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**ABSTRACT BOOK**

**45th World Conference  
on Lung Health of the  
International Union Against  
Tuberculosis and Lung Disease (The Union)**

**BARCELONA • SPAIN  
28 OCTOBER–1 NOVEMBER 2014**

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# The International Journal of Tuberculosis and Lung Disease

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TECHNICAL EDITOR IRENE ROY MEMBERSHIP/SUBSCRIPTIONS membership@theunion.org  
EDITORIAL OFFICE The International Union Against Tuberculosis and Lung Disease (The Union)  
68 boulevard Saint Michel, 75006 Paris, France  
Tel: (+33 1) 44 32 03 60 Fax: (+33 1) 43 29 90 83 e-mail: journal@theunion.org website: www.theunion.org

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# 45th World Conference on Lung Health of the International Union Against Tuberculosis and Lung Disease (The Union) Barcelona, Spain, 28 October–1 November 2014

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## Plenary session

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### Immunity to tuberculosis: reciprocity between basic research and clinical studies

Stefan H. E. Kaufmann. Department of Immunology, Max Planck Institute for Infection Biology, Berlin, Germany

Tuberculosis (TB) is both a major health threat of global dimension and an intriguing target of basic research. Iterations between basic research and clinical studies can pave the way towards better control measures that are urgently needed. In my presentation I will describe two aspects of targeted and clinical research activities: first we have rationally developed a recombinant BCG, termed VPM1002, which successfully completed two Phase I trials for safety and has also successfully completed a large Phase IIa trial in newborns in South Africa. This vaccine is currently being prepared for a Phase II trial for safety and efficacy in a larger group of infants. In experimental animal models, the vaccine has been shown to induce superior protection and to be safer than parental BCG. Second, we are involved in the identification of diagnostic and prognostic biomarkers which allow differentiation between patients with active TB and individuals with latent TB infection (LTBI). In the future we aim at developing a biosignature that can predict risk of disease in individuals with LTBI. These biosignatures are composed of transcripts and metabolites.

In the area of basic TB research we aim at elucidating the balance between inflammation and pathology on the one hand and protection on the other hand, in the control of TB. Much effort is directed toward the functional characterization of biomarkers of unknown function, which are involved in the discrimination of active TB and LTBI. In this way, microRNA223, which is differentially regulated in TB patients versus healthy individuals, was shown to control lung inflammation. In a similar way, type I interferon could be shown to control migration of inflammatory phagocytes through regulated chemokine expression. More recently, we characterized phthiocol from *Mycobacterium tuberculosis* as a pathogen-associated molecular pattern, for the aryl hydrocarbon receptor, which therefore serves as a pattern recognition receptor capable of sensing *M. tuberculosis*.

In sum, our work aims at a close crosstalk between basic research and clinical studies to make a difference in the control of one of the major infectious threats to humankind, TB.

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## SYMPOSIA: FRIDAY 31 OCTOBER 2014

### 20. COMMUNITY-DRIVEN PSYCHOSOCIAL SUPPORT: DON'T FORGET MEDICATION COUNSELLING!

#### Counselling and adherence to an arduous treatment: lessons learnt from an HIV programme

U Agarwal, J Sharma, R Sarin. Antiretroviral Therapy Centre, National Institute of Tuberculosis and Respiratory Diseases, New Delhi, India.

**Background:** Adequate adherence to treatment is a dynamic process, changing with patient's health perceptions and socio-economic pressures. Adherence to HIV treatment is further complicated by multiple drugs, difficult side effects and above all, a lifelong treatment. The 2-year MDR-TB treatment programs with multiple drug regimens face similar challenges.

**Intervention:** Structured counselling is integral component of HIV care under the National Program in India. All HIV patients undergo counselling sessions by trained staff I. Prior to ART initiation (>3 sessions)- Education about disease and need for treatment, treatment guardian identification and establishment of a contact system between patient and counsellor is undertaken initially. Subsequently, sessions focus on identification of barriers to adherence and their effective management. There is a detailed session on drugs, side effects to expect, consequences of non-adherence and follow up schedules II. After ART initiation: Adherence reinforcement sessions are undertaken in follow up.

**Findings:** Among the 539 HIV cases that were started on ART, including 4 cases co-infected with MDR-TB, lost to follow up (LFU) was on average 9.6% until March 2014 compared to the average 18% LFU in the national MDR-TB programs. Key barriers seen and addressed were : a) Lack of family support/non disclosure-Counsellor assisted communication, linkages with peer support group for guardianship b) Lack of knowledge about HIV and gravity of disease-health education sessions, use of flipcharts, models, board games etc c) Poor understanding of health care systems-use of community worker to familiarize patient with hospital facilities. d) Abject poverty, no money for food or travel- linked with CBOs for home based care, food packages and temporary monetary help e) Clash of clinic timings/ patients with travelling job (truckers, salesmen)-convenient timing for drug collection with supply for longer duration f) Drug side effects-short admissions to Community Care Centres.

**Lessons learnt:** Counsellors are vital for better patient communication and networking with local NGOs, CBOs and peer support groups to enhance adherence.

**Conclusions:** Case psychologists and structured counselling sessions as experienced in HIV programs, do not constrain program budgets. Such a structured process will be beneficial to promote improved treatment adherence in MDR-TB programs also.

#### Medication counselling and psychosocial support as part of MDR-TB control strategy

RZ Li. Department of Drug-Resistant TB Control, National Center for Tuberculosis Control and Prevention, China CDC, Beijing, China.

**Background:** To enhance patients' knowledge of MDR-TB, improve their poor psychological states and adherence through health promotion and community psychosocial support activities.

**Design/Methods:** From October 2006 to December 2012, China provided standardized MDR-TB treatment and management in 67 cities from 25 provinces with assistance from the Global Fund. From January 2011 to December 2012, The Chinese Center for Disease Control and Prevention developed an MDR-TB disease prevention and health promotion toolkit to include medication counseling component, routine health education knowledge and psychosocial support for the patients. TB prevention and treatment networks and NGOs in provinces, cities, counties, townships and villages; used the toolkit's resources for leaflets, newspapers, billboards, TV advertising, hospital electronic screens and various health promotion materials. This helped carry out extensive publicity to provide MDR-TB prevention and treatment knowledge to MDR-TB patients, their families, the public, and other groups. Approximately 7 million copies of publicity materials were distributed. Trained clinicians and nurses provided 7397 psychological counseling activities for MDR-TB patients with many psychological problems and poor compliance during hospitalization and after discharge. We studied the impact of the toolkit and counseling activities in four cities from four provinces with assistance from the Gates Foundation. Questionnaires were given to 51 MDR-TB patients in two cities about their psychological status at admission, discharge and at the end of six months of treatment.

**Results:** Patients' psychological states improved significantly after starting treatment with gradual reduction in psychological stressors. Those who had no stressors at admission accounted for 21.6% (11/51); at discharge it was 35.3% (18/51); and 70.6% (36/51) after six months of treatment ( $\chi^2=39.9$ ,  $P<0.01$ ). Sputum negative conversion rate was 58.3% (63/108) in Gates project-supported regions, and 61.2% (1703/2780) in Global Fund project-supported regions after six months of treatment. After 2 years, treatment success rate was 49.9% (572/1194) among Global Fund project-supported regions.

**Conclusion:** Health education and psychological support activities was helpful to raise patients' awareness of MDR-TB prevention knowledge, and to improve their psychological status and adherence. This process has

become an important part of China's MDR-TB control strategy.

### **Psychosocial patient support as essential element for management of DR-TB cases**

G Kaliakbarova,<sup>1</sup> S Van Den Hof.<sup>2</sup> <sup>1</sup>KNCV Representative Office in Central Asia, KNCV Tuberculosis Foundation, Almaty, Kazakhstan, <sup>2</sup>KNCV The Hague, headquarters, KNCV Tuberculosis Foundation, The Hague, Netherlands.

**Background:** In Kazakhstan treatment success rate among DR-TB patients (cohort 2009) is 75.8% and lost to follow-up rate is 5.4%. Through the USAID funded TB CAP in 2010, KNCV initiated implementation of the Psychosocial Support (PSS) Program to improve treatment adherence in East Kazakhstan Oblast (EKO). The intervention was designed to address unmet needs of patients suffering from a myriad of social and psychological problems.

**Design/Methods:** The project team established a TB patient support working group under the local government and assisted in developing the PSS model program for TB patients. PSS groups consisting of psychologists, social workers, lawyers and TB nurses were established in oblast. Based on local needs and available resources, the PSS group provided psychological counseling, treatment literacy, and medication counseling, and health education, assistance in documentation, state allowances, interim housing and jobs for the patients.

**Results:** In 2010, among 426 MDR patients starting SLD treatment, the PSS program supported 228 patients considered to be at high risk for treatment interruption and lost to follow-up. Of the 228 patients, 67% received psychological support and 77% were provided with social support. Before starting the PSS program, 23% beneficiaries had interrupted treatment at least once. After inclusion in the PSS program, only one MDR-TB patient had interrupted treatment once, due to alcohol addiction. The treatment success rate for all MDR-TB patients increased to 78.1% in EKO. Recognizing the public health implications of insufficient MDR-TB control, the impact of this project heightened local government commitment for the National TB Program. As a result, the state financial contribution increased 8-fold for direct social support of MDR-TB patients in EKO. Since 2011, social workers, psychologists and lawyers are now available for all TB/DR-TB patients in the region. Subsequently, the PSS program expanded to the Akmola oblast the following year through USAID TB CARE I programs.

**Conclusion:** . Successful treatment of patients requires innovations and strong commitment from TB programs and stakeholders for a patient-centered approach. Multidisciplinary patient-centered support is not yet available for all TB/MDR-TB patients. Given the National TB program's decision to scale up full outpatient care nationwide, it will be necessary to address psychosocial factors to improve treatment adherence and reduce treatment interruptions.

### **Multiple dimensions of counselling and options for prioritisation and intervention**

N Konduri, A Kwiecien. Management Sciences for Health, Systems for Improved Access to Pharmaceuticals and Services, Arlington, VA, USA.

**Background:** MDR-TB programs report using approaches such as psychosocial support, patient support groups, financial support, nutrition support and counseling among others to encourage patient adherence to treatment thereby minimizing default. Yet, the term "counseling" as interpreted by MDR-TB programs appears to encompass various dimensions – such as treatment literacy, adherence counseling, social support, emotional support, motivation, based on local program priorities. It is not clear to what extent is medication related counseling is applied to help patients deal with side effects and adverse events.

**Objective:** To map out how counseling is interpreted in global guidance and strategy documents and its application in country level MDR-TB programs

**Methods:** Content analysis of 14 strategies, frameworks, reports from WHO and international agencies; 9 Guidelines from WHO and international technical partners; 47 country MDR-TB guidelines and strategic plans and 190 articles retrieved from a PubMed search.

**Interim findings:** Although the Global Plan to Stop TB acknowledged importance of adherence, there was no emphasis on aspects of counseling patients on medicines use. Most of the 12 global strategies and frameworks emphasize family or social and psychological support to promote adherence but are less explicit on counseling related to medicines use. The International Standards for TB Care was explicit on patient-centered approaches since 2006 but it was not until 2009 that the problem of insufficient attention and patient communication on side effects was acknowledged. Since then, from 2011 onwards other international agencies made clear that success of treatment relies on patient understanding of DR-TB and its treatment. While analysis of country guidelines and strategic plans are ongoing, it was noticed that at least five high-burden MDR-TB countries made explicit statements to counsel patients on medicines use, side effects and adverse events. Recommendations on prioritization of patient-centered approaches based on local context will be made during the symposium with supporting examples. An operations research agenda on impact of patient counseling and prescriber drug utilization reviews will be proposed.

**Conclusion:** While educating patients on disease transmission, psychosocial support and adherence is important, MDR-TB program must ensure that the medicines related component of counseling be incorporated in a structured manner.



### Patient perspective on treatment literacy, counselling and adherence

J Hugues, B Boko, L Snyman. Khayelitsha, Medecins Sans Frontieres, Cape Town, South Africa.

**Background:** Khayelitsha is a peri-urban township with a population of ~450,000 near Cape Town in South Africa. In this setting with high HIV and TB prevalence, roughly 200 patients are diagnosed with drug-resistant TB (DR-TB) each year and 75% are HIV co-infected. Buci Boko was diagnosed with DR-TB while she was pregnant in 2005, at a time when second line TB treatment was only accessible through long term admission in a centralized hospital and with little or no information available for patients at time of diagnosis or throughout treatment. Both Buci and her child successfully completed a long and difficult treatment journey but with very limited support.

**Intervention:** MSF and local partners implemented a patient centred, decentralized model of care for DR-TB in Khayelitsha in 2007 to improve access to treatment in primary health care. Buci was subsequently employed by MSF to provide routine treatment literacy, counseling and support to patients with DR-TB in Khayelitsha. Through personal experience and support from MSF, Buci was able to mentor other DR-TB counselors and then helped to develop a counseling model to support patients through all stages of their DR-TB treatment. Results and lessons learnt: Since decentralization of care, more than 80% of DR-TB patients diagnosed in Khayelitsha are now able to start appropriate treatment in their nearest primary care clinic (compared to <20% before). DR-TB counselors are based in the community and are able to meet patients on the day of treatment start to provide ongoing counseling and support wherever necessary. The support model has been formalized and provides treatment literacy for individuals and their supporters across the entire spectrum of their treatment journey. This includes psychosocial support for patients and their families, wider community awareness and education on infection control and contact tracing, advanced adherence counseling during interruption episodes, rewards and initiatives to incentivise treatment completion, and palliative support in cases of treatment failure.

**Conclusion:** Decentralisation of care along with routine patient counseling and support enables clinically stable patients to initiate DR-TB treatment in primary care clinics and continue treatment in their own community. A routine counseling model assists counselors to cover necessary aspects of literacy and psychosocial support while allowing specific interventions to cater to individual circumstances.

### Merging mental health and medication counselling

A Pasha,<sup>1</sup> O Qureshi,<sup>1</sup> S Khowaja,<sup>1</sup> A Zaidi,<sup>1</sup> H Hussain,<sup>1</sup> A Khan,<sup>1</sup> Z Barry.<sup>2</sup> <sup>1</sup>Mental Health, Interactive Research and

Development, Karachi, <sup>2</sup>TB Clinic, Indus Hospital, Karachi, Pakistan.

In January 2014, Interactive Research and Development (IRD) launched its mental health program, which focuses on the screening, diagnosis and treatment of depression and anxiety at its recently established lung health diagnostic centers in Karachi, Pakistan. Patients who are found to be TB-positive are screened for depression and anxiety at the time they are notified of their TB status. The same algorithm is used at the Indus Hospital, whom IRD has partnered with on previous TB REACH and Global Fund grants. The Aga Khan University Anxiety and Depression Scale is used to screen for depression and anxiety. It is a 25-item, indigenous scale, developed in Urdu with demonstrated validity as a screening tool for use in community-based programs. The scale takes 8–10 minutes to administer. If a patient has a score that indicates mild or moderate depression and anxiety, they are referred to a Counsellor at Indus Hospital. If a patient has a score that indicates severe depression, they are immediately referred to a psychiatric centre. From January – July 2014, 795 TB-positive patients were screened, with a total of 245 patients (31%) screening positive for depression and anxiety. Of these, 208 (26%) patients had mild depression and 24 (3%) were moderately depressed. At the time of being notified of their TB ailment, these patients were briefly counselled on the importance of treatment adherence and reassured about their prognosis. This eased their psychological distress. They were then asked to return on a weekly basis for therapy. However, a large majority of these patients did not return on a weekly basis but did meet with the Counsellor during their monthly follow-up visits. Reasons cited for not being able to visit weekly were primarily the inability to take time away from work and in the cases of females, the inability of male family members to take time off work and accompany them to the hospital. During the monthly follow-up visits, these patients were found to have improved mental health owing to the fact that their TB related symptoms had improved after 1 month of treatment. Less than 1% screened positive for severe depression. This intervention has highlighted the need to offer mental health services for TB patients. However, since social factors, such as economics, and gender, hinder the ability of patients to access mental health treatment, psychosocial support programs need to consider community based strategies in order to be more effective.

### Multiple dimensions of counselling and options for prioritisation and intervention

A Kashyap.<sup>1</sup> <sup>1</sup>School of Pharmacy, University of North Carolina, Chapel Hill, NC, USA.

**Background:** MDR-TB programs report using approaches such as psychosocial support, patient support groups, financial support, nutrition support and counseling among others to encourage patient adherence to treatment thereby minimizing default. Yet, the term “counseling” as interpreted by MDR-TB programs appears to

encompass various dimensions – such as treatment literacy, adherence counseling, social support, emotional support, motivation, based on local program priorities. It is not clear to what extent is medication related counseling is applied to help patients deal with side effects and adverse events.

**Objective:** To map out how counseling is interpreted in global guidance and strategy documents and its application in country level MDR-TB programs

**Methods:** Content analysis of 14 strategies, frameworks, reports from WHO and international agencies; 9 Guidelines from WHO and international technical partners; 47 country MDR-TB guidelines and strategic plans and 190 articles retrieved from a PubMed search.

**Interim findings:** Although the Global Plan to Stop TB acknowledged importance of adherence, there was no emphasis on aspects of counseling patients on medicines use. Most of the 12 global strategies and frameworks emphasize family or social and psychological support to promote adherence but are less explicit on counseling related to medicines use. The International Standards for TB Care was explicit on patient-centered approaches since 2006 but it was not until 2009 that the problem of insufficient attention and patient communication on side effects was acknowledged. Since then, from 2011 onwards other international agencies made clear that success of treatment relies on patient understanding of DR-TB and its treatment. While analysis of country guidelines and strategic plans are ongoing, it was noticed that at least five high-burden MDR-TB countries made explicit statements to counsel patients on medicines use, side effects and adverse events. Recommendations on prioritization of patient-centered approaches based on local context will be made during the symposium with supporting examples. An operations research agenda on impact of patient counseling and prescriber drug utilization reviews will be proposed.

**Conclusion:** While educating patients on disease transmission, psychosocial support and adherence is important, MDR-TB program must ensure that the medicines related component of counseling be incorporated in a structured manner.

## 21. PRACTICAL CONSIDERATIONS FOR SUCCESSFUL CONTACT TRACING AND LINKAGE TO CARE IN LOW- AND MIDDLE-INCOME COUNTRIES

### TB CARE: a systematic overview of IPT delivery strategies comparing uptake, usage and completion

L Adams,<sup>1</sup> E Talbot,<sup>1</sup> K Odat,<sup>2</sup> H Blunt,<sup>2</sup> K Steingart.<sup>3</sup>

<sup>1</sup>Medicine, and <sup>2</sup>Biomedical Libraries, Geisel School of Medicine at Dartmouth, Hanover, NH, USA; <sup>3</sup>Infectious Diseases, Cochrane Infectious Diseases Group, Liverpool, UK.

**Background** Uptake of isoniazid preventive therapy (IPT) to prevent tuberculosis has been poor, particularly in the highest risk populations. Interventions to improve IPT

delivery could promote implementation. The large number of existing systematic reviews on treatment adherence has made drawing conclusions a challenge. We performed an overview of systematic reviews of interventions to improve IPT delivery in order to provide decision makers with the evidence they need.

**Methods** We searched the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects (DARE), and MEDLINE up to August 15, 2012. Two authors used a standardized data extraction form and the AMSTAR instrument to independently assess each review.

**Results** Six reviews met inclusion criteria. Interventions included changes in the setting/site of IPT delivery, use of quality monitoring mechanisms (e.g., directly observed therapy), IPT delivery integration into other healthcare services, and use of lay health workers. Most reviews reported a combination of outcomes related to IPT adherence and treatment completion rate but without a baseline or comparison rate. Generally, there was limited evidence to demonstrate that the studied interventions had a positive impact on treatment completion.

**Conclusions** While most of the interventions were not shown to improve IPT completion, integration of tuberculosis and HIV services yielded high treatment completion rates in some settings. Further research to assess different IPT delivery interventions, including those that address barriers to care in at-risk populations, is urgently needed to identify the most effective practices for IPT delivery and TB control in high TB burden settings.

### The TB REACH Initiative: driving global case finding in vulnerable populations

J Creswell,<sup>1</sup> S Sahu,<sup>1</sup> R Stevens,<sup>2</sup> L Blok,<sup>3</sup> M Bakker.<sup>4</sup>

<sup>1</sup>Secretariat, Stop TB Partnership, Geneva, Switzerland;

<sup>2</sup>Monitoring and Evaluation, HISP, London, UK, <sup>3</sup>Royal Tropical Institute, KIT Health, Amsterdam, <sup>4</sup>Royal Tropical Institute, KIT Biomedical Research, Amsterdam, Netherlands.

**Background:** Contacts of people with TB have much higher rates of TB infection and active TB than the general population. Recent WHO guidance has recommended contact investigation (CI) for TB cases. In most countries, national programmes have also recommended that contact investigation should be implemented. However, there is no guidance on practical considerations and different approaches, and in many settings CI is not carried out and/or poorly documented.

**Design/Methods:** TB REACH is an initiative that promotes innovative approaches to improve TB case finding. We compared different methods of CI implementation across 3 funding waves and a total of 48 projects. Quarterly reports as well as supplemental information documenting the different CI interventions were used.

**Results:** The 48 projects covered a wide variety of CI strategies such as using active and passive approaches, defining index cases differently, and varying criteria for symptomatic individuals to receive diagnostic testing. More than 250,000 contacts of TB index patients were

screened, yielding over 7,500 TB cases. Most projects, however, were not able to systematically implement contact investigation for all index patients. The impact on improved TB notifications at a district level was generally low even with wide coverage. Projects that used more inclusive testing algorithms (broader definitions for testing) found greater numbers of TB cases.

**Conclusion:** Contact investigation identifies cases of TB earlier among people with high risk of developing TB. Factors such as the definition of an index case, the use of active or passive CI, the definition of a person who should receive a diagnostic test, and the testing algorithm used affect yield as well as numbers of people tested. Implementing CI implies costs that may not be part of routine TB services.

### **TB REACH optimising traditional and reverse contact tracing among children in Swaziland**

P Ustero,<sup>1,2,3</sup> R Golin,<sup>1,2</sup> G Mtetwa,<sup>1</sup> M Matshaba,<sup>1,2</sup> A Mandalakas,<sup>2,3</sup> K Ngo.<sup>3</sup> <sup>1</sup>TB, Baylor College of Medicine Children's Foundation, Mbabane, Swaziland; <sup>2</sup>Pediatrics, Baylor College of Medicine, Houston, TX, <sup>3</sup>Global Tuberculosis Program, Texas Children Hospital, Houston, TX, USA.

**Background:** Despite having the world's highest Tuberculosis (TB) incidence (1349/100000), Swaziland's TB detection rate remains low (43%). Although 46% of the country's population is <14 years (y) old, childhood TB cases accounted for 14% of notified cases in 2013, underscoring a gap in TB case finding and poor access to treatment in this key population. Supported via 2012 TB Reach funding, Baylor College of Medicine Children's Foundation in Swaziland implemented a program to increase pediatric case detection and access to TB services. We report data for year one of implementation.

**Intervention:** We conducted case finding among contacts of index cases treated at 7 diagnostic and treatment centers in three of four districts. Contact tracing and reverse contact tracing procedures were designed with monitoring and evaluation tools adapted to the setting. Hard-to-reach contacts received home visits, prioritizing contacts of bacteriologically positive patients and homes housing a high number of children. On-site training was done for health care workers regarding pediatric TB and mentoring/supervisory visits were organised fortnightly to support the implementing sites. TB diagnosis was supported by GeneXpert (GXP) and chest X-ray (CXR) capacity in all facilities.

**Results:** A total of 2,928 children and 3391 adults were screened for TB. Clinical symptoms were found in 44.1% (1156/2928) of children and in 55.9% (1465/3391) of adults. Among those with positive screening, sputum was tested in 67% (773/1156) of the children and 82% (1208/1465) of the adults. A positive GXP result was obtained in 3% (20/773) of children and 7% (83/1208) of adults. Among children < 5y with a positive screen, 23.6% (106/449) had sputum tested of which 2.9% (3/106) were positive for TB. In contrast, 64.6% (450/696) of symptom screen positive children aged 5 to 14 years had sputum tested of which 1.7% (8/450) were positive for TB. Of the positive sputum samples, 43.2 % (32/74)

were collected during the home visits with 12% (4/32) being collected from children. Mathematical modeling adjusting for background changes in TB incidence suggests that our program resulted in identification of an additional 135 (92–176) cases which represent 5.6% (135/2419) of all TB notifications and 6.5% (20/308) of the pediatric case notifications in our project areas.

**Conclusions and Key Recommendations:** Contact tracing is feasible and increases TB case detection among children and adults even in TB high burden settings. Pediatric sputum can be collected during home visits and linked to new rapid diagnostics such as GeneXpert.

## **22. COUNTRIES' EXPERIENCE IN DECENTRALISING PMDT: COMMUNITY-BASED MDR-/XDR-TB CARE**

### **Developing country ownership and expanding PMDT through engaging communities: experience from Bangladesh**

M Akramul Islam,<sup>1</sup> S Islam,<sup>1</sup> M Siddiqui,<sup>1</sup> S Hossain,<sup>1</sup> MA Husain,<sup>2</sup> H Ahmed.<sup>2</sup> <sup>1</sup>TB, BRAC, Dhaka, <sup>2</sup>TB, NTP, Dhaka, Bangladesh.

**Background:** According to WHO, Bangladesh ranks 10th among 27 high burden MDR-TB countries in the world. According to recent drug resistance survey MDR-TB prevalence among new cases is 1.4% and 28.5% among retreatment cases. However, considering the size of population the estimated number of MDR-TB patients is significant—approximately 1900/year among new cases and 2300/year among retreatment cases. National Tuberculosis Control Program initiated programmatic management of DR TB cases since 2008.

**Design/Methods:** Patients diagnosed in National Institute of Diseases and Chest Hospital (NIDCH) admitted for 6 to 8 months of intensive phase of treatment initially and 18 months ambulatory phase at community. Currently intensive phase has been reduced and sputum microscopy is done weekly for admitted patients. All health care providers related to MDR-TB management receive basic one day orientation before starting MDR-TB management at community level. Monthly sputum follow up test at the field level and quarterly culture at National TB Reference Laboratory (NTRL) is done throughout the treatment course. After successful completion of treatment all patients are suggested to visit hospital 6 monthly up to 2 years for follow up with transportation and investigation support.

**Results:** In 2008, a total of 106 patients received standardized MDR-TB treatment; out of them, treatment success rate was 62% and lost to follow up rate was 29%. Gradually for strengthening the patients' adherence system through involvement of different partners (BRAC, TB CARE II) at hospital level as well as community level, success rate increased to 69% and lost to follow up rate decreased to 18 % in 1<sup>st</sup> quarter, 2012 in compare with the initial cohort (29%). Lost to follow up rate is higher (11%) during hospital stay and very low



(2%) during ambulatory care in the community. By reducing the hospital duration (at least one month), if two consecutive sputa become negative then the MDR TB patients are shifted to the community for ambulatory care which seems effective for better treatment adherence and improved treatment outcome.

**Conclusion:** Hospital stay in intensive phase for many months seems to be difficult for MDR TB patients. Early implementation of community MDRTB management helps both patients and TB program to achieve treatment compliance and improve overall treatment results.

### Transition from hospital-based care to ambulatory care for MDR-TB: Kazakhstan experience

T Abildayev,<sup>1</sup> E. Berikova,<sup>1</sup> B Toksanbaeva.<sup>1</sup>

<sup>1</sup>Management, National Center for TB Problems RK, Almaty, Kazakhstan.

The treatment was conducted by standardized chemotherapy regimens in accordance with the MoH' Order. The obligatory condition was the direct observation of daily anti-TB drugs taking by a patient. The patients were provided with obligatory consultation of the psychologist, social worker and jurist at the beginning of the treatment and, further, by indications. Also, the alimentary assistance (cost \$2 daily) and public transport month' tickets were provided. No one case of anti-TB drugs take missing did not happen. The effectiveness of treatment constituted 98.4%. Two patients turned back in TB clinics (one of them for the surgical intervention, and another patient did by reason of exacerbation of the comorbidity, namely diabetes mellitus. Thus, out-patient treatment with provision of psycho-social support showed a high effectiveness in the clinical and in psychological aspect as well.

#### Conclusions:

1. Among patients received the treatment out-patient there were prevalent the persons of working age, those which don't wish to loss a job, women having the children of younger ages and invalids.
2. As a result of treatment conducted out-patient under direct observation, cases of treatment default were absent.
3. Expansion of the experience of pilot project on out-patient treatment all over the country is foreseen in the Comprehensive Plan of TB fighting in the Republic of Kazakhstan for 2014–2020 adopted by Statement of Government n. 597 as of May 31, 2014<sup>3</sup>.

### Patients' information needs and multimedia solutions in support of integrated out-patient care in Pakistan

A Habib,<sup>1</sup> T Seimon.<sup>2</sup> <sup>1</sup>Software Development, Interactive Health Solutions, Karachi, <sup>2</sup>Health Communications, Interactive Research and Development, Karachi, Pakistan.

**Background:** In Pakistan, as in other TB endemic countries with high MDR-TB burden, diagnosis is greatly

enhanced by use of GeneXpert technology, particularly for RIF-resistant strains. To maximize benefits and affordability of GeneXpert, high quality sputum samples are essential. Research has shown that simple instructions can help patients produce better quality sputum. We have developed multimedia materials to improve patient sputum quality, for use in dedicated TB testing centres.

**Design:** In order to minimize the time burden on health workers in providing sputum submission instructions, we developed a culturally and language appropriate animated instructional video for patients. We also developed an Android app into which the video is embedded on a tablet device. A health worker logs the patient into the app via use of a unique ID, linking subsequent sputum submission outcomes with the patient's medical data. The app allows patients to select their desired voiceover language. Questions posed to the patient by way of the app before and after viewing the video draw the patient's attention to the salient messages of the video. Patient responses allow for analysis of message comprehension, with potential in the long-term to assess the video and app's effects on ability to produce sputum of sufficient quality and quantity. The app is currently in use at 2 private screening centres in Karachi.

**Results:** Thus far, the video/app combination has been used by nearly 600 patients in the 2 Karachi testing centres. Ongoing analysis of patient responses to pre- and post-viewing questions suggest increased patient self-efficacy from the watching the video. Notably, by linking the patient's history with their sputum submission data in an integrated medical record, health personnel have access to essential information as they need it.

**Conclusion:** Findings to date from the use of the instructional video and Android app suggest these multimedia materials hold great promise for scale-up to additional settings. Already, we have developed versions of the video – with revised visuals and audio tracks – in Bahasa Indonesia, Bangla, English and Swahili. The app too has been designed for ready adaptation to other languages. A rigorous evaluation will be necessary to assess the impact of these multimedia materials on patients' ability to produce high quality sputum samples, and ultimately on diagnosis and treatment outcomes.

### Experience with scale-up of community-based XDR-TB program in South Africa

R Matji. Health, University Research Company, Pretoria, South Africa.

**Background:** South Africa adopted the community based MDR TB care in 2009. This was mainly due to the increasing number of patients and limited number of hospital beds. There is also increasing evidence that there is no need to hospitalize patients for the entire duration of MDR TB treatment. The XDR TB outbreak in Tugela Ferry in South Africa, was a clear example that in countries with high HIV rates, admission to hospital can be a very dangerous practice that puts all patients at risk.



The purpose of this presentation is to highlight the lessons learnt with the management of M/XDR TB patients at community level in South Africa.

**Design/Methods:** The USAID TB Program managed by University Research Co., LLC (URC) funded by USAID is a 5 year funded project to support the South African National Department of Health on all aspects of TB prevention, care and treatment. One of the objectives of the project is to engage community based NGOs and provide technical and financial support to these NGOs. The high cost of managing M/XDR TB patients has compelled programme managers and implementers to think outside the box. For example, the more we encounter chronic cases, the more it requires funding commitment, multi-disciplinary teams to work in partnership with communities, families of the affected patients would require funding, trained medical experts. The response to M/XDR cannot only be a task to be managed by doctors; you need the engagement of nurses and community care givers. The NGOs are able to reach marginalized members of our communities. They're often at the heart of where the patients come from; therefore, they're best positioned to provide appropriate services to patients at their homes.

**Conclusion:** Good treatment outcomes can be achieved for drug resistant patients, but it requires good coordination, passionate staff such as doctors, nurses, social workers, counsellors, and patient participation with support of their families. This was demonstrated by the response and commitment shown by the district health team in Tugela Ferry.

### Developing a model for community-PMDT: the China experience in Yunnan

A Innes,<sup>1,2</sup> I Ling,<sup>1,3</sup> X Zhixiang,<sup>1,3</sup> ZH Shun,<sup>4</sup> CH Jinou,<sup>4</sup> N Guiying,<sup>4</sup> H Jinglong,<sup>4</sup> X Lin.<sup>4</sup> <sup>1</sup>USAID Regional Development Mission Asia, CAP-TB Project, Bangkok, <sup>2</sup>Asia Pacific Regional Office, Family Health International, Bangkok, Thailand; <sup>3</sup>China Country Office, Family Health International, Kunming, <sup>4</sup>Institute of TB Prevention and Treatment, Yunnan Center for Disease Control and Prevention, Kunming, China.

**Background:** Programmatic management of drug-resistant tuberculosis (PMDT) was initiated in Yunnan Province in May 2012. Multi-drug resistant tuberculosis (MDR-TB) had been treated in Yunnan for many years prior to PMDT initiation. However, standardizing MDR-TB management was challenged by the lack of coordination among clinical and public health TB centers for diagnosis, treatment, and follow-up. Ensuring standardized care and treatment completion through the 20–24 months of MDR-TB treatment requires a paradigm shift to control this complex disease.

**Intervention:** With support from the national and provincial China government and the USAID-funded Control and Prevention-Tuberculosis (CAP-TB) project, the TB Division of the Yunnan Center for Disease Control (CDC) developed a patient-centered, community-driven model for MDR-TB control. Using the GeneXpert MTB/RIF for molecular diagnosis (provided by CAP-TB), along with culture confirmation and second-

line drugs from the Global Fund, the Yunnan CDC synchronized funding from different sources to support patients from the point of identification as a presumptive TB patient, to screening, early diagnosis, treatment initiation and completion, and cure. Critical to the model's implementation was coordination among three main sectors of the health system: hospitals, TB public health centers, and the community. This coordinated approach prioritizes communication among all health system sectors through regular TB team meetings and social media platforms; standardizing MDR-TB diagnosis and treatment in alignment with international guidelines; and supporting patients using innovative initiatives through social media support groups, MDR-TB peer counsellors; MDR-TB inpatient education by nurses and health care workers; and outpatient coordination to treat complications and side effects.

**Results:** This patient-centered, community-driven model for MDR-TB has strengthened the health system and the Yunnan CDC's capacity to control MDR-TB. Treatment default rates decreased from 48% to 5% following initiation of the model. Using this model also enables early identification of initial default and treatment initiation delay, which still need to improve.

**Conclusions:** MDR-TB treatment outcomes in China are poor. Using a patient-centered, community-driven approach within a coordinated health system has potential as a cost-effective and sustainable strategy, within Yunnan and throughout China.

## 23. QMS IMPLEMENTATION AND ACCREDITATION OF TB LABORATORIES

### SLIPTA programme, SLMTA, and GLI TB tools complementarity in strengthening laboratory management system

A Umubyeyi Nyaruhirira. Laboratory services, Management Sciences for Health, Pretoria, South Africa.

Clinical laboratories in low- and middle-income countries (LMIC) need fundamental improvement because quality laboratory services are essential for the decision-making capacity of clinicians, health workers and public health authorities. To this end, a tiered accreditation scheme Stepwise Laboratory Improvement Process towards Accreditation (SLIPTA) was developed by the World Health Organization Regional Office for Africa (WHO/AFRO) and its partners, including the African Society for Laboratory Medicine (ASLM) and the United States Centers for Disease Control and Prevention (CDC). The SLIPTA framework for improving the quality of public health laboratories in developing countries was launched in 2009 in Kigali, Rwanda. It was developed with a tool "the Strengthening Laboratory Management towards Accreditation" (SLMTA) to train laboratory managers in implementing the requirements of ISO 15189. While SLIPTA provides a measure of quality improvement, SLMTA is a training program that helps laboratories improve their quality manage-

ment systems and progress through prescribed steps to prepare for accreditation. The Global Laboratory Initiative (GLI) of the Stop TB Partnership was developed to complement the SLIPTA, a TB tool used to assist laboratories in implementing a QMS (Quality Management System) that meets ISO15189 requirements. The GLI tool covers technical, managerial and TB specific requirements. During this symposium, we will review the performance of these different approaches, their complementarity and evaluate success and sustainability of the QMS (in different settings of implementation. Lessons learnt will be shared with laboratories, policy makers, and stakeholders.

### Practical issues and challenges in implementation QMS for TB laboratories in Central Asian Republics

M Jonevska,<sup>1</sup> Z Bayduloeva,<sup>2</sup> B Toxanbayeva,<sup>3</sup> M Abduloeva,<sup>4</sup> K Takieva,<sup>5</sup> G Kalmambetova.<sup>6</sup> <sup>1</sup>Europe/Eurasia, Project HOPE, Almaty, Kazakhstan; <sup>2</sup>Tajikistan, Project HOPE, Dushanbe, Tajikistan; <sup>3</sup>Kazakhstan, Project HOPE, Almaty, Kazakhstan; <sup>4</sup>NRL, Republican TB Centre, Dushanbe, Tajikistan; <sup>5</sup>Kyrgyzstan, Project HOPE, Bishkek, <sup>6</sup>NRL, National TB Centre, Bishkek, Kyrgyz Republic.

**Background:** Over the last decade the Health Sector Reform in Central Asian Republics (CAR), included major activities for quality improvement and standardization of laboratory services. To support this process, the USAID Quality Health Care Project introduced a Quality Management System (QMS) in TB laboratory networks in Kazakhstan; Kyrgyzstan and Tajikistan.

**Objective:** To review the challenges and achievements in implementation of laboratory QMS in pilot projects within the CAR region, document lessons learned and provide practical recommendations for nationwide adoption of QMS principles. Methods and materials The WHO – Global Laboratory Initiative (GLI) checklist was used and adapted for harmonization with the existing health system quality standards, addressing all quality system essentials divided into six thematic areas, in accordance with the specific institutional responsibilities. A scoring system was developed to evaluate each thematic area: organizational; infrastructure; staffing; laboratory safety; technical procedures; equipment and quality control. An overall score 85% was agreed upon with the MOH as a target for individual laboratories. Guidelines were developed and the training implemented.

**Results:** QMS Pilot sites included: 10 labs in Soghd Oblast in Tajikistan; 6 labs in Talas Oblast in Kyrgyzstan and 4 labs in Almaty Oblast in Kazakhstan. The status of QMS implementation was evaluated each quarter during the implementation period of 18 months. In Kazakhstan pilot site, the average score increased from 75% to 95%; in Kyrgyzstan from 41% to 80% and in Tajikistan from 52% to 83%. All laboratories received the highest score for technical methods and quality control, mainly as a result of well coordinated technical support, training activities and supportive supervision. Major challenge were poor infrastructure in some laboratories and lack of

funding due to reorganization of TB laboratory network and reallocation of donors funds to other sites.

**Conclusions:** QMS in laboratory services can be implemented successfully if it is an integral part of the National strategy for laboratory strengthening. Coordination of activities, provided by different international organizations and donors, as well as institutionalization of QMS principles can ensure sustainability of the system and create a solid basis for continuous quality improvement.

### GLI/QMS tool: updates and uptake

S Van Beers,<sup>1</sup> T Datema,<sup>1</sup> L Oskam,<sup>1</sup> P Klatser.<sup>1</sup>

<sup>1</sup>Biomedical Research, Royal Tropical Institute (KIT), Amsterdam, Netherlands

The GLI tool is a free, web-based tool supporting TB laboratories to provide quality assured TB diagnostic services. The tool, developed through partnerships in the TB Care I project of USAID, was launched at the Union World Conference in Lille in 2011. Version 2.0, based on the new ISO 15189:2012 standard, with extension of guided steps and activities, was launched in November 2013. The GLI tool divides the process of implementing a quality management system (QMS) into four phases, focusing on 1) assuring technical competency of testing performed, 2) implementing quality control measures and create traceability, 3) establishing the policy cycle with proper management, leadership and planning; and 4) creating continuous improvement, accumulate evidence of quality assurance. After completion of all phases a laboratory will comply with ISO 15189 requirements and be ready to apply for accreditation. In each phase the tool provides a framework with a suggested order of activities for day to day implementation of the QMS. The tool also shows which activities need to be performed for each of the CLSI defined twelve Quality System Essentials. Furthermore, the tool provides templates of QMS documents for TB laboratories such as Standard Operation Procedures, and background information for deeper insight in specific quality management principles. In each activity in the GLI tool links are provided to such materials. A separate checklist enables laboratories to perform self-assessments and monitor progress. A consistent number of users all over the world have found access to the tool at [www.GLIquality.org](http://www.GLIquality.org). Based on the success of the GLI tool for Tuberculosis Laboratories, the WHO has launched a similar tool to improve the quality of public health laboratories as part of the roll out of the International Health Regulations. This LQSI tool (Laboratory Quality Stepwise Implementation tool) can be found at <https://extranet.who.int/lqsi/>. The presentation will show updates and examples of uptake of these tools.



## 24. MATHEMATICAL APPROACHES TO BETTER UNDERSTAND AND TACKLE TUBERCULOSIS

### Mathematical models to understand transmission and to improve case detection

D Okuonghae. Mathematics, University of Benin, Benin City, Nigeria.

**Background:** This paper discusses a tuberculosis (TB) mathematical model that was formulated based on results from a survey carried out in Benin City, Nigeria. The purpose of the survey was to determine factors that could enhance the case detection rate of tuberculosis. Results from the survey identified four key factors that should be combined for an effective control of TB and increase the case detection rate: effective awareness programme, use of active cough identification, associated cost factor for treatment of identified cases and effective treatment.

**Design/Methods:** These factors (now parameterized) were then keyed into a new mathematical model that studies their effects (and other allied parameters) on the dynamics of tuberculosis in a community.

**Results:** Mathematical and statistical (uncertainty and sensitivity) analyses showed that these factors had a significant effect on the reproduction number of the model and the disease burden in the community. In fact, the analyses demonstrated that combining all four above-mentioned factors can significantly improve the case detection rate and, more importantly, lower the disease burden in the community. However concentrating on improving tuberculosis awareness programmes and encouraging the use of active cough identification as a marker to flag someone who may have developed active TB can also help in improving the TB case detection rate; these are also significant in reducing the severity of the disease when effective treatment is available. Global stability analysis of the model showed that the disease-free equilibrium (DFE) of the model is globally-asymptotically stable whenever the reproduction number is less than unity; this is guaranteed when exogenous re-infection plays no role in the transmission process of the disease.

**Conclusion:** Most TB high burden countries face the challenge of case detection in tackling and reducing the burden of the disease in a community. This study has identified and mathematically analyzed key parameters which will go a long way in improving on the case detection rate of tuberculosis in a community. Concentrating on these factors (parameters) as stated above will help health officials plan and effectively control the spread of TB in the community.

### The bubble model: mathematically explaining how active TB is possible

C Prats,<sup>1</sup> Q Valls,<sup>1</sup> Neus Sans,<sup>1</sup> D López-codina,<sup>1</sup> C Vilaplana,<sup>2</sup> E Marzo,<sup>2</sup> PJ Cardona.<sup>2</sup> <sup>1</sup>Departament de Física i Enginyeria Nuclear - Escola Superior d'Agricultura de

Barcelona, Universitat Politècnica de Catalunya - BarcelonaTech, Castelldefels, <sup>2</sup>Unitat de Tuberculosi Experimental, Fundació Institut d'Investigació en Ciències de la Salut Germans Trias i Pujol, Badalona, Spain.

**Background:** The threshold between a tuberculosis infection and an active disease is, still today, not fully understood. Experimental research point out to a delicate equilibrium between inflammatory response and immune response of individuals. Such equilibrium prevents lesions caused by *Mycobacterium tuberculosis* growth in lungs to increase in volume over a certain (unknown) threshold, presumably related with the trigger of the active disease.

**Design/Methods:** In a previous study, Marzo et al. (Tuberculosis (Edinb). 94(1):55–64, 2014) analysed the dynamics of tuberculosis lesions in mice. Their observations were taken into account for building a mathematical model that aimed to explain such dynamics. The computational model considers the spherical lesion as the basic unit, a.k.a. bubble. Variables associated to each bubble include their position in a 3D space, radius (or volume) and growth rate. Volume's increase is assumed to be driven by the own bacterial load growth in an initial stage, and modulated according to the inflammatory response (would accelerate such increase) and the immune response (could accelerate or make slower such increase, and even produce a volume's decrease). These forces are considered together when evaluating the individual growth rate. The apparition of daughter lesions is also modelled, being possible for any bubble with an age between 2 and 4 weeks and related with its size. Finally, the model also considers the merging of two lesions when they are close enough.

**Results:** The model was implemented in Matlab. Preliminary simulations to test its qualitative behaviour were carried out, showing the same dynamics that had been reported from experiments: an exponential increase in total affected area, and oscillations in the number of lesions. The need for studying simulations output in a 2D slide of the 3D space was detected and implemented. Several series of simulations to carry out a sensitivity analysis of the model and its parameterization were run. The final results were in quantitative agreement with experimental measurements.

**Conclusion:** The bubble model allowed the identification of the main forces that drive the dynamics of lesions in lungs. This is an initial step towards the fully understanding of the factors that trigger an uncontrolled growth of lesions, which would determine the apparition of an active tuberculosis.

### Spatiotemporal analysis of tuberculosis and its risk factors

C Nunes,<sup>1</sup> C Areias,<sup>1</sup> T Briz.<sup>1</sup> <sup>1</sup>Epidemiology and Statistics, National School of Public Health, NOVA University of Lisbon, Lisboa, Portugal.

**Background:** Tuberculosis (TB), the second infectious cause of death, is curable but still has a great global impact. Time and place are crucial to understand its



populational dynamics and to optimize resources allocation. In a space-time epidemiological, ecological view, regions more exposed to Pulmonary TB (PTB) risk factors are expectable to coincide with more critical PTB areas; decision-makers could use that when predicting the impact of their local programs.

**Objectives:** Through an ecological approach, to identify factors that may influence PTB local incidences, in order to characterize the TB burden in Portugal; to provide local evidence as to challenges that foster PTB incidences.

**Design/Methods:** The space-time unit is municipality-year, in three periods: 2001, 2010 and 2000–2010. Data used included: number of PTB and HIV cases, proportions of unemployment, non-standard accommodation, overcrowding, prisoners, illiterates, non-qualified workers, immigrants; a youth indicator. A multi-step approach was applied: broad literature review; data gathering on the selected factors; Pearson or Spearman tests for all factors vs PTB incidence ( $p < 0.05$ ); spatial clustering analysis for variables selected; construction of a PTB factor index; assessment of factor index validity.

**Results:** HIV, youth indicator, overcrowding and prisoners in all periods of time; unemployment (2010); non-standard accommodation (2001–2010 and 2001); immigrants (2001–2010), all positively correlated with incidence. Clustering analysis showed Metropolitan Lisbon and Oporto as consistent incidence critical areas. Critical areas for factors concentrated in the south, Lisbon and Porto Metropolitan areas, overlapping with incidence critical areas. Some factors coincided more with PTB in Lisbon (HIV, immigrants, prisoners) and others in Oporto (youth index, overcrowding, non-standard accommodation, unemployment). The new factor index showed very good sensitivity and specificity (%) for all periods (sensitivity: 94.7–100; specificity: 66.1–87.3).

**Conclusion:** factors clusters overlapped more neatly with higher incidences in PTB critical areas (Metropolitan Oporto and Lisbon), though differently. It is shown that ecological information and clustering methods can help to explain and predict PTB critical areas, thanks to a factor index. As only secondary and tertiary information is used, this approach means a cheap and easy way to assist health managers in predicting critical areas.

## 25. TOBACCO CONTROL, TRADE AND INTERNATIONAL TREATIES

### Children and young people are the primary victims of tobacco in the 21st Century: a human rights issue?

M Aghi. Behavioral Science, Free Lance Consultant, New Delhi, India.

Children are mostly in oblivion about the adverse health effects of tobacco. They are not cognizant that tobacco is addictive. The industry knows this and blatantly violates the most basic rights of the young namely Right to Knowledge and Right to Health. The tobacco industry

continues to aggressively promote its products and recognizes that children are its future. The industry is well-aware that Chronic, long-term cigarette-smoking almost invariably begins in a person's teen years. The industry views the transition from smoking the first cigarette to becoming a confirmed pack-a-day smoker as a series of stages that may extend to when a child becomes a young adult. The industry not only uses tactics to encourage initial experimentation but also to carry new smokers through each stage of this process. Its marketing encourages solidification of tobacco habits to increase consumption by focusing on key transition periods when young adults adopt new behaviors—such as entering the university, a new workplace or joining a new peer group by focusing on leisure and social activities. Tobacco companies study young adults' attitudes, social groups, values, aspirations, role models, and activities and then infiltrate both their physical and their social environments. Brands are also positioned for established users who might be thinking seriously about quitting, such as those who are concerned about health and financial costs of tobacco. The young are strategically captured by images such as “macho, strong and masculine” or “low tar, health concerned” Tobacco marketing solidifies addiction among young adults by making the product easily accessible. The recent developments of on-line sales, home-deliveries make the product always accessible.

### Trade and investment agreements: an emerging issue

M Allen.<sup>1,2</sup> <sup>1</sup>Public Policy, Allen and Clarke Policy and Regulatory Specialists Ltd, Wellington, New Zealand;

<sup>2</sup>International Union Against Tuberculosis and Lung Disease, Paris, France.

The Union has recently developed a position paper on trade and investment agreements and their impacts on tobacco control. This paper has been developed in response to increased attention at the country level on the potential impacts of an increasing number of international trade and investment agreements entered into by countries. Concerns have been expressed by many commentators regarding the potential for such commitments agreements to undermine existing tobacco control efforts, or to limit government's future regulatory flexibility. In particular, public health advocates have been concerned that the tobacco industry uses threats of litigation to chill regulatory action by governments. The presenter will outline the Union's Position Paper and its description of the myriad of international agreements that exist, concerns that have been expressed, and solutions that have been posed. These solutions include quite different approaches, and two major points of view will be discussed. The key future directions for governments concerned to retain their regulatory flexibility will be outlined.

## Global experience in tobacco buyouts and quota-based restrictions of crops

G Quan. Tobacco Control, International Union Against Tuberculosis and Lung Disease, Beijing, China.

In countries where tobacco growing is based on quotas, transitioning into a free-market system, where there are much fewer restrictions on who, where, and how much tobacco can be grown, is an option for policy makers. Quota-based system involves more government oversight and in general protects the interests of tobacco farmers as price of purchasing tobacco leaf is often set at a level higher than in a free market system. Quota-based system also tends to limit the production of tobacco leaf at a certain level whereas higher overall output of tobacco leave can be expected if tobacco leaf trade is free of restriction. From a public health perspective, quota-based system is generally favored over the free market system as it protects the interests of tobacco farmers and also limits overall tobacco leaf production. However, this might not always be the case especially as the market of tobacco leaf is increasingly becoming global. The specific country experiences on quota-based system and free market system will be discussed. Implications for public health and the wellbeing of tobacco farmers are the focus of attention.

## 26. KNOW YOUR EPIDEMIC: FUNDAMENTAL TO SOLUTIONS FOR CHILD TB

### Burden and diagnostic challenges of child TB in rural Kenya

A Brent.<sup>1,2,3</sup> <sup>1</sup>Nuffield Department of Medicine, University of Oxford, Oxford, UK; <sup>2</sup>Departments of Clinical Research and Epidemiology & Demography, KEMRI-Wellcome Trust Research Programme, Kilifi, Kenya, Kilifi, Kenya; <sup>3</sup>Infectious Diseases, Oxford University Hospitals NHS Trust, Oxford, UK.

**Introduction:** Good quality regional data on childhood TB incidence and case detection rates are lacking in most settings due to inherent challenges in diagnosing TB in children, and a lack of a consistent case definitions. Here we present results from the KIDS TB Study\* of childhood TB diagnosis and surveillance in Kenya.

**Methods:** We established intensified case finding and state of the art TB diagnostics at Kilifi District Hospital in Kenya, nested within the Kilifi Health & Demographic Surveillance Survey (KHDSS). Estimates of childhood TB incidence were derived using denominator population data from the KHDSS, and adjusted for the sensitivity of hospital-based surveillance using notification, vital registration, verbal autopsy and spatial data. We explored the effect of a range of published case definitions on the measured incidence of childhood TB, and identified epidemiological risk factors for childhood TB in a nested case control analysis.

**Results:** Estimates of the community incidence of childhood TB varied by up to two orders of magnitude

depending on the published case definitions used. Despite intensified hospital-based case finding, up to two thirds of cases may be missed. Conservative estimates suggest official notification data may underestimate the national burden of childhood TB in Kenya by a similar proportion. Known close TB contact, HIV infection and malnutrition were all identified as risk factors. Half of all childhood TB cases were attributable to a known close TB contact.

**Discussion:** This is one of very few prospective incidence studies from high burden countries. It suggests that a large proportion of cases in Kenya may not currently be diagnosed or notified, and that half of all cases are potentially preventable by implementing current recommendations for isoniazid chemoprophylaxis.

\* Kilifi Improving Diagnosis & Surveillance of Childhood TB (KIDS TB) Study

### Can mathematical modelling improve our estimates?

P Dodd,<sup>1</sup> E Gardiner,<sup>2</sup> R Coghlan,<sup>3</sup> J Seddon.<sup>4</sup> <sup>1</sup>School of Health and Related Research, University of Sheffield, Sheffield, UK; <sup>2</sup>N/A, Global Alliance for TB Drug Development, New York, NY, USA; <sup>3</sup>N/A, TESS Development Advisors, Geneva, Switzerland; <sup>4</sup>Department of Paediatric Infectious Diseases, Imperial College London, London, UK.

**Background:** Confirmation of a diagnosis of tuberculosis in children (aged <15 years) is challenging; under-reporting can result even when children do present to health services. Direct incidence estimates are unavailable, and WHO estimates build on paediatric notifications, with adjustment for incomplete surveillance by the same factor as adult notifications. We aimed to estimate the incidence of infection and disease in children, the prevalence of infection, and household exposure in the 22 countries with a high burden of the disease.

**Methods:** Within a mechanistic mathematical model, we combined estimates of adult tuberculosis prevalence in 2010, with aspects of the natural history of paediatric tuberculosis. In a household model, we estimated household exposure and infection. We accounted for the effects of age, BCG vaccination, and HIV infection. Additionally, we tested sensitivity to key structural assumptions by repeating all analyses without variation in BCG efficacy by latitude.

**Findings:** The median number of children estimated to be sharing a household with an individual with infectious tuberculosis in 2010 was 15 319 701 (IQR 13 766 297–17 061 821). In 2010, the median number of *Mycobacterium tuberculosis* infections in children was 7 591 759 (5 800 053–9 969 780), and 650 977 children (424 871–983 118) developed disease. Cumulative exposure meant that the median number of children with latent infection in 2010 was 53 234 854 (41111669–68959804). The model suggests that 35% (23–54) of paediatric cases of tuberculosis in the 15 countries reporting notifications by age in 2010 were detected. India is predicted to account for 27% (22–33) of the total burden of paediatric tuberculosis in the 22 countries. The predicted propor-

tion of tuberculosis burden in children for each country correlated with incidence, varying between 4% and 21%.

**Conclusion:** Our model has shown that the incidence of paediatric tuberculosis is higher than the number of notifications, particularly in young children. Estimates of current household exposure and cumulative infection suggest an enormous opportunity for preventive treatment.

### Disease burden and challenges estimating child TB in rural Mozambique

E Lopez Varela,<sup>1,2</sup> O Joaquim Augusto,<sup>1</sup> K Gondo,<sup>1</sup> AL Garcia-basteiro,<sup>1,2</sup> E Macete,<sup>1</sup> J Sacarlal,<sup>1</sup> P Alonso<sup>1,2</sup>

<sup>1</sup>(CISM), Centro de Investigação em Saúde de Manhiça, Manhiça, Mozambique; <sup>2</sup>Barcelona Centre for International Health Research (CRESIB), Barcelona Institute for Global Health, Barcelona, Spain.

**Background:** Although relatively neglected for many years, pediatric TB is increasingly becoming a priority for national TB programs (NTP) as it reflects ongoing transmission within a population and thus is often used as a sentinel indicator of the effectiveness of NTP. However, important limitations on the current estimates underscore the need for population-based data on the true burden of pediatric TB. Mozambique is one of the few 22 TB high burden countries with a persistent increasing trend in TB incidence rate, driven mainly by the HIV epidemic. Furthermore, it has one of the lowest case detection rates among them and improved reliable estimates are required to measure future progress. This presentation discusses the results and implementation challenges of a study aiming to estimate the minimum community based incidence rate of TB among children <3 years of age in Southern Mozambique.

**Methods and Findings:** The study was conducted in the Manhiça District (rural southern Mozambique), where the Manhiça Health Research Center (Centro de Investigação em Saúde de Manhiça, CISM) runs a Health and Demographic Surveillance System (HDSS). Between October 2011 to October 2012, we prospectively enrolled all presumptive TB cases under 3 year through passive and active case finding. Participants included all children who had either TB symptoms or were close contacts of a notified adult smear positive pulmonary TB. Children were clinically evaluated at baseline and follow-up visits. Investigation for TB disease included Chest X Ray, HIV and tuberculin skin testing as well as gastric aspirate and induced sputum sampling, which were processed for smear, culture, and mycobacterial molecular identification.

**Results:** During the study period, 13,764 children <3yr contributed to a total of 9,575py. Out of the 789 presumptive TB cases enrolled, 13 had TB culture confirmation while 32 were probable TB cases. The minimum community-based incidence rate of TB (confirmed plus probable cases) was 470/100,000 person-years (95% CI: 343 to 629/100,000). HIV co-infection was present in 44% of the TB cases and HIV infected children were six times more likely to have TB disease

than uninfected ones (OR 6.1, 95% CI 3 to 12). A wide range of implementation challenges were encountered including: reduced community health seeking behavior due to limited awareness about pediatric TB; limitations in the applicability of consensus case definition, especially in a HIV-TB setting; sub-optimal contact tracing due to difficulties in patient identification and poor recording; frequent weaknesses among the existing TB system, among others.

**Conclusion:** This study shows a high incidence of pediatric TB and adds valuable information to the global effort of producing better estimates. The data underscore the complexities of childhood TB diagnosis and the need for improved TB control strategies.

## 27. WHAT PRACTICAL STEPS ARE NEEDED TO ACHIEVE A PATIENT-CENTERED CONTINUUM OF CARE IN TB CONTROL?

### Patient-centeredness: a realist inquiry

S Massaut,<sup>1</sup> A Van Der Kwaak,<sup>2</sup> <sup>1</sup>TB CARE I, KNCV Tuberculosis Foundation, The Hague, <sup>2</sup>Health, Royal Tropical Institute, Amsterdam, Netherlands.

**Background:** Over a two year period TB CARE I pilot implemented its PCA package in five countries; Cambodia, Indonesia, Mozambique, Nigeria and Zambia. The project included an evaluation component with the goal to measure changes attributed to the implementation of the patient centered tools, and to identify reasons why or why not the intervention contributed to more patient centered services. In short, we wanted to know what worked, what did not work and why?

**Design/Methods:** The project design consists of three main parts: 1. Before study on status of TB care and treatment and the responsiveness of TB services to patients was carried out in two intervention districts and one control district 2. The intervention was carried out, PCA tool implementation (2 or 3 tools per country), within a time frame of six months covering two districts. 3. After study was carried out in two intervention districts and one control district. The study population was purposely selected and consisted of TB patients, health care providers, program managers, and key informants. A survey, in-depth interviews, FGDs and a desk review were used in both the before and after studies. At the project end, in-depth interviews were also conducted with the project implementers of each country. The goal of these interviews was to explore if the tools had created change and led to increased patient-centered care. All five countries followed the same methodology.

**Results:** Patient aware of their rights & responsibilities, empowered to ask questions and concerns. Patient engaged to help HCWs learn about patient perspective on quality services and cost barriers faced when accessing TB care. HCW empowered with tools on patients' rights and responsibilities and information on TB/HIV. HCW



better informed on quality issues and cost barriers from the patient perspective.

**Conclusion:** The PCA pilot clearly demonstrates that with a few practical approaches TB programs and health facilities can make the first steps to become more patient centered. However, a few tools do not equal patient-centered care and applying a PCA is an investment with multiple stakeholders and it takes time. Patient-centered care is a shared responsibility that needs to be defined within each cultural context before it becomes an integral part of TB programs.

### **A patient-centered continuum of care: what is it and can we afford not to do it?**

L Weber,<sup>1</sup> B Dujardin.<sup>1</sup> <sup>1</sup>Health systems and policies, Ecole de Santé Publique - Université libre de Bruxelles, Brussels, Belgium.

Despite the great results stemming from unprecedented technological and managerial advances over the past decade, the field of TB management, policies, programs and even vocabulary remain mainly centered on tuberculosis as a disease rather than focusing on patients as people suffering from TB. On the field, lack of patient-centered approach is associated with many unsolved problems in terms of accessibility, quality of care and social consequences for patients and their families. Adopting a patient-centered perspective means considering the patient with a holistic view, within the context of his family and community, educational, emotional, cultural, economic background, with their own health and non-health problems. Patients are people with complex needs, who face many barriers in the continuum of care, from being diagnosed up to achieving a successful and timely treatment. This continuum of care can only succeed if patients are welcome in friendly and supportive health systems, trust their provider and are empowered at all stages of their pathway, by attending their needs, including relief of symptoms, health education, removal of economic barriers and psychosocial support. Patient centered care increases both patient and provider satisfaction. Patients appreciate that providers are interested in their lives rather than only in the disease. In turn, good patient-provider relationship is a factor of motivation for the provider himself, as well as a great factor of compliance, leading to better cure rate and less loss-to-follow-up. Investing in patient-centered care is cost-effective for TB programs in terms of preventing future costs related to the search for missing patients, re-treatment and multidrug resistance. By improving their friendliness, health services also become more accessible and new patients consult earlier; therefore this approach allows better case detection, as well as improving cure rate. This shift is not expensive but requires behavioral changes across donors, program & facility managers, providers as well as in the field of education and training. At the facility level already, small practical steps such as promoting patient's clubs or investigating patient pathway through qualitative interviews may help to better understand and fulfill patient's needs. At the contrary,

what is very costly for all TB patients, NTPs and health systems is not to reorientate our strategies in a patient-centered way.

## **28. ADOLESCENT TB, TB-HIV AND MDR-TB: ADDRESSING A VULNERABLE POPULATION WITH UNIQUE NEEDS USING INNOVATIVE SOLUTIONS**

### **Treatment of adolescents with MDR-TB**

C Perez-Velez. Banner Good Samaritan Medical Center, University of Arizona College of Medicine, Phoenix, AZ, USA.

Many adolescents who are prescribed therapy for MDR-TB fail to complete it. These defaults lead to significant morbidity and mortality. Like all patients with MDR-TB, teenagers face obstacles to adhering to the complex medication regimens. They have unique clinical and psychosocial needs, and patient-centered approaches can improve adherence. This presentation will review the treatment of adolescents with MDR-TB, with a focus on their special needs and individualized care strategies.

## **29. MANAGEMENT OF LATENT TUBERCULOSIS INFECTION: FROM EVIDENCE TO POLICY**

### **WHO policy guidance on LTBI management**

A Matteelli,<sup>1</sup> H Getahun.<sup>1</sup> <sup>1</sup>Global Tuberculosis Program, World Health Organization, Geneva, Switzerland.

The importance of latent tuberculosis infection (LTBI) is increasingly recognized. It affects one third of the world population and significantly contributes to TB epidemiology. In countries with low incidence of the disease, TB reactivation (defined as an LTBI case progressing to active disease) accounts for a significant proportion of new TB cases. The World Health Organization (WHO) has developed an eight-point framework adapted from the post-2015 Global TB Strategy to target pre-elimination and, ultimately, elimination in countries with low levels of tuberculosis. Screening and appropriate treatment for LTBI in high-risk groups is a crucial element of the framework. Therefore, in 2014 WHO developed the Guidelines on the management of LTBI, in accordance to the requirements and recommended process of the WHO Guideline Review Committee. The guidelines intend to provide public health approach guidance on evidence-based practices for testing, treating and managing LTBI in infected individuals with the highest likelihood of progression to active disease. High-income or upper middle-income countries with an estimated TB incidence rate of less than 100 per 100 000 population are primarily targeted. The document provides the basis and rationale for the development of national guidelines. Key recommendations are provided in the following areas: 1) identification of target at-risk populations for

systematic testing and treatment of LTBI; 2) algorithmic approach to rule-in individual treatment candidates, after active disease has carefully been excluded; 3) recommended treatment options. Additional critical issues being discussed include: a) clinical monitoring of individuals receiving treatment; b) establishment of national TB drug resistance surveillance systems; c) management of contacts of multidrug-resistant TB (MDR-TB) cases; d) introduction of flexible interventions to ensure acceptable initiation of, adherence to and completion of LTBI treatment; e) documentation of treated individuals through a functional, routine monitoring and evaluation system; f) creation of conducive policy and programmatic environment, including the promotion of universal health coverage, development of national and local policies, standard operating procedures, as well as allocation of dedicated resources.

### LTBI management: who should we target?

K Kranzer,<sup>1</sup> D Govindasamy.<sup>2</sup> <sup>1</sup>Department of Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, UK; <sup>2</sup>Health Systems Research Unit, South African Medical Research Council, Cape Town, South Africa.

Systematic testing and treatment of latent tuberculosis infection (LTBI) conveys both risks and benefits. Identifying groups of individuals for whom the benefits of testing and treatment outweigh the risks is important. Two systematic reviews were conducted to determine the prevalence of LTBI and risk of progression to active TB in vulnerable groups compared to the general population. Some vulnerable groups were identified a priori (i.e. health care workers, TB contacts), whilst others were identified through the systematic reviews. The number of studies investigating the risk of progression of LTBI to active TB disease was limited. Therefore, a third review was conducted to compare the risk of active TB disease in vulnerable groups with that of the general population, taking into account that any increased risk of active disease in vulnerable groups would be influenced by the prevalence of LTBI, risk of progression and TB transmission within the vulnerable group.

### Latent tuberculosis infection beyond HIV positives: why is it important?

A Grant. Clinical Research, London School of Hygiene & Tropical Medicine, London, UK.

**Background:** One-third of the world's population is infected with *Mycobacterium tuberculosis*, although the risk of subsequent active TB disease varies greatly between individuals. Treatment of latent infection reduces the risk of subsequent active TB disease, but this intervention is relatively under-implemented. TB control programmes prioritise the treatment of active disease, particularly among individuals who are sputum smear positive and thus most infectious. In settings where the TB case load is high, treatment of latent infection is often a lower priority. However, in settings where TB incidence

is low, most TB cases arise as a consequence of reactivation of latent infection. As countries move towards TB elimination, effective and efficient treatment of latent infection will be increasingly important to prevent active disease and thus minimise continuing TB transmission. In most countries, treatment of latent infection is recommended for HIV-positive people and child contacts of people with infectious TB, groups at very high risk of subsequent disease. These recommendations are variably implemented. To maximise the effect on TB incidence at population level, better coverage and treatment of a broader range of people with latent infection will be needed. Programmes will none the less need to target individuals at high risk of reactivation in order to ensure that the benefits of testing and treatment outweigh the risks at individual level. Better diagnostic tests to identify individuals at higher risk of reactivation, and effective, short, well-tolerated regimens for the treatment of latent TB infection are needed. Effective treatment regimens for people likely to have latent infection with drug-resistant organisms are also urgently needed.

**Conclusion:** New WHO guidelines will encourage wider use of treatment for latent TB infection in intermediate and low burden countries, in line with the post-2015 Global TB Strategy.

## 30. TB IN EUROPE: MDR-/XDR-TB CONTROL AND CHALLENGES OF HIGH RISK GROUPS

### MDR-TB in Belarus, the role of psychosocial care.

A Skrahina,<sup>1</sup> H Hurevich,<sup>1</sup> V Solodovnikova,<sup>1</sup> D Klimuk,<sup>2</sup> A Astrauko,<sup>2</sup> V Rusovich,<sup>3</sup> M Dara.<sup>4</sup> <sup>1</sup>Clinical Department, Republican Research and Practical Centre for Pulmonology and Tuberculosis, Minsk, Belarus, <sup>2</sup>Monitoring and Evaluation Department, Republican Research and Practical Centre for Pulmonology and Tuberculosis, Minsk, Belarus, <sup>3</sup>Country Office, World Health Organization, Minsk, Belarus, <sup>4</sup>Regional Office for Europe, World Health Organization, Copenhagen, Denmark.

TB incidence and mortality in Belarus has been progressively falling from 54 to 41 and from 12.1 to 6.8 per 100 000, accordingly, for last 7 years. Nevertheless the number of HIV/TB co-infected rises dramatically and according to recent nationwide drug resistance survey MDR-TB was found in 32.3% of new and in 75.6% of previously treated TB cases. Results of treatment of MDR-TB are far from satisfactory (51% treatment success, 11% death). Risk factors for MDR-TB acquisition and unfavourable treatment outcome are the following: young age, drug and alcohol abuse, HIV, history of imprisonment, unemployment, homeless. Most of such events as treatment failure and loss to follow up occur at outpatient treatment phase particularly in patients from above risk groups. One of the key elements of outpatient care strengthening is psychosocial



support. An Operational Research conducted with 40 MDR-TB patients showed that treatment cost can be reduced of more than 5200 US dollars per patient using outpatient care with social support instead of existing care based on long hospitalization. Another study showed that MDR-TB patients with psychosocial support (n=1057) had better treatment outcomes in compared with conventionally managed patients (n=3514): treatment success 70% vs. 53%; mortality 2% vs. 6%; treatment failure 27% vs. 40%. Along with adequate diagnostics and therapy psychosocial support is an important element in achieving good treatment outcomes and reducing the cost of treatment of MDR-TB.

### **The Rotterdam case study: challenges after controlling an outbreak in an urban setting**

G Devries,<sup>1</sup> R Van Hest.<sup>1,2</sup> <sup>1</sup>KNCV Tuberculosis Foundation, The Hague, <sup>2</sup>Municipal Public Health Service Rotterdam-Rijnmond, Rotterdam, Netherlands.

**Background:** Rotterdam, a city with 600,000 inhabitants in the Netherlands, faced a tuberculosis (TB) outbreak among illicit drug users and homeless persons during the beginning of this century. Since May 2002 a mobile radiographic screening program was implemented as outbreak management which resulted by the end of 2005 in a decrease of the annual number of notified TB cases among these risk groups and DNA fingerprinting showed reduced transmission among these populations (results published in 2007). Few studies however report on what happens after an outbreak. Objective: To study the incidence of TB and characteristics of TB cases during and after an outbreak.

**Methods:** Description of TB trends, recent transmission, efficiency (numbers needed to screen) and yield of active case-finding during the two study periods.

**Results:** Comparing May 2002–2005 (outbreak period) and 2006–2013 (post-outbreak period) the average annual number of all notified TB cases among illicit drug users and homeless persons declined from 19 to 5, representing 12.6% versus 4.7% of the total TB caseload in Rotterdam respectively. The proportion of TB cases attributable to recent transmission reduced from >80% in 2002 to 45% in 2005 during outbreak management and averaged 38% post-outbreak management. The numbers needed to screen reduced from 325 to 2,088 during the two periods and the yield of the screening program declined from 39.4% to 10.0% for the target population. Eighty-nine percent of the 111 notified TB cases among illicit drug users and homeless persons during May 2002–2013 completed treatment.

**Conclusion:** TB screening among illicit drug users and homeless persons in Rotterdam, together with social interventions, such as supervised small-scale housing projects and detox, had considerable impact on TB incidence and recent transmission among these risk groups. Efficiency and yield of the screening program substantially reduced. As a consequence the program was scaled down. Measures to prevent future outbreaks and to reduce TB disease burden among these risk groups

should maintain, such as early and low-threshold referral services for symptomatic clients, and awareness and education activities for the most relevant medical specialists. Screening for latent TB infection, either opportunity-based during contact investigation or targeted for the risk groups, should be considered.

## **31. IMPLEMENTING "FAST": A RE-FOCUSED APPROACH TO INSTITUTIONAL TB TRANSMISSION CONTROL**

### **FAST in Viet Nam**

H Le. TB-HIV, University Research Co., LLC, Hanoi, Viet Nam.

**Background:** Quang Nam province in Vietnam, with 1.4 million population, reports approximately 1,700 TB cases annually. The Provincial Hospital of TB and Lung Diseases (PHTB&LD), diagnoses the majority of TB cases and transfers them to 18 district facilities for registration and treatment. Therefore, the PHTB&LD had no system tracking and reporting all TB cases diagnosed and initiated treatment at Out-Patient Department (OPD) and Intensive Care Unit (ICU) as entry points and clinical wards. The TB CARE II project assisted to introduce the FAST strategy to improve patient screening and triaging at OPD and ICU, and patient tracking and management at the PHTB&LD.

**Methods:** FAST supported the PHTB&LD to develop and execute a patient protocol and integrate recording, monitoring and reporting tools into the current system. Since May 2014, the PHTB&LD started using simple MS Excel sheets and MS Access database to track all patients from registration at OPD and ICU to TB diagnosis and treatment initiation at all departments. FAST also supported practical trainings and routine review meetings to improve data utility and exchangeability and strengthen collaboration among departments.

**Results:** From May to July in 2014, among 2066 patients visiting OPD, 167 pulmonary TB cases, 39 extra-pulmonary TB cases and 5 MDR-TB cases were diagnosed at the PHTB&LD. Out of 2066 patients, 235 patients were tested with Xpert, yielding 51 pulmonary TB cases and 5 MDR-TB cases. During the same period, among 209 patients admitted to ICU, 26 pulmonary TB cases, 12 extra-pulmonary TB cases and 4 MDR-TB cases were detected. Out of 209 patients at ICU, 71 patients were tested with Xpert, detecting 5 pulmonary TB cases and 4 MDR-TB cases. Average times from visit to pulmonary TB treatment initiation were 5.7 days and 8.2 days for patients first received at OPD and ICU respectively. The average times were longer - 6.8 days and 12.0 days, for patients diagnosed with Xpert, received at OPD and ICU respectively while average time from Xpert test to treatment initiation was 2 days. The average time to MDR-TB treatment initiation from visit was about 9 days, including about 5 days from Xpert test.

**Conclusion:** The monitoring system, well operated since May 2014, provided strong evidences for additional

number of pulmonary TB and MDR-TB cases detected by Xpert and a great need to increase earlier accessibility to Xpert test with the FAST strategy to effectively and rapidly diagnose TB and MDR-TB cases.

Visiting patients diagnosed with Pulmonary TB and MDR-TB at the PHTB&LD in May-Jul, 2014

Patients diagnosed with pulmonary TB and MDR-TB	No. of patients diagnosed	No. of patients enrolled in treatment	Average time (days) to treatment initiation	
			from visit	from Xpert test
<b>1. Pulmonary TB patients</b>				
First received at OPD				
All patients	167	164	5.7	
Patients diagnosed with Xpert	51	50	6.8	2.3
First received at ICU				
All patients	26	25	8.2	
Patients diagnosed with Xpert	5	5	12.0	2.2
<b>2. MDR-TB patients</b>				
First received at OPD	5	5	8.6	5.4
First received at ICU	4	3	8.7	4.7

## FAST in Bangladesh

AE Barrera-Cancedda,<sup>1</sup> S Islam,<sup>2</sup> R Sultana,<sup>2</sup> E Nardell.<sup>3</sup>

<sup>1</sup>Tuberculosis, Partners In Health, Boston, MA, USA; <sup>2</sup>MDR-TB, University Research Co. Bangladesh, Dhaka, Bangladesh; <sup>3</sup>Global Health and Social Medicine, Harvard Medical School, Boston, MA, USA.

**Background/Introduction:** Globally more than half of multidrug resistant TB cases occur in persons not previously treated, the result of transmission, and probably reinfection in many cases – although reinfection is difficult to prove. Here we introduce a refocused, intensified administrative approach to TB transmission control we call FAST: Finding cases Actively by cough surveillance and rapid diagnostics, Separating safely, and Treating effectively based on rapid drug susceptibility testing. This approach is based on the assumption that most transmission occurs not from known TB patients on effective therapy, but from persons with unsuspected TB or unsuspected drug resistance. Our hypothesis is that if unsuspected/undiagnosed TB and/or drug resistance is eliminated from hospitals and clinics, there should be no one able to transmit infection.

**Methods:** The National Institute of Diseases of the Chest and Hospital (NIDCH), a 680-bed facility in Dhaka, Bangladesh, implemented the FAST strategy in its inpatient departments starting February 1, 2014. All newly admitted patients, irrespective of symptoms, were immediately tested using GeneXpert® MTB/RIF.

**Results:** From February 1, 2014, to May 1, 2014, a total of 1062 sputum samples from discrete patients admitted to one of the IPDs at NIDCH were tested using GeneXpert® MTB/RIF. Of these 1062 samples, approximately 11% and 1% unsuspected cases of TB and MDR-TB were identified, respectively. Of the 850 patients admitted to the facility as non-TB patients with other respiratory diseases, roughly 9% actually had TB and were misclassified upon admission. Furthermore, of the 42 TB patients on treatment admitted to the facility,

approximately 7% were identified as Xpert-confirmed MDR-TB cases.

**Conclusions:** Implementing the FAST strategy at NIDCH led to a sharp increase in the number of unsuspected TB and MDR-TB cases that were identified compared to historical control data. If not for the FAST strategy, these cases would have likely gone unidentified and untreated - potentially transmitting to other patients or staff - until the patient's continued clinical deterioration led to a diagnosis, or they were discharged or died. Due to the rapid nature in which these cases were identified using GeneXpert® MTB/RIF, treatment was initiated far faster than with the standard practice of waiting for culture or DST results with drug-resistant cases.

## FAST in Russia

V Livchits,<sup>1</sup> D Taran,<sup>1</sup> S Kornienko,<sup>2</sup> R Nikitin,<sup>2</sup> J Kononenko,<sup>3</sup> S Keshavjee,<sup>4</sup> E Nardell.<sup>4</sup> <sup>1</sup>PIH-Russia, Partners in Health (PIH), Moscow, <sup>2</sup>Voronezh Regional Clinical TB Dispensary, Voronezh, <sup>3</sup>Republic of Karelia clinical TB Dispensary, Petrozavodsk, Russian Federation; <sup>4</sup>Department of Global Health and Social Medicine, Harvard Medical School, Brigham and Women's Hospital, Boston, MA, USA.

**Introduction:** Nosocomial transmission of DR-TB in Russian TB hospitals is believed to be an important factor in the epidemiology of DR-TB in the region. Uninterrupted transmission of DR-TB has a direct impact on both patient treatment outcomes and health system costs (financial and other). Working with the Lilly MDR-TB Partnership, Partners In Health (PIH) and Brigham & Women's Hospital/Harvard University have developed a program based on the F-A-S-T approach (Find patients Actively, Separate them as required; and Treat them appropriately) to build up a strong, adaptable and sustainable hospital infection control strategy, and interrupt nosocomial DR-TB transmission. The program: (1) uses rapid TB diagnostic methods to identify DR-TB patients early and separate them from those with drug-susceptible TB; and (2) initiates the correct therapy as rapidly as possible. Although its primary purpose is to provide evidence-based guidance for regional infection control activities, the initiative is also designed to identify high yield interventions that provide value for money.

**Methods:** Multi-center study to assess the impact of the F-A-S-T strategy on MDR-TB infection control indicators and outcomes for patients admitted to Voronezh and Petrozavodsk (Russia) regional TB hospitals from May 2013 to December 2015. The main objective is to compare several process indicators and treatment outcomes between two cohorts: those admitted during the two years that preceded implementation of F-A-S-T, and those admitted with the F-A-S-T strategy in place.

**Results:** From May 2013 to July 2014, we have studied 1,174 patients admitted to inpatient care facilities with clinical and radiological suspicion of pulmonary TB in Voronezh and Petrozavodsk. From them, 1,165 (99.2%) patients were tested with Xpert MTB/RIF molecular technique at a point of admission. Of these patients, 43.7% (509/1,165) were MTB positive and 41% (209/509) had RIF-resistant TB strains. 93.0% (1,084/1,165)

of patients have undergone the test in the first two days after admission and 99% (200/202) of patients were placed on the MDR-TB chemotherapy within 3 days after testing.

**Conclusion:** The F-A-S-T strategy has resulted in a significant improvement in routine policies of patients being diagnosed early, appropriately separated, and rapidly and correctly treated for TB. This is an essential intervention to interrupt MDR TB transmission at Russian regional TB hospitals.

## 32. CHANGING THE STATUS QUO IN TB DRUG AND REGIMEN R&D

### Barriers for combination trials

R Horsburgh. Department of Epidemiology, Boston University School of Public Health, Boston, MA, USA.

**Background:** New anti-tuberculosis agents are becoming available, but little information has been generated to guide clinicians on how to use them in combination with each other and/or with existing second-line drugs.

**Design/Methods:** Survey of clinical trial investigators designing ongoing and planned clinical trials.

**Results:** The following barriers were identified: 1) Studies that combine more than one investigational agent do not advance either product towards regulatory approval and are thus not prioritized by manufacturers; 2) Concern about overlapping toxicity that might be attributed to the manufacturer's product further limits willingness to participate in combination trials; 3) Time frames expected by manufacturers are difficult to achieve in large publicly supported networks; 4) Numerous trial networks exist, leading to competition for investigational products; 5) Each network develops its own study designs without regard to complementarity; and 6) Small focused trials that could produce results on which other studies might build are not prioritized. Current TB clinical trials using new drugs are shown in the table.

**Conclusion:** Clinical trials combining investigational agents are not likely to be implemented until the new drugs come on the market. Careful planning and continued communication between investigators and networks will be essential to avoid duplication of efforts and to maximize the number of regimens that are evaluated.

Study Name/Number	Description	Current Status
Delamanid Phase 3 Trial	Safety and Efficacy Trial of Delamanid for 6 Months in Patients With Multidrug Resistant Tuberculosis	In follow-up
Delamanid 6 month safety study in children and young adults	A 6-Month Safety, Efficacy, and Pharmacokinetic Trial of Delamanid in Pediatric Patients With Multidrug Resistant Tuberculosis	Enrolling
Delamanid PK study in Children	Phase I Pharmacokinetic and Safety Trial to Determine the Appropriate Dose for Pediatric Patients With Multidrug Resistant Tuberculosis	Enrolling
Bedaquiline/PA-824/PZA (GATB NC-005)	8-week SSC Study of Bedaquiline plus PA-824 plus PZA	In preparation
PA-824/moxi/PZA (GATB NC-006)	Treatment shortening trial of PA/M/Z for 4 or 6 months compared to HRZE for 6 months	In preparation
NIX-TB	PA-824, linezolid and bedaquiline; single arm for 6 or 9 month duration depending on rate of sputum culture conversion.	In preparation
DDI of bedaquiline+delamanid (ACTG A5343)	A Trial of the Safety, Tolerability, and Pharmacokinetics of Bedaquiline and Delamanid	In preparation

### A novel solution to the current R&D problem

M Balasegaram. Access Campaign, Medecins Sans Frontieres, Geneva, Switzerland.

There is a desperate need for a new multi-drug resistant TB (MDR-TB) treatment. To achieve this new regimen there needs to be a healthy drug pipeline to supply new classes of drugs to be combined into regimens. The current pipeline will not be able to provide this, with no drugs in phase one trials and only 4 new classes of drugs in later clinical development. With little commercial market for TB and the withdrawal of large pharmaceutical companies from the area there is a need to relook at how TB R&D is incentivised. What is needed for more compounds to enter phase 1 trials? Can the collaboration required for regimen development be ensured? MSF in collaboration with a number of stake holders examined various forms of incentivising mechanisms to establish an open collaborative framework for drug and regimen development. The 3P Project implements three mechanisms to facilitate R&D for TB medicines: push funding to finance R&D activities upfront (i.e. through grants) pull funding to incentivise R&D activities through the promise of financial rewards on the achievement of certain R&D objectives (i.e. through milestone prizes) pooling of intellectual property to ensure open collaborative research and to ensure fair licensing for competitive production of the final products The current status quo in TB R&D cannot continue. Innovative ways of stimulating the TB drug R&D pipeline, such as the 3P proposal, require political will and financial commitment.

## 33. TB PATIENTS: LEARNING FROM THE EXPERIENCE OF THOSE PERSONALLY AFFECTED

### Take That TB: online platform for patients, created by patients to address information gap

C Ehlers. Head, Take That TB, Hamburg, Germany.

Take That TB is the tuberculosis patient organization affiliated with the TBNET. It was founded as a website ([www.takethattb.com](http://www.takethattb.com)) by Cordula Ehlers in July 2012 as a result of many impressions during a TB course and many personal experiences in the field of TB since 2008. Since November 2012, this page is available on Twitter (@TakeThatTB) and since February 2013 on Facebook (Take That TB). Take That TB is member of the STOP TB Partnership and is furthermore intended as a platform for the exchange of information but also serve as a forum for concerns, questions and experiences. The target group are former and current TB and MDR-TB patients, doctors, nurses, hospital staff and relatives of patients with tuberculosis. Take That TB is a group of former patients from Europe (mostly Moldova, Spain and Germany), India, Africa and Australia and they are trying to build a meeting area "From Patients For Patients". The primary aim is the exchange between



patients and the discussion about their experiences with TB. Take That TB wants to be a platform for patients on treatment and for former patients who want to exchange about their experiences with TB. Take That TB wants to be a chat room for patients in isolation. Collectively, the group can offer great support to each other, and help raise the awareness of TB in our communities, and help remove the stigma this disease has unfortunately associated with it.



### 34. SUPERVISION OR SUPPORT? A DEBATE PANEL ON CHALLENGES AROUND DOT AND PATIENT-CENTERED CARE

#### Engaging communities: BRAC innovative strategies to TB treatment in Bangladesh

M Akramul Islam,<sup>1</sup> S Islam,<sup>1</sup> M Rana,<sup>1</sup> S Munim,<sup>1</sup> R Amzad,<sup>1</sup> H Ahmed.<sup>2</sup> <sup>1</sup>TB, BRAC, Dhaka, <sup>2</sup>TB, NTP, Dhaka, Bangladesh.

**Background and challenges:** TB is a major public health concern in Bangladesh. BRAC, a development organization initiated community based tuberculosis control program in 1984 in one sub-district. This model was gradually expanded since 1994 in collaboration with National Tuberculosis Control Program (NTP) and currently covering two-third of the country covering approximately 93 million population. Community engagement and assessing the needs and expectations of TB patients is essential for universal access to TB care. As a part of the community engagement BRAC established strong networking with different care providers.

**Intervention or response:** BRAC addressed the barriers of treatment adherence and high treatment completion in early 1980s by introducing incentive system for the female frontline Community Health Worker (Shasthya Shebikas) who plays an important role in implementing community based DOT. BRAC has mobilized the community and involved Shasthya Shebikas to reach the poor, and people living in area with limited access to services. They disseminate TB messages in the community during their routine household visits and refer TB symptomatic for sputum examination at NTP designated laboratories. Outreach sputum collection centers are conducted to improve the accessibility of services. For enhancing referral linkage to increase presumptive TB cases referral, diagnosis and treatment adherence, BRAC

conducted different orientation activities for different health care providers under the guidance of NTP. Treatment for all TB patients is initiated by graduate medical doctors and daily DOT is ensured by SS.

**Results and lessons learnt:** In 2013, a total of 1, 24,906 TB patients were diagnosed in BRAC supported areas. Of them, new smear positive (NSP) cases were 71,903. New smear negative and extra-pulmonary cases were 18,475 and 30,827 respectively. Case notification rate of NSP was 77/100,000 population against the national target of 70 and all types of TB case notification rate was 132/100,000 population against the national target of 116. Treatment success rate of new sputum positive TB patients diagnosed in 2012 was 94%.

**Conclusions and key recommendations:** Community engagement by involving community people showed better result in TB control. This approach could increase early case detection and maintain high cure rate. DOTS expansion by involving community health workers is found to be effective as they are well valued by the community.

#### An ethical reflection on DOT: supervision X support

J Denholm.<sup>1,2,3</sup> <sup>1</sup>Victorian Tuberculosis Program, Melbourne Health, Melbourne, VIC, <sup>2</sup>Microbiology and Immunology, University of Melbourne, Parkville, VIC, Australia; <sup>3</sup>Ethics Advisory Group, International Union against Tuberculosis and Lung Disease, Paris, France.

While the DOTS strategy involves a number of pillars, the 'directly observed' component is controversial, with both the clinical value and ethical appropriateness of the practice questioned. In particular, the use of universal direct observation of therapy has been suggested to be unreasonably restrictive and in conflict with the autonomy of those undergoing TB treatment. This talk will review frameworks for public health ethics, including human rights approaches, and discuss how practices relating to the implementation of DOTS have ethical significance.

#### Delivering TB treatment in the Rocinha community, Rio de Janeiro: nurses' perspective on DOT in Brazil

F Assumpção De Souza,<sup>1</sup> F Cortines Carvalho,<sup>1</sup> J Siqueira Lima,<sup>1</sup> L De Souza Velasque,<sup>1</sup> T Sousa,<sup>1</sup> G Schuabb,<sup>1</sup> M Ramos Guimaraes,<sup>1</sup> A Monroe.<sup>2</sup> <sup>1</sup>Escola de Enfermagem Alfredo Pinto, Universidade Federal do Estado do Rio de Janeiro, Rio de Janeiro, RJ, <sup>2</sup>Escola de Enfermagem de Ribeirao Preto, Universidade de São Paulo, Ribeirao Preto, SP, Brazil.

**Setting:** The incidence rate of tuberculosis (TB) in Rocinha community is 300/100.000 inhabitants.

**Objectives:** describe the structure and care provided to patients with TB in Family Health Program (FHP) in Rocinha; analyze the performance of TB treatment and the connection establishment of health professionals of the FHP with TB cases on DOT; identify the performance of social movements in DOT; investigate the application

of SNC by nurses; investigate the transition from the Program Community Health Workers to FHP.

**Methods:** exploratory descriptive study with a qualitative study using content analysis, and a quantitative approach elaborated based on assessing standard of the quality of health services, having as basic ground the components: structure-process-result. Approved by the Ethics Committee in Research of the Municipal Health Secretariat. Interviews based on studies and documents of the Ministry of Health were performed with nurses in the 3 units of FHP in Rocinha, totaling 171 respondents.

**Results:** the Structure component showed the deficiency in professional training and lack of incentives for TB patients; the Process component revealed that the supervised treatment isn't performed in patient's workplace and educational actions in the community doesn't happen routinely. In the Result component, there was an increase in the number of TB cases. The majority of answered had heard about a social movement that works with the reintegration of TB cases, but nurses doesn't maintain contact with it. The majority of the nurses do not follow the SNC process, and the reasons are intense workload and complexity of SNC. The transition of the Programme of Community Health Workers for FHP occurred gradually, and reports reveal improved access to treatment.

**Conclusions:** the study allowed a health service evaluation in Rocinha. The units' structure shows failures in professional training and a lack of incentives to patients and professionals who could help to decrease the stigma of disease. Nurses recognize the contribution of representative groups of society in the fight against TB in the community but there are no communication and integration activities of such groups and nurses. The results associated with local extreme poverty can be the determinants of so many cases of the disease, high treatment dropout and low cure rate.

### **A patient's voice on TB-MDR treatment: a long path to the cure**

C Amaechi. Program, The Good Neighbour, Lagos, Nigeria.

**Background:** Treatment support for TB patients has been a mirage and shadow of a reality that is yet to come. Africa is worse over shadowed by very limited support for TB patients. In an era where TB drugs are free (only drug kit), and the principle of cough to cure ideal pathway to tuberculosis control is partially considered in planning TB treatment, then supportive care for TB patients is lost in the process of drug procurement, diagnosis, active case finding and advocacy for more resources for TB control.

**Design/Methods:** TB patients need psychosocial support, treatment adherence counseling, home visit, nutritional support and medical personnel friendly attitude to help them complete treatment. These treatment supportive cares has been partially ignored in treatment planning for TB patients and when part of treatment, it is haphazardly implemented. In fact MDR patients are not considered in this plan at all due to fear infection.

**Results:** Treatment without lost to follow up that leads to cure must be accompanied with nutrition support. Improved health personnel attitude to TB patients ensure treatment completion

**Conclusion:** DOTS center that has no treatment to cure plan for TB MDR patients is simply a patient waiting room for consultation. DOTS scale up has only been in the multiplication of centers but not in delivery of quality service for TB MDR patients. DOTS scale up would be meaningful to TB MDR patients if only quality services and care are incorporated, and then we can say that DOTS is patient centered.

### **Treatment support in South Africa: TB/HIV Care Association experiences**

M Grant. TB/HIV Care Association, Cape Town, South Africa.

**Background:** In Cape Town "treatment had to be seen to be taken" when rifampicin was first administered to tuberculosis patients. Later it became known as DOT (directly observed treatment). Daily DOT proved to be a barrier to treatment adherence. People most affected by tuberculosis relied on casual work as their source of income. Health facilities with rigid opening hours were difficult to access.

**Intervention:** In 1992 we participated in a community based DOT pilot project. Buy in from health service providers, civil society, patients, community and especially nurses was challenging. The first group of community treatment supporters were trained and ready to receive patients after a year. At facilities patients were mapped and allocated to treatment supporters nearest to the patients' homes. Patients were given the option of community supervision or clinic supervision. Lessons learnt: Benefits included patients being able to negotiate the time of their visit with their supporter, numbers of patients attending the facility daily were reduced - less demand on staff, supporters were better able to communicate and understand their patients, small stipends paid to treatment supporters boosted the family income and treatment supporters experienced greater self-actualisation. The model was adopted by the health department. Dr Karl Styblo visited Cape Town and urged the head of health to provide the financial support to nongovernmental organisations for community DOT to be a sustainable method of access to treatment. The patient centred programme worked well, cure rates for the city improved and a WHO study on community based TB treatment in Africa proved that community based DOT was cost effective. 5000 patients were supervised daily in the community. The introduction of ART for patients with HIV brought a new model of patient support. Many TB patients were dually infected and integrating the two models of care became a necessity. Having two carers visiting the same patient was neither cost effective nor patient-centred. A mindset change was required to move from DOT as we knew it to empowering TB patients with treatment literacy and allowing them to take their treatment in their own home.

**Conclusion:** In the integrated programme we have facility based counsellors providing treatment literacy on HIV and TB and community care workers who support patients on TB and ART weekly and monitor their medication. Patients receive enhanced care in an integrated way.

### **Treatment support in South Africa: TB/HIV Care Association experiences**

C Jaftha. HIV, AIDS, STIs and TB, TB/HIV Care Association, Cape Town, South Africa

Community care workers (CCWs) are a cadre of lay health worker that developed from the Directly Observed Treatment Short Course (DOTS) supporter in response to a need for an integrated worker who could handle both TB and HIV support in the Western Cape, South Africa. Community care workers live within the community with whom they work, and form a link between the clinic and the community. CCWs visit patients in their homes to provide information on TB and HIV (as well as a variety of other health issues), to perform pill counts, to offer treatment support, to deliver medication, and to trace and recall patients lost to follow up. They meet weekly with a clinic team including doctors, nurses, counsellors, a social worker and a psychologist. CCWs are vital to the success of TB and HIV programmes as they know the physical and social landscape of the community and are able to spend time locating patients. They are also able to speak the patient's language and may have a similar life experience. This means it is easier for patients to relate to them. CCWs also have the time to provide additional support that patients may need, such as listening to concerns, answering questions and referring patients for other services. Both supervision and support are used by CCWs when interacting with patients as the CCW will adapt the approach they use to the patient they are supporting. Every patient is unique and will require a different strategy of support. Case studies are examined to illustrate this. CCWs programmes face a number of challenges; including staff leaving for financial reasons, stigma around HIV and TB, extreme weather conditions, violence and crime against patients and CCWs, and the general living conditions of communities. It is recommended that CCW programmes provide fulltime work for CCWs, that CCWs work in pairs to increase safety and that the scope of CCWs work be increased to include chronic diseases, wound care, first aid and counselling.

## **36. TOBACCO, POVERTY AND POSSIBLE SOLUTIONS: HEALTH PROMOTION FUNDING MODELS**

### **Health promotion funding models: experiences and lessons**

L Wood,<sup>1,2</sup> G McKie,<sup>1</sup> A Carroll,<sup>2</sup> A Jones.<sup>3</sup> <sup>1</sup>School of Population Health, University of Western Australia, Perth,

WA, Australia; <sup>2</sup> Tobacco Control Department, International Union Against Tuberculosis and Lung Disease, Paris, France; Perth, WA, <sup>3</sup>Tobacco Control, International Union Against Tuberculosis and Lung Disease (The Union), Sydney, NSW, Australia.

Effective tobacco control requires long term sustainable funding but health promotion and prevention are often 'poor cousins' when compared to the resources drained by the immediacy of health services and treatment. One of the most innovative solutions to this dilemma is to raise tobacco taxes and direct resultant funds to tobacco control. This presentation draws particularly on the experiences of countries that have used funds generated through tobacco taxation to establish an organisation or foundation dedicated to supporting tobacco control programmes and capacity building. In some nations, the remit is to fund health promotion beyond just tobacco, but many of the principles and lessons learnt are the same. The success of this approach to securing sustainable funding for health promotion is also being increasingly seen as a model for addressing the escalating health burdens associated with alcohol misuse and unhealthy food and beverage consumption. Raising tobacco taxes and directing the funds into tobacco control is a fair, logical and cost effective way to accelerate action on tobacco control, and has been shown to be a viable approach for low to middle income countries. The preferred model is to legislate the establishment of an independent or semi-autonomous organisation (often called a foundation) dedicated to administering these funds for health promotion. There is no 'one size fits all' template to follow however, as such organisations need to take into account a nation's existing tobacco control capacity and adapt to its economic, social and political context. The size, structure and activities funded by foundations also varies from country to country, but there are some common critical success factors and characteristics that can be distilled. Capacity building is a core tenet, as effective tobacco control needs the support of a wide range of government agencies, sectors, health professionals and civil society groups. History shows that there are also some common challenges (including political or tobacco industry impediments), hence it is valuable to consider the experiences of other countries in anticipating and countering challenges that may arise. Reviewing these shared experiences and lessons learnt offers insights for those wishing to secure a more sustainable base for tobacco control or health promotion more broadly.

### **Health promotion funding models: how they can contribute toward universal healthcare and poverty reduction**

A Jones,<sup>1</sup> Lisa Wood,<sup>2,3</sup> A Carroll,<sup>2</sup> G McKie.<sup>2,3</sup> <sup>1</sup>Tobacco Control Department, The Union, Sydney, NSW, <sup>2</sup>Tobacco Control Department, The Union, Perth, WA, <sup>3</sup>School of



Population Health, University of Western Australia, Perth, WA, Australia.

While the vicious circle between tobacco and poverty is well established, effective measures and mechanisms for alleviating poverty are being undermined and delayed by a lack of sustainable funding and capacity for tobacco control in low-resource countries. The tobacco epidemic is predicted to rise rapidly in LMICs where tobacco taxes remain low, tobacco consumption is high and governments despite facing rising healthcare costs, are delaying the adoption of sustainable funding models for health financing. With 180 parties to the WHO Framework Convention on Tobacco Control and global pressure to reach poverty reduction goals, governments are beginning to tackle health disparities and the growing burden of healthcare costs by raising tobacco taxes and directing funds to pay for universal health care and health promotion. This paper will review how raising tobacco and some other taxes to fund health promotion fund models are being used in several countries and regions to create sustainable health financing aimed at: improving population health outcomes; reducing healthcare costs; and preventing or reducing tobacco use and other non-communicable diseases. Success factors and lessons learnt will be presented to demonstrate how a multi-sectoral partnership between government and civil society and best practices can be used to secure a more sustainable base for tobacco control measures, reducing health disparities, increasing productivity and addressing health promotion more broadly.

### **Taxation as a tobacco control policy to reduce inequalities in Mexico**

**B Saenz.**<sup>1,2</sup> <sup>1</sup>Social Policy, London School of Economics and Political Science, London, UK; <sup>2</sup>Tobacco Control, Interamerican Heart Foundation Mexico, Mexico City, Mexico.

**Background:** Tobacco use is a leading cause of impoverishment. Sickness and premature mortality associated with smoking increase health care costs and reduce family income. Spending on tobacco also affects expenditure patterns and therefore households' wellbeing. Tobacco use is an important cause of inequalities too. Smoking prevalence is usually higher among low-income individuals and declines in cigarette smoking are commonly concentrated in high-income rather than low-income individuals. Tobacco taxes are the most cost-effective tobacco control intervention but their effect across income groups is not clear. While some studies argue that the impact of tobacco taxes on consumption is higher among low-income groups, other studies argue that the impact does not differ substantially across income-groups.

**Objective:** The objective of this presentation is to discuss the role of taxes as a tobacco control policy to reduce inequalities using recent evidence for Mexico and Uruguay.

**Data:** Data from nationally representative surveys is used, namely the Global Adult Tobacco Survey (GATS) implemented in Mexico and Uruguay in 2009 and eleven

rounds of the National Income and Expenditure Survey (ENIGH) for Mexico.

**Results:** Smoking prevalence is higher among the poorest in Uruguay; in Mexico the opposite pattern is observed. Tobacco expenditure as a share of total income is higher for the poorest in both countries, however. Total price elasticity estimates (the price elasticity of consumption uptake plus the price elasticity of consumption for those who decide to smoke) are similar across income groups for both countries but the price elasticity of consumption uptake is relatively higher for low-income groups.

**Conclusions:** Taxes are an important tobacco control policy and may help narrowing inequalities in some contexts. It is important, however, to implement other measures for the poorest that continue smoking such as targeted cessation services, as well as measures to combat illicit trade. Also, tobacco taxes must be equivalent across products; prices of roll-your-own cigarettes are significantly lower than prices of manufactured cigarettes in Uruguay since taxes for the former are lower. Future research should evaluate existing tobacco control policies across income groups and study the effects of alternative policies.

### **Sub-national tobacco tax: an initiative to build and sustain tobacco control in Indonesia**

**T S Bam.** Tobacco Control, International Union Against Tuberculosis and Lung Disease (The Union), Singapore, Singapore.

**Background:** In Indonesia, smoking kills more than 200,000 people every year. About 80% of Indonesian households are exposed to SHS every day. Smoking prevalence in males was 67% and in females was 2.7%. Government regulation on tobacco control was passed in 2012 which includes provision of smoke-free and pictorial health warning.

**Objectives:** To share sustainable funding mechanism establishing in Indonesia. Approach: National law no. 28 year 2009 concerning the regional tax and retribution which is in consideration of the decentralization law no. 32 year 2004 and the fiscal balance between the national and sub-national government law no. 33 year 2004. It provides financial resources for the regional government through extension of taxes and retributions, including sharing of 10% tobacco tax revenue to subnational government.

**Results:** The law mandates the sub-national government to spend at least 50% tobacco surcharge for health services. However, Jakarta Provincial government has adopted a tobacco tax law which defines the 70% of allocation should be spent on tobacco control including mass media, smokefree enforcement, monitoring, and smoking cessation. Jakarta has set an example to establish a sustainable funding and resources for tobacco control.

**Conclusion:** Indonesia has set a system of utilization of tobacco tax at national and sub-national level for health services including tobacco control. A monitoring framework needs to be adopted for effective use of the resources.

## ABSTRACT PRESENTATIONS FRIDAY 31 OCTOBER 2014

### e-POSTER SESSIONS

#### 02. MULTI-DISCIPLINARY APPROACH TO TB CONTROL

##### EP-112-31 Strengthening politico-administrative commitment: UP, India

L Reza,<sup>1</sup> A Das,<sup>1</sup> M Ubaid,<sup>2</sup> S Chadha,<sup>1</sup> S Mohanty.<sup>1</sup>

<sup>1</sup>Tuberculosis, International Union Against Tuberculosis and Lung Disease, New Delhi, <sup>2</sup>Tuberculosis, Catholic Bishops' Conference of India, New Delhi, India.

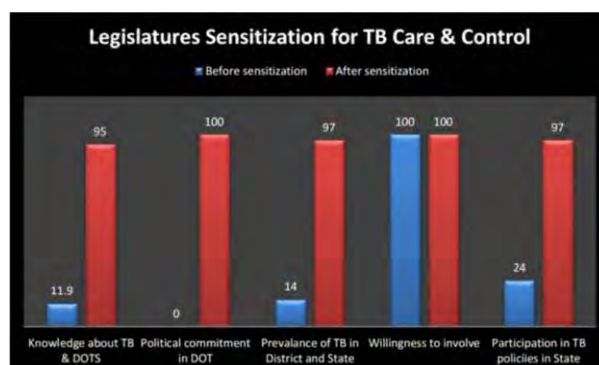
e-mail: lwreza@theunion.org

**Background** – Political and administrative commitment is the first and most important components of the DOTS strategy but Quite neglected. UP is an Indian state having 210 million population. The Legislative assembly & council of UP consist of 512 members and government have 3.5 years in hand. According to India TB report 2013, TB symptomatic examined per lac is 150 and below the national average. It also varies significantly across districts i.e. below 100 to 200+. The cure rate of new sputum positive cases is below the national average i.e. 81%. The services of DR-TB diagnosis are also poor and 6 CBNAAT machines and 2 IRLS are supporting the diagnosis of DRTB. The district has good diagnostic service to DR-TB examination, have over 300 DR-TB case. As far as trained staff is concerned, only 33% of the sanctioned post of medical officer is filled. According to STO, TB control programme in the State has received only 38 crore in lieu of sanctioned 110 crore and salaries of staff has been pending also long delayed. With these chronic problem legislature has been approached for their engagement in the strengthening of the programme. The objective of study was to record the knowledge and outcome of sensitization for engagement of legislatures. **Method** – In the process, 42 legislatures were contacted for learning about their understanding and perspective on TB by TB forum members. The current scenario and challenges of TB in global, national, state and local context were discussed and contextual solutions with possible areas of engagement were presented.

**Results** – The important finding of the study was that legislatures were ready to extend their support for TB care and Control. Nearly 90% of them were surprised that TB still being prevalent and a challenging health problem. They said, "We heard it is disease of previous centuries." They called up district health administrator of their district and asked for the status of TB care activities. They also agreed to raise the matter in the state assembly.

2–3 legislatures also came forward with the suggestion of nutrition policies for TB patients.

**Conclusion** – The knowledge about tuberculosis is poor among the politicians of the state, leading to poor political commitment. Their sensitisation on the TB situation and engagement with willing legislatures will help the effective programme management. Thus political will would go a long way to solve the TB Programme issues thereby leads to effectual disease control.



##### EP-113-31 Competence of primary healthcare to take role in tuberculosis control in Serbia

V Kuruc,<sup>1</sup> D Kukavica,<sup>1</sup> M Stosic,<sup>2</sup> L Ristic,<sup>3</sup> M Ilic.<sup>1</sup>

<sup>1</sup>Tuberculosis, Institute for Lung Diseases of Vojvodina, Novi Sad, <sup>2</sup>Control of Tuberculosis in Serbia, Ministry of Health of Republic of Serbia, Beograd, <sup>3</sup> Tuberculosis, Clinic for Lung Diseases Knez Selo, Nis, Serbia. Fax: (+381) 2 1527 960.

e-mail: vesnakuruc@gmail.com

**Background and challenges to implementation:** Due to implementation of tuberculosis control programme in Serbia, in accordance with WHO strategies, burden of tuberculosis in Serbia significantly decreased. Within the reform of the health care system in Serbia, when pneumophthysiological service as a pillar of tuberculosis control in Serbia loses its importance, it is necessary to design and build an organizational scheme within the system that can maintain a successful model for the disease control. Primary health care providers can play an important role in TB control through early detection of the disease, referral for treatment, and involvement in directly observed treatment. Education of PHCPs on TB has therefore taken a prominent place in the Control of Tuberculosis in Serbia, the project carried out under the supervision of Ministry of Health and financed by GFATM.

**Intervention or response:** To establish how much do PHCPs really know about the basic features of TB, its transmission, paths, diagnostic criteria, treatment procedures and epidemiological relevance; to define the improvement in PHCPs knowledge on TB obtained after the active training course on TB; and to establish the correlation between the former PHCPs' knowledge on TB and its incidence in the area of a PHSP's competence.

**Results and lessons learnt:** The study included 1300 PHCPs at the mean age of 45.7, and the mean 18.7-year



working experience, coming from 10 regions of Serbia. PHCPs are found not to have sufficient up-to-date knowledge on TB and its early detection: false answers in the pre-test amounted to 29%. A questionnaire including 15 questions on basic TB features was given to the PHCPs participating in this study prior and after the training course. The training efficacy was assessed by increased number of true answers in the post-questionnaire. The percentage of false answers in the pre-questionnaire was also correlated to the TB incidence rate in a particular region.

**Conclusions and key recommendations:** The active training course PHCPs received has resulted in a significant improvement of their knowledge on TB (19% on the average). The regions with a lower level of PHCPs' knowledge have a higher TB incidence rate. The positive linear correlation between the percentage of false answers and the TB incidence rate was confirmed. The attention to further education of PHCP should be paid in the future.

#### **EP-114-31 Progress and implementation of surveillance of Directly Observed Treatment, Short-Course (DOTS) for tuberculosis in Taiwan**

SH Huang,<sup>1</sup> CB Hsu,<sup>1</sup> K-F Wang,<sup>1</sup> S-L Yang,<sup>1</sup> Y-F Huang,<sup>1</sup> C-H Chen.<sup>1</sup> <sup>1</sup>Centers for Disease Control, Ministry of Health and Welfare, Taipei City, Taiwan. e-mail: minjulu@cdc.gov.tw

On April, 2005, Taiwan initiated DOTS program for smear-positive patients, and extended coverage for other patients gradually, inclusive of culture-positive patients, clinically diagnosed patients with poor compliance, homelessness patients, relapsed patients, patients in mountainous area, aboriginal patients, etc. Nowadays, all patients undergoing TB medication are required to participate in DOTS. And for patients who start anti-TB treatment yet waiting for the bacteriological evidence, DOTS will include the patients for at least 2 months. Besides increase of participation rate, Taiwan CDC pursues high-quality DOTS as well by developing DOTS quality monitoring system. Audition of DOTS program was started on July, 2010, staff of local health bureau and CDC would check DOTS supporters' schedule of drug delivery and records of DOTS on the web-based system. Taiwan CDC also announces DOTS performance of each county regularly. By December, 2013, participation rate and proportion of quality level A, which means DOT  $\geq$  70% among treatment duration in the first 2 months, and overall  $\geq$  60%, both exceed 90% for bacteriologically confirmed patients. There are now more than 700 DOTS supporters to help patients taking treatment correctly. And the DOTS program was achieving phenomenal results that TB relapse rate in Taiwan decreased from 1.3% in 2005 cohort to 0.6% in 2009 cohort. For people who can't accommodate observer's schedule, Taiwan plans eDOTS. First of all, eDOTS will be applied for people receiving LTBI treatment (eDOPT), if there are no negative results, then next step eDOTS will expand to TB patients.

#### **EP-115-31 Market assessment of tuberculosis diagnostics in Brazil in 2012**

M Hammerle,<sup>1</sup> R Souza,<sup>1</sup> J N Lima,<sup>1</sup> D Barreira,<sup>1</sup> A Trajman,<sup>2</sup> P Chedore,<sup>3</sup> S Kik.<sup>3</sup> <sup>1</sup>National Tuberculosis Program, Ministry of Health, Brasilia, DF, <sup>2</sup>Tuberculosis, Gama Filho University, Rio de Janeiro, RJ, Brazil; <sup>3</sup>McGill International TB Centre, McGill University, Montreal, QC, Canada. e-mail: mari.hammerle@terra.com.br

**Background:** In August 2013, the National Tuberculosis Program of Brazil (NTP) in partnership with McGill University, conducted a study to assess the served available market for TB diagnostics in Brazil in 2012, as well as the market segmentation in the public and private sectors. This data will support new product development by test developers and investors.

**Design/Methods:** Data were collected on the volumes of tests done for the diagnosis of TB and latent TB in the public and private sectors (for diagnosis and follow-up). The tests included were tuberculin skin tests, interferon-gamma releases assays, smear microscopy, solid and liquid cultures, nucleic acid amplification tests and phenotypic drug susceptibility tests. The data were collected by an electronic survey via Central Laboratories of Public Health of each state of Brazil, as well as from sales information from manufacturers. Costs in the public sector were calculated using a component approach, while costs for the private sector were based on prices paid by patients. The overall market value for the entire country was calculated using the public sector test costs.

**Results:** In Brazil, the total market value was USD 17.2 million in 2012. The public sector accounted for 91% of the test volumes and 88% of the overall market value. An average of USD 208 was spent on TB diagnostics per notified TB case. Smear microscopy (SSM) was the most commonly used single test (n=1.3 million; 55% of total); 0.3 million cultures were done.

**Conclusion:** The private sector market for TB diagnostics is relatively small in Brazil. Considering the prevalence of TB in Brazil, both cultures and SSM are underutilized, suggesting low coverage of respiratory symptomatic patients investigation and poor adherence of healthcare professionals to the recommended monthly treatment follow-up. The market is likely to change with the introduction of Xpert MTB/RIF replacing SSM in 92 cities (55% of notified cases) in 2014, and revised algorithms for diagnostic testing for those screened by Xpert MTB/RIF. New trends will be captured in a future update of our analysis. These results will be useful for test developers.

### EP-116-31 Disseminating operational research: converting a problem into a knowledge resource while re-engaging national priorities

A Jacob,<sup>1</sup> S Chadha,<sup>1</sup> K Sagili,<sup>1</sup> N Wilson.<sup>2</sup> <sup>1</sup>TB, International Union Against Tuberculosis and Lung Disease, New Delhi, <sup>2</sup>TB Care and Control, Independent Consultant, New Delhi, India. e-mail: ajacob@theunion.org

**Background:** Despite a significant body of Operational Research (OR) studies on TB control in India, its difficulty of access, collation and connection with issues that national programme policymakers dealt with on a routine basis constituted a real challenge. In order to convert this problem into an opportunity for India's national TB Control programme, the need was felt for a collated collection of the most relevant OR studies by bringing together research institutions, implementing bodies, academia and practitioners.

**Intervention:** In collaboration with the Government of India's Central TB Division, United States Agency for International Development (USAID), the USEA office organized a by-invitation national meeting to consult with the *crème de la crème* of India's past and present scientific experts to take OR forward in India. For this meeting, the USEA Office developed a Summary OR Document spanning 20 years of OR studies from 1993–2013: 450 OR studies were line-listed based on criteria recommended by the WHO's STOP TB Partnership Report. Experts located, accessed, analysed and systematically organized these along the lines of the research questions and implications of each study. This survey covered work done at India's national institutions, open- and private-access databases and the gray literature. Circulated during the August 26 and 27, 2014 meeting of the National OR Dissemination workshop, this document became the basis for discussion in addition to topics that the Government had highlighted; experts prioritized key areas for research. Further, engagements in September 2013 and January 2014 with national stakeholders helped complete the follow-through cycle going well above and *beyond* the immediate objectives of the National OR Dissemination Workshop, and continuing into the present.

**Results/Lessons Learned:** To move an initiative from potential success to complete institutional buy-in requires not only collaboration and cooperation, but active engagement with multiple stakeholders both pre- and post-intervention. Timing is important: engaging with the Government of India before the intervention is a key lesson.

**Conclusions:** Identifying a national need and strategizing collaboration with a stakeholder is a necessary but not sufficient condition for intervention success. This has differentiated our intervention: it increased buy-in for OR and our good will with the Government. In-principle assent for a Knowledge Hub has also been attained

### EP-117-31 Working in network: the Brazilian tuberculosis committee network

C Oliveira Dantas,<sup>1</sup> P Werlang,<sup>1</sup> A Paranagua Fraga,<sup>1</sup> J Veloso,<sup>1</sup> F Moherdau,<sup>1</sup> D Barreira.<sup>1</sup> <sup>1</sup>National TB Programme, Ministry of Health, Brasília, DF, Brazil. e-mail: cintia.dantas@saude.gov.br

**Background and challenges to implementation:** The Brazilian Tuberculosis (TB) Committee Network is a participatory advisory collegiate body with the mission of articulating among government and civil society, in order to contribute to the public TB policies in the country, giving visibility to mobilization, advocacy, social communication and monitoring and evaluation (M&E). Moreover, it aims to ensure citizenship according to the Unified Health System. It was established in 2007 to monitor the Global Fund TB project in Brazil, in 10 metropolitan areas high TB burden.

**Intervention and response:** Considering that the Committees contribute to the qualification of public policies on the fight against TB, once the Global Fund project ended in Brazil in 2012, the National TB Programme (NTP) decided to support the continuity of the network. In this sense, the NTP organizes annually meetings for the Steering Committee, represented by civil society and local government of each Committee, the Committees' Assembly, technical visits and trainings annually. All activities aim to qualify members of the Network from different regions of the country, in the development of policies always considering issues such as human rights, social mobilization and M&A.

**Results:** As a result of the political articulation, five local Committees were formally recognized in their respective Local Health Secretariats. Committees have been successfully articulating with the legislative power, in order to establishing State Parliamentary Fronts to Fight TB, an example is the Parliamentary Front of Sao Paulo, created in 2013.

**Conclusion and recommendations:** Aligned with international guidelines related to community participation, the NTP considers strategic the expansion of this Network and the implementation of new Committees in states in which they do not exist. This strategy is already ongoing with the creation and consolidation of a committee in the state of Santa Catarina. Other states have also started to mobilize in this sense.

### EP-118-31 Computerising TB registers: our response to our current and changing needs

T Raphael,<sup>1</sup> N Larme.<sup>2</sup> <sup>1</sup>TB DOTs, World Vision PNG, Kokopo, <sup>2</sup>Health, East New Britain Provincial Administration, Kokopo, Papua New Guinea. Fax: (+675) 9828470. e-mail: raphaeltapin@gmail.com

**Background and challenges to implementation:** East New Britain (ENB) is a volcanic island province of Papua New Guinea. It has 4 districts with a land area of 15,724 km<sup>2</sup> and population of around 270,000. DOTs started only in 2012. Quarterly reporting from 17 BMUs was a major problem. Common ones were errors in transferring data from TB Registers to the quarterly

reports, calculation errors, and classifying patients. Manually calculating was also time consuming.

**Intervention or response:** We decided to come up with our own electronic database to minimize these problems. We started with thorough study of the TB Register, how the data is transferred into the BMU quarterly reports. We used MS Access for data entry and MS Excel for analysis and generating reports (Figure 1). All information in the TB Register was used with simple coding and formulas that are easier to understand by the designer and user. The system is programmed in a way that after the data has been entered into MS Access, it automatically updates the data in MS Excel. In MS Excel, the raw data from MS Access is used to routinely complete the whole BMU quarterly booklet. Laboratory activities, TB/HIV data, and drug orders were also included. The system is regularly updated during supervisory visits, and a template was also designed for the BMU staff to fill and submit to the provincial health office.

**Results and lessons learnt:** The system is now running, with frequent improvement to suit the program's and stakeholders' needs. BMU Quarterly Reports can be verified and confirmed using the system, which also cuts down on human errors. When BMUs are not coming in on time with their manual quarterly reports, their reports can be printed or emailed straight from the system to national office on a timely manner. Whenever information is needed, they are readily available, and can be customized to suit the user's requirements. Analysis results can be presented in different ways including tables, graphs and charts. Currently we have 2,796 cases registered in the database dating back to 2010. Almost all BMUs are already showing interest for the system to be installed in their computers and to be customized for individual facility use and updating.

**Conclusions and key recommendations:** This home-grown TB database system is our solution for the next generation. We have proven that this could work for our province, and hopefully for the entire country.

### EP-119-31 Impact of nutritional support to patients on first line anti-TB treatment in India: a case control study

A Pandey,<sup>1</sup> K Rade,<sup>1</sup> N Mannan,<sup>1</sup> N Kulshreshtha,<sup>2</sup> R S Gupta,<sup>2</sup> P Maheshwari,<sup>3</sup> P Malik,<sup>1</sup> A Sreenivas.<sup>1</sup>

<sup>1</sup>Country Office for India, World Health Organization, New Delhi, <sup>2</sup>DGHS/MOHFW, Central TB Division, New Delhi, <sup>3</sup>TB, Clinton Health Access Initiative, New Delhi, India.  
e-mail: drkiranrade@gmail.com

**Background:** Malnutrition, poverty and tuberculosis (TB) is a vicious cycle. Systematic reviews indicate a strong and consistent log-linear relationship between TB incidence and Body Mass Index (BMI). However, there is insufficient evidence to suggest improved TB treatment outcomes with additional nutritional support to patients. There has been no policy to provide nutritional support to tuberculosis patients under Revised National TB Control Programme (RNTCP). However, it was known that many organizations offer such support to patients.

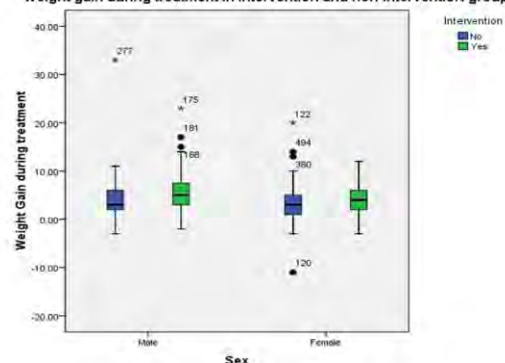
Therefore, assessing its impact would help in practicing evidence based policy.

**Design/Methods:** Retrospective case-control study design. Line list of 56 districts was prepared with average number of TB patients receiving additional nutritional support and 10 districts were selected using probability proportionate to size of number of such patients. Patients registered in RNTCP between 1st April 2012 to 31st March 2013 and had received additional nutritional supplement, were line listed. Pediatric patients (14 years and below) were excluded from the study and 25 patients were selected using systematic random sampling, which comprised 'intervention arm'. One TB patient from same unit who did not receive any nutritional support, and of same sex and age ( $\pm 3$  yrs but above 14 yrs) comprised the 'control arm'. Selected 500 patients were interviewed using semi-structured questionnaire in addition to extraction of information from treatment cards.

**Results:** 219 (87.6%) patients in intervention group and 214 (85.6%) patient in control group were successfully treated out of 250 in each. Treatment default among control group was 22(9%) and intervention group was 11(4.5%). Odds ratio of favorable and unfavorable outcomes was 1.66 (0.87-3.18). 9(3.6%) patients in intervention group and 4(1.6%) patients in control group were switched to multi-drug resistant tuberculosis (MDRTB) regimen. Average weight gain during treatment was 4.9 kg in intervention group (n=222) and 3.9 kg in non-intervention group and the difference was significant ( $p=0.007$ ). Percentage weight gain was 12.2% and 11.2% respectively, the difference of which was however not significant.

**Conclusion:** Additional nutritional support to patients on Anti-TB treatment marginally improves treatment success, default is prevented and, as patients adhere to treatment, there is opportunity for drug susceptibility testing, which increases their chances to receive more appropriate regimen.

Figure: Weight gain during treatment in intervention and non-intervention groups





## EP-120-31 A user-friendly model to evaluate cost-effectiveness of shortened first-line treatment regimens for TB

A Zwerling,<sup>1</sup> J Pennington,<sup>1</sup> G Knight,<sup>2</sup> R White,<sup>2</sup> G Gomez,<sup>3</sup> A Vassall,<sup>4</sup> F Cobelens,<sup>3</sup> D Dowdy.<sup>1</sup>

<sup>1</sup>Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA; <sup>2</sup>Infectious Disease Epidemiology, London School of Hygiene & Tropical Medicine, London, UK; <sup>3</sup>Amsterdam Institute for Global Health and Development, University of Amsterdam, Amsterdam, Netherlands; <sup>4</sup>Department of Global Health & Development, London School of Hygiene and Tropical Medicine, London, UK. e-mail: azwerlin@jhsph.edu

**Background:** Novel first line anti-TB treatment regimens are under development, with potential to shorten therapy from 6 to 4 months. Cost-effectiveness models can help understand how to implement such novel regimens, but the methodological details of advanced economic models may be obscure to most real-world decision-makers, who may also want to tailor the results of such models to their local settings.

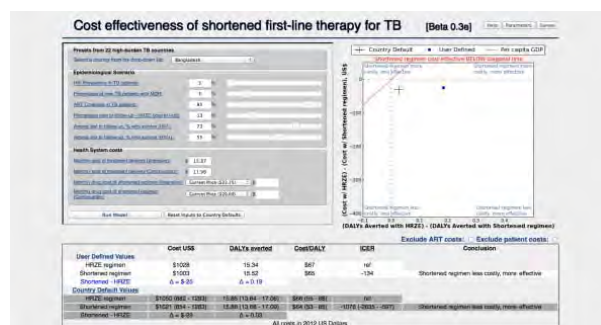
**Methods:** We simplified a detailed decision-analytic model describing the cost-effectiveness of novel TB drug regimens. Using a series of sensitivity analyses, we identified those parameters that were most influential on final model output. We then took these influential parameters plus other parameters identified as important by a convenience sample of end-users to create a user-friendly (UF) cost-effectiveness model. We designed a web interface (Figure 1, valueTB.modelTB.org) for the UF model that allows end-users to modify a series of parameters (e.g., TB incidence, MDR-TB prevalence, retention rates, drug and treatment delivery costs), providing cost-effectiveness results for user-defined scenarios within seconds. We also created country-specific scenarios that include 95% uncertainty ranges based on probabilistic uncertainty analysis of all model parameters. End-users are given the option to include or exclude patient-level costs and costs of antiretroviral therapy. All costs are measured in 2012 USD. Here, we compare results from the UF model to those of the complete, more complex model in South Africa, Tanzania, and Bangladesh – three countries for which empirical cost data were directly collected.

**Results:** Through examination of the complex model, we were able to develop a user friendly, with a highly simplified structure, improved speed of calculation, and ability for users to define key parameter values, that provided output that was very similar to that of the full model. For example, in all three countries, both the UF and full model projected 0 to 0.1 incremental disability-adjusted life years (DALYs) averted per patient.

**Results** on cost-effectiveness were also in line with the more complex model.

**Conclusion:** We successfully developed a simplified user-friendly model of cost-effectiveness for novel TB drug regimens that produces real-time, web-based results tailored to user-defined scenarios that are consistent with those of a more detailed model that is calibrated to

specific country settings. Figure 1. Screenshot of online user-friendly model



## EP-121-31 Cost-effectiveness of community-based TB care in Namibia

K Vaughan,<sup>1</sup> T N. Shilongo,<sup>2</sup> V Remi,<sup>3</sup> D Witbooi,<sup>4</sup> M Samahiya,<sup>5</sup> F Mavhunga,<sup>2</sup> A Zesai,<sup>6</sup> R Indongo.<sup>7</sup>

<sup>1</sup>Health, KIT, Amsterdam, Netherlands; <sup>2</sup>NTLP, MOHSS, Windhoek, Namibia; <sup>3</sup>Verduin Consult, Verduin Consult, Oegstgeest, Netherlands; <sup>4</sup>Daab Consulting, Daab Consulting, Windhoek; <sup>5</sup>Polytechnic of Namibia, Polytechnic of Namibia, Windhoek; <sup>6</sup>KNCV Tuberculosis Foundation, Windhoek; <sup>7</sup>TB/HIV, USAID, Windhoek, Namibia. e-mail: k.vaughan@kit.nl

**Background:** Namibia has a high per capita TB burden, with a case notification rate of 487/100,000 in 2013. 45% of TB patients are HIV co-infected. To build and further expand the implementation of community-based TB care (CBTBC), the National TB and Leprosy Programme (NTLP) commissioned a USAID-funded cost-effectiveness assessment (CEA) of the different CBTBC models in the country. CBTBC-related challenges in Namibia include the large geographical area, low population density and the diversity of populations.

**Design/Methods:** Data on costs and effects were collected from non-governmental organisations (NGOs) providing CBTBC in 17 of 34 districts in the country. Costs were based on actual 2012 expenditure records. Case finding and treatment outcome data was retrieved from district registers for the first two quarters of 2012 and then doubled for an estimated annual total. Cost-effectiveness was measured in terms of cost per new smear positive (NSP) TB patient successfully treated (completed treatment or cured).

**Results:** Findings to date show cost-effectiveness of NGO approaches vary widely from US\$266.25 to US\$4,292.58 per NSP TB patient successfully treated. Up to 33% of NGO spending is on M&E and supervision. Amongst comparable districts (primarily urban, primarily rural, HIV prevalence, case finding load, presence of special populations), there are variations in both treatment success and cost per NSP TB patient successfully treated. Even within organizations using the same approach in multiple districts, we found large differences in cost-effectiveness.

**Conclusion:** Using WHO's guideline that an intervention is highly cost-effective if it falls below the country's GDP per capita and Namibia's GDP per capita in 2012 of

US\$5,786 (World Bank), CBTBC implemented by NGOs in Namibia is highly cost-effective in all districts. However, below the GDP per capita of \$5,786 we found a wide range of costs per NSP TB patient successfully treated, suggesting that there are opportunities for improving the cost-effectiveness of some approaches, even when taking into consideration unique district characteristics. Suggestions for improving cost-effectiveness include making better use of HIV/AIDS community volunteers for TB, reviewing the service packages offered by NGOs, considering new CBTBC delivery models in areas with a small number of patients and combining or streamlining M&E and supervision with Ministry efforts.

### EP-122-31 Incentives for tuberculosis care in the private sector in India: a qualitative study

V Yellappa,<sup>1</sup> N Rao.<sup>1</sup> <sup>1</sup>Public Health, Institute of Public Health, Bangalore, India. e-mail: vijayashreehy4@gmail.com

**Background:** In India, private practitioners (PPs) are the first choice for seeking care. Government (Govt) is engaging PPs in the National TB programme, through public private mix schemes (PPMS). However no PP in our study area had signed up for any PPMS. Hence, we sought to understand the private TB market and estimate earnings of PPs.

**Methods:** Data was collected in 2013 from Bangalore (urban) and Tumkur district (rural) in Karnataka, India. Semi-structured interviews were conducted with private sector providers of TB care (n=38), patients on private TB treatment (n=28), private pharmacies (n=40) and labs (n=40).

**Results:** Patients spent ranging from 3,685- 42,750 rupees (US\$61-705) on direct costs of TB care. PPs earned from commissions from pharmacies and labs more than twice what they received from consultation fees. About 30% of lab and pharmacy revenues from TB diagnostic tests and anti-TB medicines were paid to the referring PPs. Overall, PPs could expect earnings from a TB patient ranging from 660 to 7,500 rupees (US\$ 11-123). Kick-backs are well ingrained in the system to the extent that bigger labs maintain systematic ledgers for this purpose. Both urban and rural pharmacists stock anti-TB drugs and catered self-referred TB suspects. A majority of them noted that no patients purchase the entire course of medication at one time. One stated, "They are daily wage people. They get money in the evening. Hence they come here in the evening and buy medicines."

**Table:** Range of earnings of interviewed PPs from TB patients

Item	Amount (Range)	Remarks
Consultation fees	Rs.180-1,800 (US\$ 3-28)	Average of six consultations
Commissions to PP	Rs.300-5,700 (US\$ 5-90)	Around 30% of lab and drug costs
Laboratories (gross revenue)	Rs.100-1,000 (US\$ 2-16)	One time
Pharmacies (gross revenue)	Rs.900-18,000 (US\$ 14-28)	Cost for 6 months treatment
Total Earnings of PP from a TB patient	Rs.660-7,500 (US\$ 10-120)	Consultation fees and commissions

**Discussion:** Unlike other studies, this research collected information from TB patients receiving TB care exclusively in the private sector. It finds that TB patients incur large costs and are at risk of interrupted treatment. PPs have a significant financial incentive to retain TB patients. Nonetheless, the range of earnings estimated by this study suggests that it may be feasible to provide sufficient financial incentives for PPs to report and refer TB patients to free-of-charge government TB services earlier in the course of treatment.

### EP-123-31 Mapping TB campaigns for local politicians in high-burden settings

A Davids,<sup>1</sup> E Hoosain.<sup>1</sup> <sup>1</sup>HAST, Human Sciences Research Council, Port Elizabeth, South Africa. e-mail: asdavids@hsrc.ac.za

**Background and challenges to implementation:** The Nelson Mandela Bay Health District (NMBHD) reported a tuberculosis (TB) incidence rate of 1155/100 000 persons for the 2010/11 reporting year. This was higher than the national incidence rate of TB in South Africa (805/100 000 persons) in 2010. The TB cure rate in NMBHD was lower than the national target, with a defaulter rate of 11.5% in 2012, almost double the national target of less than 6%. The very high TB caseload and defaulter rates fuel the waves of drug-resistant TB cases in NMBHD. The tremendous scourge of TB and HIV co-morbidity requires the pursuit of high-quality Directly Observed Treatment (DOT) support expansion and enhancement demanded by the STOP TB Strategy. Whilst political commitment in South Africa is evident at a national level, lower level involvement in combating TB is not as high a local political priority when compared to unemployment, crime and housing shortages.

**Intervention or response:** The aim of this study was to use Geographical Information Systems (GIS) mapping to assist local politicians to track TB campaign activities within their electoral wards. The objectives were to map the locations of TB patients; map their DOT supporters; track patients' two-month sputum tests and TB patients at risk of non-adherence; and mapping cured TB patients. Data on newly diagnosed smear positive TB patients that participated in a four-pillared intervention were used. Physical addresses of 77 TB patients and 25 active DOT supporters were extracted and plotted using data available from the cadastral office of the Nelson Mandela Bay Municipality. Data for the three participating health facilities were extracted using Google Maps.

**Results and lessons learnt:** Fifteen maps were created in electronic and hard copy formats; one for each of the objectives at each of the three health facilities. The electoral ward boundaries and the relative location of health facilities are also included. All locations are off-set by a set factor to protect the anonymity of TB patients.

**Conclusions:** Mapping of TB cases should be a routine activity and its outputs should be part of local political agendas, as well as reports to local health committees to

address risks of non-adherence and to track cure rates within local areas.

**Results** of active TB case finding activities should also form part of TB mapping to monitor and evaluate TB campaigns in support of the STOP TB strategy.

### EP-124-31 Evaluating the effective coverage of new rural cooperative medical scheme on the costs of tuberculosis treatment in China

X Wei,<sup>1</sup> G Zou,<sup>2</sup> J Yin,<sup>1</sup> J D Walley,<sup>2</sup> Q Sun,<sup>3</sup> X Zhang.<sup>1</sup>

<sup>1</sup>School of Public Health and Primary Care, The Chinese University of Hong Kong, Hong Kong, China; <sup>2</sup>Nuffield Centre for International Health and Development, University of Leeds, Leeds, UK; <sup>3</sup>Centre for Health Management and Policy, Shandong University, Jinan, China. Fax: (+86) 21 6404 7075. e-mail: zgy1021@hotmail.com

**Background:** The New Medical Cooperative Schemes (NMCS) in China has covered nearly all rural residents. However, its effect on reducing patient out-of-pocket medical cost remained controversial. Only around half of NCMS schemes covered outpatient service for TB patients treated in the county TB dispensary. Many TB patients sought care in general health facilities before receiving standard treatment in the TB dispensary. This study is to examine to what extent the policy of the covering TB dispensary could contribute to the overall reimbursement of the TB treatment in Zhejiang (ZJ) and Sichuan (SC) provinces.

**Design/Methods:** Four counties were selected in each province, including two with NSMS covering TB dispensary ('covered group') while the other two not ('uncovered group'). In each county, we randomly selected 50 uncomplicated TB patients from the TB dispensary registered in 2009 and successfully completed treatment by August 2010. In total, the covered and uncovered groups included 97 and 89 in ZJ, and 98 and 108 in SC respectively.

**Results:** In the TB dispensary, the average cost per patient from the covered group was significantly lower than that from the uncovered group (RMB931 vs RMB1,660  $P < 0.001$ ) in ZJ, though vice versa in SC (RMB1,790 vs RMB1,041,  $P < 0.001$ ). The covered group had significantly higher average reimbursement rate per patient than the uncovered group in both provinces (ZJ: 5% vs. 0,  $p < 0.001$ ; SC: 14% vs 0,  $P < 0.001$ ). In total, each patient from the covered group spent significantly lower on treatment than that from the uncovered group (RMB4,660 vs. RMB5,895,  $P = 0.005$ ) in ZJ, though vice versa in SC (RMB4,161 vs RMB3,879,  $P = 0.001$ ). In both provinces, the covered group had significantly higher average reimbursement rate per patient than the uncovered group (ZJ: 13% vs. 8%,  $P = 0.002$ ; SC: 17% vs 8%,  $P < 0.001$ ), which coincided with results from the sensitivity analysis. The binary logistic regression analysis suggests that inpatients and patients from the covered group were more likely to be reimbursed  $> 10\%$  of the total cost than the outpatients and those from the uncovered group respectively (OR 3.989; 4.171).

**Conclusion:** Covering TB dispensary contributed to the overall reimbursement of the TB treatment in both

provinces. However, the effective coverage of NCMS was low. Policy actions such as including TB into the special disease category at higher reimbursement rate are needed to improve the benefit package of NCMS for TB patients.

## POSTER DISCUSSION SESSIONS

### 23. TB IN CHILDREN: OUTCOMES, EXTRA PULMONARY TB, BCG AND OTHER

#### PD-758-31 Sickle cell disease and tuberculosis in children living in a low-incidence setting

A Cruz,<sup>1</sup> G Airewele,<sup>1</sup> J R Starke.<sup>1</sup> <sup>1</sup>Pediatrics, Baylor College of Medicine, Houston, TX, USA. Fax: (+1) 832 825 1182. e-mail:acruz@bcm.edu

**Background:** Few published data exist on the burden and outcomes of tuberculosis disease (TB) in children with hemoglobinopathies, including sickle cell disease (HgbSS). Children with anatomic or functional asplenia are not considered high-risk conditions for progression from latent tuberculosis infection (LTBI) to disease.

**Design/Methods:** This was a descriptive case series of a single-center experience of TB in children with HgbSS in a low-incidence TB setting from 1993–2013 and literature review (1963–2013).

**Results:** 4 children (14 months–18 years) were diagnosed with pulmonary TB (2 with hilar adenopathy and infiltrates, 1 with isolated hilar adenopathy, 1 with multifocal infiltrates and mycobacteremia). 2 were US-born, 2 were born in Nigeria. One child, who had received a bone marrow transplant (BMT), was diagnosed post-mortem from blood and lung cultures shortly after BMT engraftment. The other 3 had tuberculin skin tests  $> 10$ mm. Only 1 had positive cultures; 3 met the standard definition of probable disease. 2 died: 1 prior to diagnosis; 1 with known cardiomyopathy had cardiac arrest 3 months into therapy. Only one child had been screened for LTBI prior to diagnosis. Literature review found 9 additional pediatric cases (6–18-years-old): 7 in HgbSS, 1 HgbSC, 1 HgbEE. 2 each had cervical adenitis, miliary disease, meningeal involvement, and musculoskeletal disease; one had isolated pulmonary disease. Outcomes were reported for 7: all survived, 2 (1 with meningitis, 1 with synovitis) with sequelae.

**Conclusions:** These cases demonstrate several commonalities: the difficulty in making epidemiologic links to adults known to or suspected of having TB disease; challenges in obtaining microbiologic confirmation; the potentially preventable nature of some of the cases; and the morbidity and mortality of TB in this population. Children with medical comorbidities often are screened for infections less common than TB, or are screened for infections which currently lack available preventive or treatment strategies. However, integration of screening guidelines for TB into algorithms used by most professional organizations caring for children with medical comorbidities has lagged. Given the morbidity and



mortality of disease in sickle cell patients and the low risk of adverse effects of LTBI therapy, consideration should be given to screening sickle cell disease patients for LTBI.

### PD-759-31 Vitamin D status of Batswana children with and without active TB: a pilot study

J Ludmir,<sup>1,2</sup> L Mazhani,<sup>3</sup> M Cary,<sup>2</sup> U Chakalisa,<sup>4</sup> J Pettifor,<sup>5</sup> M Molefi,<sup>6</sup> R Gross,<sup>1,2</sup> A Steenhoff.<sup>1,2,7</sup>

<sup>1</sup>Research, Botswana-UPenn Partnership, Gaborone, Botswana; <sup>2</sup>Epidemiology, Pediatrics or Medicine, Perelman School of Medicine University of Pennsylvania, Philadelphia, PA, USA; <sup>3</sup>Paediatric & Adolescent Health, University of Botswana, Gaborone; <sup>4</sup>Research, Botswana Harvard Partnership, Gaborone, Botswana; <sup>5</sup>Paediatrics, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa; <sup>6</sup>Public Health, University of Botswana, Gaborone, Botswana; <sup>7</sup>Pediatrics, The Children's Hospital of Philadelphia, Philadelphia, PA, USA.  
e-mail: steenhoff@email.chop.edu

**Background:** Strategies are needed to prevent and treat tuberculosis (TB). Although vitamin D has antituberculous effects, whether low vitamin D confers risk for TB in children is unknown. We assessed 25-hydroxyvitamin D (25OHD) levels in children with and without active TB in Gaborone, Botswana (latitude 24.6°S).

**Methods:** Between September 2010 and November 2012, we conducted a case-control study of 80 black children <2 years old from clinical sites in Gaborone. Cases had a first occurrence of active TB diagnosed by a pediatrician and <21 days of TB treatment. Controls, with active TB excluded, were similarly evaluated. The mean plasma 25OHD level was compared between groups using rank sum test and multivariate logistic regression was used to control for confounders. Linear regression was used to assess weight, HIV status, parental education, formula and sunlight effects on 25OHD levels.

**Results:** The 39 cases did not differ from the 41 controls by clinical criteria or 25OHD levels (Table). 25OHD was <20ng/mL in 8/39 (21%) cases and 7/41 (17%) controls ( $p=0.69$ ,  $X^2$ ). The odds of being a case conferred by low 25OHD levels was 0.997 (95% CI 0.967 to 1.027,  $p=0.82$ ). 25OHD levels were associated with age (+0.87ng/mL/month [95% CI 0.36 to 1.38],  $p<0.001$ ), time in the sun (0.34ng/mL per hour/week [95% CI 0.15 to 0.54],  $p<0.001$ ) and formula feeding (7.58ng/mL [95% CI 1.17 to 13.99],  $p=0.02$ ) for exclusive formula feeding compared with other feeding. Higher parental education (secondary/tertiary vs none/primary) was associated with lower 25OHD levels by -10.2ng/mL (95% CI -18.07 to -2.35,  $p=0.01$ ). For TB cases, number of days of TB treatment did not predict 25OHD levels (-1.1ng/mL/day [95% CI -2.22 to 0.02],  $p=0.06$ ). In multivariable regression, increased 25OHD was predicted by increased age (+0.70 ng/mL/month [95% CI 0.16 to 1.25],  $p=0.01$ ), exclusive formula feeding (7.89ng/mL [95% CI 1.99 to 13.80],  $p=0.01$ ), and lower educational level (-8.96ng/mL [95% CI -16.41 to -1.50]  $p=0.02$ ). Total sun exposure did not

significantly influence 25OHD (0.20ng/mL [95% CI -0.01 to 0.40],  $p=0.06$ ).

**Conclusion:** Vitamin D status was similar between children with and without active TB. Lower vitamin D status may not be a risk factor for TB in this setting. Several other factors were identified which might have implications for other health manifestations in these children.

Table: Study population.

	Active TB (n=39)	No Active TB (n=41)	Comparison
25-hydroxyvitamin D ng/mL (mean, IQR)	31.9 (21.5, 40)	32.7 (22.6, 41.9)	$p=0.84\#$
Age in months (mean, IQR)	10.8 (5, 16)	8.5 (5, 13)	$p=0.15\#$
Weight in kg (mean, IQR)	7.0 (5.2, 8.5)	6.6 (5.2, 7.4)	$p=0.45\#$
Length in cm (mean, IQR)	69.3 (61, 75)	65.8 (60.3, 72.3)	$p=0.35\#$
Male	16 (41%)	22 (54%)	$p=0.26^*$
HIV infected			$p=0.926^*$
Yes	6 (15%)	7 (18%)	
No	25 (64%)	26 (65%)	
Unknown	6 (15%)	7 (18%)	
Child on HAART medications in past 6m	8 (23%)	13 (33%)	$p=0.35^*$
Child has chronic diarrhea	6 (17%)	8 (21%)	$p=0.71^*$
Exposure to PMTCT	11 (31%)	19 (48%)	$p=0.16^*$
Weekly hours outside from 1000-1600 (mean, SD)	18.2 (3%)	13.3 (2%)	$p=0.18\ddagger$
Any sunburn in past 12m	8 (21%)	7 (18%)	$p=0.77^*$
Total sun protection score (high=more protection) (mean, SD)	7.6 (4%)	8.1 (3%)	$p=0.50\ddagger$
Family member with cough for $\geq 2$ weeks	21 (54%)	14 (34%)	$p=0.08^*$
Family member with unintended weight loss for 2m	22 (56%)	14 (34%)	$p=0.045^*$
Child received only formula	23 (58%)	15 (41%)	$p=0.14^*$
Parental educational level - none /primary compared to secondary/tertiary	8 (20%)	8 (21%)	$p=0.96^*$

IQR, interquartile range; m, months; #ranksum; \*chi square; †t-test

### PD-760-31 Treatment outcome of TB-HIV positive and TB-HIV negative children in Lagos, Nigeria

O Adejumo,<sup>1</sup> O Daniel,<sup>2</sup> H Abdur-Razzaq,<sup>3</sup> J O Obasanya,<sup>4</sup> Ayo Awe,<sup>5</sup> E Jaiyesimi,<sup>6</sup> O Odusanya.<sup>1</sup>

<sup>1</sup>Community health and Primary Health Care, Lagos State University Teaching Hospital, Lagos, <sup>2</sup>Tuberculosis, World Health Organization (WHO), Lagos, <sup>3</sup>Lagos State TB and Leprosy Control Programme, Lagos State Ministry of Health, Lagos, <sup>4</sup>National TB and Leprosy Control Programme, Federal Ministry of Health Nigeria, Abuja, <sup>5</sup>TB Control Programme, WHO, Abuja, <sup>6</sup>Reproductive Health, Center for Research for Reproductive Health, Sagamu, Nigeria.  
e-mail: oluadejumo75@gmail.com

**Background:** Tuberculosis (TB) has been reported to be among the top ten causes of death among children worldwide. The diagnosis of TB in children is difficult because the symptoms are not specific and access to specialized equipment for diagnosis is difficult especially in resource poor country like Nigeria. Although the principles of management of childhood TB are similar to that of adults, treatment outcomes in children are rarely evaluated at the end of treatment by most national TB programmes in sub-Saharan Africa. Thus this study was embarked upon to examine the treatment outcomes of children diagnosed and treated for TB in Lagos State, Nigeria

**Design/Methods:** A retrospective review of programme data submitted to the Lagos state TB and Leprosy control programme by TB treatment centres in Lagos state Nigeria. A data extraction form was used to collect data on children treated for TB from January to December 2012. The duration of treatment was 6 months which consist of a two month intensive phase and a four month continuation phase. Rifampicin, Isoniazid and Pyrazinamide were given at the intensive phase while Rifampicin and Isoniazid were given at the continuation phase as fixed dose combinations. Treatment outcomes were categorized as treatment success, died, default, failure and transferred out according to the national TB guidelines. The Statistical Package for Social Sciences (SPSS) version 19 was used for data analysis.

**Results:** A total of 535 TB cases of children aged 0–14 years were notified in Lagos State Nigeria in 2012. This represents 6.3% (535/8455) of the total TB cases notified for the state in 2012. The prevalence of TB/HIV co infection was 29% which was higher than the national average of 4.6%. The overall treatment success rate was 77.0%. The treatment success rate was 79.2% in TB/HIV negative children compared with 73.4% in TB/HIV positive children ( $P = 0.1268$ ). Children less than one year had a significantly lower treatment success (59.4%), higher deaths (13.0%) and default (27.5%) compared with children between 1–4 years and those between 5–14 years ( $P < 0.001$ ).

**Conclusion:** The number of childhood TB cases notified by the Lagos State TB programme is low. The need to intensify effort at improving notification and the treatment outcomes in children especially those below the age of one year in the State cannot be over emphasized.

#### PD-761-31 The Mbeya Advanced Pediatric TB Centre: a partnership between Baylor Tanzania, Mbeya Medical Research Centre (MMRC) and Mbeya Referral Hospital (MRH)

J Bacha,<sup>1</sup> L Campbell,<sup>1</sup> B Kasambala,<sup>1</sup> L Mwita,<sup>1</sup> C Mangu,<sup>2</sup> P Clowes,<sup>2</sup> K Ngo,<sup>3</sup> A Mandalakas.<sup>3</sup>

<sup>1</sup>Pediatrics, Baylor College of Medicine Children's Foundation - Tanzania, Mbeya, <sup>2</sup>NIMR-MMRC, National Institute of Medical Research - Mbeya Medical Research Centre, Mbeya, United Republic of Tanzania; <sup>3</sup>Pediatrics - Retrovirology & Global Health, Baylor College of Medicine, Houston, TX, USA. e-mail: bacha@bcm.edu

**Background:** In March 2013, the Baylor Tanzania Center of Excellence (COE) in Mbeya, MMRC and the Mbeya Referral Hospital partnered to create a centre offering comprehensive TB diagnostics including sputum work-up, tuberculin skin testing (TST), fine needle aspiration (FNA), and chest x-ray (CXR) interpretation for children identified with presumptive TB. This abstract provides a description of robust patient assessments, diagnostic findings and treatment during the first 10 months of program evaluation.

**Design/Methods:** Retrospective chart review at the COE between March 2013 and December 2013. Baseline and outcome data were captured using a standardized data collection tool and unique data base. Data is summarized

by means and standard deviations for continuous variables and by frequency and proportion for categorical variables.

**Results:** Baseline data: 203 patients with presumptive TB were referred. 47% female (95/203); age 0.3–19.7 years (median 5.3yr). 61% (123/203) HIV-infected, 7% (14/203) HIV-exposed, HIV-uninfected, and 32% (66/203) HIV-negative. Of HIV-infected, 66% (82/124) were on ART at time of referral. 26% (52/203) reported a known TB contact. For HIV-infected presumptive TB, mean CD4 count 650 (3–4387, SD 640). Of all patients evaluated, 76% (155/203) had sputa (44% induced, 56% spontaneous), 96% (194/203) had TSTs, 8% (17/203) FNAs, and only 51% (104/203) had CXRs due to mechanical and logistical challenges. Outcome data: 78 of the 203 (38%) were diagnosed with TB disease and 95% (74/78) initiated on TB therapy. 35% (27/78) were confirmed TB, 38% (38/78) probable TB, and 17% (13/78) possible TB. 10 patients were LTFU or died (4 of which had bacteriologically-confirmed TB results). Of those diagnosed, 76% (59/78) had pulmonary TB, 10% (8/78) lymph node TB, and 14% (11/78) extrapulmonary TB. HIV-infected accounted for 59% (33/59) of PTB, 50% (4/8) of LNTB and 73% (8/11) EPTB diagnosed. Table 1 lists the results and performance of the TB diagnostic tests in our patients. Median time from referral for TB diagnostics to initiation of TB therapy was 3 days (range 0–98 days) **Conclusion:** Advanced TB diagnosis is possible in our resource-constrained setting, and successfully led to increased TB case finding and prompt initiation of anti-TB in children. However, our results show that despite having access to state of the art diagnostics, positive test results are still low, stressing the importance of clinical TB diagnosis in children.

Table 1: TB diagnostic test results and test performance measures for pediatric patients with presumptive TB (with "TB Disease" diagnosis used as reference standard)

All patients (n=203)							
Diagnostic Test (# performed)	% tests with positive result (n)	PPV	NPV	Sensitivity	Specificity	PLR	NLR
Sputum GeneXpert (n=155)	3% (4/155)	1.00	0.37	0.07	1.00	0.07	0.93
Sputum smear (n=155)	3% (4/155)	1.00	0.37	0.07	1.00	0.07	0.93
Sputum culture (n=155)	17% (26/155)	0.92	0.29	0.39	0.98	0.65	0.62
TST (n=194)	13% (25/194)	0.80	0.35	0.27	0.95	0.37	0.76
FNA (n=17)	41% (7/17)	1.00	0.67	0.64	1.00	1.75	0.36
Chest x-ray (n=104)	35% (36/104)	1.00	0.17	0.75	1.00	3.00	0.25
HIV-infected patients only (n=123)							
Diagnostic Test (# performed)	% tests with positive result (n)	PPV	NPV	Sensitivity	Specificity	PLR	NLR
Sputum GeneXpert (n=101)	3% (3/101)	1.00	0.36	0.08	1.00	0.09	0.92
Sputum smear (n=101)	2% (2/101)	1.00	0.36	0.05	1.00	0.06	0.95
Sputum culture (n=101)	15% (15/101)	0.93	0.28	0.37	0.98	0.58	0.64
TST (n=106)	11% (12/106)	0.83	0.35	0.23	0.97	0.30	0.79
FNA (n=8)	38% (3/8)	0.75	0.50	0.60	0.67	1.50	0.60
Chest x-ray (n=59)	36% (21/59)	1.00	0.20	0.72	1.00	2.62	0.28

TST: Tuberculin Skin Test; FNA: Fine Needle Aspiration; PPV: Positive Predictive Value; NPV: Negative Predictive Value; PLR: Positive Likelihood Ratio; NLR: Negative Likelihood Ratio.

#### PD-762-31 High prevalence of abdominal tuberculosis in children: experience from the Indus TB control programme, Karachi, Pakistan

F Amanullah,<sup>1</sup> F Khatoon,<sup>1</sup> A Malik,<sup>2</sup> S Hussain,<sup>1</sup> U Qazi,<sup>1</sup> S Shahid,<sup>1</sup> L Samad,<sup>3</sup> A Khan.<sup>2</sup> <sup>1</sup>Pediatrics, The Indus Hospital, Karachi, <sup>2</sup>International Health, Interactive Research and Development, Karachi, <sup>3</sup>Pediatric Surgery, The Indus Hospital, Karachi, Pakistan.

e-mail: farhana.maqbool@irdresearch.org

**Background:** In developing countries, as much as 40% of the tuberculosis (TB) burden may occur in children of



which 10 to 25% is extrapulmonary TB (EPTB). Abdominal TB is known to be the 6<sup>th</sup> most common type of EPTB. Our study objective was to assess the presentation, course and outcomes of abdominal TB in children at the Indus Hospital TB program.

**Methods:** We retrospectively reviewed medical records of all children 0–14 years age who were treated for abdominal TB at the Indus Hospital from March 2008 to March 2014

**Results:** The Indus Hospital TB program has registered and treated 1346 children with TB disease from 2007 to date. EPTB comprises 45% (603/1346) of all cases. Abdominal TB (27%) is the second most common cause of EPTB after lymph node TB. It is a significant cause of pediatric TB deaths, with 30% of mortality from all TB cases occurring secondary to abdominal TB and its complications. Abdominal TB occurs predominantly in female children (62%). Detailed analysis of these children with abdominal TB indicates that at presentation, abdominal pain (n=120, 74%), weight loss (n=120, 74%), fever (n=114, 70%), and loss of appetite (n=101, 62%) were the most commonly reported symptoms.

**Conclusion:** Abdominal TB is a common cause of EPTB in children in our program and is twice as common in females who are more likely to present with marked weight loss and severe disease. Difficulties with early diagnosis, lack of intravenous first line TB drugs, significant surgical morbidity and mortality in advanced cases remain challenges.

#### **PD-763-31 Characteristics and risk factors of extrapulmonary tuberculosis in children from low-burden country: EREMITA Study Group**

B Santiago,<sup>1</sup> F Baquero-artigao,<sup>2</sup> MJ Mellado Peña,<sup>2</sup> D Blázquez Gamero.<sup>3</sup> <sup>1</sup>Laboratorio Inmunobiología Molecular, Hospital Universitario Gregorio Marañón, Madrid, <sup>2</sup>Servicio de Pediatría, Enfermedades Infecciosas y Patología Tropical, Hospital Universitario La Paz, Madrid, <sup>3</sup>Servicio de Inmunodeficiencias Primarias, Hospital Universitario 12 de Octubre, Madrid, Spain. e-mail: bsantiagogarciar@gmail.com

**Aims:** To determine the prevalence, clinical characteristics and risk factors of pediatric extrapulmonary tuberculosis (EPTB) in children from a low burden setting.

**Design/Methods:** A retrospective multicenter study in children <18 years diagnosed with tuberculosis (TB) between 2005 and 2013 was developed among 21 hospitals from Madrid region. Demographic and clinical characteristics of EPTB cases were compared to pulmonary TB (PTB) cases, as well as among different sites of EPTB disease. Risk factors for EPTB were determined by multivariate analysis

**Results:** Among 522 children diagnosed with TB disease, 97 (18.5%) were EPTB cases (median age 3.5 years [1.7–11], 19.8% male). *M. tuberculosis* was identified in 63 EPTB children (65.6%) by culture (n=54) or PCR (n=9). The most frequent site was lymphatic (n=39; 40.2%) followed by CNS (n=23; 23.7%), disseminated (n=22; 22.6%), osteoarticular (n=16; 16.4%), abdominal

(n=7; 7.2%), pericardial (n=2; 2%), genitourinary and laryngeal TB (n=1; 1%). Compared with PTB, EPTB was more frequent in children born to foreign parents (80% vs. 69.9%, p=0.05) and among immunocompromised (13.4% vs. 3.8%, p<0.0001). CNS TB was more frequent among infants <2 years (p=0.006), whilst osteoarticular TB was more common in children between 2 and 5 years (p=0.034). EPTB cases presented smaller PPD induration compared to PTB cases, being <5mm in 16.5% of EPTB cases compared to 4.5% of PTB (p<0.0001). Besides, EPTB cases showed more complications (42.9% vs. 14.8%; p<0.0001), especially CNS TB cases (68.2%, p<0.0001). Overall, drug resistant TB was more frequent among EPTB cases compared to PTB (p=0.009). Risk factors associated with EPTB were immune suppression (OR 8.8[2.8–27.6]), drug resistance (OR 2.6[1.2–5.5]) and parents' immigrant status (OR 2.3[1.02–5.4]).

**Conclusion:** In our setting, EPTB is more common among children born to foreign parents and immunocompromised children, and features a high rate of complications and resistance to first-line drugs.

#### **PD-764-31 Childhood TB: experience from the largest private pediatric TB programme in Pakistan**

A Malik,<sup>1</sup> F Amanullah,<sup>2</sup> F Khatoon,<sup>2</sup> R Hashmi,<sup>1</sup> M Jaswal,<sup>2</sup> A Khan,<sup>1</sup> H Hussain.<sup>2</sup> <sup>1</sup>International Health, Interactive Research & Development, Karachi, <sup>2</sup>TB Control, The Indus Hospital, Karachi, Pakistan. e-mail: amyn.malik@irdresearch.org

**Background:** WHO estimates that almost 0.5 million children become infected with TB every year with a 6–10% contribution towards all notified TB cases. In 2012 child TB (<15 year olds) comprised 10% of all reported TB cases in Pakistan. This is likely a gross underestimate of the true child TB burden, owing to poor access to diagnostics and underreporting.

**Design/Methods:** We retrospectively reviewed medical records of all children 0–14 years old who were registered for TB treatment at the Indus Hospital from 2007 to March 2014.

**Results:** A total of 1346, 0–14 year olds children were registered for treatment at the Indus Hospital Pediatric TB program. Majority of the 0–14 year olds, 85% were registered after 2010 with the highest number of cases registered in 2012 (following implementation of active case finding strategies). The M:F ratio is 0.56 (64% children are female). Extra pulmonary TB accounted for 45% childhood TB, with lymph nodes being the commonest site (46%) followed by abdominal TB (27%). The treatment success rate was 80% overall (PTB- 78.4% and EPTB-81%). The default rate was 15.8 overall and dropped from 23 to 13.9 from 2008 to 2013.

**Conclusion:** The Indus Hospital Pediatric TB program is the largest private child TB program in Pakistan. Review of programmatic data indicates a significant increase in pediatric TB case detection as of 2012 when active case finding strategies involving the private sector were

implemented. Strong community linkages through health care workers and awareness campaigns have resulted in improved treatment outcomes.

### PD-765-31 The peculiarities of bone and joint TB (BJTB) confirmed by *M.tuberculosis* isolates in pediatric patients

A Mushkin,<sup>1</sup> Nola Solovieva,<sup>1</sup> E. Malyarova,<sup>1</sup> V. Vatutina,<sup>1</sup> A. Inozemtseva,<sup>1</sup> S. Mazokhina.<sup>1</sup>

<sup>1</sup>Extrapulmonary Tuberculosis, St. Petersburg Research Institute of Phthisiopulmonology, St.Petersburg, Russian Federation. e-mail: baclab@spbnif.ru

**Background:** Despite the relative rarity of the defeat of BJTB is the most common extrapulmonary tuberculosis in children.

**Design/Methods:** The peculiarities of BJTB destruction, intrathoracic TB (ITTB) and resistance of *Mtb* to the anti-TB drugs were compared. 27 pediatric patients aged from 2 till 16 yrs. were consistently operated due to BJTB in the clinic of St. Petersburg Research Institute of Phthisiopulmonology in 2009–2013. It was not patients with primary immune insufficiency in this cohort. Criteria for inclusion was confirmation of TB by isolates of *Mtb*. Drug resistant (DR) of *Mtb* was determined by method of absolute concentration on Lewenstein-Jensen medium. BJTB included 6 osteitis, 9 arthritis and 12 spondylitis cases. CT signs of ITTB were absent in 7 children (2 osteitis, 2 arthritis and 3 spondylitis). 14 ones had multi-groups intrathoracic lymph nodes TB, 6 more patients had complicated ITTB forms, incl. poliserositis (pleuritis, pericarditis), the bronchial and bronchopulmonary TB pleuritis, primary TB complex with dissemination into the lung. All locations of BJTB were accompanied by the paraossal/paraarticular/perivertebral abscesses. All children were operated with maximal debridement of destroyed tissues and reconstruction by bone plastics and instrumentation (in spondylitis cases).

**Results:** *Mtb* isolates were revealed in 26 cases from the zone of operation and just in one case from the sputum. The total level of the isolates' DR was found in 82.8 % of cases: 5 isolates had mono-DR; one had poli-DR to the 3 components (SHZ). The majority isolates (17/27 or 62.7%) had MDR, 16(94.1%) strains with resistance to the 4 and more medicines and 1 with XDR. The same time, 7 cases of BJTB without ITTB included 3/5 TB cases caused by completely drug sensitive *Mtb*, 1/5 MonoDR and 3/17 MDR *Mtb*. From other side, 4/6 complicated ITTB cases were caused by MDR *Mtb*, 1 – by poli-DR and just 1 – by sensitive *Mtb* culture. After surgery all patients are received the target anti-TB chemotherapy based on the drug sensitivity data. The recurrences of TB were found in two cases, both were caused by MDR *Mtb*.

**Conclusion:** It was found that 20/27 patients (74.1%) had generalized TB with ITTB, incl. 5(18.5%) complicated intra thoracic processes; 17/27(62.7%) *Mtb* isolates had MDR and just 5(18.5%) were completely sensitive to the anti-TB medicines. It was not found influence of DR to the forms (location) of BJTB.

### PD-766-31 Evolution of the BCG lesion in neonates and adults

M Van Rooyen,<sup>1</sup> K Luabeya,<sup>1</sup> M Hatherill,<sup>1</sup> M Tameris,<sup>1</sup> G Saxon,<sup>2</sup> J Foster,<sup>2</sup> D Zehrung,<sup>2</sup> H Geldenhuys.<sup>1</sup> <sup>1</sup>SATVI, University of Cape Town, Worcester, South Africa; <sup>2</sup>PATH, Seattle, WA, USA. e-mail: m.vanrooyen@uct.ac.za

**Background:** BCG is routinely administered to newborns in South Africa. There is also renewed interest in BCG re-vaccination later in life. There are limited data describing the evolution of the BCG lesion in adults and neonates. Our objective was to describe progression of the injection site lesion in HIV negative adults and HIV unexposed neonates after BCG vaccination in a clinical trial.

**Design/Methods:** In a blinded study we vaccinated 30 adults and 66 newborns with standard dose intradermal BCG (0.1 ml adults, 0.05 ml neonates) via investigational Disposable Syringe Jet Injector or syringe and needle in a ratio 1:1. Follow-up was for 3 months. The BCG lesion was observed and measured with diary cards and follow up visits at 1 month and 3 months post-vaccination.

**Results:** At 4 weeks post-vaccination mean erythema of the BCG lesion in neonates was 1.8 mm (95% CI 1.5-2.1), mean induration 0.3 mm (0.2-0.4), with no ulcers and 2% of lesions with scarring. In adults, mean erythema was 2.2 mm (0.5-3.9), induration 0.3 mm (0–1.1), 48% with ulcers and none with scarring. At 3 months, mean erythema in neonates was 0.4 mm (0.2-0.5), 0 mm induration, 5 (8 %) ulcer and 45 (69%) scar. In adults, no erythema or induration was present, 3 (10%) ulcer and 27 (90%) scar.

	Neonates	Adults	Neonates	Adults
	4 weeks		3 months	
Erythema (mean, CI)	1.8 mm (95% CI 1.5-2.1)	2.2 mm (0.5-3.9)	0.4 mm (0.2-0.5)	0 mm
Induration (mean, CI)	0.3 mm (0.2-0.4)	0.3 mm (0–1.1)	0 mm	0 mm
Ulcer formation (n (%))	0 (0%)	14 (47%)	5 (8 %)	3 (10%)
Scarring (n (%))	1 (2%)	0 (0%)	45 (69%)	27 (90%)

**Conclusion:** BCG lesions consisted of overlapping early erythema then induration, followed by ulcer formation and scarring in neonates and adults. BCG lesions appeared to evolve later in neonates and were smaller. By 3 months post-vaccination the BCG lesion had resolved in most adults, but was on-going in up to a third of neonates.

### PD-767-31 BCG associated lymphadenitis in the country of Georgia

G Kuchukhidze,<sup>1</sup> A Kasradze,<sup>1</sup> T Dolakidze,<sup>1</sup> D Baliashvili,<sup>1</sup> H Blumberg,<sup>2</sup> R Kempker.<sup>2</sup> <sup>1</sup>Communicable Diseases, National Center for Disease Control and Public Health, Tbilisi, Georgia; <sup>2</sup>Department of Medicine, Emory University School of Medicine, Atlanta, GA, USA. e-mail: giokuchu@gmail.com

**Background:** Georgia is a high-burden multidrug resistant (MDR) tuberculosis (TB) country. To help prevent miliary TB and TB meningitis, BCG vaccine is adminis-

tered to children after birth; estimated vaccine coverage is 96%. After a switch to exclusive use of the Danish 1331 BCG strain, several cases of BCG-associated lymphadenitis were reported to public health officials. We sought to quantify the increase in cases of BCG lymphadenitis, identify the relationship to the introduction of a new BCG vaccine strain, and to evaluate clinical management of the cases.

**Methods:** A retrospective study design was utilized. Pertinent data was abstracted from the medical charts of all infants (<2 years) reported to the National TB Program (NTP) and additional cases found through inquiry at the largest children's hospital in the country. All cases of BCG lymphadenitis occurring from January 2012 through July 2013 were included. BCG-associated lymphadenitis was defined clinically as a case of ipsilateral axillary lymph node enlargement developing within 2 years after vaccination. Treatment was at the discretion of clinicians. During the study, the NTP treatment guidelines did not include any mention of BCG related adverse events including lymphadenitis.

**Results:** From 2007–2011, only 6 cases of BCG lymphadenitis were reported to the Georgian NTP. During our study period, we identified a total of 23 cases of BCG associated lymphadenitis (20 suppurative, 3 non-suppurative); 15 cases were reported to the Georgian NTP and 8 diagnosed at the children's hospital. The Danish 1331 strain was used in all cases of lymphadenitis; the cases received BCG at 8 different maternity hospitals. The estimated incidence of BCG related lymphadenitis in 2012 was 1.3 per 1000 infants. The median time from vaccination to presentation of lymphadenitis was 5 months. All 15 cases seen at the NTP were treated with first-line anti-TB drugs including pyrazinamide and four patients had adjunctive surgical excision performed along with treatment. Of the 8 patients treated at the children's hospital, 6 received surgical excisions alone and 2 were managed conservatively.

**Conclusion:** We found a substantial increase in the known prevalence of BCG associated lymphadenitis after a switch in BCG vaccine strain. Given the findings of this report, management recommendations for BCG lymphadenitis were included in updated national Georgian NTP pediatric TB guidelines; this should lead to more appropriate treatment.

#### **PD-768-31 Occurrence and treatment outcomes of TB in an urban pediatric HIV clinic in Kampala, Uganda**

F Kanyike,<sup>1</sup> M Sekadde,<sup>2</sup> B Nsangi,<sup>1,3</sup> A Kekitiinwa,<sup>1,3</sup> A Mandalakas.<sup>3</sup> <sup>1</sup>Pediatrics, Baylor College of Medicine Children's Foundation Uganda, Kampala, <sup>2</sup>Pediatrics, National TB and Leprosy Program, Kampala, Uganda; <sup>3</sup>Pediatrics, Baylor College of Medicine, Houston, TX, USA. e-mail: bnsangi@baylor-uganda.org

**Background:** In 2012, children under 15 years accounted for 2.5% of Uganda's notified smear positive TB cases. Under diagnosis and underreporting of pediatric TB presumably contribute to rates that are far below the expected 15%. HIV is the leading risk factor for develop-

ment of TB; TB is the leading cause of mortality among HIV infected patients. The magnitude and treatment outcomes of TB among HIV infected Ugandan children are unknown. We determined the occurrence and treatment outcomes of TB in an urban pediatric HIV clinic.

**Design/Methods:** We reviewed medical records of all HIV-infected children <15 years who attended the Baylor-Uganda clinic between 1<sup>st</sup> October 2012 to 31<sup>st</sup> August 2013. Children diagnosed with TB were identified and treatment outcomes examined. Sputum was collected by expectoration and lymph node aspirates and biopsy were also done. Bacteriologically confirmed (BC) TB was defined as smear or gene Xpert positive TB. Clinically diagnosed (CD) TB was defined as TB that did not fulfill the criteria for bacteriological confirmation but was diagnosed by a clinician who made a decision to initiate the patient on TB treatment. Extrapulmonary TB (EPTB) was defined as BC or CD TB involving organs other than the lungs. We determined TB occurrence, treatment success rate (TSR), death rate, cure rate, and loss to follow up rate using proportions.

**Results:** 80/3,964 (2%) HIV infected children were newly diagnosed with TB in the review period; median age was 4 years (IQR: 8.1). 47/80 (58.8%) were female. 5/80 (6.3%) had BC TB; these children were all aged 5 – 15 years. 75/80 (93.8%) had CD TB. 8/80 (10%) children had EPTB. All children with BC TB were cured. 61/80 (76.3%) children had treatment success, 5/80 (6.3%) were lost to follow up and 14/80 (17.5%) died.

**Conclusion:** Pediatric TB/HIV co-infection rate was lower than the reported rate of 6% in Ugandan adults living with HIV. Our TSR was equal to the national TSR of 77% but the death rate was almost four fold higher than the national death rate (4.7%). Our results highlight the increased risk of mortality among TB-HIV co-infected children and the urgent need to improve treatment outcomes. Identification of factors associated with increased mortality may inform interventions to improve TB treatment outcomes.

#### **PD-769-31 A baseline assessment of tuberculosis outcomes and diagnostic practices to inform development of a community-based TB-HIV programme in central Malawi**

R Flick,<sup>1,2</sup> A Munthali,<sup>1</sup> K Simon,<sup>1,3</sup> C Buck,<sup>1,4</sup> A Dimba,<sup>5</sup> Y Lo,<sup>1</sup> P Kazembe,<sup>1,3</sup> S Ahmed.<sup>1,3</sup> <sup>1</sup>Baylor College of Medicine Children's Foundation Malawi, Lilongwe, Malawi; <sup>2</sup>University of Colorado School of Medicine, Denver, CO, <sup>3</sup>Pediatrics, Baylor College of Medicine, Houston, TX, <sup>4</sup>Pediatrics, University of Colorado School of Medicine, Denver, CO, USA; <sup>5</sup>Malawi National Tuberculosis Control Programme, Lilongwe, Malawi. e-mail: robbie.flick@gmail.com

**Background:** Baylor College of Medicine Children's Foundation Malawi has a well-established community health worker program called Tingathe focused on improving outcomes by strengthening the continuum of care in the treatment and prevention of pediatric HIV. As the immunocompromised and pediatric populations served by the program are two of the highest risk groups



for TB disease progression, Tingathe is developing a TB-specific program to layer onto existing activities. To inform the development of this TB module, a baseline assessment of TB outcomes and diagnostic practices at intervention sites was conducted.

**Methods:** Data from January 2011 through July 2013 from the National TB Control Programme (NTP) paper registers at 11 public health facilities in Malawi's central region was aggregated, de-identified, and compiled into a Microsoft Excel database. Demographics of caseload, diagnostic practices, and treatment outcomes were assessed by simple comparative analysis.

**Results:** Pediatric patients <15 yrs represented 8% (368/4765) of total TB caseload. Children were significantly less likely than adults to be diagnosed by sputum smear (22% vs 79%, OR=.07, CI=.05-.09); when sputum was obtained, pediatric patients were less likely to have smear-positive disease (49% vs 61%, OR=.60, CI=.39-.94). As a result, cure rates – defined by smear conversion – were 7% in children vs 30% in adults (OR=.17, CI=.11-.27). A subgroup analysis of patients with final outcomes at time of data collection was done (Table 1); of 299 pediatric patients in this cohort, 20 (7%) were cured and 195 (65%) completed treatment; 23 (8%) died, 59 (20%) were lost to follow up, and 2 (<1%) transferred out. Of 3416 adult patients in this cohort, 1018 (30%) were cured and 1214 (36%) completed treatment; 401 (12%) died, 637 (19%) were lost to follow up, 48 (1%) failed treatment, and 98 (3%) transferred out.

**Conclusions:** Children are under-represented in TB case notifications at these facilities. They also have low rates of bacteriologic diagnosis due to inadequate capacity for obtaining sputum specimens. Adult and pediatric patients exhibit high rates of lost to follow up from TB treatment. Based in part on these findings, the Tingathe TB program will include intensified TB case finding in HIV-infected children and adults, community-based TB/HIV treatment support, and improved access to induced sputum and GeneXpert for pediatric diagnosis. Program outcomes relative to these findings will be shared.

Table 1. Treatment outcomes

	Cured	Completed Treatment	Died	Failed Treatment	Lost to follow-up	Transfer out
Children (n=299)	20 (7%)	195 (65%)	23 (8%)	0	59 (20%)	2 (<1%)
Adults (n=3416)	1018 (30%)	1214 (36%)	401 (12%)	48 (1%)	637 (19%)	98 (3%)

### PD-770-31 Mothers and caretakers understanding and care-seeking practices for paediatric tuberculosis in a rural district of southern Mozambique

K Munguambe,<sup>1,2</sup> C Mindu,<sup>1</sup> E Lopez Varela,<sup>1,3</sup> A García-Basteiro,<sup>1,3</sup> O Augusto,<sup>1</sup> K Gondo,<sup>1</sup> P Alonso,<sup>1,3</sup> J Sacarlal.<sup>1,2</sup> <sup>1</sup>Social Sciences, Manhica Health Research, Maputo, <sup>2</sup>Social Science, Eduardo Mondlane University, Maputo, Mozambique; <sup>3</sup>CRESIB, Barcelona Centre For International Health Research, Barcelona, Spain.  
e-mail: carolina.mindu@manhica.net

**Background** Children contribute to 15–20% of the global TB burden. Mozambique is among the 22

countries with the highest TB figures. However, figures are not precise, partly due to a suboptimal notification system. Caregivers and traditional healers recognition of paediatric TB could contribute to improved detection and treatment of paediatric TB cases. This study sought to understand care-seeking practices for paediatric TB and to link such practices to the local understanding of signs and symptoms, aetiology, prevention, and treatment of TB.

**Methods** A qualitative study nested in a prospective study to determine the community-based incidence of childhood TB in Manhica was conducted from October 2011 to October 2012. The incidence study recruited children under 3 years of age, who were presumptive TB cases. Diagnosis was through chest X-Ray, tuberculin skin test, gastric aspirate, and induced sputum. Qualitative data was collected through in-depth and semi-structured interviews with 21 caregivers and 37 traditional healers. Data was analysed by grounded theory using Nvivo-10.

**Results** Despite being at risk or showing signs suggestive of TB (prolonged coughing, fever, weight loss and breathing difficulties), very few caretakers (all of which were TB patients themselves or had household TB contacts) thought it could be TB. Most believed that the child was healthy; others suspected flu, HIV, asthma, malaria, xilala (a form of malnutrition), and illness of the moon (convulsions linked to the moon phases). Most went to the hospital as a result of the incidence study tracking system, but the majority had previously sought traditional healers. Most caregivers of confirmed TB cases remained unconvinced of the diagnosis because TB is believed to affect adults who do not undergo purification upon a death of a relative. Although diagnostic techniques, especially the induced sputum, are perceived by caretakers as harmful for children, they are tolerated.

**Conclusion** There is limited awareness about paediatric TB, even among caregivers of presumptive TB cases. Despite certain knowledge of transmission, the belief that TB results from transgression of local norms prevails. Misinterpretation of TB, coupled by the current invasive diagnostic procedures, may discourage appropriate care-seeking. Community sensitization should emphasise messages about the reality, risks and consequences of paediatric TB. Traditional healers may constitute an entry-point for case detection.



## 24. COPD AND OUTCOMES POST-TB

### PD-771-31 ACE2 deficiency promotes pathological imbalance of MMPs/TIMPs expression in the early stage of chronic obstructive pulmonary disease

Y-H Hung,<sup>1</sup> W-Y Hsieh,<sup>2</sup> J-S Hsieh,<sup>1</sup> FC Liu,<sup>1</sup> C-L Wu,<sup>2</sup> C-S Lin.<sup>1</sup> <sup>1</sup>Biological Science and Technology, National Chiao Tung University, Hsinchu, <sup>2</sup>Internal Medicine, Division of Chest Medicine, Mackay Memorial Hospital, Hsinchu, Taiwan. Fax: (+886) 3-572 9288. e-mail: lincs@mail.nctu.edu.tw

**Background:** Abnormal renin-angiotensin system (RAS) function has been implicated in the pathogenesis of fibrosis diseases, including chronic obstructive pulmonary disease (COPD). However, RAS-related mechanism of COPD development is still largely unclear. In this study, angiotensin converting enzyme II (ACE2) knock-out (KO) mice were used to investigate the role of ACE2, an enzyme converting Ang II into Ang-(1-7), in the COPD development at early stage. Molecular mechanism of the disease associated with ACE2 deficiency was also investigated.

**Design/Methods:** Wild-type (WT; C57BL/6) and ACE2 KO mice were exposed to cigarette smoke four times per day and 7 days per week to induce COPD. After 1, 2 and 3 weeks of the smoke exposure, body weight and resting respiratory rate (RRR) of the mice were measured and the mice were sacrificed to collect lungs for further biochemical, pathological and molecular examinations.

**Results:** Body weight and RRR of the mice was decreased and increased with the increasing time of smoke exposure. Both changes in ACE2 KO mice were more severe in compared with those in WT mice. In the pathological findings, infiltration of white blood cells, alveolar damage and airway epithelial thickening in the lung of ACE2 KO mice were significantly increased compared with those in WT mice. The markedly increases of pulmonary ACE, matrix metalloproteinase-2 (MMP-2) and MMP-9 activity in ACE2 KO mice were determined. Simultaneously, the pulmonary tissue inhibitor matrix metalloproteinase (TIMP-1) and TIMP-2 expression in ACE2 KO mice were markedly decreased. Therefore, it can be proposed that imbalance expression of MMPs/TIMPs is associated with the COPD development at the early stage. In addition, the level of STAT-3 phosphorylation was obviously increased in the lung isolated from ACE2 KO mice treated with smoke exposure, but not WT mice. Such STAT-3 activation in ACE2 KO mice can be attenuated by pulmonary Lenti-ACE2, the recombined lentivirus that can overexpress human ACE2 protein, delivery.

**Conclusion:** Loss of ACE2 would induce excessive angiotensin II to stimulate more inflammatory responses when the ACE KO mice challenged with the exposure of cigarette smoke. In the mice, imbalance of MMP-2/MMP-9 expression via at least STAT-3 activation was proposed and elucidated. Our results imply that RAS dysregulation plays a pivotal role in the development of

COPD. The role of novel ACE2/Ang-(1-7) axis in the COPD pathogenesis remains to be explored.

### PD-772-31 Scintigraphic parameters of patients with pulmonary tuberculosis in chronic obstructive pulmonary disease

T Ageeva,<sup>1</sup> Anna Dubodelova,<sup>1</sup> S Mishustin,<sup>2</sup> E Mishustina,<sup>1</sup> N Krivonogov.<sup>3</sup> <sup>1</sup>Department of Internal Disease Propedeutics, Siberian State Medical University, Tomsk, <sup>2</sup>Department of Phthisiopulmonology, Tomsk Tuberculosis And Pulmonary Disease Medical Center, Tomsk, <sup>3</sup>Laboratory of Radionuclide Research Methods, Institute of Cardiology, Tomsk Research Center of RAMS, Tomsk, Russian Federation. e-mail: ts.ageeva@gmail.com

**Background:** The research was designed to study diagnostic capabilities of pulmoscintigraphy from the viewpoint of the assessment of pulmonary microcirculation and ventilation disorders in case of infiltrative pulmonary tuberculosis (IPT) in COPD vs. COPD.

**Design/Methods:** 30 patients of both genders and the verified diagnosis of IPT in Stage I-II COPD (n=10) and COPD I-II COPD (n=20) underwent ventilation-perfusion pulmoscintigraphy to study the ventilation-perfusion ratio (V/Q), apex-base gradient of ventilation (U/L-V) and perfusion (U/LQ) and alveolar-capillary permeability (ACP). The scintigraphic studies were performed by means of the Omega 500 gamma camera (Technicare, USA-Germany). The subject of the research was an examination of ACP in the right (RL) and left (LL) lungs in the process of radiopharmaceutical derivation, static conditions, during the 1st, 10th and 30th min after 99mTc DTPA inhalation.

**Results:** IPT in COPD was characterized with the reduced apical-basal grade of perfusion in both the right and left lungs as well as the bilateral increase in the alveolar-capillary permeability from the first minutes of the examination as compared with the similar parameters of the COPD patients. The patients with IPT in COPD were characterized with reduced U/LQ in both the affected and intact lungs, 0.63 (0.48-0.80) and 0.70 (0.69-0.87) vs. similar indicators in the COPD patients, 1.01 (0.87-1.15) and 0.8 (0.81-1.06), p=0.02 and 0.001, respectively. The ACP value in case of IPT in COPD in the affected lung amounted to 47.05% (35.05-52.01%) during the 10<sup>th</sup> minute, 52.65% (50.25-55.30%) during the 30<sup>th</sup> minute; as for the intact lung, the indicator amounted to 33.35% (31.95-44.75%) during the 10<sup>th</sup> minute and 50.01% (48.70-56.45%) during the 30<sup>th</sup> minute. These values were meaningfully higher vs. the same indicators of ACP in case of COPD (p=0.00005, 0.00006, 0.0004 and 0.00005, respectively).

**Conclusion:** The detected changes in the parameters of ventilation-perfusion pulmoscintigraphy can be used as additional criteria to diagnose IPT in COPD.

**PD-773-31 Prevalence of COPD in a rural area of sub-Saharan Africa: FRESH AIR Uganda survey**F Van Gemert,<sup>1</sup> B Kirenga,<sup>2</sup> N Chavannes,<sup>3</sup> M Kamya,<sup>2</sup> P Musinguzi,<sup>2</sup> C De Jong,<sup>1</sup> R Jones,<sup>4</sup> T Van Der Molen.<sup>1</sup><sup>1</sup>Department of General Practice, University of Groningen, University Medical Centre Groningen, Groningen, Netherlands; <sup>2</sup>Department of Medicine, Makerere University, Mulago Hospital, Kampala, Uganda; <sup>3</sup>Department of Public Health and Primary Care, Leiden University Medical Centre, Leiden, Netherlands; <sup>4</sup>Peninsula Medical School, University of Plymouth, Plymouth, UK. Fax: (+31) 517 418 712. e-mail: frgemert@xs4all.nl**Background** In sub-Saharan Africa, little is known about the damage to respiratory health caused by biomass fuel use and tobacco smoke. The aim of this survey was to collect data on prevalence of chronic obstructive pulmonary disease (COPD) and related risk in a rural area of Uganda.**Methods** Population-based cross-sectional epidemiological survey of 588 randomly selected adults above age of 30. Trained local healthcare workers conducted interviews using validated questionnaires, and performed pre- and post-bronchodilator spirometry. The lower limit of normal threshold, i.e. the fifth percentile of the predicted FEV1/FVC ratio, was used as defining criterion of COPD.**Results** The study population had a mean age of 45 (SD 13.7) with 50.5% women; 93% of subjects were exposed to indoor biomass smoke (men: 91%, mean 3.1 hours/day; women: 95%, mean 5.2 hours/day). Kerosene lamps were used by 94% of subjects. The prevalence of COPD was 16.2% (53% women): 78% GOLD 1, 20% GOLD 2 and 2% GOLD 3. Prevalence was highest in age group 30–39 years: 38% of men and 40% of women. In the COPD group, many young men smoked: 44% current smokers (mean age 41) and 24% former smokers (mean age 48); 8% women smoked (mean age 53), 18% were former smokers (mean age 63). Total mean Clinical COPD Questionnaire score, measuring the health-related quality of life, was 0.81 (SD 0.78) and MRC dyspnoea score was 1.33 (SD 0.65); 30% had one or more exacerbations during the last 12 months, increasing with age. COPD was associated with wheeze OR 2.19 (95%CI: 1.09-4.37;  $p=0.026$ ) and former smoker OR 1.93 (95%CI: 1.05-3.52;  $p=0.033$ ).**Conclusion** In Uganda, with a life expectancy of 52 years, the prevalence of COPD is high, especially in lower age groups. In addition to a high smoking prevalence in young men, biomass fuel smoke is almost uniform in this population. COPD represents a major threat to men and women of all ages in rural areas of Uganda. A major priority is to increase the knowledge of harmful effects of biomass fuel use and tobacco smoke in the various communities and to promote awareness among healthcare workers and policy makers. More research is needed to understand the short- and long-term effects of these risk factors, and their association in the early development of COPD.**PD-774-31 Impact of chronic respiratory symptoms in a rural area of sub-Saharan Africa**F Van Gemert,<sup>1</sup> N Chavannes,<sup>2</sup> N Nabadda,<sup>3</sup> S Luzige,<sup>4</sup> B Kirenga,<sup>4</sup> C De Jong,<sup>1</sup> C Eggermont,<sup>5</sup>T Van Der Molen.<sup>1</sup> <sup>1</sup>General Practice, University of Groningen, University Medical Centre Groningen, Groningen; <sup>2</sup>Public Health and Primary Care, Leiden University Medical Centre, Leiden, Netherlands; <sup>3</sup>Sociology, Multi Consults Research Ltd, Kampala; <sup>4</sup>Medicine, Makerere University, Mulago Hospital, Kampala, Uganda; <sup>5</sup>Faculty of Medicine, University Medical Centre Utrecht, Utrecht, Netherlands. Fax: (+31) 517 418 712. e-mail: frgemert@xs4all.nl**Background** Chronic obstructive pulmonary disease (COPD), once regarded as a disease of developed countries, is now recognized as a common disease in low- and middle- income countries. No studies have been done examining how the community in resource-poor settings of a rural area in sub-Saharan Africa lives with chronic respiratory symptoms. The aim was to explore beliefs and attitudes concerning health, particularly respiratory illnesses, use of biomass fuels, tobacco smoking, and the use of health services.**Methods** A qualitative study in a rural area of Masindi district in Uganda, using focus group discussions (FGDs) with 10–15 members of the community in 10 randomly selected villages.**Results** In most FGD the word asthma was known, although they did not understand the implication of the disease. The word COPD, however, was totally unknown. Most participants knew tuberculosis as a serious disease. Respiratory symptoms were common among men, women and children. In several communities respiratory symptoms were stigmatized and often associated with tuberculosis. Almost all the households used firewood for cooking, and the majority cooked indoors without any ventilation. The extent of exposure to tobacco and biomass fuel smoke was largely determined by their cultural tradition and gender, tribal origin and socio-economic factors. Many people were unaware of the damage to respiratory health caused by these risk factors, notably biomass smoke disproportionately affecting women and children. The trust in the health centres was low, particularly when it concerned chronic respiratory symptoms. The communities often used local herbs as treatment (boiled mango leaves) for respiratory symptoms. Salbutamol tablets were only available at the district hospital. Inhaled medication was not available at all.**Conclusion** The results of the FGDs reveal that many people of all ages have respiratory symptoms. The knowledge of chronic respiratory diseases, particularly COPD, is poor. The lack of knowledge in the rural community has created different beliefs and attitudes concerning respiratory symptoms. A priority should be increasing the knowledge of COPD in the various communities, and promoting awareness among healthcare workers about the detrimental health effects of these risk factors. .

**PD-775-31 Profile and risk factors of patients with obstructive airway diseases at Tikur Anbessa Specialised Hospital Chest Clinic, Addis Ababa, Ethiopia**

T Bayisa,<sup>1</sup> M Parekh,<sup>2</sup> J Tewodros,<sup>3</sup> F Oumer,<sup>1</sup> A Binegdie Bekele,<sup>1</sup> O Braendli,<sup>4</sup> C Sherman,<sup>5</sup> N Schluger.<sup>2,6</sup> <sup>1</sup>Division of Pulmonary and Critical Care Medicine, Addis Ababa University, Addis Ababa, Ethiopia; <sup>2</sup>Division of Pulmonary and Critical Care Medicine, Columbia University, New York, NY, <sup>3</sup>East African Training Initiative, Mailman School of Public Health at Columbia University, New York, NY, USA; <sup>4</sup>East African Training Initiative, Swiss Lung Foundation, Lausanne, Switzerland; <sup>5</sup>Division of Pulmonary and Critical Care Medicine, Brown University, Providence, RI, <sup>6</sup>East African Training Initiative, World Lung Foundation, New York, NY, USA. e-mail: madhavi.j.parekh@gmail.com

**Background:** Obstructive airway diseases are a major cause of morbidity and mortality worldwide. There is limited published data describing the characteristics and risk factors of obstructive airway diseases in Ethiopia. Understanding the characteristics of these patients and identifying risk factors is an important first step in developing effective interventions and future research. Therefore, the purpose of this study is to characterize and identify the risk factors of patients with obstructive airway diseases at Tikur Anbessa Specialized Hospital (TASH) chest clinic, in Addis Ababa, Ethiopia.

**Methods:** A retrospective, cross-sectional review of a clinical database of patients seen at TASH chest clinic, between April 2013-February 2014, was performed. All adult patients with a diagnosis of obstructive airway disease were identified; their demographic and clinical data were included in the analysis.

**Results:** During the study period, there were 144 patients seen with a clinical diagnosis of obstructive airway disease. Asthma was the primary diagnosis among 86% of patients; the remainder carried a diagnosis of chronic obstructive pulmonary disease (COPD). Spirometry was obtained for 56% of the patients; all patients with COPD and 57% of patients with asthma had an obstructive ventilatory defect (FEV1/FVC ratio of less than 0.7). Fifty six percent were females and 74.6% were from Addis Ababa. The mean age was 52.8 years. Only 16 were HIV positive. Among the participants, 26% and 27% had history of prior tuberculosis treatment, and prior pneumonia, respectively. Fifty percent were educated only to less than high school. Approximately 17% had ever smoked cigarettes, which was exclusively among men. Among COPD patients, 40% were ever smokers, and 40% were females. Among patients who reported symptoms 73%, 83% and 75% presented with cough, wheezing and dyspnea respectively.

**Conclusions:** The majority of patients with obstructive lung disease at TASH chest clinic are female, non-smoking asthmatics. Of those with spirometry, the majority demonstrated an obstructive ventilatory defect. Other risk factors, such as exposure indoor and/or outdoor air pollution are likely contributing to these findings. Future study will incorporate bronchodilator and/or methacholine challenge testing to improve accu-

racy of disease diagnosis, and will incorporate a broader study population to improve generalizability.

**PD-776-31 Sequelae of patients treated for pulmonary tuberculosis in Chest Clinic, Tikur Anbessa Specialized Hospital (TASH), Addis Ababa, Ethiopia**

A Binegdie Bekele,<sup>1</sup> M Parekh,<sup>2</sup> T Bayisa,<sup>1</sup> F Oumer,<sup>1</sup> O Braendli,<sup>3</sup> E J Carter,<sup>4</sup> C Sherman,<sup>4</sup> N Schluger.<sup>2,5</sup> <sup>1</sup>Pulmonary and Critical Care Medicine, Addis Ababa University, Addis Ababa, Ethiopia; <sup>2</sup>Pulmonary and Critical Care Medicine, Columbia University, New York, NY, USA; <sup>3</sup>East African Training Initiative, Swiss Lung Foundation, Lausanne, Switzerland; <sup>4</sup>Pulmonary and Critical Care Medicine, Brown University, Providence, RI, <sup>5</sup>East African Training Initiative, World Lung Foundation, New York, NY, USA. e-mail: madhavi.j.parekh@gmail.com

**Background** Pulmonary tuberculosis (TB) is one of the most common infectious diseases worldwide, and contributes significantly to morbidity and mortality in developing countries. Despite availability of effective treatment, a significant number of patients will suffer from permanent lung damage, which predisposes patients to numerous pulmonary complications. The purpose of this study is to examine the spectrum of chronic pulmonary disease encountered among patients who have been treated for tuberculosis at an outpatient chest clinic at Tikur Anbessa Specialized Hospital (TASH) in Addis Ababa, Ethiopia.

**Methods** This is a retrospective, cross-sectional analysis of patients registered in a clinical database at the chest clinic of TASH between January and December 2013. Patients with a history of pulmonary tuberculosis treatment were identified and included in the analysis.

**Results** During the study period, 676 patients were seen at the chest clinic of TASH. Among these patients, 134 (19.8%) presented with chronic pulmonary complications of TB. Three hundred seventy two patients (55%) were male, and the mean and median ages were 40 and 37 years, respectively. Of the study population, 83 (61.9%) patients had clinically significant parenchymal scarring and fibrosis, 40 (29.9%) had bronchiectasis, 5 (3.7%) had aspergillomas, 4 (3%) had granuloma/calcification, one (0.7%) had pleural thickening and one (0.7%) underwent pneumonectomy during the study period. In all age groups, fibrosis and bronchiectasis were the most common complications seen among patients who had previously treated for TB. Both fibrosis and bronchiectasis were more commonly seen among women than men.

**Conclusions** Fibrosis and bronchoectasis are the most common pulmonary complications of tuberculosis among patients encountered at the TASH chest clinic during the study period. This demonstrates the impact of pulmonary tuberculosis is beyond only management of active disease, but chronic disease as well. Additionally, the high prevalence of clinically significant sequelae of TB underlies the need for earlier diagnosis and institution of therapy. The recent addition of Xpert technology (rapid nucleic acid amplification testing for *M. tuberculosis*) to



TASH may assist in earlier diagnoses. Future study will include prospective collection of sequelae of tuberculosis and risk factors, and a broader population sample for analysis.

### PD-777-31 Minimally invasive extra-pleural thoracoplasty in the treatment of patients with destructive pulmonary tuberculosis

D Krasnov,<sup>1</sup> D Skvortsov,<sup>1</sup> M Reihrud,<sup>1</sup> Y Petrova,<sup>1</sup> M Chernova.<sup>1</sup> <sup>1</sup>Surgical, Novosibirsk Tuberculosis Research Institute, Novosibirsk, Russian Federation. Fax: (+738) 320 37 825. e-mail: kamenskaya\_85@bk.ru

A new version of extrapleural osteoplastic thoracoplasty with minimal access was developed in order to avoid complications of the classical approach: severe pain, significant cosmetic effect and, as a consequence, poor adherence of patients to this method of surgery.

**Materials and methods:** A randomized study of 288 patients who underwent osteoplastic thoracoplasty for destructive pulmonary tuberculosis. Group I (n=130) - patients osteoplastic thoracoplasty with minimal access, Group II (n=158) - a similar surgery is performed by classical method. Worsening of tuberculosis process prior to the surgery was observed by radiology in the majority of patients in group I - 129 (99,2 ± 0,8%), in group II - 138 (87,3 ± 2,7%) (p = 0,001,  $\chi^2$ ). Patients were bacillary in preoperative period in group I - 126 (96,9 ± 1,5%), in group II - 141 (89,2 ± 2,4%) (p=0,01,  $\chi^2$ ), it has been massive in 108 (85,7 ± 3,1%) and in 106 patients (75,2 ± 3,6%) (p = 0,03,  $\chi^2$ ). MDR was detected in 95 (73,1 ± 3,9%) and 119 (75,3 ± 3,4%) patients (p=0,67,  $\chi^2$ ).

**Results.** There were no intraoperative complications. Intraoperative blood loss was less than 400 ml in group I in 119 patients (91,5 ± 2,4%), in the comparison group - in 96 (60,8 ± 3,9%) (p = 0,00001,  $\chi^2$ ). In the postoperative period, complications occurred in group I in 15 (11,5 ± 2,8%) cases (1 patient was bleeding in the early postoperative period, and in 7 - the progression of respiratory failure, and 4 patients were with the progression of TB disease, in 3 patients - deep suppuration of surgical wounds occurred). In group II, complications were observed in 35 (22,2 ± 3,3%) patients (8 patients had a bleeding in the early postoperative period, and 9 patients were with the progression of respiratory failure, and 8 cases had the progression of TB disease, in 10 - deep suppuration of surgical wounds occurred) (p = 0,018,  $\chi^2$ ). Application of OT led to cease of bacterial discharge in 87 (69,0 ± 4,1%) patients of the study group and 103 (73,0 ± 3,7%) of the comparison group (p=0,76,  $\chi^2$ ). Closure of cavities was achieved in 96 (73,8 ± 3,9%) and 115 (72,8 ± 3,6%) patients, respectively (p=0,84,  $\chi^2$ ).

**Conclusion:** New method of surgical treatment of patients with destructive pulmonary tuberculosis will reduce the risk of postoperative complications by 10.7 % and significantly reduce intraoperative blood loss.

### PD-778-31 Pulmonary tuberculosis sequel

J De Los Rios,<sup>1</sup> Y Bravo,<sup>1</sup> E Mori.<sup>1</sup> <sup>1</sup>Medicine, Maria Auxiliadora Hospital, Lima, Peru. e-mail: jodelosrios@yahoo.com

**Background:** Describe the characteristics of patients with sequel of pulmonary tuberculosis.

**Design/Methods:** Descriptive Study. We evaluated 118 patients diagnosed with tuberculosis sequel attending the outpatient pulmonology office of Maria Auxiliadora Hospital during 2012–2013, to whom apply a data collection sheet to obtain demographic and clinical information.

**Results:** Of the total 118 cases, 66.1 % were women. The average age was 54.4 years, 50 % had a normal BMI, 68.64 % had only one episode of tuberculosis in his life, 79.66 % reported having completed treatment, 75.4% reported a regular treatment, 94.9% did not smoke, 36.4 % had a diagnosis of asthma, of which at 88.37 % the diagnosis was after episode of TB, 17.8 % had a diagnosis of pulmonary fibrosis, of which at 100% the diagnosis was later the episode of TB, 22.9% had a diagnosis of bronchiectasis, of which at 21.2% the diagnosis was after episode of TB, 10.2% had undergone chest surgery, of which at 100% had an indication for management of the sequel, 78 % present with wheezing, 61.9 % had dyspnea, 50.8 % have chronic cough, 44.9 % have at least 2 episodes of respiratory infections per year, 43.2 % present with hemoptysis, 22% has been hospitalized at least one time by a reason related to the sequel, 33% had emergency visit at least once, 45.7% had used antibiotics, 45.7% short-acting Beta 2 agonists and 43.2% short-acting anti-cholinergics in their management. Only 19.4% had received influenza vaccination and 6.7% received anti pneumococcal vaccination.

**Conclusion:** The sequel of tuberculosis has significant morbidity and its impact must be quantified as a public health problem.

## 25. ASTHMA, SPIROMETRY AND ARIS

### PD-779-31 Asthma and allergy among adults in Stockholm (3-HE study): associations with energy use, maintenance and the home environment in multi-family houses

D Norback,<sup>1</sup> E Lampa,<sup>1</sup> K Engvall.<sup>1</sup> <sup>1</sup>Department of Medical Sciences, Uppsala University, Uppsala, Sweden. Fax: (+48)18 51 9978. e-mail: dan.norback@medsci.uu.se

**Background** There are few population studies on associations between asthma and allergies in adults and energy consumption, maintenance and other home environment factors.

**Design/methods** Risk factors for asthma and allergy were studied in a stratified random sample of adults in Stockholm. Totally 7554 subjects participated (73%) (one invited subject/dwelling). Cluster analysis was used to select 20 variables. Associations were studied by multiple



logistic regression analysis, including 16 home environment variables with additional adjustment for gender, age, current smoker, being foreign born, family income/year, and number of years in the current dwelling.

**Results** Totally 10.9% reported doctor's diagnosed asthma, 22.0% doctor's diagnosed allergy and 22.6% pollen allergy (hay fever). Younger subjects had more pollen allergy ( $p<0.001$ ) and doctor's diagnosed allergy ( $p<0.001$ ) but there were no associations between asthma and allergy and family income (socioeconomic status) or being foreign born. Doctor's diagnosed asthma was more common in dwellings with humid air ( $OR=1.71$ ;  $p=0.03$ ). Humid air was defined as either window pane condensation or slowly drying towels. Doctor's diagnosed allergy was more common in buildings with mechanical supply-exhaust ventilation system ( $OR=1.45$ ;  $p=0.02$ ), in redecorated apartments ( $OR=1.50$ ;  $p=0.01$ ) and in apartments with mouldy odour ( $OR=2.47$ ;  $p=0.01$ ). Management accessibility influenced doctor's diagnosed asthma ( $p=0.03$ ) and allergy ( $p=0.009$ ). Pollen allergy was less common in buildings consuming more energy for heating ( $OR=0.75$  for an interquartile (IQR) change;  $p=0.005$ ) (IQR=28 kWh/m<sup>2</sup> and year) and less common where the work management was on contract ( $OR=0.67$ ;  $p=0.008$ ) as compared to management by the building owner. Moreover, pollen allergy was more common in apartments with humid air ( $OR=1.74$ ;  $p=0.001$ ) and mould odour ( $OR=2.48$ ;  $p=0.003$ ).

**Conclusions** Asthma and allergies among adults in Stockholm are more common in buildings with less energy use for space heating and in dwellings with recent redecoration, mould odour, water leakage and humid air. There is a need to reduce chemical indoor emissions and control building dampness and microbial growth in dwellings. Increasing the energy efficiency in the existing buildings stock may have consequences for health. More studies are needed on the health consequences of different types of building management.

#### **PD-780-31 Increasing prevalence of complicated pneumonia in children after routine pneumococcal vaccination**

G Wong.<sup>1</sup> <sup>1</sup>Paediatrics, Chinese University of Hong Kong, Shatin, Hong Kong. Fax: (+852) 264 51570. e-mail: wingkinwong@cuhk.edu.hk

**Background:** Several studies suggested that use of PCV-7 may be associated with increased incidence of complicated pneumonia. From September 2009 PCV7 was included in Hong Kong's publicly funded immunization schedule.

**Methods:** We conducted a retrospective study using data from the central computerized database of all public hospitals in Hong Kong for children 18 yrs or below to determine the standardized rates of hospitalization pre- and post-PCV7 vaccination by retrieving all cases with a discharge diagnosis of pneumonia, complicated pneumonia, invasive pneumococcal diseases, pneumococcal bacteremia from Jan 2005 to Dec 2013. Records from

one tertiary university hospital were analyzed in details to evaluate the types of invasive pneumococcal diseases.

**Results:** The adjusted incidence rates of complicated pneumonia for children under 18 years and under 5 years have increased from 6.9 (2005 to 2008) to 13.6/100,000/yr (2010 to 2013) ( $P<0.01$ ), and 14.1 to 28.5 respectively ( $P<0.01$ ). In our tertiary care hospital, 51 children were admitted with complicated pneumonia over the 9 year period with 35 (69%) presenting in the post-PCV period. 17 were due to Strept pneumoniae with 4 deaths in the post-PCV7 period (due to serotype 3 and 19A). There was also a statistically significant increase of pneumococcal related hemolytic uremic syndrome.

**Conclusion:** A significant increase of complicated pneumonia was found in children shortly after PCV7 vaccination was started in Hong Kong. Severe cases were caused by serotypes not covered by PCV7 or 10. PCV-13 for all at risk children may reduce severe infections due to serotypes 3 and 19A but on-going surveillance of possible serotype replacement is needed as we move to newer types of PCV.

#### **PD-781-31 Effects of pharmacist counseling in inhalation medication adherence and asthma control in asthma patients at one stop service clinic**

P Junlaor,<sup>1</sup> Visa Boontod,<sup>1</sup> N Chindavech.<sup>2</sup> <sup>1</sup>Ambulatory Clinic. Pharmacy Department, Buriram Hospital, Buriram, <sup>2</sup>Intensive Care Medicine, Buriram Hospital, Buriram, Thailand. e-mail: wanumrung1589@gmail.com

**Backgrounds:** Asthma is a leading cause of death and major health problem and costs in Thailand. Patient adherence in asthma is essential to optimize disease control. However in real life practice, poor adherence to inhalation medication is common. At asthma clinic, pharmacists play a critical role for help patients understand the disease, educate inhaler devices technique to improve adherence and that it might control asthma symptom.

**Methods:** A descriptive study of 82 asthma patients who consecutively follow up at least 4 times per year at one stop service asthma clinic from October 2011 to February 2014 before and after pharmacist counseling in term of adherence, lung functions and asthma control. Counseling included teaching and demonstration inhaler device and also educate in disease to patients one by one.

**Results:** Before pharmacist counseling, we found that patients with good adherence was 31.7% and after counseling by brief educate in disease knowledge and demonstration inhaler devices technique adherence increase to 63.4%, 84.1% in 3 months and 1 year follow up ( $p<0.05$ ). The peak expiratory flow rates measured before and after improved with statistical significance ( $p<0.05$ ). Asthma total control was also increased from 12.2% to 30.5%, 42.7% in 3 months and 1 year follow up ( $p<0.05$ ).

**Conclusions:** Pharmacist counseling in asthma patients at one stop service clinic can intervene to help patients improve their adherence and asthma control.

### PD-782-31 Tuberculosis en pacientes ingresados, como neumonía adquirida en la comunidad en sala de emergencia de un hospital público del Perú

M Paredes Moreno,<sup>1</sup> O Gayoso,<sup>2,3</sup> J Alave,<sup>4</sup> G Mas.<sup>5</sup>

<sup>1</sup>Neumología, Hospital Maria Auxiliadora, Lima,

<sup>2</sup>Neumología, Hospital Nacional Cayetano Heredia, Lima,

<sup>3</sup>Medicina, Universidad Peruana Cayetano Heredia, Lima,

<sup>4</sup>Infectología, Asociación Civil Impacta Salud y Educación, Lima, <sup>5</sup>Medicina, Hospital Arzobispo Loayza, Lima, Peru.

e-mail: mariangelica\_78@hotmail.com

**Background:** Tuberculosis (TB) representa un gran problema de salud pública en el mundo. En países con alta prevalencia de tuberculosis los pacientes acuden frecuentemente a recibir atención médica ambulatoria y/o emergencia. La presentación clínica inespecífica y la diversidad de los hallazgos radiográficos, a veces no permiten diferenciar tuberculosis pulmonar de la neumonía adquirida en la comunidad (NAC). Se plantea el estudio con el objetivo de determinar la frecuencia de tuberculosis en pacientes admitidos como neumonía adquirida en la comunidad en un servicio de emergencia de un hospital público.

**Table** Características socio demográfico y clínico de los pacientes ingresados como NAC en el Servicio de emergencia – Periodo de octubre 2012 – febrero 2013

Variables	TB (n = 19)%	No TB (n = 120)%	p?
Edad ¶	39.05 (± 22.48 )	60.75 (± 21.42)	< 0.001
Sexo			NS
Mujer	(11 )57.89%	(58) 48.33%	
Contacto TB			< 0.001
Intra domiciliario	(5) 26.32%	(1) 0.83%	
Comorbilidades			NS
VIH	(3) 15.79%	(10) 8.33%	
DM2	(1) 5.26%	(13) 10.83%	
TB previa	(1) 5.26%	(19) 15.83%	
Tiempo de enfermedad			<0.05
Menor a 7 días	(10) 52.63%	(29) 24.17%	
De 7 días a 2 semanas	(2) 10.53%	(56) 46.67%	
Más de 2 semanas	(7) 36.84%	(35) 29.17%	
Uso de antibióticos previo	(3) 15.78%	(16) 13.33%	NS
Síntomas Principales			
Tos	(18) 94.74%	(116) 96.67%	NS
Expectoración	(13) 68.42%	(89) 74.17%	NS
Fiebre	(14) 73.68%	(69) 57.50%	<0.05
Disnea	(15) 78.95%	(65) 54.17%	NS
Hemoptisis	(3) 15.78%	(10) 8.33%	NS
Baja de peso	(7) 36.84%	(22) 18.33%	<0.05
Bioquímica			
Leucocitos mm3 ¶	10.103x10 <sup>3</sup> (±4.556)	12.606x10 <sup>3</sup> (±6.688)	NS
PO2	70.05 (± 13.26)	73.89 (±16.56)	NS
SIRS	(14) 73.68%	(80) 66.66%	NS

¶ Se reporta la mediana (+/- desviación estándar) para las variables continuas y el porcentaje para las categóricas. El valor de p corresponde a la comparación entre TB y No TB ? Valor de p < 0.05 en negrita y NS representa p > 0.05 (pruebas de  $\chi^2$ , exacta de Fisher o Kruskal-Wallis de acuerdo a si la variable es categórica o continua).

**Design/Methods:** Estudio descriptivo, transversal exploratorio de la información clínica de pacientes

admitidos como NAC al Hospital Nacional Cayetano Heredia desde Octubre 2012 a Febrero 2013. Se excluyó a pacientes hospitalizados los últimos tres meses o que tuvieran tuberculosis activa. Tuberculosis fue definido como la identificación del *M. tuberculosis* por métodos microbiológicos o hallazgos histopatológicos.

**Results:** De 186 pacientes que fueron admitidos como NAC durante el periodo de estudio, 160 cumplieron los criterios de inclusión. La frecuencia de tuberculosis fue 11.88%, la mediana de la edad fue 39.05 años, 57% de los pacientes fueron mujeres. El tiempo de enfermedad menor a 7 días se reportó en 52% de los pacientes. En el análisis multivariado la edad y contacto intradomiciliario se asociaron independientemente con el diagnóstico de TB.

**Conclusion:** La frecuencia de TB fue 11.88%, y las características clínicas encontradas en este estudio podrían ser utilizadas para proponer estrategias de control nosocomial de TB en los hospitales públicos peruanos, específicamente en las unidades de emergencia.

### PD-783-31 Spirometry reference values and predictive equations for elderly north Indians

A K Janmeja,<sup>1</sup> P Mohapatra,<sup>2</sup> R Gupta.<sup>3</sup> <sup>1</sup>Pulmonary Medicine, Government Medical College & Hospital, Chandigarh, <sup>2</sup>Pulmonary Medicine, AIIMS, Bhubaneswar, <sup>3</sup>Pulmonary Medicine, Government Medical College & Hospital, Chandigarh, India.

e-mail: ashokjanmeja@hotmail.com

**Background:** Spirometry is the most common test used for assessing pulmonary functions and the standard parameters of utmost value in various respiratory diseases are FVC, FEV1 and PEFR. The reference values in the elderly population of north India is lacking. The aim of this study was to generate normal spirometry reference values and derive predictive equations for the elderly north Indian subjects.

**Design/Methods:** A total of 366 subjects of both gender (123 females and 243 males) above 60 years of age, non smoker and without prior respiratory or cardiac disease were randomly selected from the general population of a north Indian city. Spirometry was performed by a trained technician as per ATS standards using the same equipment. The predictive equations were derived separately for males and females using multiple regression analyses.

**Results:** Mean FVC, FEV1 and PEFR calculated for male subjects were 2.70 +/- 0.64 litres, 2.16 +/-0.51 litres and 7.23 +/- 2.13 L/s respectively. In females, the values for mean FVC, FEV1 and PEFR were 2.06 +/- 0.90 litres, 1.70 +/- 0.80 litres and 4.96 +/- 1.68 L/s respectively. Observed spirometry parameters revealed negative correlation with advancing age whereas positive correlation with height. On comparison, a statistically significant difference was found between our results and available spirometry values in elderly from various parts of world including India. The equations derived for the spirometry values were dependent on age and height of the subjects.

**Conclusion:** The present study further emphasises that reference spirometry values and predictive equations

should come from the population on which they are to be applied. In the Northern India scenario, the reference values derived through this study may help clinicians averting over diagnosis/treatment of elderly and to look for alternative causes of dyspnoea other than the respiratory ones. However, more data may be collected from the region.

**PD-784-31 Changes in severity of pandemic influenza A H1N1/2009 Infection from pandemic to post pandemic period, Himachal Pradesh, India**

V Mehta,<sup>1</sup> P Sharma,<sup>1</sup> R Guleria,<sup>1</sup> S Ganju,<sup>1</sup> D Singh,<sup>1</sup> A Kanga.<sup>1</sup> <sup>1</sup>Microbiology, Indira Gandhi Medical College, Shimla, Himachal Pradesh, India. Fax: (+91)1772627601. e-mail: vinodkholighat@gmail.com

**Background:** To strengthen public health intervention strategies, data on severity of pandemic and post-pandemic influenza infection are scarce. To assess associated morbidity and mortality, we determined factors influencing the outcome of pandemic and post pandemic influenza A H1N1/2009 (pH1N1) infection.

**Design/Methods:** Retrospective hospital based study was done from 1<sup>st</sup> August 2009 - 9<sup>th</sup> August 2010 (pandemic) to 10<sup>th</sup> August 2010 to 31<sup>st</sup> March 2013(post-pandemic) by reviewing medical records using close-ended instrument for collecting demographic & clinical profile of the study samples. Nasopharyngeal/throat swabs, collected in viral transport media, processed using QI Amp® viral RNA Mini Kit from Qiagen, USA for RNA extraction and reverse transcription & amplification of the target genes was done by real time reverse transcriptase polymerase chain reaction using CDC primers and probes. Data was analysed using Epi info 7.1.3, 2013.

**Results:** Out of 969 samples processed, 48.67% (55) were reported in pandemic and 51.33% (58) in post pandemic period. Sex distribution, mean age, & hospital stay were 56.36% (31) females, 29.34 years and 2.87 days vs. 53.45%(31) females, 41.54 years and 4.3 days respectively for pandemic & post pandemic period. Infection of pH1N1 was observed in healthier [80% (44)] in pandemic period as compared to comorbid 53.45% (31) during post pandemic period ( $\chi^2=12.12$ ,  $p<0.000$ ). Case fatality rate was 34.54% (19) and 18.96% (11) in pandemic and post pandemic period respectively which was statistically significant ( $\chi^2=2.76$ ,  $p<0.03$ ). Mortality shift was observed from younger, 31–40[52.63% (10)] years to older,  $\geq 50$  [82.73% (8)] years and from healthier, 84.21% (16) to co-morbid, 90.91% (10) during pandemic to post pandemic period.

**Conclusion:** We observed decreased virulence and low mortality from pandemic to post pandemic period. It affected young healthy adults in the pandemic period, with shift to old and co-morbid during post pandemic, may be attributed to lack of immune memory among younger population as compared to the elderly who had acquired it during previous pandemics. We suggest the need of early public health interventions and access to

diagnostic methods with initiation of treatment as early as possible.

**PD-785-31 School-based asthma screening: state of asthma for undeserved population in Bogotá**

D Crispin Cruz,<sup>1</sup> J Jurado,<sup>1</sup> A Casas,<sup>1</sup> J Berrio,<sup>1</sup> M González-García,<sup>1</sup> E Duenas,<sup>1</sup> D Maldonado,<sup>1</sup> C A Torres-Duque.<sup>1</sup> <sup>1</sup>Fundacion Neumologica Colombiana, Bogota, Colombia. e-mail: dncrispin@gmail.com

**Background:** Lack of access to health care services and scarce ability to detect asthma by the primary care services are crucial determinants of failure to reach international asthma management goals: early diagnosis and control; School-based screening and educational programs might be good option to reduce asthma morbidity. The aim of this research is to describe asthma screening process and the situation of asthma in two public schools located in deprived areas in Bogotá.

**Design/Methods:** Crosssectional survey. A health care team using a mobile health care unit (Asmamóvil) went to two public schools to screening children from 7 to 11 years old using an International Study of Asthma and Allergies in Childhood (ISAAC) written questionnaire. The format was sent to home to be filled by a caregiver. If any positive answer was detected in the questionnaire the child and its caregiver were given an appointment at mobile unit where a trained physician evaluated clinical status, lung function was assessed by spirometry. Diagnosed of asthma was based on NAEPP guidelines criteria. Results were analyzed using SPSS software.

**Results:** A total of 920 school children were screened with a median age of  $9.1\pm 1.1$ ; 54 % males. ISAAC questionnaire response rate was 85 % (790) of which 30% (229) reported at least one positive answer. After a phone request 203 children were evaluated, 55% (113) of them were diagnosed with asthma, given an asthma prevalence of 14%, when asking about previous asthma diagnosis 75% (85) has not been diagnosed before despite history of symptoms. Asthma severity according to guidelines was as follows: intermittent 14 %, mild 38%, 42% moderated, 4% severe. Ninety percent have not well or poorly asthma control.

**Conclusion:** Asthma prevalence is high; in spite of asthma management guidelines widespread, under diagnosed rates and lack of control remains problematic. Screening at school setting gives a good opportunity to detect children with asthma evidenced the reality of communities with low access to health care services. Parallel, mobile health care unit might become an opportunity to detect and offer education and treatment for children with asthma.



### PD-786-31 Economic burden of acute respiratory infections in a rural community in north India

R Amarchand,<sup>1</sup> DR Purkayastha,<sup>2</sup> SK Peasah,<sup>3</sup> FS Dawood,<sup>4</sup> M-A Widdowson,<sup>4</sup> RB Lal,<sup>4</sup> CS Pandav,<sup>2</sup> A Krishnan.<sup>2</sup> <sup>1</sup>Projects, INCLEN Trust International, New Delhi, <sup>2</sup>Centre for Community Medicine, All India Institute of Medical Sciences, New Delhi, India; <sup>3</sup>Pharmacy Practice, Mercer University College of Pharmacy, Atlanta, GA, <sup>4</sup>Influenza Division, Centers for Disease Control, Atlanta, GA, USA. e-mail: kanandiyer@yahoo.com

**Background:** The economic burden of Acute Respiratory Infection (ARI), a major cause of mortality and morbidity among children < 5 years in developing countries, where health insurance is typically unavailable, needs to be better understood. The study estimates the annual cost of ARI among children aged <5 years in a rural community in northern India.

**Methods:** Data from population-based ARI surveillance in Ballabgarh and a cost of illness study of ARI from the same area and time were used. Under ARI surveillance, all children aged <10 years of in four villages were screened weekly for symptoms of ARI, who then underwent clinical examination to be categorized as no pneumonia, pneumonia, or severe pneumonia/severe illness as per WHO criteria. The outpatient and inpatient costs were estimated among subjects attending hospitals in the study area while costs among medically non-attended was from those identified in the surveillance. Total direct costs included medical (consultation, investigations, and medications) and non-medical (travel and food) costs while loss of income was taken as indirect cost derived by multiplying days lost with per capita income. For public institutions, WHO-CHOICE estimates were added as provider costs. The analysis was restricted to data from children aged <5 years. The number of episodes was multiplied by median cost of ARI in non-medically attended, outpatient, and inpatient care in public and private settings. These were totaled and divided by mid-year under-five population to get annual cost per child.

**Results:** During August 2012 to Aug 2013, 11,292 ARI episodes were reported among under children <5 years (n=1,506), of which 29% were non-medically attended, 71% were seen at outpatient and 0.4% were admitted. Of all ARI episodes, 2.6% (291) were classified as pneumonia and 1.3% (152) as severe pneumonia or severe disease. The total annual cost due to ARI among under-fives in this community was US\$60,217 (US\$3,596 for non-medically attended, US\$49913 for outpatient care and US\$6708 for Inpatient care) and the annual cost per child was US\$39.98. Most of this cost was direct cost of treatment.

**Conclusions:** The cost of ARI to the community was considerable; especially for the poor (annual income below US\$163) who comprise almost one quarter of population. In order to support informed decision making, there is a need to conduct economic evaluation of different approaches to reduce the ARI burden including relevant immunization This study was sup-

ported in part by cooperative agreement U01 IP000492 from the Centers for Disease Control and Prevention, Atlanta, USA

Table 1. Annual Cost (US\$) due to ARI among under-five children (n = 1506) in rural North India

ARI Episode classification depending on Health care sought	Number of episodes	Median Direct cost	Median Indirect cost	Median Total cost	Total cost
Non-medically attended	3269	1.1	--	1.1	3596
outpatient (public)	4490	4.9	--	4.9	22001
outpatient (private)	3489	8	--	8	27912
Inpatient (public)	2	54	24	78	156
inpatient (private)	42	135	21	156	6552
Total episodes	11292	--	--	--	60217

### PD-787-31 Influence of abdominal obesity on pulmonary function indices of abdominal surgery patients

A Akinremi,<sup>1</sup> A Orotokun,<sup>1</sup> A Sanya.<sup>1</sup> <sup>1</sup>Department of Physiotherapy, College of Medicine, University of Ibadan, Ibadan, Nigeria. e-mail: ogooluwa2@yahoo.com

**Background:** Abdominal surgery patients are usually prone to post-operative respiratory complications. Pre-operative assessment is aimed at identifying and addressing modifiable risk factors such as obesity. Preliminary studies show that the impact of abdominal obesity on pulmonary function indices in this group of patients is often overlooked. In addition to the effects of general anesthesia and incision pain on respiration, abdominal obesity may further compromise pulmonary function and consequently heighten the risk of pulmonary complications after surgery. We investigated the influence of abdominal obesity on pulmonary function indices of abdominal surgery patients with abdominal obesity.

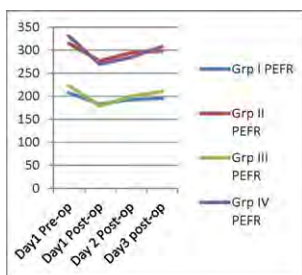
**Design/Methods:** A total of 50 patients, comprising of 25 male and 25 female patients in the surgical wards of a tertiary teaching hospital in Ibadan, Nigeria participated in this study. Participants were between the ages of 20–60 years with no history of smoking and were able to perform spirometric manoeuvre. Waist circumference (WC) were measured and participants classified into 4 groups: group 1-male with WC>102cm; 2-male with WC<102cm, group 3-females with WC>88cm and group 4-female with WC<88cm. Weight, height, body mass index, Forced expiratory volume in first second (FEV1), forced vital capacity (FVC) and peak expiratory flow rate (PEFR) of participants were taken day-1 pre-op; while FEV1, VC, PEFR and pain score using visual analogue scale were taken day-1, -2, -3 post-surgery. Data summarized using mean and standard deviation and analyzed using independent t-test; while p was set < 0.05.

**Results:** At baseline there was significant difference in FEV1 (1.18±0.02 vs. 1.85±0.69), FVC (1.32±0.59 vs. 2.25±0.75) and PEFR (207.5±9.57 vs. 314.5±50.63) between participants in group I and group II; while for the female category (group III vs group IV) there was significant difference in FVC (1.67±0.75 vs. 2.52±0.79) and PEFR (222.86±18.90 vs. 330.77±37.74) but no significant difference was observed in FEV1 (1.45±0.60



vs.  $2.00 \pm 0.78$ ) and FER ( $0.88 \pm 0.05$  vs.  $0.79 \pm 0.14$ ). There was no significant difference in the pain score between the groups across the various assessment periods. Day-3 post surgery, there was significant difference in FEV1 ( $1.09 \pm 0.04$  vs.  $1.68 \pm 0.55$ ), FVC ( $1.21 \pm 0.53$  vs.  $1.95 \pm 0.65$ ) and PEFR ( $195.0 \pm 5.77$  vs.  $298.10 \pm 51.15$ ) between group I and II. In the female category however, significant difference was observed in FVC ( $1.44 \pm 0.50$  vs.  $2.04 \pm 0.64$ ) and PEFR ( $210.0 \pm 20.82$  vs.  $307.86 \pm 38.06$ ) between participants in group III and group IV. Pulmonary function impairment persisted and worsened in all the groups by day-3 post surgery; but the impairment in the male and female obese groups was 40% more compared with the non-obese groups

**Conclusion:** Respiratory function indices (FEV1, FVC and PEFR) in males, FVC and PEFR in females were influenced by abdominal obesity among surgery patients. Abdominal obesity should be considered when assessing patients for risks of post-operative respiratory complications and adequate steps taken to maximize lung function before the surgery.



**Figure** PEFR of participants in Groups I, II, III and IV across the assessment periods

**Key:**

Grp I PEFR - Peak expiratory flow rate of male participants with abdominal obesity  
 Grp II PEFR - Peak expiratory flow of male participants without abdominal obesity  
 Grp III PEFR - Peak expiratory of female participants with abdominal adiposity  
 Grp IV PEFR - Peak expiratory of female participants without abdominal adiposity

### PD-788-31 Ethnic differences in adverse drug reaction of asthma medication: a systematic review

Y Hu,<sup>1</sup> L Cantarero Arévalo.<sup>1</sup> <sup>1</sup>Pharmacy, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark. e-mail: wvj202@alumni.ku.dk

**Background:** Adverse drug reactions (ADRs) of asthma medications attract widespread attention because of the high prevalence and long-term use of these drugs. In the American context, there is evidence suggesting that African Americans are facing higher risk when using  $\beta_2$ -adrenergic receptor agonists. However, information on ethnic diversity of ADRs of asthma medications is rare.

**Objectives:** To investigate how ethnic minorities are involved in adverse reaction assessment in clinical trials and observational studies, and to examine the relationship between ethnic background and ADRs of different asthma medications.

**Methods:** PubMed was searched from origin until March 2014 for studies reporting ADRs for asthma medications

according to ATC RO3 involving ethnic minorities. Information on ethnic background, stage of disease, type of intervention, ADR reporting rates, type and seriousness of ADRs and study design was extracted.

**Results:** 29 research papers were included in the systematic review, in which 15 were randomized clinical trials, 6 were pooled analysis of randomized clinical trials, 6 were prospective observational studies and 2 were case reports. Subjects were categorized into ethnic groups as 'White (Caucasian)/Black (African American)/Asian (Oriental)/Hispanic/other'. All drug groups within ATC RO3 were involved. Among all the research papers except the case reports, 1 was conducted exclusively on African Americans, while the remaining 26 were conducted on at least two ethnic groups. Only 7 of them mentioned comparisons of ADRs in different ethnic groups. Such comparisons were either statistically insignificant or not able to lead to results due to lack of power in study samples.

**Conclusions:** Few studies reporting ADRs from use of asthma medications in different ethnic groups were identified in the literature. Ethnic diversity of ADRs of asthma medications were hardly stated, regardless of drug types.

### PD-789-31 Pulmonary hydatid cyst: clinical features and outcome

A Ayari,<sup>1</sup> S Bacha,<sup>1</sup> N Chaouech,<sup>1</sup> H Blibech,<sup>1</sup> H Racil,<sup>1</sup> S Cheikh Rouhou,<sup>1</sup> M Zarrouk,<sup>1</sup> A Chabbou.<sup>1</sup> <sup>1</sup>Tunis El Manar University. FMT. Abderrahmen Mami Hospital, Laboratoire de recherche Etude et prévention des maladies liées au tabac, Ariana, Tunisia. e-mail: han-no@hotmail.fr

**Introduction:** Hydatid pulmonary disease is one of common world-wide health problems especially in endemic countries. The aim of this study was to assess clinical presentations, surgical approach and outcome of this disease.

**Methods :** Retrospective study of all pulmonary hydatid cysts diagnosed in our Department of Respiratory Pathology in The university hospital of Ariana, from January 2006 to December 2013.

**Results :** Twenty one patients are included. The median age was 36,35 years old (range 15 to 70). Smoking was found in 11 (52%) cases. The most common presenting symptoms were cough (86%) and chest pain (78%). Hemoptysis was found in 4 (20%) cases. Single sharply demarcated round or oval homogenous opacity was the commonest radiological sign (81.13%). CT scan was performed in 10 cases essentially when a complication was suspected. Serological test was performed in only 77% of patients and it was positive in all cases. At presentation, 7 patients have complicated hydatid cyst, lung abscess in 10,38%, pleural involvement in 13,21% and pneumonitis in 7.55% of the cases. Bilateral involvement occurred in 3 patients (14%), simultaneous hepatic cysts in 5 (23%) and intrathoracic extrapulmonary involvement in 1 (4%). 76% of patients presented a single hydatid pulmonary cyst. Ninety five percent (95%) of patients underwent surgery. 5 (23%) of them received additional chemotherapy with Albendazole.

Surgery consists of pericystectomy in 17(84%) and lobectomy in 3 (15%).

**Conclusion :** All pulmonary hydatid cysts should be surgically treated as soon as possible after the diagnosis in order to avoid complications, preserve the maximal lung parenchyma and yield excellent outcomes.

## 26. XPERT MTB/RIF: IMPLEMENTATION AND PERFORMANCE

### PD-790-31 The utility of Xpert® MTB/RIF as a screening tool among medical in-patients

C Heidebrecht,<sup>1</sup> L J Podewils,<sup>2</sup> A Pym,<sup>3</sup> T Cohen,<sup>4,5</sup> T Mthiyane,<sup>1</sup> D Wilson.<sup>6</sup> <sup>1</sup>Clinical And Biomedical Tuberculosis Research Unit, Medical Research Council, Durban, South Africa; <sup>2</sup>Division of Tuberculosis Elimination, Centers for Disease Control and Prevention, Atlanta, GA, USA; <sup>3</sup>KwaZulu-Natal Research Institute for Tuberculosis and HIV, Durban, South Africa; <sup>4</sup>Division of Global Health Equity, Brigham and Women's Hospital, Boston, MA, USA; <sup>5</sup>Epidemiology, Harvard School of Public Health, Boston, MA, USA; <sup>6</sup>Medicine, Edendale Hospital, Pietermaritzburg, South Africa. e-mail: christine.heidebrecht@gmail.com

**Background** The discovery that a substantial fraction of medical inpatients in South Africa have active and drug-resistant forms of tuberculosis (TB) suggests an urgent need to improve screening of patients upon admission. Xpert® MTB/RIF (GeneXpert) detects both active TB and resistance to rifampicin (RIF) within two hours and can be administered at the point of care. We conducted a study at Edendale Hospital in Pietermaritzburg, South Africa, to assess the yield, feasibility, and utility of GeneXpert as a screening tool for medical inpatients.

**Methods** All newly-admitted adults ( $\geq 18$  years) who had received fewer than three doses of TB treatment and could provide informed consent were eligible to participate. Consecutive patients admitted to Edendale's five medical wards were enrolled between 12 March and 13 June 2013. Each consenting patient was asked to provide a sputum sample for GeneXpert, smear and culture. Demographic, clinical and exposure data were obtained through patient interviews and chart abstraction.

**Results** Among 709 patients admitted to medical wards during the study period, 346 (49%) patients were eligible, and 291 (41%) were enrolled and able to provide a sputum sample. GeneXpert results were available for 271 patients. TB was detected by GeneXpert in 16% (n=44) of participants, and among these, RIF-resistance was detected in 9% (n=4). GeneXpert-positive patients comprised 58% of those diagnosed with TB. In addition to bacteriological tests, TB diagnoses were based on chest radiography (CXR) (performed on all newly-admitted inpatients), extra-pulmonary imaging and clinical observations. When patients in whom TB was suspected, investigated or identified by other means were excluded, GeneXpert testing yielded only two additional TB cases. However, GeneXpert testing resulted in immediate detection of RIF-resistance in four patients, followed by transfer to a specialized TB facility.

**Conclusions** In institutional settings where CXR and the initiation of TB therapy without microbiological confirmation is routine, the utility of GeneXpert as a TB screening tool may be limited. Its value in rapidly detecting drug resistance and informing infection control procedures, including appropriate treatment initiation and patient relocation, may be considerably higher. In high-prevalence HIV-TB settings and open medical wards, GeneXpert has a role and should be considered for integration as a screening tool for all patients entering the hospital.

### PD-791-31 Xpert MTB/RIF test implementation in a resource-limited setting with high MDR-TB and HIV burden

K Oh,<sup>1</sup> A Tesfaye,<sup>2</sup> JY Kim,<sup>1</sup> A Endris,<sup>3</sup> H Kumssa,<sup>4</sup> G Yosef,<sup>4</sup> EJ Park,<sup>1</sup> BH Lee.<sup>3</sup> <sup>1</sup>Department of Program Cooperation, Korean Institute of Tuberculosis, Chungbuk, Republic of Korea; <sup>2</sup>Addis Ababa Health Regional Laboratory, Addis Ababa, <sup>3</sup>Ethiopia Representative Office, Korea International Cooperation Agency, Addis Ababa, <sup>4</sup>TB-HIV team, Addis Ababa City Administration Health Bureau, Addis Ababa, Ethiopia. e-mail: kyunghyun.oh@gmail.com

**Background:** Although Xpert MTB/RIF test is a promising new diagnostic technology, its optimal usage in real settings is not established yet. Hence it is critical to assess its feasibility in various settings, especially with high multidrug-resistant tuberculosis (MDR-TB) and/or HIV burden. This study was aimed to evaluate the feasibility of Xpert MTB/RIF test for the diagnosis of sputum smear-negative tuberculosis (TB) and/or rifampicin (RMP) resistance among MDR-TB suspects and people living with HIV at regional level with high MDR-TB and HIV burden.

**Design/Methods:** Xpert MTB/RIF test was conducted among MDR-TB suspects and people living with HIV in Addis Ababa after sputum smear microscopy at Addis Ababa Health Regional Laboratory between April 2013 and Jan 2014.

**Results:** Of a total of 312 cases requested for Xpert MTB/RIF test, 201 (64.4%) were positive for MTB. A total of 66 rifampicin resistant results were found (32.8% of positive tests). Of all tests conducted, 4 (1.3%) failed. Among those who had TB suggestive symptoms with smear negative results and a previous anti-TB treatment history (n=15), 33.3% were MTB positive, of whom 20% were proved to be rifampicin resistant. Among those who were smear positive cases experiencing a previous anti-TB treatment (n=146), 87% were positive for MTB, among whom 37% showed rifampicin resistant results. Among the people living with HIV who had TB suggestive symptoms with smear negative results (n=33), 9.1% were found positive for MTB, none of whom were rifampicin resistant.

**Conclusion:** Xpert MTB/RIF test achieved additional yield of TB cases among MDR-TB suspects and people living with HIV and identified substantial amount of rifampicin resistance prior to conventional drug susceptibility test (DST) in the study. If Xpert MTB/RIF test is routinely implemented at regional level with high MDR-

TB and HIV burden, it will play an important role for controlling TB within the national TB control program.

### PD-792-31 Role of Xpert MTB/RIF to detect rifampicin resistant tuberculosis among the presumptive drug-resistant tuberculosis patients in Bangladesh

S Hossain,<sup>1</sup> M Akramul Islam,<sup>1</sup> S Islam,<sup>1</sup> M Siddiqui,<sup>1</sup> A Hossen,<sup>1</sup> M Rahman,<sup>2</sup> S Sultana.<sup>3</sup> <sup>1</sup>HNPP, BRAC, Dhaka, <sup>2</sup>DGHS, NTP, Dhaka, <sup>3</sup>MDR-TB, WHO, Dhaka, Bangladesh. Fax: (+880)28823542. e-mail: sthossain22@gmail.com

**Background:** Xpert MTB/RIF has been introduced as a first line tool for rapid diagnosis of Multi Drug Resistant-Tuberculosis (MDR-TB) on April, 2012 in Bangladesh. Patients identified as Rifampicin Resistant-TB (RR-TB) are directly enrolled for MDR-TB treatment as per present National TB Control Program (NTP) policy. All presumptive Drug Resistant-TB (DR-TB) patients were classified as nine criteria by NTP. The study was aimed to determine the proportion of Rifampicin Resistant (RR) among the presumptive MDR-TB patients and to assess the implication of their categorization in routine programmatic setting.

**Methods:** The study was conducted in 12 Xpert centers. Tests results of Xpert MTB/ RIF for all 5,988 presumptive DR-TB patients were collected through structured data collection proforma between April, 2012 to March, 2014. The nine criteria of presumptive DR-TB patients as adopted by NTP are failures of CAT-I (remain positive at month 5 and later); failures of CAT-II (remain positive at month 5 or 8); non converters of CAT-I (remain positive at month 3); non converters of CAT-II (remain positive at month 4); all relapses; all return after default; close contacts of MDR-TB patients with symptoms; all HIV infected patients; and others.

**Results:** Out of 5,988 tests, the overall proportion of Mycobacterium TB and RR-TB detected were for 36.24% (2170) and 436 7.28% (436) respectively. The category wise proportion of RR-TB was for failures of CAT-I 26.72% (93 out of 348), failures of CAT-II 36.7% (40 out of 109), non converters of CAT-I 14.88% (64 out of 430), non converters of CAT-II 33.33% (13 of 39), all relapses 19.4% (180 out of 928), all return after default 11.54% (18 out of 156), close contacts of MDR-TB patients with symptoms 10.34% (6 out of 58), all HIV infected patients 0.63% (1 out of 158) and others 0.56% (21 out of 3762).

**Conclusion:** Rapid detection of MDR-TB cases and prompt initiation of treatment is a cornerstone to prevent the transmission of disease and reduce the morbidity and mortality. Risk categorization of all presumptive DR-TB patients under nine criteria was proved effective to ensure their rapid diagnosis by Xpert MTB/RIF. So, rational utilization of Xpert MTB /RIF to test all presumptive DR-TB patients will be a key factor for effectively controlling the MDR-TB burden in Bangladesh.

### PD-793-31 GeneXpert early implementation experience in Ethiopia: how to plan for implementation and address challenges before further roll out

E Mengesha,<sup>1</sup> D Jerene,<sup>2</sup> J Seid,<sup>2</sup> M Melese,<sup>2</sup> G Ayana,<sup>3</sup> P Suarez,<sup>4</sup> <sup>1</sup>Federal Ministry of Health of Ethiopia, Department of Disease Prevention and Control, Addis Ababa, <sup>2</sup>Help Ethiopia Address the Low TB Performance project, Management Sciences for Health (MSH), Addis Ababa, <sup>3</sup>Ethiopian Public Health Institute, Department of Regional Laboratories' Capacity Building Directorate, Addis Ababa, Ethiopia; <sup>4</sup>MSH, Center for Health Services, Arlington, VA, USA. Fax: (+251)11 372 4473. e-mail: degujerene@gmail.com

**Background:** GeneXpert MTB/RIF is a tool that can simultaneously diagnose TB and test for drug resistance in just two hours. Further documentation on GeneXpert implementation experiences in resource-limited settings, such as Ethiopia, is needed to address implementation challenges and inform future implementation efforts.

**Interventions:** As part of the national GeneXpert implementation scale up efforts by Ethiopia's Ministry of Health (MOH), the USAID-funded Help Ethiopia Address the Low TB Performance (HEAL TB) project supported implementation of GeneXpert at the initial sites in four locations. As per MOH's GeneXpert guidelines, site selection criteria included high TB burden, high TB/HIV co-infection rate, and availability of electricity, a dedicated space, and laboratory staff. We trained laboratory staff at the selected sites to use GeneXpert, installed GeneXpert machines at two of the hospitals, provided technical and material support to the two additional sites that already had GeneXpert machines. HEAL TB provided regular, on-site mentoring, documented implementation challenges, and collected data on sample processing and outcomes.

**Results:** After two months of implementation, the sites had processed 696 sputum samples and found 2.4% to be Rifampicin resistant (MTB+/RIF+) and 12.8% to be Rifampicin-sensitive (MTB+/RIF-). The cartridge wastage rate was 10.4% including errors (4.7%), invalid results (3.7%), and no results in 2.3% (Table). The combined rate of invalid results and errors varied considerably between sites and was as high as 21% at one site. Frequent power outages and incomplete installation of the GeneXpert machines contributed most significantly to higher rates of cartridge wastage. On-site refresher trainings for laboratory staff helped to address some of the identified implementation challenges.

Table. GeneXpert results after 2 months in Ethiopia, March 2014

Variable	Results (%) N=696
MTB not detected	73.7
MTB+/RIF-	12.8
MTB+/RIF+	2.4
MTB+/RIF Indeterminate	0.6



### PD-794-31 Effectiveness of introducing Xpert MTB/RIF for individuals at risk of TB and MDR-TB in Kazakhstan

S Van Kampen,<sup>1</sup> A Tursynbayeva,<sup>2</sup> A Koptleuova,<sup>3</sup> L Murzabekova,<sup>4</sup> L Bigalieva,<sup>5</sup> M Aubakirova,<sup>6</sup> S Van Den Hof,<sup>1</sup> S Pak.<sup>2</sup> <sup>1</sup>Knowledge Policy and Research, KNCV Tuberculosis Foundation, The Hague, Netherlands; <sup>2</sup>M&E, KNCV Tuberculosis Foundation, Representative Office for Central Asia, Almaty, <sup>3</sup>Reference Laboratory, National Center of TB of Ministry Health of Republic Kazakhstan, Almaty, <sup>4</sup>Laboratory, Akmola Regional TB Dispensary, Kokshetau, <sup>5</sup>Laboratory, East Kazakhstan regional TB Dispensary, Oskemen, <sup>6</sup>Laboratory, ALMATY city TB Dispensary, Almaty, Kazakhstan. Fax: (+7) 7272 93 86 58. e-mail: a.tursynbaeva@gmail.com

**Background and challenges to implementation:** With support from USAID/TB CARE I, Xpert MTB/RIF (Xpert) was introduced in the national TB control program (NTP) of Kazakhstan as routine test to detect TB and rifampicin resistance (RR) among eleven groups at risk of TB or multidrug resistant (MDR-)TB. This study set out to inform national scale-up of Xpert by assessing the uptake of Xpert, effectiveness of the diagnostic algorithm, and linkage between laboratory and clinics.

**Intervention or response:** Xpert was implemented under programmatic conditions in three provincial laboratories and the national TB reference laboratory (NTRL). From August 2012 to May 2013, individual patient data was gathered from electronic laboratory and treatment registers. Outcomes measured were: the proportion of individuals that received an Xpert test; that tested positive for TB and RR; that started treatment for TB or RR-TB; turn-around-time of Xpert results; and time from suspect registration to treatment initiation.

**Results and lessons learnt:** Uptake of Xpert testing was immediate with on average 140 tests per month per site. The type of individuals tested varied per site, reflecting linkages with e.g. prisons and AIDS centers. (Ex-)prisoners and people living with HIV/AIDS (PLWHA) suspected of TB showed a high proportion of RR among TB positives (59% and 53%), comparable to that of retreatment patients (58%, see Table). Two sites started 89% of RR patients on MDR-TB treatment, while in the two other sites this was 43–50%. In one site, 23% of individuals started TB treatment despite negative Xpert and culture results. The median turn-around-time of an Xpert result to the clinic was one day. Median time from diagnosis to start of TB treatment was 4 (IQR 2–10) days and for RR-TB treatment 8 (5–19) days.

**Conclusions and key recommendations:** Uptake of Xpert in provincial laboratories was rapid. Efforts should go towards testing more prisoners and PLWHA suspected of TB with Xpert and strengthen linkages with penitentiary and HIV centers. Xpert has been taken up without problems by clinicians for treatment decisions, as shown by the short time needed to start patients on TB and MDR-TB treatment after a test result. As next step, reasons for the gap between diagnosis and treatment registration should be assessed, as well as whether patients may be treated unnecessarily.

Table. Proportion of TB positive and RIF resistant Xpert results among eleven eligible groups in four laboratories in Kazakhstan

Eligible group	Total tested	TB positive (among all tested)	RIF resistant (among TB positives)
<b>Presumptive MDR-TB patients treated previously for TB</b>			
Retreatment patients	1252	57%	58%
Smear-positive after intensive phase	358	59%	53%
Acute progressive TB	139	50%	42%
TB/HIV co-infected patients	128	65%	42%
Previous treatment not in line with national guidelines	22	43%	33%
<b>Presumptive MDR-TB patients not previously treated for TB</b>			
(Ex-)prisoners suspected of TB	205	36%	59%
PLWHA suspected of TB	128	34%	54%
Close MDR-TB contacts	1439	39%	43%
Medical/prison staff suspected of TB	62	25%	43%
Group type not recorded	451	41%	43%
Others (i.e. mostly TB suspects and TB patients not previously treated)	1332	36%	38%
Pregnant women or after delivery suspected of TB	201	13%	32%

### PD-795-31 Assessment of the Xpert MTB/RIF assay for rapid diagnosis and treatment of tuberculosis in a setting with limited laboratory resources

CS Jang,<sup>1</sup> WL Huang,<sup>2</sup> KK Yang,<sup>1</sup> MS Li,<sup>1</sup> S-H Wei,<sup>3</sup> R Jou.<sup>2,4</sup> <sup>1</sup>Department of Internal Medicine, Puli Christian Hospital, Nan-Tao, <sup>2</sup>Reference Laboratory of Microbiology, Centers for Disease Control, Taipei, <sup>3</sup>Central Regional Center, Centers for Disease Control, Taichung, <sup>4</sup>Institute of Microbiology and Immunology, National Yang-Ming University, Taipei, Taiwan. Fax: (+886) 2-2653-1387. e-mail: rwj@cdc.gov.tw

**Background:** To evaluate diagnostic algorithms targeting specific categories of patients based on rapid and simultaneous testing for *Mycobacterium tuberculosis* complex (MTBC) and rifampicin (RIF) resistance using the point-of-care Xpert MTB/RIF (Xpert) assay.

**Design/Methods:** This is a prospective cohort study evaluating impact of the Xpert assay when used in a setting with no TB laboratory during the period of June 3 to November 5, 2013. Consecutive adult patients with high clinical suspicion of TB based on clinical symptoms, medical and social history, TB contact history, and/or chest x-ray findings and patients returning after TB treatment default. The first sputum sample was tested using the Xpert assay and conventional acid-fast bacilli (AFB) smear microscopy, culture, and phenotypic drug susceptibility testing. The performance of the Xpert assay and time-to-initiating appropriate treatment were assessed.

**Results:** We enrolled 76 TB suspected cases in outpatient service. Their median age is 65.5 years old, male to female ratio is 1.72, and 19 (25%) were retreated cases. Of the 67 cases with chest X-ray examination, 100% had abnormal findings. Of the 76 cases, 19 (25%) cases were MTBC positive including 1 case with RIF resistance using the Xpert assay, and 18 (23.7%) cases were MTBC culture positive. Of the 19 Xpert positive cases, 18 were new cases including 10 cases with TB contact history and



1 treatment failure case. Major clinical findings included cough (78.9%), weight loss (63.2%) and fever (52.6%). 16 cases were AFB smear positive and 3 cases were culture negative. Overall, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for AFB smear positive cases were 100%. While, the sensitivity, specificity, PPV and NPV for AFB smear negative cases were 33.3%, 100%, 100% and 75%, respectively. The average turn-around-time of positive MTBC reports using the Xpert assay and conventional methods were 0.37 and 16.9 days, respectively. The time-to-initiating appropriate treatment in 24 and 48 hours were 57.9% and 78.9%, respectively.

**Conclusion:** In settings with limited laboratory resources, the Xpert assay is recommended for clinical and programmatic decision making to diagnose TB suspected cases with chest X-ray and symptom findings and/or with contact history.

### PD-796-31 Market analysis of South African tuberculosis diagnostics in 2012

L Berrie,<sup>1</sup> K Schnippel,<sup>2</sup> W Stevens,<sup>1,3</sup> S Kik,<sup>4</sup> M Pai,<sup>4</sup> Pam Chedore,<sup>4</sup> TB Diagnostics Market Analysis Consortium.<sup>4</sup> <sup>1</sup>National Priority Programmes, National Health Laboratory Service, Johannesburg, <sup>2</sup>Health Economics and Epidemiology Research Office, University of the Witwatersrand, Johannesburg, <sup>3</sup>Molecular Medicine and Haematology, University of the Witwatersrand, Johannesburg, South Africa; <sup>4</sup>McGill International TB Centre, McGill University, Montreal, QC, Canada.  
e-mail: leigh.berrie@nhls.ac.za

**Background:** South Africa has the 3rd highest TB burden globally with 349582 notified TB cases in 2012, prevalence for pulmonary disease of 857/100 000, and an incidence of 1003/100 000. It also has the world's largest population of HIV-infected individuals and high rates of HIV/TB co-infection. This market analysis, collaboratively done by multiple partners and supported by the Bill and Melinda Gates Foundation, was to estimate the served available TB diagnostic market in South Africa in 2012.

**Design/Methods:** The public laboratory network in South Africa is operated by the National Health Laboratory Service, servicing 80% of the country's population. A small number of private laboratory networks also offer TB diagnostic services. The Xpert MTB/RIF test was being implemented in the public sector, reaching 57% coverage by December 2012. Three methods were used for the data collection on test volumes and costs: a top-down, bottom-up and middle-out approach. Volume of tests done in the public and private sectors was collected for: tuberculin skin test, interferon-gamma release assays, sputum smear microscopy, culture, NAATs (Xpert MTB/RIF and line probe assays), commercial M.tb speciation tests, 1st and 2nd line drug susceptibility testing and adenosine deaminase for extrapulmonary TB. TB diagnostic market values were calculated for the public sector, private sector and overall TB market.

**Results:** 9.2 million TB diagnostic tests were performed in the public and private sectors. 93% of these tests were done in the public sector. The TB diagnostic test most often used in both sectors was fluorescence smear microscopy (55%). An estimated total of 91.1 million USD was spent on TB diagnostics in the public sector of which 16.4 million was spent on Xpert MTB/RIF. In the private sector, almost 19 million USD was spent. 87% of the overall diagnostics market expenditure was spent on tests used for the diagnosis and treatment of active TB. Tests used for any form of drug susceptibility testing made up 31% of the overall market value while LTBI tests accounted for 12%.

**Conclusions:** Successful implementation of Xpert MTB/RIF in South Africa has shown that there is a market for new TB diagnostic tools with increased sensitivity and faster turnaround times. This study will enable test developers to understand the current and potential market for new replacement or add-on technologies and their possible applications in a middle-income, high TB incidence country as South Africa.

### PD-797-31 Point-of-Care implementation of Xpert: evaluating the impact of product and process innovation in TB diagnosis

D Christopher,<sup>1</sup> C Denking,<sup>2,3</sup> B Thangakunam,<sup>1</sup> J Sarojini,<sup>4</sup> M Pai,<sup>2</sup> S Schumacher.<sup>2</sup> <sup>1</sup>Pulmonary Medicine, Christian Medical College, Vellore, India; <sup>2</sup>Epidemiology & Biostatistics and McGill International TB Centre, McGill University, Montréal, QC, Canada; <sup>3</sup>Infectious Disease, Beth Israel Deaconess Medical Centre, Boston, MA, USA; <sup>4</sup>Microbiology, Christian Medical College, Vellore, India.  
e-mail: samuel.schumacher@mail.mcgill.ca

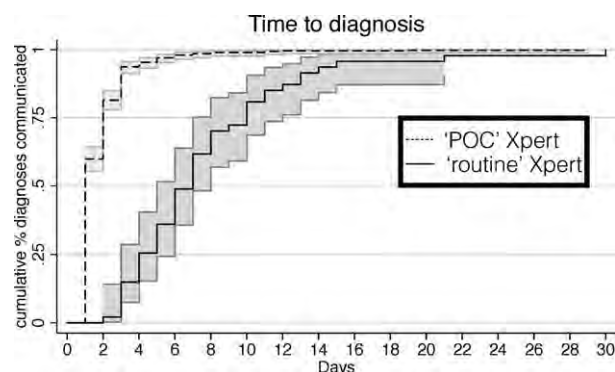
**Background:** Both product innovation-like Xpert MTB/RIF- and process innovation-like a point-of-care (POC) testing program to reach same-day diagnosis- may improve patient care. No published studies have directly compared routine versus POC implementation of Xpert. We assessed feasibility of Xpert implementation in a POC testing program, its performance in this context and the impact on time to diagnosis.

**Methods:** We implemented a POC testing program using Xpert to test TB suspects (n=743) in the pulmonary outpatient department of an Indian tertiary care hospital. We compared accuracy to MGIT 960 and incremental yield over fluorescence microscopy. In a pre/post implementation comparison we also assessed time to diagnosis of 'routine Xpert', i.e. routine testing in the hospital's microbiology department, versus 'POC Xpert', i.e. rapid testing, reporting and patient follow-up. Confidence intervals for the reduction in median time to diagnosis were calculated with the non-parametric bootstrap.

**Results:** POC implementation of Xpert was feasible but required two dedicated full-time staff and substantial adaptation of clinic flow to accommodate same-day follow-up. High accuracy (Sensitivity 82%, Specificity 97%) was maintained when running 'POC Xpert' by a health-care worker without technical background. Sensitivity varied substantially between spontaneously ex-

pectorated (91% [95%CI 80–97]) and induced sputa (63% [95%CI 42–81]). The incremental value of one Xpert over two smears was only 2.5% (95%CI 0.3–8.6). In the study setting, time to diagnosis was not shortened by routine implementation of Xpert itself due to lab processing time and how patient follow-up visits were scheduled. In contrast, the POC testing program shortened median time to diagnosis by 6.0 days (95%CI 4.7–7.3, Figure). Same-day diagnosis was achieved in 32% of patients (73% after 1 day, 96% after 3 days), and same-day treatment was started in 23% of TB cases.

**Conclusions:** Incremental value of Xpert was low, likely due to a combination of high-quality microscopy and patient spectrum. Routine, lab-based Xpert did not shorten time to diagnosis while implementation within a POC testing program did. Depending on the setting, innovation in care delivery may yield greater benefits than innovative tests per se or lead to complementary improvements in patient care. Careful consideration of context-specific factors is key to optimal decision-making about choice of interventions to improve TB diagnosis.



#### PD-798-31 Use of Xpert MTB/RIF for the identification of TB and drug resistance among smear-negative and re-treatment cases in Sidama zone, Ethiopia

M Agonafir,<sup>1</sup> M Yassin,<sup>1</sup> M A Yassin,<sup>2</sup> D Datiko,<sup>1</sup> S Theobald,<sup>3</sup> L Cuevas.<sup>4</sup> <sup>1</sup>LSTM TB Reach Project, Reach Ethiopia, Hawassa, Ethiopia; <sup>2</sup>Tuberculosis and Malaria, The Global Fund, Geneva, Switzerland; <sup>3</sup>Social Science and International Health, Liverpool School of Tropical Medicine, Liverpool, UK; <sup>4</sup>Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, UK. e-mail: macagonafir@gmail.com

**Background:** Tuberculosis (TB) diagnosis relies on smear-microscopy, which has low sensitivity. Smear-negative patients could benefit from more sensitive tests. Cases who receive treatment and continue to be symptomatic are likely to have drug resistance and should be screened.

**Methods:** We used Xpert MTB/RIF (Xpert) to confirm PTB among new smear-negative cases and to identify drug resistance. The study was embedded in a TB-REACH project in 19 districts of Sidama zone to increase

case detection. Health extension workers (HEWs) identified adults with cough >2 weeks; collected specimens and sent smears for examination. If symptoms persisted, the HEW collected new specimens. Xpert became available in 2012 and new patients with negative smear-microscopy and patients formerly treated for TB who continued to have symptoms were screened.

**Results:** 1959 Xpert MTB/RIF were conducted among 1895 cases (March 2012 - February, 2014). 186 tests failed (156 (83.9%) errors, 22 (11.8%) no results, and 8 (4.3%) invalid). Most errors were due to power outages. 198 (10.4 %) patients were Xpert-positive, with 151 (76.3%) RIF-negative, 12 (6%) RIF-indeterminate and 35 (17.7%) RIF-positive. The proportion of Xpert and RIF positivity varied between new and re-treatment patients.

**Conclusion:** Xpert provides additional tool for the diagnosis of TB, with at least 10% of new and retreatment cases obtaining information that is useful for clinical management. However there were many operational challenges to implement the technology. A high proportion of re-treatment cases were confirmed to have drug resistance and were referred for MDR-TB treatment.

#### PD-799-31 Performance of the Xpert MTB/RIF in MTB and Rifampin resistance detection among Pulmonary TB suspects in Georgia

N Tukvadze,<sup>1</sup> N Bablishvili,<sup>1</sup> N Lomtadze,<sup>1</sup> T Chkhutiashvili,<sup>1</sup> M Japaridze,<sup>1</sup> R Kempker.<sup>2</sup> <sup>1</sup>Research, National Center for Tuberculosis and Lung Diseases, Tbilisi, Georgia; <sup>2</sup>Infectious Diseases, Emory University School of Medicine, Atlanta, GA, USA. Fax: (+995) 322 910 467. e-mail: marikushane@yahoo.com

**Background:** Accurate and rapid detection of tuberculosis (TB) and associated drug resistance are critical for improving patient care and decreasing transmission of *Mycobacterium tuberculosis*. The Xpert MTB/RIF assay has been endorsed by WHO since 2010 and recently has been rolled out in the country of Georgia. We evaluated the performance of the Xpert assay among patients suspected of having TB in Georgia.

**Methods:** A prospective study conducted from November 2011-June 2013 among patients suspected of having pulmonary TB (based on clinical symptoms and CXR findings) with sputum smear positive (SS+) or sputum smear negative (SS-) microscopy. Sputum samples were processed with standard methodology and a resuspended pullet was split into two equal portions for culture and the Xpert assay. Drug susceptibility testing (DST) was performed on all cultures positive for *M. tuberculosis*. All testing was carried out at the National TB Reference Laboratory in Tbilisi, Georgia. Performance parameters of the Xpert assay in detection of *M. tuberculosis* and rifampin (Rif) resistance as compared to conventional culture and DST were determined.

**Results:** Among 2068 pulmonary TB suspects, 1938 had both Xpert and culture results available (469 SS+ and 1469 SS-). A total of 576 (30%) had positive cultures for *M. tuberculosis*. The pooled sensitivity (89.6%), specificity

(93.9), positive predictive value (PPV) (87.9), and negative predictive value (NPV) (94.8) of the Xpert in detecting *M. Tuberculosis* were all high. The sensitivity of the Xpert among SS+ samples was excellent at 100%, but specificity was relatively poor at 37.1% (due to 22 false positive Xpert results), while sensitivity and specificity for SS- culture positive samples was 67.9% and 95.5%, respectively. Of 75 cases with contaminated cultures, 22 had a positive Xpert result. There were 64 Xpert assay failures; 18 had a positive culture result. The Xpert detected Rif resistance in 118/134 (88%) cases as compared to DST. The overall agreement between the Xpert and DST in the detection of Rif resistance and MDR-TB detection were  $k=0.90$  (95%CI 0.86-0.94) and  $k=0.88$  (95%CI 0.83-0.93) respectively.

**Conclusion:** Overall, the Xpert MTB/RIF assay performed well when compared to conventional culture and DST in detecting *M. tuberculosis* and Rif resistance. False positive Xpert results need further investigation. Clinical impact studies are now needed to assess the public health impact of the Xpert assay.

Table 1

	All Cases (N=1938)	Smear + (N=469)	Smear - (N=1469)
True Positive	576	434	142
True Negative	1216	13	1203
False Positive	79	22	57
False Negative	67	0	67
Sensitivity	89.6 (87.2-91.9)	100	67.9 (61.6-74.3)
Specificity	93.9 (92.5-95.1)	37.1 (21.1-53.2)	95.5 (94.3-96.6)
PPV	87.9 (85.2-90.3)	95.2 (93.2-97.1)	71.4 (65.1-77.6)
NPV	94.8 (93.6-96.0)	100	94.7 (93.5-96.0)
Kappa	0.83 (0.81-0.86)	0.52 (0.35-0.69)	0.65 (0.59-0.70)

#### PD-800-31 Evaluation of Xpert MTB/RIF for rapid detection of multidrug-resistant tuberculosis in Korea

C K Kim,<sup>1</sup> SW Choi,<sup>1</sup> KH Oh,<sup>2</sup> H J Kim.<sup>2</sup> <sup>1</sup>Department of Laboratory Medicine, Korean Institute of Tuberculosis, Osong, <sup>2</sup>Department of Education and Training, Korean Institute of Tuberculosis, Osong, Republic of Korea. Fax: (+82)43-249-4987. e-mail: psoas95@gmail.com

**Background** Tuberculosis (TB) is still a public health threat in Korea. Emergence and spread of drug-resistant TB is the major obstacle to control TB. However,

diagnosis of multidrug-resistant (MDR) TB takes long time and is not feasible in many settings. Xpert MTB/RIF (Xpert) is an innovative diagnostic tool, which can rapidly detect tubercle bacilli and rifampicin (RIF) resistance in clinical samples. The aim of this study was to evaluate the feasibility of Xpert for rapid detection of MDR-TB in Korea.

**Methods** From June through December in 2013, a total of 6,838 sputum samples were collected from TB suspects who visited health centers in Korea. All samples were examined by smear microscopy, culture, and Xpert. When there was indeterminate result such as error, invalid or RIF indeterminate result, Xpert was repeated with the same sample. Xpert was also repeated for RIF-resistant samples to confirm the result. If culture was positive for *Mycobacterium tuberculosis* (MTB), drug susceptibility testing (DST) was performed using Lowenstein-Jensen absolute concentration method at the Korean Institute of Tuberculosis (KIT). *rpoB* gene was sequenced to detect mutation for isolates showing discrepancy between Xpert and DST.

**Results** MTB was detected in 1,818 (26.6%) samples by Xpert and 224 (3.3%) showed error result and 35 (0.5%) had invalid result. With one repeat test using remained sample, 85.7% (203/237) of samples with an indeterminate result became to be appropriate. Only 12 of 39 samples with RIF indeterminate turned to be valid after repeating. Compared to culture, sensitivities of Xpert were 99.5% and 61.9% for smear positive and negative samples, respectively and specificity was 95.9%. Xpert correctly identified 69 of 71 samples with RIF resistance and 1,293 of 1,390 samples susceptible to RIF. Repeat tests with Xpert RIF-resistant samples showed that results of nine (8.2%) changed to be susceptible. Among them, six had DST results and all were susceptible to RIF. Mutations in *rpoB* gene were found in nine of 15 RIF-susceptible isolates from Xpert RIF-resistant samples. Mean turnaround time (TAT) of Xpert was 4.1 days while TAT of DST was 57.7 days.

**Conclusion** Xpert would be useful for rapid detection of MDR-TB in Korea. Sample preparation-related error was common but easily resolved by repeating test with the same sample. However, RIF resistance results should be confirmed by other DST method or repeating Xpert due to low positive predictive value of Xpert.

#### PD-801-31 EXPAND-TB: strengthening TB laboratories in resource limited settings - focus on existing challenges

A Korobitsyn,<sup>1</sup> D Orozco,<sup>1</sup> K Kao,<sup>1</sup> J Wambugu,<sup>1</sup> C N Paramasivan,<sup>1</sup> J Lemaire,<sup>1</sup> T Verges,<sup>2</sup> F Mirzayev.<sup>3</sup> <sup>1</sup>EXPAND-TB, FIND, Geneva, <sup>2</sup>Global Drug Facility, STOP TB Partnership, Geneva, <sup>3</sup>Global TB Programme, WHO, Geneva, Switzerland. Fax: (+996) 312 62 43 20. e-mail: alexei.korobitsyn@gmail.com

**Background:** The EXPAND-TB project is focused on accelerating access to new, rapid and WHO-endorsed diagnostic technologies for patients at risk of MDR-TB in 27 low and middle-income countries in Africa, Central Asia, Eastern Europe, Latin America, and South-East



Asia. We summarize the achievements, challenges of the project and describe its transitioning process.

**Methods:** The EXPAND-TB project has entered a sixth year of operations, which is critical time to analyze its achievements; challenges and successfully transition the laboratory support to partners. Throughout the project we have assured political commitment and policy review; upgraded laboratory facilities; delivered commodities for liquid culture and drug susceptibility testing (DST), line probe assay (LPA), and rapid speciation; and initiated a capacity building and mentoring program for laboratory staff in collaboration with partners. At final stage of the project a transitioning strategy was developed to ensure that certain level of operations is maintained beyond the project, which will allow governments and local/international partners to provide the necessary support. A number of laboratory strategic plans were developed.

**Results:** By the end of 2013, 71,824 cases of MDR-TB were detected in 92 laboratories in 27 countries (62% of the global target). In the operational laboratories the supported technologies have been integrated into the national diagnostic algorithms but continued support is required to ensure their rational use.

**Conclusion:** The EXPAND-TB project has successfully supported TB laboratory work in 27 countries, contributing to narrowing the diagnosis gap for MDR-TB cases. Obstacles faced at the initial stage of the project (laboratory preparedness) directly relate to the strengthening political commitment, coordination between ministries and agencies involved in a project, costly infrastructure and biosafety upgrades. The critical constraints during the second stage of the project (technology transfer) were related to the human resources, complex nature of diagnostic and biosafety technologies, complex importation regulations, new technology validation requirements in selected countries. The difficulties at the third project stage (routine testing and monitoring) included coordination and cooperation at the national level, limited possibilities for equipment maintenance and poor sample transportation systems.

## 27. EXTERNAL QUALITY ASSURANCE FOR TB: GETTING BETTER ALL THE TIME!

### PD-802-31 Review of EQA on sputum AFB microscopy in Myanmar

TT Mar,<sup>1</sup> T Lwin,<sup>2</sup> TL Swe,<sup>3</sup> D Ti Ti,<sup>4</sup> A Fujiki.<sup>5</sup> <sup>1</sup>National TB Programme, National TB Reference Laboratory, Yangon, <sup>2</sup>Department of Health, Disease Control, Nay Pyi Taw, <sup>3</sup>National TB Programme, Upper Myanmar TB Reference Laboratory, Mandalay, <sup>4</sup>Expand TB Project, Foundation for Innovative New Diagnostics, Yangon, Myanmar; <sup>5</sup>Japan Anti-TB Association, Research Institute of Tuberculosis, Tokyo, Japan. Fax: (+95) 67-421201. e-mail: mywaddy@gmail.com

**Background and challenges to implementation:** Sputum microscopy for Acid Fast Bacilli (AFB) is the crucial tool for tuberculosis (TB) case finding. National Tuberculosis

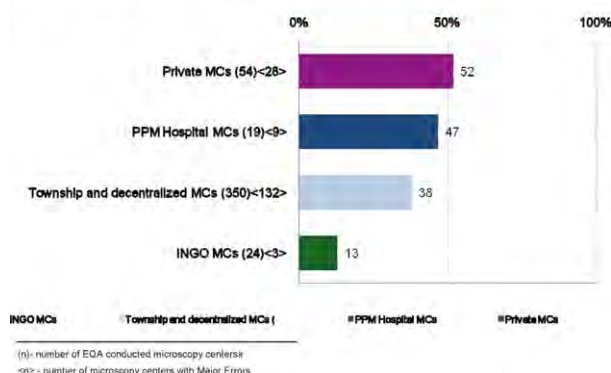
Programme (NTP), Myanmar started the External Quality Assessment (EQA) for sputum smear microscopy applying Lot Quality Assurance Sampling (LQAS) method with the support of JICA-MIDCP in 2007. NTP aimed to ensure the quality of sputum microscopy services and expanded EQA system on 464 microscopy centers (MC) including public and private MCs. The objectives are (1) to review the quality of the MCs doing sputum for AFB microscopy and (2) to identify the factors to be improved in sputum for AFB microscopy.

**Intervention or response:** After 3 years experiences of EQA introduction in Myanmar, this is the first systematic review of EQA reports of 2012. Slides from MCs were selected by township supervisors using LQAS method and sent monthly to Regional EQA centers concerned. Quarterly feedback reports from Regional EQA centers were sent to township supervisors and to the national EQA unit, where the data verification and data management were conducted.

**Results and lessons learnt:** Total EQA coverage on TB microscopy was 96% (447/464). Seventeen percent (78/447) of the MCs was under private sector and 83% (369/447) was under public sector. Thirty eight percent (172/447) of MCs had major errors. They were 47% (9/19) of MCs from Public-Public Mix hospitals and 38% (132/350) of MCs from district/township and station hospitals. In private sector, 13% (3/24) of MCs from INGOs and 52% (28/54) of MCs from private MCs had major errors. The improvement of 103 MCs was observed due to EQA feedback, follow-up supervisory visits and immediate action taken on the findings and recommendations of the laboratory supervisors from NTP. However, 68 MC had persistent major errors. The reasons of having major errors were identified as over workload on some laboratory technicians, inadequate refresher training, defect in binocular microscopes and weak supervision by immediate supervisors. Apart from that, the smear preparation could contribute to have major errors while size, thickness and evenness of smears were found not fully qualified.

**Conclusions and key recommendations:** Performance of MCs needs to be strengthened by providing frequent supportive supervision, effective training and reinforcement to follow standard operating procedures (SOP) and provision of good microscopes. It is important to maintain the quality of MCs.

Major Errors in Different Groups of Microscopy Centers, 2012





### PD-803-31 Implementation of a decentralised AFB microscopy quality assurance system in the Amhara and Oromia Regions of Ethiopia, 2014

J Seid,<sup>1</sup> B Girma,<sup>1</sup> M Melese,<sup>1</sup> G Alemu,<sup>2</sup> Z Habtamu,<sup>3</sup> D Jerene,<sup>1</sup> P Suarez.<sup>4</sup> <sup>1</sup>Help Ethiopia Address the Low TB Performance (HEAL TB) Project, Management Sciences for Health (MSH), Addis Ababa, <sup>2</sup>Amhara Regional Health Bureau, Department of Disease Prevention and Control, Bahir Dar, <sup>3</sup>Oromia Regional Health Bureau, Department of Disease Prevention and Control, Addis Ababa, Ethiopia; <sup>4</sup>MSH, Center for Health Services, Arlington, VA, USA.  
e-mail: jseid@msh.org

**Background:** Ensuring quality AFB microscopy is a challenge in Ethiopia due to the lack of capacity at the national and four Regional reference laboratories (RRLs) to conduct external quality assessment(EQA) at more than 2,500 TB diagnostic units spread throughout the country. This prompted the Ministry of Health in collaboration with TB implementation partners to develop a strategy for decentralization of AFB microscopy quality assurance system.

**Intervention:** From October 2011 to December 2013, the MOH and the Amhara and Oromia Regional Health Bureaus, with support from the USAID-funded Help Ethiopia Address the Low TB Performance project, implemented a decentralized EQA system in Amhara and Oromia regions. The system tasks the RRLs with conducting EQA at their regional hospitals to capacitate them to conduct EQA at all diagnostic units in their catchment areas. To support this process, the partners trained staff from regional hospitals on AFB microscopy and blind slide rechecking. Each quarter, district TB focal staff selected a random sample of slides from the diagnostic units in their districts using the Lots Quality Assurance Sampling model and delivered these to the hospitals' EQA centers. At these centers staff examined the slides using a blinded slide rechecking process. In case of discordant slides, an RRL expert visits the diagnostic unit that made the error to provide corrective feedback.

**Results:** At baseline, only 104 of the 691 diagnostic units had on-site evaluation and none had regular or blinded slide checking. After the intervention, 626 diagnostic units were participating in EQA and the number of facilities conducting EQA had increased from RRLs to include 38 hospitals. After the intervention, false positivity rate dropped from 6.76% to 2.14% (Table). Frequent turnover of trained staff was a challenge.

Table EQA performance indicators, Ethiopia, 2012–2013

Indicators	Number of slides collected	False positive (%)	False Negative (%)	≥95% concordance (%)
April-June 2012	13,354	7.6	0.53	90.3
July-Sep 2012	16,184	8.95	0.59	94.2
Oct-Dec 2012	21,682	6.6	0.34	95.4
Jan-Mar 2013	27,450	7	0.2	97
April-June 2013	23,507	5.9	1.7	97.3
July-Sep 2013	24,703	6.76	0.22	95.4
Oct-Dec 2013	25,262	2.14	0.14	99.5

**Conclusion:** This decentralized system contributed to a rapid expansion of TB diagnostic units participating in EQA. Mechanisms should be put in place to retain trained and experienced laboratory staff to maintain this work. The model can be replicated in similar settings.

### PD-804-31 Proficiency testing of detecting *M. tuberculosis* and DST in Russian Federation

L Domotenko,<sup>1</sup> NI Mezentseva,<sup>2</sup> V Malakhov,<sup>2</sup> T Morozova,<sup>1</sup> M Khramov.<sup>1</sup> <sup>1</sup>Diagnostic Preparations, State Research Center for Applied Microbiology & Biotechnology, Obolensk, <sup>2</sup>Federal System for External Quality Assessment in Laboratory Medicine, National Centre for External Quality Assessment in Laboratory Medicine, Moscow, Russian Federation.  
e-mail: domotenko@obolensk.org

**Background:** In Russian laboratories, detecting and drug susceptibility testing (DST) of *M. tuberculosis* is performed by both traditional and new methods. The reliability of results obtained by different methods affects the accuracy of TB diagnosis.

**Aim:** To evaluate the performance of detecting *M. tuberculosis* and DST by traditional and new methods in frame of annual proficiency testing (PT) in Russian Federation.

**Methods:** Two PT panels were sending in 155 Labs. Each PT panel consisted of 12 samples: 11 of them were well characterized *M. tuberculosis* strains and one sample was a negative sample. The strains were susceptible or resistant to 1<sup>st</sup> and/or 2<sup>nd</sup> line drugs. *M. tuberculosis* strains were suspended into Middlebrook 7H9 broth. Among the *M. tuberculosis* samples there were six strong positive samples containing 10<sup>5</sup>-10<sup>6</sup> CFU/mL and five samples with 10<sup>3</sup>-10<sup>4</sup> CFU/mL. The negative sample was bovine albumin solution or *M. avium* strain. All samples were coded. PT panels were prepared in the Russian expert laboratory from *M. tuberculosis* strains obtained from the WHO Supranational Reference Laboratory at the Swedish Institute for Communicable Disease Control, in 2005–2012. *M. tuberculosis* was detected by microscopy, culture and molecular methods. DST was performed by the absolute concentration method, the BACTEC 960 MGIT and molecular method. Obtained results were compared with the expert laboratories consensus results.

**Results:** Of 125 Labs using the culture method on eggs media, 80 Labs obtained the true results. Of 28 Labs using the BACTEC system, all laboratories identified correctly all samples. Of 30 Labs using molecular methods, only 26 Labs reported correct results. In many laboratories problems are faced by testing the sample with 10<sup>3</sup> CFU/mL, negative sample and the *M. avium* sample. A total of 17 laboratories using the absolute concentration method demonstrated the correct results for eight drugs of 1<sup>st</sup> and 2<sup>nd</sup> line. Average value of sensitivity obtained by the BACTEC 960 MGIT was 93–98 % for INH, RIF and STR, 90% for EMB and 84% for AM. The true DST results obtained with the molecular method were reported by 62,5% of laboratories.

**Conclusion:** PT of detecting *M. tuberculosis* and DST performed as the traditional methods as new methods is one of the most feasible and effective technique to monitor the technical ability of laboratory staff in proper identification of TB.

#### **PD-805-31 Strengthening TB laboratory performance: role of external quality assurance (EQA) system in BRAC supported areas**

D-U- Mesbah,<sup>1</sup> K Uddin,<sup>1</sup> M Siddiqui,<sup>1</sup> S Reza,<sup>1</sup> MA Husain,<sup>2</sup> M Akramul Islam,<sup>1</sup> S Islam.<sup>1</sup> <sup>1</sup>HNPP, BRAC, Dhaka, Bangladesh, <sup>2</sup>TB, NTP, Dhaka, Bangladesh. e-mail: shayla.dhaka@gmail.com

**Background and challenges to implementation:** AFB microscopy is an effective method for diagnosis and monitoring of treatment progress of infectious TB. Therefore, laboratory capacity and quality are crucial components of successful TB control programme. BRAC has country network of peripheral laboratories for sputum microscopy to support national TB program (NTP). To ensure quality microscopy and accurate diagnosis it has developed external quality control mechanism through external quality assurance (EQA) laboratories in 2004.

**Intervention or response:** BRAC is operating 26 EQA centres to oversee 709 laboratories run by Government and BRAC. EQA centres are lead by EQA coordinators and most are placed at Chest Disease Clinics (CDC) under CDC consultants. EQA supervisor (district manager of BRAC) and medical officers of Upazila Health Complexes randomly collect five slides from each laboratory every month and send to EQA coordinator for rechecking. After assessment of these slides regular feedback is provided from EQA to microscopy centres. The discordant slides found by first controller are sent to second controller for further rechecking at central level laboratories under NTP. The first controllers also visit laboratories for assessing the overall laboratory conditions and performances. BRAC also provides basic and refresher training for laboratory technicians.

**Results and lessons learnt:** From 2009 to September 2013, a total of 58 basic and refresher training on laboratory have been conducted with 754 participants. BRAC also arranged training on EQA in every year. In 2011, 2012 and 2013 (up to September) 41984, 43026 and 32747 slides were rechecked for EQA respectively. Out of them 173 (0.41%), 152 (0.35%) and 111 (0.33%) slides were found discordant by first controller which were confirmed by 2<sup>nd</sup> controller respectively.

**Conclusions and key recommendations:** EQA system helps to monitor quality of laboratory activities and ensure better performance. Thus efforts need to be continued for strengthening laboratory activities, capacity building of laboratory technicians and ensure proper diagnosis of infectious TB.

#### **PD-806-31 Long-term results of smear microscopy External Quality Assurance (EQA) in Ukraine's tuberculosis (TB) control system**

M Karnaukhova,<sup>1</sup> A Barbova,<sup>2</sup> O Pavlova,<sup>3</sup> O Kheylo,<sup>1</sup> A Chaika,<sup>4</sup> M Dolynska.<sup>1</sup> <sup>1</sup>USAID| Strengthening Tuberculosis Control in Ukraine Project, USAID| Strengthening Tuberculosis Control in Ukraine Project, Kyiv, <sup>2</sup>National TB Reference laboratory, National TB Reference laboratory, Kyiv, <sup>3</sup>Ukrainian Center for Disease Control, Ukrainian Center for Disease Control, Kyiv, <sup>4</sup>Bacteriology, TB hospital #1, Symferopol, Ukraine. e-mail: mdolynska@stbcu.com.ua

**Background and challenges to implementation:** Before 2014, EQA in Ukraine's TB control system had been mainly implemented through the support of USAID-funded projects since the development of relevant state regulations was still in progress. Consequently, EQA was not always consistently applied between projects and often did not meet WHO-recommended standards.

**Intervention:** Since mid 2012, the USAID Strengthening Tuberculosis Control in Ukraine Project began implementing the EQA system in 10 regions of Ukraine. The project simultaneously focused on facilitating the development of national regulations in line with the WHO approach, assisting with updates to local regulations, and helping implement routine EQA procedures.

**Results and lessons learnt:** The USAID-supported regions experienced two years of fully comprehensive EQA of sputum smear microscopy by the date of the final endorsement of Ukraine's National Guidelines on EQA in January 2014. This experience included use of panel testing and/or blinded rechecking, and/or on-the-job training. In accordance with WHO recommendations, the project advocated for a flexible approach which included increasing of coverage for those regions which had been poorly integrated into EQA, and more difficult cases sent to some laboratories that already maintain a relative proficiency in EQA. Whereas the rest of Ukrainian regions are still initiating the EQA process, 340 Level 1 laboratories from USAID-supported regions achieved 99.7% coverage by panel testing, 36.2% coverage by blinded rechecking and 52.1% by on-the-job training. The quality of tests has significantly improved within the last two years, confirmed by 88.2% of laboratories undergoing panel testing with 95% and more correct results in 2013 versus 78.6% in 2012. This led to almost three times as effective smear TB detection among TB suspects in the USAID-supported region compared to non-supported regions (2.82% versus 1.07%, p-value<0.05).

**Conclusion:** Experience in EQA implementation in the USAID-supported regions of Ukraine has demonstrated the benefits of how accurate testing and sustainable improvements, which now are institutionalized country-wide through the new national legislation, can benefit both targeted regions and those beyond direct donor support.

### PD-807-31 Implementing national EQA scheme for first- and second-line DST services in Pakistan

S Tahseen,<sup>1</sup> A Hussain,<sup>1</sup> E Qadeer.<sup>1</sup> <sup>1</sup>National TB Reference Laboratory, National Tuberculosis Control Programme, Islamabad, Pakistan. e-mail: sabira.tahseen@gmail.com

**Background and challenges to implementation:** Pakistan is 4th high burden country for MDR. There is limited capacity in public sector for DST services, however plans to expand DST services are in process. National TB reference laboratory Pakistan was made operational in 2009 and proficiency of First and second line DST was achieved. Currently NRL and two private sector laboratories are enrolled in Global EQA scheme with target performance both for FL and SLD For scale up for PMDT plan there is need for increasing access to quality assured DST. There are other TB laboratories performing DST both in public and private sector but quality of services being offered is mostly unknown. Implementation of Quality assessment is needed to facilitate TB programme in decision making for engaging TB laboratories in diagnostic services required for Programmatic management of drug resistant TB (PMDT)

**Intervention or response:** Baseline assessment was done by NTRL through questionnaire to gather information on DST services offered by TB laboratories and subsequently invitation was sent for first time in 2010 to 5 and in 2013 to 11 TB laboratories performing DST for voluntary enrollment in national EQA scheme Subsets of panels was prepared from EQA panel received from SRL and was dispatched to consenting laboratories. First round of national EQA scheme for DST services was conducted in 2010 and by 2013 results of four round of panel testing were reported .

**Results and lessons learnt:** Number of participating laboratories increase from 4 in 2010 to 7 in 2013. Out of these only 2 in 2010 and one in 2013 laboratory submitted result for SLDST Proportion of laboratories qualifying FLDST results increase from 50%(2/4) laboratories in 2010 to 71%( 5/7) in 2013. None of the participating laboratory qualified SLDST performance target . Two laboratories in public sector which failed to achieve proficiency to FLD were advised to stop DST services . However same could not be applied to underperforming laboratories in Private sector

**Conclusions and key recommendations:** EQA scheme helped in improving FLDST services but none of laboratory developed capacity for QA second line DST. Introduction of GeneXpert has minimized need of phenotypic FLDST for diagnosis of MDR but at same time there is increase need to build capacity of laboratories to perform QA SLDST

		R-1 (2010)		R-2 (2011)		R-3 (2012)		R-4	
		# enroll	# qual	# enroll	# qual	# enroll	# qual	# enroll	# qual
FLDST	Public	2	1	3	2	4	1	3	2
	Private	2	1	4	2	4	2	4	3
SLDST	Public	1	0	1	0	1	0	1	0
	Private	1	0	1	0	1	0	0	0

Table : Summary of laboratories enrolled in EQA scheme for first line and second line DST

### PD-808-31 Proficiency testing as measurement tool for quality of service of laboratory personnel in Nigeria: a method for training impact evaluation

A Hassan,<sup>1</sup> F Sarkinfada,<sup>2</sup> G. T Ojika,<sup>3</sup> R Olukolade,<sup>1</sup> L Okwuonye,<sup>1</sup> K Osinowo,<sup>1</sup> C Ogbuji,<sup>1</sup> O Ladipo.<sup>1</sup>

<sup>1</sup>Monitoring and Evaluation, Association for Reproductive and Family Health, Abuja, FCT, <sup>2</sup>Department of Medical Microbiology and Parasitology, Faculty of Medicine, Bayero University, Kano, Kano State, <sup>3</sup>Laboratory Services, National Tuberculosis and Leprosy Control Programme, Abuja, FCT, Nigeria. e-mail: abiodunhassan@gmail.com

**Background:** Laboratory diagnosis of TB remains the main fulcrum for management of Tuberculosis. In Nigeria, use of sputum smear microscopy is the most preferred laboratory technique. In order to guarantee the reliability and accuracy of laboratory results, high level of accuracy and precision is required from the testing laboratories through regular external quality assurance.

**Methodology:** A total of thirty laboratory staff that has been trained in sputum smear microscopy from the existing DOTS centres participated in a proficiency testing. Panel slides were prepared by the National reference laboratory and used to assess the proficiency of the individual trainees in staining and reading of smears. Ten panels (comprising of 2 scanty, positive with 1+, 2+ and 3+, and negative slides) were issued to each of the selected laboratory personnel.

**Results:** Of the 30 trainees targeted for the evaluation, scores from 28 participants were obtained while 2 results were rejected. The overall average of the aggregate scores of the trainees was 78% (range 40 – 100). Of the 269 panel slides evaluated, a relatively high Concordance in 222 slides (82.5%) was recorded while among 47 discordant slides, up to 25 (9.3%) and 20 (7.4%) were High and Low False Negatives (FN) respectively. Quantification Error (QE) was observed in 18 (6.7%) among the positive slides. The participants demonstrated a high relative specificity of 95.1%, reflecting a high proficiency in identifying AFB when present in sputum sample. The relative sensitivity of 76.7% and FN results were due to the deficiencies in identifying scanty AFB in sputum smears. Up to 16 of the participants had at least 1 FN result, while 14 of the participants commit at least 1 QE.

**Conclusion:** Scale up of microscopy centres to improve active TB case finding should be matched with regular sustained follow up & supportive supervision of laboratory personnel to consolidate the gains of the training programmes.



### PD-809-31 Implementation of blinded rechecking method for external quality assessment (EQA) for smear microscopy in Tajikistan

Z Bayduloeva,<sup>1</sup> G. Kasymova,<sup>2</sup> M Joncevska.<sup>1</sup>

<sup>1</sup>Tuberculosis, Project HOPE, Dushanbe, <sup>2</sup>Laboratory, Republican TB Center, Dushanbe, Tajikistan. Fax: (+992)372244720. e-mail: Zamira\_Bayduloeva@qhcp.net

**Aim:** To evaluate the results from the countrywide implementation of blinded rechecking method for EQA for smear microscopy in Tajikistan

**Method:** Blinded rechecking method for smear microscopy in Tajikistan was implemented with a stepwise approach, a situation analysis followed by protocol development and then training. The implementation process started in 2005 with pilot projects in Dushanbe, Rudaki, Machiton, Kulyab, continuing until 2007, 100 % of the national TB laboratory network (97 microscopy laboratories) was covered.

**Results:** Analysis of blinded rechecking results is done regularly on a quarterly basis, evaluating the progress in quality improvement, including: smear preparation; staining procedure and reading of slides. Quarterly analysis enabled prompt reaction and remedial action in laboratories performing below the required standard. Comparison of the results from 2011 to 2013 showed an overall improvement in quality. The total number of laboratories with unsatisfactory results decreased from 33 to 10 (36% to 11%). Significant improvement was also registered in the quality of smear preparation and staining.

**Conclusion:** Conducting the blinded rechecking method for EQA for smear microscopy helps the NTP to identify existing problems in microscopy laboratories in a timely manner, to react and make decisions to solve identified problems, and improve the quality of work in microscopy laboratories.

Table 1.

Region	Total labs	Number of labs with unsatisfactory results (False results)		
		2011 (%)	2012 (%)	2013 (%)
Dushanbe	9	4 (44%)	3 (33%)	3 (33%)
Sogd	25	10 (40%)	4 (16%)	4 (16%)
Kurgan-Tyube	17	6 (35%)	0	0
GBO	8	1 (13%)	1 (13%)	0
DRS	18	4 (22%)	3 (17%)	3 (17%)
Kulyab	13	6 (46%)	4 (31%)	0
Prison system	5	2 (40%)	1 (20%)	0
Total	92	33 (36%)	16 (17%)	10 (11%)

### PD-810-31 Initiating an innovative External Quality Assurance programme for evaluating the use of Xpert MTB/RIF in Ghana

A Umubyeyi Nyaruhirira,<sup>1</sup> C Mundy,<sup>2</sup> R Chimzizi,<sup>3</sup> F Dzata,<sup>4</sup> S Molapo,<sup>5</sup> L Scott,<sup>5,6</sup> P Suarez,<sup>2</sup> F Bonsu.<sup>4</sup>

<sup>1</sup>Department of Laboratory Services, Management Sciences for Health (MSH), Pretoria, South Africa; <sup>2</sup>MSH, Centre for Health Services, Arlington, VA, USA; <sup>3</sup>TB CAREI, MSH, Accra, <sup>4</sup>National TB Control Programme, Accra, Ghana; <sup>5</sup>National Laboratory Health Services, Department of TB Laboratory, Johannesburg, , <sup>6</sup>University of the Witwatersrand, Department of Hematology, Johannesburg, South Africa. e-mail: alainenyaruhirira@hotmail.com

**Background:** Internationally approved external quality assurance (EQA) programs are well-defined for TB microscopy, culture, and susceptibility testing. However, EQA has not yet been evaluated or demonstrated as feasible and useful for Xpert MTB/RIF testing. Consequently, countries have not initiated an EQA program for regularly measuring the technical performance of staff using Xpert MTB/RIF. In 2011, the National Health Laboratory Service (NHLS) in South Africa addressed this gap by developing a program that uses EQA to evaluate Xpert MTB/RIF testing of dried culture spots (DCS). Ghana's National TB Program, with support from TB CARE I, pilot tested the NHLS' program at four sites in Ghana.

**Design/Methods:** Four study sites each received four spot panels that included a DCS of a MTB-positive Rifampin-sensitive strain, a MTB-positive Rifampin-insensitive strain, non-TB mycobacteria, and a negative control. The NTP conducted one-day training on EQA implementation before launching the EQA program. Participating facilities sent data reports to the NHLS for analysis through email or tbgxmonitor.com and received annual certificates of completion. The NTP conducted supervision and corrective action, as they routinely do for microscopy.

**Results:** Three DCS batches with 48 DCS were shipped to Ghana for 4 GX4.

**Results** on three panels were 100% accurate. At the four study sites, 100% of laboratory staff participated in the process.

**Conclusion:** This pilot project demonstrates that the use of inactive *M. tuberculosis* coupled with easier transportation of DCS material can be safely evaluated for an EQA program that highlights expected staff error and site non-conformities. Cost needs to be established for global participants (currently \$135/panel by module), but the use of a DCS format allows the material to be shipped as non-biohazardous and at one tenth the cost of transporting then other EQA material. Monitoring of the GeneXpert instrument and cartridge performance should be complemented with monitoring of the complete testing process. The NHLS' DCS test proved to be an appropriate vehicle for pilot testing the use of EQA for Xpert technology. The World Health Organization should endorse the dissemination of this approach, and thus, the cost reduction.



### PD-811-31 External quality assessment of *Mycobacterium tuberculosis* drug susceptibility testing in Peru, 2006–2009

G Obregon Boltan,<sup>1</sup> N Quispe,<sup>1</sup> M Acurio.<sup>1</sup>

<sup>1</sup>Mycobacteriology Laboratory, National Health Institute, Lima, Peru. e-mail: flankan.damagon@gmail.com

**Background:** External quality assessment (EQA) of *Mycobacterium tuberculosis* drug susceptibility testing (DST), using proficiency testing in public health laboratories in the Peru.

**Design/Methods:** Six rounds of DST proficiency testing were conducted between 2006 and 2009, using *Mycobacterium tuberculosis* strains provided by the World Health Organization Supranational Reference laboratories. In total, 6 public health laboratories in the public sector participated in the rounds.

**Results:** The accuracy average in six rounds for the 6 public health laboratories was 92.3% (Isoniazid), 98.3% (Rifampicin), 91.8% (streptomycin) and 91.8% (Ethambutol).

**Conclusion:** EQA of test susceptibility to first-line drugs, has shown significant improvement in each of the participating laboratories in the public health peruvian laboratories network.

### PD-812-31 The use of archived results of Xpert MTB/RIF testing for data triangulation in improving data quality from four GeneXpert sites in Nigeria

E Oyama,<sup>1</sup> A Awe,<sup>1</sup> J O Obasanya,<sup>2</sup> A F Omoniyi,<sup>1</sup> E Elom,<sup>2</sup> M Gidado,<sup>3</sup> J Onazi.<sup>3</sup> <sup>1</sup>Tuberculosis, World Health Organization, Abuja, <sup>2</sup>Public Health, Federal Ministry of Health, Abuja, <sup>3</sup>TB CARE I Project, KNCV Tuberculosis Foundation, Abuja, Nigeria. e-mail: oyamae@ng.afro.who.int

**Background:** In December 2010, WHO recommended the use of the Xpert MTB/RIF technology for the detection of tuberculosis and drug resistant tuberculosis by National TB programmes (NTPs) in low-income countries. The Nigerian TB programme commenced implementation of the technology in a few secondary as well as tertiary health care facilities. The collation and reporting of the Xpert MTB/RIF test results continued to pose a challenge of data quality. This study was to determine whether archived computer Xpert MTB/RIF test results can contribute to data validation and quality of reported Xpert MTB/RIF data to National TB programme in 4 of the initial GeneXpert sites in Nigeria.

**Design/Methods:** Routine supervisory visit was conducted to four GeneXpert sites which included Central Hospital, Benin City (CHB), St Patrick Hospital, Abakaliki (PHA), State Specialist hospital (SSH), Gombe and Zankli Medical centre (ZMC), Abuja from 15–18 May 2012. All Xpert MTB/RIF tests conducted from 1 January to 31 March 2012 and archived in the computers of the centres were copied in a recordable CD disc and the results analyzed centrally. The results were verified with the Q1 2012 summary Xpert MTB/RIF reports submitted to NTP.

**Results:** A total of 193 Xpert MTB/RIF results reported from the 4 sites during the period were validated by the archived computer results. There was variation in the reported data from 3 of the 4 evaluated sites. In 2 sites, there was underreporting (CHB, Benin, 11%; ZMC, Abuja, 7%) and over reporting of the results in one (St Patrick Hospital, Abakaliki, 9%). The variations occurred in all 4 key outcomes of the Xpert test results (MTB detected, MTB detected, Rif resistance not detected; MTB detected, Rif resistance detected and errors).

**Conclusion:** There was significant variation in the reported Xpert MTB/RIF outcome results from 3 of 4 GeneXpert sites (7–11%) though no difference in the total reported data. Computer archived Xpert MTB/RIF results provided a means for data triangulation of Xpert MTB/RIF results reported to the National TB programme. The NTP should incorporate evaluation of computer archived Xpert MTB/RIF results collected during routine supervisory visits for the purpose of data triangulation as it scales up the Xpert MTB/RIF intervention in the country.

### PD-813-31 Quality assessment of AFB microscopy in tuberculosis laboratories in Kyrgyzstan

G Kalmambetova,<sup>1</sup> A Kadyrov,<sup>1</sup> A Adambekova,<sup>1</sup> K Takieva,<sup>2</sup> M Sydykova,<sup>1</sup> A Iskakova.<sup>1</sup> <sup>1</sup>NRL, National Center of Phthisiology, Bishkek, <sup>2</sup>TB, Quality Health Care Project, Bishkek, Kyrgyzstan. e-mail: gulmira.kalmambetova@gmail.com

**Background and challenges to implementation:** *Mycobacterium tuberculosis* infection remains a major cause of global mortality and morbidity. The diagnosis of pulmonary tuberculosis (TB) has based on smear microscopy which provides the basis of treatment worldwide. Precision level in microscopy procedures is the most important steps for accurate diagnosis of the disease and to initiate proper treatment. Therefore, the implementation of the external quality assessment (EQA) is important to provide the reliability and validity of tests. One of the major issues in the functioning of laboratory services in Kyrgyzstan is the lack of a standardized system for internal quality control and EQA. The system has been partly developed in the TB laboratory network, but it was not fully implemented.

**Intervention or response:** For the past year, with a support of the USAID funded Quality Health Care Project (QHCP) the National TB Reference Laboratory (NRL) has launched EQA program. Chyi region, Bishkek city and penal sector's labs started EQA in 2006 and 2009. A staff of 120 laboratories participated at the EQA trainings done by QHCP. Blind re-checking method (re-examination of randomly selected slides) was used for the evaluation, and the slides were sent to the regional TB labs on quarterly basis. Slides were selected according to LQAS (Lot Quality Assurance Sampling) guides.

**Results and lessons learnt:** In the re-evaluation of the slides, false positivity (FP), false negativity (FN) and

quantification errors (QE) were noted. District labs sent totally 2220 slides to 7 regional and 2 cities laboratories between March 31, 2013 and December 31, 2013. In the result of re-checking, 2115 (96,1%) slides were found concordant, and 85 (3.9%) were discordant (15 FP, 36 FN and 34QE).

**Conclusions and key recommendations:** Following EQA, on-site evaluation of the laboratories with major errors was performed and necessary adjustments were done. Two workshops for the Heads of regional labs were conducted with support of the QHCP and the defined problems were discussed thoroughly. Due to the turnover of lab staff, re-fresh trainings should be considered. In conclusion, external quality control for the AFB microscopy is crucial and essential for the improvement of tuberculosis laboratory to ensure accurate and reliable results.

## 28. CULTURE AND PHENOTYPIC DRUG SUSCEPTIBILITY TESTING

### PD-814-31 Surveillance of anti-tuberculosis drug resistance in Cuba, 2010–2012

D Lemus,<sup>1</sup> M Echemendia,<sup>1</sup> R Díaz,<sup>1</sup> A Llop,<sup>2</sup> M J Llanes-Cordero.<sup>3</sup> <sup>1</sup>National Reference Laboratory on Tuberculosis, Leprosy and Mycobacteria, Institute of Tropical Medicine Pedro Kouri, Havana, <sup>2</sup>Microbiology, Institute of Tropical Medicine Pedro Kouri, Havana, <sup>3</sup>National Tuberculosis Program, Ministry of Public Health, Havana, Cuba. e-mail: dlemus@ipk.sld.cu

**Background:** Antituberculosis drug resistance surveillance is very important to identify multidrug resistant and extremely drug resistant *Mycobacterium tuberculosis* isolates. The aim of this study was to determine prevalence of resistance in *M. tuberculosis* strains isolated in 2010 – 2012 and to demonstrate the laboratory performance in the external quality control of drugs susceptibility testing.

**Design/Methods:** A prospective longitudinal study was carried out. Antituberculosis drug resistance was determined in 989 *M. tuberculosis* isolates obtained throughout the country. Nitrate reductase assay was used to investigate resistance to isoniazid and rifampicin. Proportion method was performed to verify resistance to these drugs and further to investigate in multidrug resistant isolates their susceptibility to streptomycin, ethambutol, ofloxacin, kanamycin and capreomycin. Additionally, the laboratory achieved the external quality control of drug susceptibility testing

**Results:** The 96,02% of the isolates fitting in the category new cases were classified as sensible and multidrug resistance was confirmed in seven of them (0,93%). The 81,54% and 7,0% of isolates belonging to previously treated patients were sensible and multidrug resistant, respectively. Four multidrug resistant isolates were extensively drug resistant. Except ethambutol and capreomycin, for all drugs the efficiency was 100% during the execution of the external quality control.

**Conclusion:** This study demonstrates a low prevalence of *M. tuberculosis* multidrug resistant isolates in Cuba. The laboratory achieved excellent results in the execution of the two external quality control of drug susceptibility testing.

### PD-815-31 Exploring anti-tuberculosis activity from actinobacteria from mangrove sediment in Papua Island, Indonesia

H Krismawati,<sup>1</sup> L Salim,<sup>1</sup> A Oktavian,<sup>1</sup> I Wike,<sup>1</sup> Eva Fitriana,<sup>1</sup> O Karapa.<sup>1</sup> <sup>1</sup>Ministry of Health, Institute of Research and Development for Biomedicine Papua, Jayapura Papua, Indonesia. e-mail: hkrismawati@gmail.com

**Background:** Explore the potential use of bioactive compounds produced by Actinobacteria as anti-tuberculosis therapy

**Design/Methods:** The samples were collected from 4 mangrove area: Asmat and Jayapura in Papua and Seged and Raja Ampat in West Papua. Isolation of Actinobacteria was carried out using selective media Starch Casein and Raffinose Histidin Agar. Identification of Actinobacteria was done base on morphology, color grouping, gram staining and form of spore chain. The first screening of ability to produce bioactive compound was been done using inhibition tests on two tests bacteria: *Escherichia coli* ATCC 35218 and *Staphylococcus aureus* ATCC 25923. Anti-tuberculosis assay were done using inhibition test of *Mycobacterium tuberculosis* H37RV. The Drugs Sensitivity Assay that recommended by WHO were applied to observe the ability of Actinobacteria inhibit the growth of *Mycobacterium tuberculosis* H37RV.

**Results:** The result show that 100% Actinobacteria strains identified as *Streptomyces* sp. The inhibition test indicate that 4/20 strain of *Streptomyces* sp potentially produce bioactive compounds that posses anti-Tuberculosis activity. The inhibition test reveals that 9 starins inhibit growth of *Staphylococcus aureus*, one of which revealed duo activity against *Mycobacterium tuberculosis* H37RV

**Conclusion:** Actinobacteria that produce bioactive compounds with anti-Tuberculosis activity were isolated from mangrove sediment on Papua Island. However further experiment are needed identify the active ingredients and optimization is needed.

### PD-816-31 Limited access to diagnosis of drug-resistant TB among high-risk groups in a central province in Thailand

W Kateudomsup,<sup>1</sup> S Jittimanee.<sup>2</sup> <sup>1</sup>Disease Control, Kamphaengphet Public Health Provincial Office, Kamphaengphet, <sup>2</sup>Department of Disease Control, Bureau of Tuberculosis, Bangkok, Thailand. Fax: (+66)55705189. e-mail: wirachtb@gmail.com

**Background and challenges to implementation:** A policy of culture and Drug Susceptible Testing (DST) among high-risk groups to diagnose drug-resistant TB (DR-TB) has been implemented countrywide since 2009. Well-

established laboratory capacity and funding from multiple resources are allocated to ensure that the high-risk groups universally access to the services. However, translation from policy to practice frequently varies based on local context.

**Intervention or response:** This retrospective study was to examine percentages of culture and DST among high-risk groups of DR-TB in 11 districts in a central province covering 714,779 population. This study was also to assess recovery rate (RR) of sputum culture and turn around time (TAT) of both culture and DST. Out of 795 tuberculosis (TB) patients registered in 2012, 100 TB patients with risk-groups were eligible and were enrolled. Based on the province policy, the risk-groups were (i) re-treatment patients with smear-positive, (ii) non-converters at the end of month three or five, and (iii) smear-positive patients with HIV infection. Costs of culture and DST for all eligible patients were routinely supported by the insurance schemes or other government budget. Sputum specimens were sent to three nearby laboratories where MGIT 960 was used for culture & DST. A standard form was used to collect data from the study settings.

**Results and lessons learnt:** Out of 100 patients with high-risk of DR-TB, 59% had their sputum submitted for culture and DST. Sputum submission was mostly performed among non-converters (89%), while re-treatment patients and HIV positive patients were reported 61% and 9% respectively. Recovery rate of culture was 60% due to 30% of no growth, 7% of non-TB and 3% of contamination. One-third (36%) received culture results during 31–60 days, 26% between 61–90 days, and 27% more than 90 days. Only 29% (29/100) of patients with risk-group, DST results were available and its TAT (after receiving culture results) was observed that 31% (9/29) for more than 5 months and 24% (7/29) during 91–120 days. MDR-TB was reported 10% (3/29). **Conclusions and key recommendations:**

#### PD-817-31 Analysis of cross resistance between kanamycin and amikacin in extensive drug resistant tuberculosis isolates

A K Verma,<sup>1</sup> Gavi Kumar,<sup>1</sup> J Arora,<sup>1</sup> Vith Myneedu,<sup>1</sup> R Sarin.<sup>1</sup> <sup>1</sup>Microbiology, National Institute of TB and Respiratory Diseases, New Delhi, India.  
e-mail: akv\_680@yahoo.co.in

**Background:** The aminoglycosides (kanamycin and amikacin) and macrocyclic peptide (capreomycin) are key drugs for treatment of multidrug resistant tuberculosis (MDR-TB). Increasing resistance to these drugs and possible cross-resistance between amikacin and kanamycin is a concern for MDR-TB therapy. The present study was undertaken to assess the cross resistance phenomenon in extensive drug resistant tuberculosis (XDR – TB) between amikacin and kanamycin.

**Design/Methods:** The study was undertaken in the Dept of Microbiology at National Institute of TB and RD, New Delhi during August 2012 to September 2013. 480 MDR *M. tuberculosis* strains were subjected to suscep-

tibility testing using critical concentration against kanamycin (2.5µg/ml), amikacin (1.0µg/ml) and capreomycin (2.5µg/ml) and ofloxacin (2.0 µg/ml) by MGIT 960 system.

**Results:** During the study it was found that 502/627(80%) strains were sensitive to all the 3 injectable drugs and 125/627 (20 %) was resistant to at least one of the injectable drug. Out of 125 mycobacterial strains 81/627(14%) strains were resistant to all the three injectable drugs and quinolone. 22/627 (3.5%) strains were resistant to kanamycin but sensitive to amikacin and capreomycin. whereas a single strain (0.16%) was resistant to amikacin and capreomycin but sensitive to kanamycin. The cross resistance between kanamycin and amikacin were observed in 86/111 (78%) of mycobacterial strains. The different resistance pattern of mycobacterial strain showed that capreomycin was least resistant amongst the 2<sup>nd</sup> line injectable ATT drugs.

**Conclusion:** The aminoglycosides are more resistant than macrocyclic drugs. High rate of resistance among injectables warns the clinician of using these drugs judiciously to avoid emergence of XDR TB.

#### PD-818-31 Successful replication of the Tanzanian tuberculosis detection rat programme in Mozambique

E Valverde,<sup>1</sup> N Beyene,<sup>2</sup> I Manhiça,<sup>3</sup> T Edwards,<sup>2</sup> A Mahoney,<sup>2</sup> S Viegas,<sup>4</sup> C Cox,<sup>2</sup> C Mulder.<sup>2</sup> <sup>1</sup>TB Program, APOPO, Maputo, Mozambique; <sup>2</sup>TB Program, APOPO, Morogoro, United Republic of Tanzania; <sup>3</sup>Tuberculosis National Control Program, Ministry of Health, Maputo, <sup>4</sup>National Institute of Health, Ministry of Health, Maputo, Mozambique. e-mail: emilio.valverde@apopo.org

**Background and challenges to implementation:** The TB case detection rate in the World Health Organization Africa Region was estimated to be 59% in 2012, meaning that close to half of active tuberculosis (TB) cases remain undetected and continue to transmit TB. The unavailability of rapid diagnostic tools is one of the main challenges for TB control in resource-limited settings.

**Intervention or response:** Trained giant African pouched rats have been used in Tanzania to detect TB in human sputum samples in DOTS center microscopy negative TB suspects since 2008. In January 2013, a second laboratory located in the city of Maputo, Mozambique, started to use the same method in collaboration with 8 health units.

**Results and lessons learnt:** In 2013, TB detection rats at the Maputo laboratory evaluated 18,475 samples from 9,238 patients. Microscopy performed at health units found 1,262 (14%) of these patients positive for TB. Trained TB detection rats detected 556 additional TB patients, accounting for a 44% increase in TB detection rates. During the same period, TB detection rats at Morogoro laboratory in Tanzania evaluated 49,973 samples from 25,966 patients. For these samples, DOTS center microscopy identified 4,015 patients as positive. Tanzania TB detection rats identified 1,793 additional patients, which mean a 45% increase in TB detection



rates. All the additional TB patients found by TB detection rats were confirmed by concentrated sputum-smear microscopy by auramine staining and LED examination.

**Conclusions and key recommendations:** Both Maputo and Morogoro results are very similar, indicating that TB detection rats are a scalable and replicable tool to screen large numbers of individuals in a relatively short period of time. TB detection rats revealed a significant number of patients missed by conventional microscopy, thus suggesting that TB detection using trained rats can contribute to accelerate TB control in resource-limited settings.

### PD-819-31 Pattern of anti-tuberculosis drugs resistance among Pakistani population: a six-year study

M Javaid,<sup>1</sup> S Asif,<sup>1</sup> A Ahmed,<sup>1</sup> S Siddiqi.<sup>1</sup> <sup>1</sup>Laboratory, The Indus Hospital, Karachi, Pakistan. Fax: (+92) 21 3511 2718. e-mail: moona\_javaidd@yahoo.com

**Background:** Pakistan ranks fifth amongst TB high-burden countries worldwide. Facilities of drug susceptibility testing especially for 2<sup>nd</sup> line TB drugs are not available in most of the testing labs in Pakistan. This study was conducted to establish the drug resistance pattern among newly diagnosed and treated TB patients in Pakistan.

**Design/Methods:** A hospital based retrospective study was used to evaluate the pattern of anti-TB drugs resistance among new and previously treated patients at The Indus Hospital from Nov. 2007 to Dec. 2013. Clinical specimens were processed by NaOH-NALC method and inoculated in BACTEC MGIT 960 as well as LJ medium and DST for the first & 2<sup>nd</sup> line drugs was performed by MGIT 960.

**Results:** A total of 5100 suspected/treated TB patient's specimens were processed. There were 2456 new/Treated cases of Tuberculosis. Among these 44.9% were sensitive to all drugs, 55.1% had some level of drug resistance with 37.47% being MDR and 1.42% XDR. Among resistant cases INH resistance was the highest (52.1%), while resistance to STR was 38%, RIF 6.6%, EMB 1.17% and PZA 2%. The percentage of drugs resistance among poly-resistant cases INH+STR was 53%, INH+STR+PZA 19%, INH+PZA 5%, INH+EMB 4%, INH+STR+ETB 5%, INH+PZA+ETB 2.7%, while resistant to all the five drugs was 4.8%. Among MDR cases additional resistance to other first-line drugs was INH+RIF only 17%, with STR 11.5%, with EMB 5%, with PZA 13%, with EMB+PZA 10%, with STR+EMB 6%, with STR+PZA 13.5% and with STR+EMB+PZA were 23.7%. Second-line drugs resistance among MDR cases was as follows: resistance to FQ 54%, ETH 19.7%, CM 0.7%, AK 0.5%, KM 0.7%, FQ+ETH 18%, FQ+AK 1.2, FQ+CM 0.5%, CM+AK 0.7% while 3.1% were resistant to all drugs. In Non-MDR cases resistance to FQ was 19.7%, ETH 10.5%, AK 2.3%, FQ+ETH 3.4%.

**Conclusion:** Among the first-line drugs 52% cases showed resistance to INH. In general drug resistance especially MDR/XDR is high in our study population. This indicates that second-line drug susceptibility testing is critical in this setting to treat patients effectively. More widely availability of drug susceptibility testing facilities would help in TB control in Pakistan.

### PD-820-31 Validation of thin layer agar assay for direct rifampicin and isoniazid drug susceptibility testing in rural Shiselweni, Swaziland, 2012

G Obregon Boltan,<sup>1</sup> B Kerschberger,<sup>1</sup> G Maphalala,<sup>2</sup> A Antierens,<sup>1</sup> R Dela Tour.<sup>1</sup> <sup>1</sup>Operational Centre, Médecins Sans Frontières, Geneva, Switzerland; <sup>2</sup>National Reference Laboratory, Ministry of Health, Mbabane, Swaziland. e-mail: flankan.damagon@gmail.com

**Background:** We evaluated the performance of the non-commercial low cost method thin layer agar assay (TLA) for drug resistant tuberculosis (DRTB) detection in Shiselweni, Swaziland. Currently there is no data on the validation that has been carried out by WHO to enable routine program use of TLA, thus is the aim of to inform decision makers on its accuracy and feasibility in a high TB/HIV prevalence context.

**Design/Methods:** From January to October 2012, all presumptive TB cases presenting to one secondary and 7 primary health facilities in Swaziland were eligible for inclusion. Samples were processed in parallel by Lowenstein-Jensen (LJ), TLA, Xpert® MTB/RIF and acid-fast microscopy (auramine-rhodamine staining) in Nhlanguano Microbiology laboratory; strains were tested for rifampicin (RIF) and isoniazid (INH) susceptibility by the proportion method by a supra-national reference laboratory (Mycobacteriology Laboratory, Institute of Tropical Medicine-Antwerp, Belgium). Test accuracy was assessed by computing sensitivity and specificity estimates for TLA in comparison with the reference methods.

**Results:** 1,113 samples corresponding to 1,061 patients were evaluated. 1,027 (92.3%) were SM-negative. A good agreement between TLA and the LJ-culture reference method was observed for TB detection. Sensitivity of TLA was 100% (95% CI 96.5–99.9), significantly higher ( $p < 0.05$ ) than for Xpert® MTB/RIF (83.2%; 95% CI 75.7–88.8). Contamination rate was 18.6% ( $n=207$ ) for LJ, and 3.8% ( $n=43$ ) for TLA. For detection of INH and RIF resistance, we observed high sensitivity and specificity of the TLA assay when compared to the DST reference method. Sensitivity was 92.6% (IC95% 74.2–98.7) for INH and 100% for RIF, and specificity was 100% for both drugs. Sensitivity of Xpert® in the detection of RIF-resistance was 80% (95% CI 44.2–96.5), and specificity was 98.7% (95% CI 92.1–99.9). Median time to detection was decreased by 22 days ( $p < 0.01$ ) for TLA (9 days); IQR 6–13.5) when compared with LJ (31; IQR 27–43.8).

**Conclusion:** TLA was feasible in a programmatic context and performed better than LJ and Xpert®. Because of its



reduced costs, ease of performance, lack of sophisticated equipment and reduced laboratory infection control needs, TLA supports sustainable scale-up of TB/DRTB diagnostic and thus contributing to the control of the TB epidemic. The WHO guidelines on the use of TLA need to be reviewed to allow for expansion of DRTB diagnostic in resource constraint settings.

### PD-821-31 Prevalence of ofloxacin resistance among DR-, MDR- and XDR-TB patients in a TB centre, Karachi

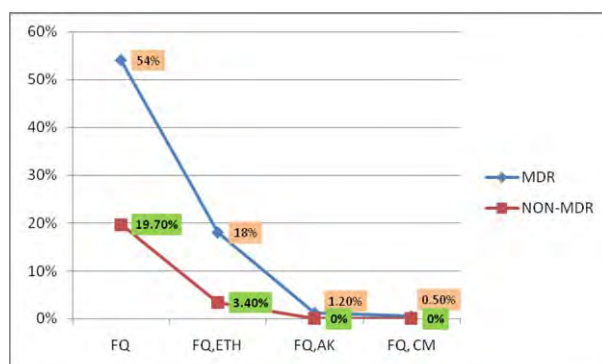
A Ahmed,<sup>1</sup> M Javaid,<sup>1</sup> S Asif.<sup>1</sup> <sup>1</sup>Laboratory, The Indus Hospital, Karachi, Pakistan. Fax: (+92) 21 3511 2718. e-mail: moona\_javaid@yahoo.com

**Background:** Fluoroquinolones are key second line anti-tuberculosis drugs, usually used in the treatment of Multi-Drug Resistant Tuberculosis (MDR-TB). Therefore fluoroquinolones resistance in *Mycobacterium tuberculosis* (MTB) makes the disease worse and chances of getting extensive-drug Resistant Tuberculosis (XDR-TB) becomes higher. It is therefore very important to determine the frequency of Ofloxacin resistance among DR, MDR and XDR TB patients.

**Design/Methods:** A total of 2456 culture positive clinical specimens including pulmonary and extra pulmonary TB were submitted to The Indus Hospital diagnostic laboratory from 2008 to 2013 for AFB culture and DST (Drug susceptibility testing). Their culture and DST were performed by liquid (7H9) MGIT 960 method. Culture positive samples after confirmation of *Mycobacterium tuberculosis* were subjected to Drug susceptibility testing by liquid (MGIT 960) method.

**Results:** Out of 2456 TB positive specimen, 1105 (44.9%) were sensitive to all first line drugs and 1351 (55.1%) showed resistance to anti-TB drugs. Among these 1351 patients 255 (18.77%) were mono drug resistant, 145 (5.88%) Poly drug resistant (PDR), 923 (67.96) Multi-drug resistant (MDR) and 35 (2.58%) were XDR. Out of 923 MDR TB patients, Ofloxacin resistance was 54%, PDR was 19.7% while in 35 extensive-drug resistant TB, Ofloxacin resistant was 100%.

**Conclusion:** Resistance to Ofloxacin is significantly high in MDR and PDR TB patients hence there is an urgent need to improve drug susceptibility testing in Pakistan and for accurate treatment.



### PD-822-31 Evaluation first line anti-tuberculosis drugs of the nitrate reductase assay for detection of resistance to the

S Fourati,<sup>1</sup> M Kaffel,<sup>1</sup> c Marouane,<sup>1</sup> S Kammoun,<sup>1</sup> L Slim-saidi,<sup>2</sup> F Messadi.<sup>1</sup> <sup>1</sup>Microbiology, Regional Laboratory of Hygiene Sfax Tunisia, Sfax, <sup>2</sup> Microbiology, Microbiology Laboratory, Pneumology Hospital, Ariana, Tunisia. e-mail: smaoui\_salma@yahoo.fr

**Background:** The emergence of *Mycobacterium tuberculosis* multi-drug-resistant strains has hindered tuberculosis control. So, the rapid diagnosis of TB drug resistance is a priority to avoid dissemination of resistant strains. The nitrate reductase assay (NRA) is a rapid and low-cost drug susceptibility test for detection of Multi-drug-resistant. **Aim:** To evaluate the performance of the NRA for detection of resistance to the first line anti-tuberculosis drugs.

**Methods:** the NRA was used as an alternative for resistance detection to the first line anti-tuberculosis drugs: isoniazid, rifampicin, ethambutol and streptomycin. A total of 73 strains of *M. tuberculosis* were studied during 2013 and the results were compared with the proportion method (PM) on Lowenstein Jensen medium.

**Results:** The majority of NRA results (65%) were available at day 14 after inoculation. The sensibility of the NRA was 100% streptomycin, rifampicin and isoniazid. It was 98.5% for ethambutol. The specificity was 100% for streptomycin, isoniazid and ethambutol. It was 66% for rifampicin. The overall agreement between the NRA and the PM was 94.5%.

**Conclusion:** The NRA constitutes a useful tool for detection of TB drug resistance in Low Countries with limited laboratory facilities due to its low costs, ease of performance and lack of requirement for sophisticated equipment.

### PD-823-31 Antimycobacterial activity of 22 Malian medicinal plants used against *Mycobacterium tuberculosis*, H37Rv

M Ballo,<sup>1,2</sup> M Sanogo,<sup>1</sup> B Diarra,<sup>1</sup> A Somboro,<sup>1</sup> M Maiga,<sup>1</sup> O Koita,<sup>1</sup> R Sanogo,<sup>2</sup> D Diallo.<sup>2</sup> <sup>1</sup>Faculté de Médecine et d'Odonto-Stomatologie (FMOS)/Faculté de Pharmacie (FAPH), Université des Sciences des Techniques et des Technologies de Bamako (USTTB), Centre de Recherche et de Formation sur le VIH et la Tuberculose, Bamako, <sup>2</sup>Institut National de Recherche en Santé Publique (INRSP) du Mali, Département de Médecine Traditionnelle, Bamako, Mali. Fax: (+223) 20 22 75 13. e-mail: mballo87@gmail.com

**Background:** Global Tuberculosis (TB) control is facing major challenges such as coinfection with HIV (TB/HIV), and the occurrence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis. The current TB drugs are getting less effective and associated with side effects limiting their use, especially with MDR and XDR infected patients. In Mali, many medicinal plants are used against various diseases including bacterial infections. The objectives of this study are to evaluate the in vitro antimycobacterial activities of 60 aqueous and organic crude extracts from 22 Malian

medicinal plants for their ability to inhibit the growth of MTB.

**Design/Methods:** TLC phytochemical screening was done for extract to determine the main chemical groups and the antibacterial activity against MTB (ATCC 27294) was evaluated with the Microplate Alamar blue assay (MABA).

**Results:** We found that 11 extracts from 9 plants were able to prevent the growth of MTB, with minimal inhibitory concentrations (MICs) in the range of 125µg/ml-625µg/ml. The best MIC (125µg/ml) was obtained with Ethanol extract of leaves of *Saba senegalensis*, *Vitellaria paradoxa*, dichloromethane extract of leaves of *Cola cordifolia*, root of *Strychnos spinosa* and *Ximenia americana*. Ethanol extract of leaves of *Guiera senegalensis*, root of *Zizyphus mauritiana* as well as methanol extract of leaves of *Anthocleista djalensis* inhibited the grow of MTB with a MIC at 250µg/ml. Methanol and dichloromethane extracts of bark of *Cola cordifolia* was also active at a MIC of 312.5µg/ml, 156.2µg/ml respectively. Dichloromethane extract of leaves of *Opilia celtidifolia* was less active with a MIC of 625µg/ml. We found that all the aqueous extracts were inactive on *M. tuberculosis*. Main chemical groups found in the active plants were: flavonoids, sterols and triterpenoids.

**Conclusion:** This study demonstrated the antimycobacterial activity of some Malian medicinal plants against MTB in vitro. More studies are needed to determine the in vitro toxicity before heading to the in vivo evaluations of the extracts.

#### PD-824-31 Resistance aux antituberculeux de première ligne dans les maisons d'arrêt à propos de 28 cas au Mali

F Camara,<sup>1</sup> A Cisse,<sup>1</sup> S Diarra,<sup>1</sup> K Traore,<sup>2</sup> L Keita,<sup>2</sup> F Bougoudogo,<sup>1</sup> A Van Deun.<sup>3</sup> <sup>1</sup>Bamako, Institut National de Recherche en Santé Publique, Bamako, <sup>2</sup>Bamako, Direction Nationale de la Santé, Bamako, Mali ; <sup>3</sup>Anvers, Institut de médecine Tropicale Prince Léopold, Anvers, Belgium. e-mail: fatimacamara\_fr@yahoo.fr

Malgré la mise en œuvre en 2007 de la stratégie Halte TB dans les maisons d'arrêt du Mali par le Programme National de Lutte Contre la Tuberculose (PNLT), la prise en charge de la tuberculose de 2007 à 2010 a montré des insuffisances. La stratégie avec un accent particulier sur laco-infection TB/VIH et la multirésistance n'était pas suffisamment intégrée. Cette étude prospective se propose de déterminer la proportion des cas ratés par la microscopie, les taux de résistance primaire et secondaire et le taux de co-infection dans 3 prisons. Le diagnostic a été passif et les suspects identifiés lors des consultations ont fourni des échantillons de crachats qui ont été traités par la méthode de Ziehl Nielsen à chaud dans les centres de santé de rattachement et par la culture au Laboratoire National de Référence. Les tests de sensibilité pour Isoniazide, Rifampicine, Ethambutol et Streptomycine ont été réalisés par la méthode des proportions sur Lowenstein Jensen (LJ), selon la technique standard sur toutes les souches de *Mycobacterium tuberculosis* obtenues. Tous les suspects ont été conseillés et ceux

qui ont accepté ont été testés au VIH. Sur 1900 détenus des trois maisons d'arrêt, 213 suspects de tuberculose ont été identifiés, soit 198 nouveaux jamais traités et 15 déjà traités. Vingt-cinq cas de tuberculose pulmonaire prouvée par la bactériologie ont été détectés parmi les jamais traités, et trois parmi les déjà traités soit une prévalence de 1,3%. Parmi les 28 cas détectés au cours de l'étude, sept l'ont été par la culture soit 25% représentant les cas ratés par la microscopie. Les tests de sensibilité parmi les vingt cinq jamais traités ont montré cinq cas de polyrésistance à l'Isoniazide et à la Streptomycine, ainsi que six cas de monorésistance à la Streptomycine. Toutes les souches des déjà traités ont été sensibles aux quatre antituberculeux testés. Aucun cas de MDR n'a été détecté. Sur 213 suspects, 199 (93,4%) ont accepté le test VIH et quatre (2%) sont positifs. Et parmi les 28 tuberculeux détectés deux (7%) sont co-infectés. Des séances régulières de dépistage actif, organisées par le programme national, utilisant les méthodes rapides de diagnostic et de détection de la résistance, associées à une bonne observance du traitement, permettront une réduction du poids de la tuberculose dans nos maisons d'arrêt.

#### PD-825-31 Estimating the operational costs of tuberculosis diagnosis in Perú

T Wingfield,<sup>1,2</sup> E Ramos,<sup>1,2</sup> T Valencia,<sup>1,2</sup> S Carrera,<sup>1,2</sup> M Ching,<sup>1,2</sup> Tom Tovar,<sup>2,3</sup> M Tovar,<sup>1,2</sup> C Evans.<sup>1,2,3</sup>

<sup>1</sup>IFHAD: Innovation For Health And Development, Universidad Peruana Cayetano Heredia LID218, Lima,

<sup>2</sup>Asociacion Benefica PRISMA, IPSYD: Innovacion Por la Salud Y el Desarrollo, Lima, <sup>3</sup>IFHAD, Infectious Diseases & Immunity, Wellcome Trust Imperial College Centre for Global Health Research, Lima, Peru. e-mail: thea.wingfield@gmail.com

**Background:** Research concerning tuberculosis (TB) diagnostic costs is limited, especially in resource-constrained settings. The data that are available are usually restricted to the costs of materials purchased in well-resourced countries. Accurate operational TB diagnosis costs are required to plan and implement feasible TB control programs. **Objective:** To undertake an analysis of the economic costs of TB smear and culture tests in a TB research laboratory in Lima, Perú.

**Methods:** From June to December 2013, direct costs were recorded for sputum smears (n=5061) and 3 culture-based TB diagnostic tests: thin-layer agar MDR/XDR-TB "Colour Test" (n=5061); Microscopic-Observation Drug-Susceptibility (MODS, n=1333); and Tetrazolium Microplate Assay (TEMA, n=420). TEMA culture was only performed on positive TB cultures growing in the Colour Test or MODS. "Unit" (per test) costs were calculated using both traded goods (laboratory equipment and materials purchased in Peru) and non-traded goods (staff time, rent, maintenance and overheads). Sample collection and transportation costs were not considered. The "time-observation" method was used to assess costs from a laboratory services perspective: average time and proportion of total laboratory working time required to perform each test; and total number of tests performed. Two complimen-

tary analyses of MODS costs were performed: assuming batched MODS testing (5 samples processed simultaneously) and without batched testing (<5 samples available). All costs were converted to US\$.

**Results:** The unit cost of a smear test was US\$3.23. Of the 3 culture tests, the Colour Test had the lowest unit cost (US\$10.43), followed by MODS (US\$18.68), and TEMA (US\$41.22, Figure). Traded goods as a proportion of total test costs was lowest for smear (28%), followed by the Colour Test (41%), TEMA (53%) and MODS (55%). When MODS samples were not batched, the unit cost was up to 3-times higher.

**Discussion:** It is difficult to give reliable unit costs for diagnostic tests because the calculations are influenced by: national market price and importation costs; laboratory practices such as processing rates, batching, shelf-life of materials and biosafety levels and human resource costs. Non-traded goods make up a significant proportion of overall TB diagnostic costs, therefore, considering only traded goods when budgeting TB control program activities will underestimate overall costs and is not recommended.

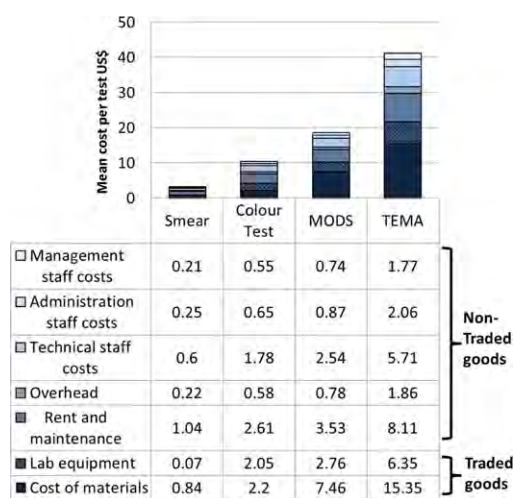


Figure: Average costs in US\$ for 4 tuberculosis diagnostic tests (Smear, Colour Test, MODS, TEMA)

### PD-826-31 High-tuberculosis diagnostic yield from culturing salivary sputum samples

E Ramos,<sup>1</sup> A Sloutsky,<sup>2</sup> CE Osorio,<sup>1</sup> T Valencia,<sup>1</sup> M Llacza,<sup>1</sup> M Ching,<sup>1</sup> M Tovar,<sup>1,3</sup> C Evans.<sup>1,3,4</sup> <sup>1</sup>IFHAD: Innovation For Health And Development, Universidad Peruana Cayetano Heredia, San Martin de Porres, Lima, Peru.; <sup>2</sup>Massachusetts Supranational TB Reference Laboratory, Shrewsbury, MA, USA; <sup>3</sup>Innovación por la Salud y el Desarrollo (IPSYD), Asociación Benéfica Prisma, San Miguel, Lima, Peru; <sup>4</sup>Section of Infectious Diseases & Immunity, Wellcome Trust Centre, Imperial College London, UK. Fax: (+511) 483 2942. e-mail: ericsteverm@yahoo.com

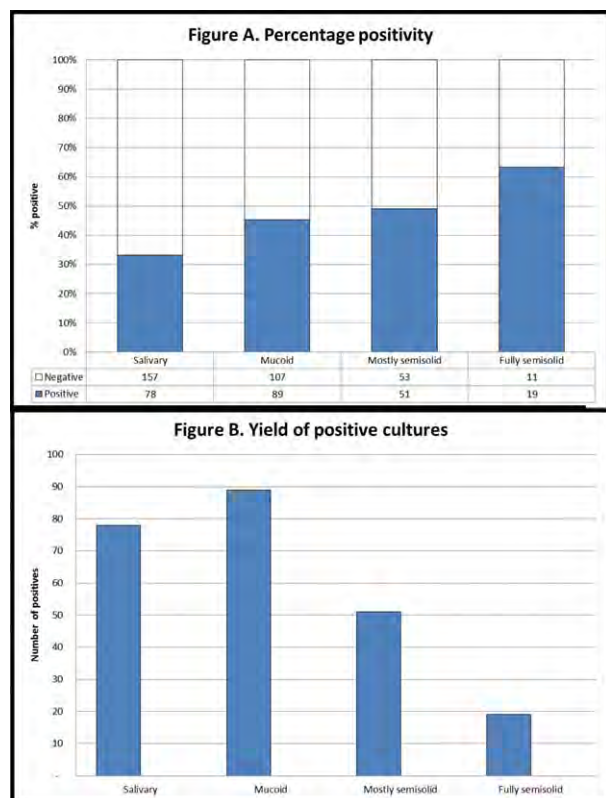
**Background:** TB diagnosis culture is influenced by sputum sample consistency. Some laboratories reject or discard salivary sputum samples because it is believed that TB diagnosis is reduced when the quality of sputum is low.

**Objective:** To characterise the effect of sputum consistency on TB culture diagnosis, including defining the contribution from salivary sputum samples.

**Methods:** Sputum specimens were collected from people about to commence treatment for TB disease who lived in the study site of Ventanilla, on the outskirts of northern Lima, Peru, between May 2013 and February 2014. Sputum specimens (n=565) were decontaminated by mixing with trisodium phosphate in the sputum pot then were cultured using thin-layer agar (TLA) with Middlebrook 7H11 culture medium with supplements to promote growth and reduce contamination. The identification of positive culture was determined by naked-eye by colorimetric indicator 2,3-Diphenyl-5-(2-thienyl)tetrazolium chloride (STC).

**Results:** The percentage positivity of TLA culture was lower for salivary samples (P=0.0012): 33% of salivary sputum samples; 45% of mucoid samples; 49% of mostly semisolid sputum samples; and 64% of fully semisolid samples (Figure A). However, because salivary sputum samples were frequent, they yielded 33% of all positive cultures (Figure B).

**Conclusions:** Salivary sputum were least likely to be TB culture positive but should not be refused or discarded by TB diagnostic laboratories because they provided one third of patients with confirmation of their TB diagnosis and an opportunity for drug-susceptibility testing.





## 29. AFB SMEAR MICROSCOPY

### PD-827-31 Tests de sensibilité aux antituberculeux de première ligne à Kayes (Mali): utilisation du transport public pour l'acheminement des prélèvements

A Cisse,<sup>1</sup> H Touré,<sup>2</sup> B Diarra,<sup>3</sup> K Traore,<sup>4</sup> F Camara,<sup>1</sup> J Kamaté,<sup>2</sup> MH Kaba,<sup>3</sup> F Bougoudogo.<sup>1</sup> <sup>1</sup>Institut National de Recherche en Sante en Publique, Bamako, <sup>2</sup>Hopital Fousseyni Daou, Kayes, <sup>3</sup>Centre de Recherche et de Formation sur la Tuberculose et le VIH, Bamako, <sup>4</sup>N'tomikorobougou, Programme National de Lutte Contre la Tuberculose, Bamako, Mali. e-mail: aissatacisse@yahoo.fr

**Introduction:** Au Mali, le diagnostic de la tuberculose multi-résistante (TB-MR), envisagé en cas d'échec de retraitement, rarement pour rechute ou pour co-infection TB/VIH et son traitement se font uniquement à Bamako, la capitale. Le patient suspect non résident, voyage et reste à sa propre charge avant confirmation entraînant refus et perte de vue. Le but de cette étude est de diagnostiquer la tuberculose et la TB-MR à partir de prélèvements acheminés par le transport public de Kayes, à 420 km de Bamako.

**Méthodologie:** Les patients à frottis positif et les patients VIH+ en présomption de TB ont été recrutés après consentement éclairé de Mai 2012 à Avril 2013. Les échantillons ont été envoyés le jour de la collecte ou conservés à 4°C avant envoi sous financement du GIP-Esther. Le container tertiaire, une glacière pouvait accepter 10 crachoirs et des accumulateurs de froid. La culture, les identifications morphologique et antigénique (TBciId MPT64) et les tests de sensibilité aux antituberculeux de première ligne ont été réalisés par le MGIT Bactec 960 au laboratoire de référence. Les atypiques ont été identifiés par le GenProbe au CEREF.

**Résultats:** Les 102 patients inclus avaient 32 ans comme âge médian et comme sexe ratio 2,92 (76/26). Parmi ces patients, le test VIH a été réalisé chez 96 dont 59 négatifs et 37 positifs au VIH-1, non proposé à 2; 2 sont perdus de vue et 2 ont refusé. Parmi 112 crachats collectés, 89% ont été reçus et traités au laboratoire soit 100 prélèvements. Une glacière était envoyée à 1000 FCFA (1,52 euro) contre 10000 (15 euros) pour le malade. Le délai moyen entre l'envoi et la réception était de 20 h. Un délai de 1 à 8 jours se sont écoulés entre la collecte et la mise en culture. Sur les 66 cultures positives, 56 contenaient une mycobactérie du complexe tuberculis. Deux TB-MR ont été observées sur 10 cas de résistance. Un malade MR est décédé avant les résultats, le second a été référé à Bamako pour le traitement de seconde ligne. Neuf patients étaient co-infectés TB/VIH. Deux patients VIH+ portaient une mycobactérie du complexe avium-intracellulaire.

**Conclusion:** Le transport des échantillons permet un diagnostic et une prise en charge rapides et a été intégré dans la politique de diagnostic de la TB-MR au Mali. Cependant le délai d'envoi et ou la température de conservation n'étant pas toujours respectés, des tech-

niques ne nécessitant pas une chaîne de froid devraient être envisagées.

### PD-828-31 Comparative yielding of acid fast bacilli from three specimen examinations: experience from a high-burden laboratory in Bangladesh

S M M Kamal,<sup>1</sup> MS Hossain,<sup>1</sup> M Chawdhury,<sup>1</sup> S K Sarker,<sup>1</sup> O Ahmed,<sup>1</sup> U Habiba,<sup>1</sup> R Sultana,<sup>2</sup> MA Husain.<sup>3</sup> <sup>1</sup>National Tuberculosis Reference Laboratory(NTRL), National Institute of Diseases of the Chest and Hospital(NIDCH), Dhaka, <sup>2</sup>TB CARE II, University Research Corporation (URC), Dhaka, <sup>3</sup>National Tuberculosis Control Program(NTP), Dhaka, Bangladesh. e-mail: ntrlnidchbd@yahoo.com

**Setting:** National Tuberculosis Reference Laboratory (NTRL), National Institute of Diseases of the Chest and Hospital (NIDCH), Bangladesh.

**Background:** Smear microscopy is still the gold standard for diagnosis of pulmonary tuberculosis in high burden countries like Bangladesh. Though WHO recommended 2 smear (spot and morning) examinations, but still there is no study regarding this experience in Bangladesh.

**Objective:** This retrospective study was carried to see effectiveness of morning and spot smear examination for diagnosis of pulmonary tuberculosis in Bangladesh.

**Patients and methods:** All patients attending in and out patient departments of NIDCH with respiratory symptoms and or abnormal chest X-rays provided three sputum samples each for acid-fast bacilli smear microscopy were considered. Systematic external quality assurance was done by designated EQA center as per national tuberculosis control program guideline. A total of 16,144 TB suspects submitted three samples on two consecutive days (spot, early morning, spot) had been considered for this study between January 2013 and December 2013. Smears were prepared and stained by Auramine O staining method under LED Fluorescence Microscopy as per standard operating procedure.

**Results:** Out of total 48432 smears examined a total of 4476 smears including 1806 cases were positive. The smear and case positivity rate were 9.24% and 11.1% respectively. Total 3 samples were positive in 1069 cases. Only 1<sup>st</sup> and 2<sup>nd</sup> samples detected 486 cases, 1<sup>st</sup> and 3<sup>rd</sup> 27 cases and 2<sup>nd</sup> & 3<sup>rd</sup> 19 cases only. 1<sup>st</sup> sample alone detected 160 cases, 2<sup>nd</sup> sample alone 31 cases and 3<sup>rd</sup> sample 14 cases. Therefore it is evident that spot and early morning sample will be enough for the diagnosis of pulmonary tuberculosis.

**Conclusion:** This retrospective analysis from a high burden laboratory indicated that spot and early morning smears examination will be sufficient for routine sputum microscopy. This observation therefore correlative with the WHO recommendation.

### PD-829-31 A novel automated microscope system for detection of mycobacteria in acid-fast stain procedures via image recognition technology

Y Lin,<sup>1</sup> Y Sun,<sup>2</sup> J Chen,<sup>3</sup> J Chen,<sup>2</sup> Z Chen,<sup>2</sup> C Lee,<sup>2</sup> F Huang,<sup>1</sup> Y Lee.<sup>1</sup> <sup>1</sup>Human Resource and Knowledge Management, National Kaohsiung Normal University, Kaohsiung, <sup>2</sup>Computer Science and Information Engineering, National Cheng Kung University, Tainan, <sup>3</sup>Biomedical Engineering, National Chiao Tung University, Hsinchu, Taiwan. Fax: (+886)76051379. e-mail: easonlin@ncku.edu.tw

**Background:** Tuberculosis is an emerging infectious disease worldwide. The most robust and economical method for laboratory diagnosis of pulmonary tuberculosis is based on sputum smears stained by the acid-fast stain method for acid fast bacilli (AFB). However, it mostly relies on human examination, which is tedious and error-prone. The objective of this study is to develop a novel automated system for identification of AFB under microscope using image recognition technology.

**Design/Methods:** An automated microscope system was developed with (1) microscopic imaging system with auto-focusing and slide-scanning mechanism; (2) image recognition system for detection of positive AFB (Figure 1). The microscopic images were digitally captured at 400x (instead of 1000x) from each smear. In detection phase, candidate AFBs were marked and differentiated from other tissues in smear based on color/geometrical characteristics. In classification phase, the feature parameters were applied to a proprietary classifier software. The slide was recognized as positive if any AFB was identified in the image. We compared our computer results with laboratory technicians (human) using the same slide in two Veterans General Hospitals in Taiwan (VGH-A and VGH-B).

**Results:** The accuracy of computer results in VGH-A (n=146) was 90.5% (Sensitivity 68.6% and Specificity 97.3%) which performed better than human (Accuracy 86.3%, Sensitivity 35.5%, and Specificity 100%). Human missed 20 positive slides that were detected by computer. However, computer missed 11 positive slides which may be due to the insufficient coverage of smear when taking images. This shortcoming was later improved by increasing the image coverage area. In VGH-B (n=193), the accuracy of computer results was 99.0% (Sensitivity 100% and Specificity 97.5%) which performed better than human (Accuracy 96.9%, Sensitivity 94.5%, and Specificity 100%). Human missed 6 positive slides which were detected by computer. It is noteworthy that VGH-B used expensive fluorescent stain as screening follow by AFS, and still missed 6 slides.

**Conclusion:** The automated microscope system exhibits excellent sensitivity and specificity in detecting AFB which can significantly decrease the false-negative results due to human errs. Our automated system requires only minimal technician skill when staining and loading the slides. Such system could achieve higher laboratory quality and efficiency to detect AFB and halt the TB pandemic worldwide.



### PD-830-31 Evaluation of TBDx, an automated platform for fluorescence smear microscopy in Abuja, Nigeria

L Lawson,<sup>1</sup> R Dacombe,<sup>2</sup> J O Obasanya,<sup>3</sup> S T Abdurrahman,<sup>4</sup> O Oladimeji,<sup>1,2</sup> C Iweha,<sup>1</sup> C Okoli,<sup>1</sup> L Cuevas.<sup>2</sup> <sup>1</sup>Tuberculosis Research Unit, Zankli Medical Centre, FCT-Abuja, Nigeria; <sup>2</sup>Tropical Medicine, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, UK; <sup>3</sup>National Tuberculosis and Leprosy Control Programme (NTBLCP), Federal Ministry of Health, Nigeria, FCT-Abuja, <sup>4</sup>FCT Tuberculosis and Leprosy Control Programme (TBLCP), FCT Ministry of Health, FCT-Abuja, Nigeria. e-mail: droladfb@gmail.com

**Background:** Most patients with symptoms of TB in Nigeria are screened using smear microscopy. However smear microscopy is labour intensive and laboratories often have a high workload. Automating the reading of smear microscopy would increase the efficiency of diagnostic centres with high patient turnout. A new platform called TBDx with a robotic arm can load and process up to 200 smears per day. However there is limited data on its performance in the field

**Design/Methods:** This prospective study compared head to head TBDx and LED-FM and TBDx against culture. Consecutive patients submitted two sputum specimens on the spot. Specimens were stained for LED-FM and one specimen underwent GeneXpert and one culture in solid media (x2).

**Results:** A total of 250 patients were enrolled per month, with 600 enrolled by end of April 2014. 14% of patients are LED-FM positive and 21% are culture positive. All specimens are processed by TBDx and a log of errors and experiences by lab staff is being generated. The study is blinded and test results will be available by August 2014.

**Conclusion:** The implementation of an automated platform in a very busy reference laboratory allowed the screening of larger number of specimens. Its use within a screening algorithm with GeneXpert may allow screening patients rapidly and efficiently. Full results will be presented at the Union.

### PD-831-31 Strengthening TB specimen referral in Zambia to improve diagnostic capacity: a stepwise approach

G Kahenya,<sup>1</sup> R Chibumba,<sup>2</sup> S Kaminsa,<sup>2</sup> M Muvwimi,<sup>3</sup> C Mulenga,<sup>2</sup> N Kapata.<sup>3</sup> <sup>1</sup>Management Sciences for Health (MSH), Centre for Pharmaceutical Services, Lusaka, <sup>2</sup>TB CARE I, FHI360, Lusaka, <sup>3</sup>Ministry of Health, National TB Program, Lusaka, Zambia. Fax: (+260) 211 261614. e-mail: gkahenya@msh.org

**Background and challenges to implementation:** TB continues to be a major public health problem in Zambia where the estimated prevalence is 388 per 100,000 population. Many Zambians infected with TB are left undiagnosed because they cannot afford to travel to a diagnostic facility or are too ill to make the journey. Fortunately, the nation is now using GeneXpert testing for rapid TB and drug resistant TB diagnosis. This system allows health facilities to test residents at the community-level and then send their TB specimen to the GeneXpert test facility in their catchment areas. Unfortunately, Zambia has yet to establish or formalize a specimen referral system for GeneXpert testing; so many infected residents remain undiagnosed.

**Intervention or response:** From January to June 2012, the National TB Program (NTP), with support from the USAID-funded TB CARE I project, conducted a baseline assessment to evaluate the quality of the TB specimen referral processes in four provinces. The team found the provinces did not have a standardized specimen referral mechanism, guidelines, protocols, or funds to pay for specimen transportation. To address these issues, the partners developed and distributed specimen referral standard operating procedures and flow charts to 27 facilities in the four provinces. They also introduced a specimen courier service, purchased and distributed specimen packaging and transportation materials, and conducted on-site training on specimen referral for all clinicians, nurses, laboratory technicians, and courier service staff. The NTP and TB CARE I then conducted regular, supportive supervision visits to monitor the facilities' progress in using the new referral system.

**Results and lessons learnt:** From November 2013 to March 2014, the NTP and TB CARE I collected and analyzed data from the intervention sites and compared it to baseline data.

**Results** showed that the number of diagnosed samples had increased by 29% (from 145 to 187 samples) and the turn-around time for diagnosis had reduced from 6 months to 2 months.

#### Conclusions and key recommendations:

**Interventions** to improve the TB specimen referral system in Zambia contributed to an increased number of diagnosed samples and a reduced diagnosis turn-around time. The NTP should sustain and expand these interventions to further improve access to rapid TB diagnosis so patients can initiate early treatment and break the cycle of TB transmission in Zambia.

### PD-832-31 Implementation experience of light-emitting diode fluorescence microscopy TB in TB microscopic centers in Amhara region of Ethiopia, 2013–2014

G Alemu,<sup>1</sup> J Seid,<sup>2</sup> A Alem,<sup>2</sup> M Melese,<sup>2</sup> Y Kassie,<sup>2</sup> M Melese,<sup>2</sup> B Girma,<sup>2</sup> D Jerene,<sup>2</sup> P Suarez.<sup>3</sup> <sup>1</sup>Amhara Regional Health Bureau, Disease Prevention and Control, Departement of Disease Prevention and Control, Bahir Dar, <sup>2</sup>Help Ethiopia Address the Low TB Performance (HEAL TB) project, Management Sciences for Health (MSH), Addis Ababa, Ethiopia; <sup>3</sup>MSH, Center for Health Services, Arlington, VA, USA. e-mail: jseid@msh.org

**Background:** Light-emitting diode microscopy (LED-FM) is recommended by the WHO for TB diagnosis at health facilities serving large populations. In line with this guidance, the Ethiopian Ministry of Health (MOH) purchased LED microscopes and prepared standard operating procedures for LED microscope utilization. In 2013, the Amhara Regional Health Bureau (RHB) then worked with the USAID-funded Help Ethiopia Address the Low TB Performance (HEAL TB) to pilot test the use of LED microscopes in Amhara.

**Interventions:** The RHB and HEAL TB distributed LED microscopes to 150 health facilities in Amhara and trained laboratory staff at the facilities to use these microscopes. The partners also provided the facilities with reagents and other supplies and prepared a designated space at each facility for reagent preparation. Senior laboratory specialists from regional referral laboratories and HEAL TB provided quarterly on-site supervision and mentoring to ensure the laboratory staff were following the standard operating procedures and using the LED microscopes correctly. The RHB and HEAL TB then analyzed performance indicators at 31 of the health facilities that were serving the highest volume of patients.

**Result and lessons learnt:** From October to December of 2012, the 31 health facilities examined 9,346 TB sputum slides using Ziehl-Neelson staining. After LED implementation, the number of examined slides increased to 12,470 in the final quarter of 2013. The number of presumptive TB cases identified increased from 3,721 to 4,311, and among those cases, the facilities identified 569 sputum smear positive slides at baseline and 805 in the final quarter of 2013. The slide positivity rate was 6.08% Ziehl-Neelson staining was used and 6.46% when LED microscopy was implemented. This translates to an increase in slide positivity rate of 6% with LED implementation.

Table. Comparison TB sputum smear results before and after the introduction of LED microscopy (2012–2013)

variables	Oct-Dec, 2012 (Baseline)	Oct-Dec, 2013
Number of slides examined	9,346	12,470
Number of presumptive TB case identified	3,721	4,311
Number of sputum smear positive case identified	569	805
Slide positivity rate	6.08%	6.46%

**Conclusion:** Use of LED microscopy increased the number of sputum smear positive cases diagnosed among



the presumptive TB cases identified. The use of LED microscopy should be scaled up to further improve TB case detection in Ethiopia.

#### PD-833-31 Quality of sputum specimen samples submitted for culture and drug susceptibility testing to the National Tuberculosis Reference Laboratory in Uganda

L Bulage,<sup>1,2</sup> J Imoko,<sup>1,3</sup> B Kirenga,<sup>4</sup> T Lo,<sup>5</sup> H Byabajungu,<sup>1,2</sup> K Musisi,<sup>1,2</sup> M Joloba,<sup>1,2</sup> E Bloss.<sup>5</sup>

<sup>1</sup>Central Unit, National Tuberculosis and Leprosy Programme - Uganda, Kampala, <sup>2</sup>Central Unit, National TB and Reference Laboratory-Uganda, Kampala, <sup>3</sup>TB Control Office, World Health Organization - Uganda, Kampala, <sup>4</sup>Division of Pulmonary Medicine, Makerere University College - Department of Medicine, Kampala, Uganda; <sup>5</sup>Division of TB Elimination, Centers for Disease Control and Prevention, Atlanta, GA, USA. e-mail: vtu3@cdc.gov

**Background:** A good quality sputum sample is important for obtaining accurate and timely tuberculosis (TB) drug susceptibility testing (DST) results. To date, no systematic evaluation of the quality of sputum samples submitted to the Uganda National Tuberculosis Reference Laboratory (NTRL) has been conducted. We determined the proportion of poor quality specimens received for DST at the NTRL and assessed the factors contributing to poor specimen quality.

**Design/Methods:** A cross-sectional study of sputum samples received at the Uganda NTRL from patients at high risk for multidrug-resistant (MDR) TB (e.g., previously treated cases, MDR-TB contacts, and health care workers) was conducted during July-October 2013. Demographic, clinical, and bacteriological data were abstracted from laboratory records. The following sputum sample quality indicators were also abstracted: timeliness, volume, packaging, and appearance. A good quality sample met all the four quality criteria:  $\geq 3$ ml volume, delivered within 72 hours from time of collection, triple packaged, and appearance of either muco-salivary, mucoid, muco-purulent, purulent, or blood stained. A poor quality sample failed to meet any one of the four indicators. Frequencies and proportions were calculated. Odds ratios (ORs) and 95% confidence intervals (CI) were used in bivariate and multivariate analyses.

**Results:** Overall 365 out of 556 (64%) samples included in the study were of poor quality; 16 percent (89/556) were not triple packaged, 8 percent (44/556) were  $< 3$ mls, 30 percent (164/556) were not delivered on time, and 39 percent (215/556) were salivary in appearance. In multivariate analysis, poor quality specimens were more likely to be collected during the eighth month of TB treatment (OR=2.2, CI=1.1-4.5), from the northeast or eastern zone (OR=2.1, CI=1.0-4.5), and from patients who had previously defaulted from treatment (OR=1.7, CI=1.0-2.9).

**Conclusion:** The majority of sputum samples received at the NTRL did not meet all the four quality indicators. Additional efforts are needed to improve quality of samples collected at the end of treatment in the northeast

and eastern zones and from patients who had previously defaulted.

#### PD-834-31 The contribution of light-emitting diode fluorescence microscopy (LED-FM) to smear positive TB case detection in the Tigray region of Ethiopia

P Nano,<sup>1</sup> C Kagoma,<sup>2</sup> B Woldemariam,<sup>3</sup> N Fituwi,<sup>4</sup> G Ayana,<sup>5</sup> P Suarez.<sup>6</sup> <sup>1</sup>TB CARE I, Management Sciences for Health (MSH), Centre for Health Services (CHS), Addis Ababa, Ethiopia; <sup>2</sup>MSH, Centre for Pharmaceutical Service, Dar es Salaam, Tanzania; <sup>3</sup>MSH, CHS, Addis Ababa, <sup>4</sup>Regional Reference Laboratory, National TB Programme, Tigray, <sup>5</sup>Ethiopia Public Health Institute, Ministry of Health, Addis Ababa, Ethiopia; <sup>6</sup>MSH, CHS, Arlington, VA, USA. e-mail: ckagoma@msh.org

**Background:** In resource constrained countries, microscopy using the conventional Ziehl Neelsen (ZN) method is widely used for TB case detection. However, ZN has low sensitivity compared to other tests, like culture. As an alternative, fluorescence microscopy (FM) is recommended, as it is about 10 percent more sensitive than the ZN method. In 2013, Ethiopia's National TB Program (NTP) introduced FM using light-emitting diode (LED) to improve TB case detection. The main challenge of rolling out LED-FM countrywide was sustained distribution of Auramine O stain, because the stain has a three-month shelf life.

**Intervention:** In 2013, the NTP introduced LED-FM at 12 hospitals in the Tigray region of Ethiopia, with support from the USAID-funded TB CARE I project. NTP and TB CARE I trained laboratory staff at each site on LED-FM and Auramine O stain preparation and then distributed LED microscopes and supplies to the hospitals. The partners conducted quarterly supervision visits to support FM implementation and performed external quality assurance panel testing to ensure staff proficiency in FM. To assess the benefits of the new method, the NTP and TB CARE I evaluated laboratory data from before LED-FM implementation (December 2012 to February 2013) to data after LED-FM implementation (December 2013 to February 2014).

**Results:** Data from the 12 hospital showed that, before LED-FM implementation, laboratories detected sputum smear positive (SS+) TB in 139 out of 2,420 presumptive TB case samples. After LED-FM implementation, the laboratories detected SS+ TB in 173 out of 2,745 presumptive TB case samples. The proportion of SS+ cases detected before and after LED-FM implementation was 5.7% and 6.3%, respectively, representing a 10.5% increase in the case detection yield. On-site preparation of Auramine O stains at the laboratories circumvented the challenge of stain's short shelf life and related distribution difficulties. Staff LED-FM proficiency was high due to the initial trainings and regular supervision. The EQA results showed that 9 sites tested 100% of their slides accurately, 2 tested 90% accurately, and 1 tested 80% accurately.

**Conclusion:** LED-FM implementation substantially increased the yield of smear positive TB cases at the 12

hospitals. This improvement can be attributed to LED-FM's increased sensitivity, staff trainings, follow-up supervision and EQA proficiency testing. This approach is being scaled up in Ethiopia and can be replicated in similar settings.

**Table1:** Smear positive TB cases detected before and after introduction of LED-FM at 12 hospitals in the Tigray region of Ethiopia

	Presumptive TB cases tested	Smear positive TB cases detected	Percentage	Increase in the yield of ss+ve TB cases
Before LED-FM implementation (December 2012-February 2013)	2,420	139	5.7%	Baseline
After LED-FM implementation (December 2013-February 2014)	2,745	173	6.3%	10.5%

### PD-835-31 Evaluation of cellScope-based digital LED fluorescence microscopy in Hanoi, Viet Nam

C Reber,<sup>1</sup> H Nguyen,<sup>2</sup> L Chaisson,<sup>3</sup> F Meyers,<sup>1</sup> V N Nguyen,<sup>2</sup> P Nahid,<sup>2,3</sup> D Fletcher,<sup>1</sup> A Cattamanchi.<sup>2,3</sup>  
<sup>1</sup>Bioengineering, University of California, Berkeley, Berkeley, CA, USA; <sup>2</sup>University of California Research Collaboration, Viet Nam National Tuberculosis Programme, Hanoi, Viet Nam; <sup>3</sup>Medicine, University of California, San Francisco, San Francisco, CA, USA. Fax: (+1)415-695-1551. e-mail: chaissonl@medsfgh.ucsf.edu

**Background.** Expanding access to sputum smear microscopy is a key priority for global TB control. Currently, TB microscopy services are limited to central health facilities in most high burden countries because of the need for standard lab microscopes and well-trained technicians. We evaluated the accuracy of digital smear microscopy using CellScope – a compact platform based on camera components found in a typical mobile phone. **Methods.** Consecutive patients evaluated for TB at Hanoi Lung Hospital from May-September 2013 were enrolled. Lab technicians prepared Auramine-O stained sputum smears and used a second sputum specimen for Xpert MTB/RIF testing. Technicians reviewed and interpreted the sputum smears using CellScope and a conventional LED fluorescence microscope (Primo Star iLed, Zeiss). Smear images captured by technicians were also analyzed by a computer vision algorithm. We compared the sensitivity and specificity of conventional LED FM to that of manual and automated reading of CellScope LED FM digital images, using Xpert as a gold standard.

**Results.** Of 333 patients enrolled, 100 (30%) were women, the median age was 53 (IQR 36–62), and 97 (29%) had Xpert-positive TB. Conventional LED FM was positive in 41 of 97 Xpert-positive TB cases (sensitivity 42%, 95% CI 32–53%) and negative in 234 of 236 (specificity 99%, 95% CI 97–100%) patients with negative Xpert results. Technicians achieved similar sensitivity (40% vs. 42%, difference –2%, 95% CI –16 to +12%) and specificity (100% vs. 99%, difference 1%, 95% CI –1 to +2%) as conventional LED FM when manually reviewing and interpreting smears using CellScope. While technicians reviewed a full length of the smear with CellScope, they only captured a median of 4

(range 1–8) images of each sputum smear, corresponding to 1/10<sup>th</sup> of the area covered by a full length of the smear. Automated analysis had a sensitivity of 21% (95% CI 13–31%), and specificity of 99% (95% CI 97–100%). Automated image acquisition and analysis of the full length of sputum smears with a second-generation CellScope platform are ongoing.

**Conclusions.** Diagnostic accuracy of CellScope for Xpert-positive TB was equivalent to conventional LED FM. Automated image analysis had nearly perfect specificity and reasonable sensitivity even when analyzing a small area of a sputum smear. CellScope has potential to increase quality of existing microscopy services and to further decentralize TB microscopy in low-income, high-burden settings.

**Table.** Diagnostic accuracy of Conventional LED FM, Manual reading of CellScope images, and Automated reading of CellScope images for Xpert-positive TB (N=333)

	Conventional LED FM n/N, % (95% CI)	Manual CellScope n/N, % (95% CI)	Automated CellScope* n/N, % (95% CI) (95% CI)
Sensitivity	41/97 42% (32%-53%)	39/97 40% (30%-51%)	17/82 21% (13%-31%)
Specificity	234/236 99% (97%-100%)	235/236 100% (98%-100%)	207/209 99% (97%-100%)
Positive predictive value	41/43 95% (84%-99%)	39/40 98% (87%-100%)	17/19 90% (67%-99%)
Negative predictive value	234/290 81% (76%-85%)	235/293 80% (75%-85%)	207/272 76% (71%-81%)

**Abbreviations:** 95% CI, 95% Confidence Interval; ZN, Ziehl-Neelsen; LED FM, Light-emitting diode fluorescence microscopy

\*N=291

### PD-836-31 A cross-sectional study of factors associated with tuberculosis diagnostic delay for smear microscopy in Namibia

I Mwaningange,<sup>1</sup> E Shipiki,<sup>2</sup> F Mavhunga,<sup>1</sup> B Bayer,<sup>1</sup> H Zaire,<sup>3</sup> E H Mitchell,<sup>4</sup> A Zezai.<sup>5</sup> <sup>1</sup>National Tuberculosis and Leprosy Program, Ministry of Health and Social Services, Windhoek, <sup>2</sup>Mycobacteriology, Namibia Institute of Pathology, Windhoek, <sup>3</sup>School of Medicine, University of Namibia, Windhoek, Namibia; <sup>4</sup>Headquarters, KNCV Tuberculosis Foundation, The Hague, Netherlands; <sup>5</sup>Namibia Country Office, KNCV Tuberculosis Foundation, Windhoek, Namibia. Fax: (+264)61252740. e-mail: zezai.a4@gmail.com

**Background:** Namibian TB policy states that results of sputum smears should be available to those with presumed TB within 2 days. A review in one region revealed a turnaround time (TAT) of 5 to 8 days for patients to receive a result. This study was designed to measure TAT in a nationally representative sample of Namibian health facilities and to investigate factors affecting turnaround time for sputum smear microscopy.

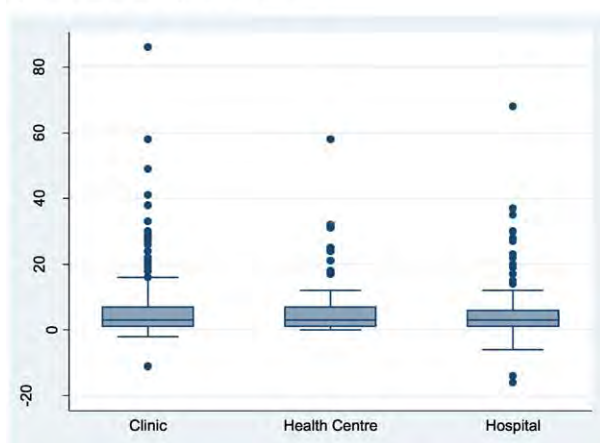
**Design/Methods:** A cross-sectional study was conducted in public health facilities from April to June 2012. TAT was defined as the time from sputum collection to decision to treat for TB. Stratified random sampling was used to recruit a sample size of 110 facilities (64 clinics, 15 health centres and 31 hospitals). A total of 153 point-of-service interviews were conducted and TAT calculated for 505 persons with presumed TB consecutively quota sampled from selected facilities. Data were double entered and analysis done using STATA version10.

**Results:** Clinics, health centres and hospitals had median TAT of 3 days with interquartile ranges (IQR) of 1–7, 1–7 and 1–6 respectively. The median TAT for smear

microscopy results was 5 days (IQR 2–23) among smear negative cases and 3 days; (IQR 1 to 7) in smear positive cases. The overall median TAT was 3 days (IQR 1–7 days) implying that in more than 50% of the cases evaluated, the TAT fell short of the NTLP benchmark of two days. Non-availability of a vehicle for TB control (OR 1.6, CI 1.1–2.4), experience of less than six months (OR 1.5, CI 1.0–2.3), and not having lab SOPs (OR 0.2, CI 0.0–1.2) were associated with prolonged TAT for smear microscopy. Work load of more than ten patients a day, distance from the lab, and not having been trained in past year did not have an effect on TAT. Surprisingly, good practices such as training of health care workers and linking laboratory computers to health facilities were not associated with rapid TAT.

**Conclusion:** Prolonged TAT is primarily due to inadequacies in the health system. There is need to address transport issues as well as strengthening the use of laboratory SOPs to improve TAT for smear microscopy in Namibia. These health systems related factors can be addressed by the ministry and the laboratory services as soon as possible. This study provides a national baseline to measure efficiencies gained via scale up of rapid diagnostics.

Figure1. Box Plot: TAT (days) by type of facility



### PD-837-31 Auramine staining and fluorescent microscopy for TB diagnosis: a controlled comparison of sputum smear microscopy protocols

S Datta,<sup>1,2</sup> M Ching,<sup>1,3</sup> T Valencia,<sup>1,3</sup> E Ramos,<sup>1,3</sup> M Tovar,<sup>1,3</sup> D Coleman,<sup>4</sup> C Evans.<sup>1,2,3</sup> <sup>1</sup>IFHAD: Innovation For Health And Development, Universidad Peruana Cayetano Heredia, Lima, Peru; <sup>2</sup>Infectious Diseases & Immunity, Wellcome Trust Imperial College Centre for Global Health Research, London, UK; <sup>3</sup>IPSYD: Innovacion Por la Salud Y el Desarrollo, Asociación Benéfica Prisma, Lima, Peru; <sup>4</sup>Microbiology, St Georges Hospital Medical School, London, UK. e-mail: sumonadatta@doctors.org.uk

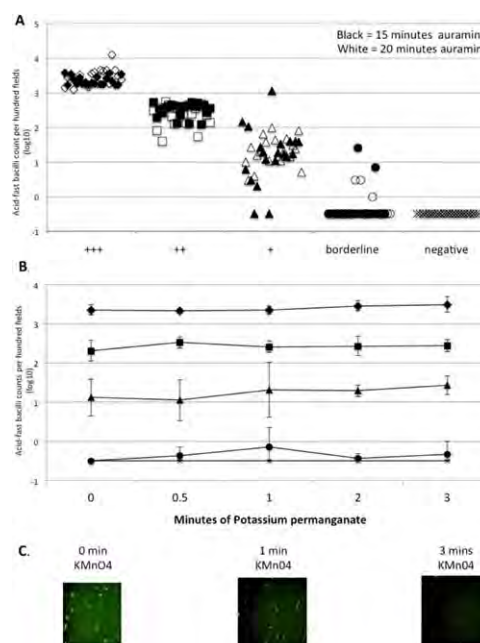
**Background:** Fluorescent sputum smear microscopy with auramine staining is the recommended tuberculosis (TB) microscopy method, due to its increased sensitivity and time efficiency compared to light microscopy with Ziehl-

Neelsen staining. However, international and national auramine staining standard operating procedures vary.

**Objectives:** To determine the effects on auramine microscopy results of the duration of: 1. auramine staining; 2. potassium permanganate (KMnO<sub>4</sub>) quenching of background fluorescence, and 3. to clarify the optimum auramine staining protocol.

**Methods:** A total of 200 sputum smear microscopy slides were made from vortex-homogenised sputum samples that were from patients with pulmonary tuberculosis that was graded by prior microscopy to be smear negative, borderline, +, ++ and +++. Each slide had 40 micro-litres of sputum spread over a 2 × 2 cm area. Slides were stained with auramine for either 15 or 20 minutes. After 2 minutes decolourisation with 0.05% acid-alcohol, background fluorescence was quenched by flooding with potassium permanganate for either 0.5 minutes (local recommendation), 1 minute (WHO protocol), 2 minutes (CDC recommendation), 3 minutes (positive control) or without quenching (negative control). Quadruplicate slides were used for each protocol. Slides were blinded and read the same day using 100x magnification, Nikon iLED microscope, with 10% of slides being re-read for quality control. All results were recorded as counts per hundred microscopy fields.

**Findings:** The duration of auramine microscopy staining had no effect on microscopy results (see figure A; 15 (black) versus 20 minutes (white),  $p=1.0$ ). Slides that had no KMnO<sub>4</sub> quenching had more background fluorescence (see figure C) that made microscopy less comfortable and slides stained with auramine for 20 minutes had lower TB counts ( $p=0.02$ ). However, whether quenching duration was 0.5, 1, 2 or 3 minutes had no effect on TB counts (see figure B, all  $p>0.3$ ). Linear regression shows that neither auramine nor KMnO<sub>4</sub> time had an effect on counts per hundred fields (coef=0.03  $p=0.7$  and coef=0.00  $p=1.0$  respectively).





**Conclusions:** For fluorescent sputum smear microscopy with auramine stain, the quenching step facilitates microscopy. However, the duration of auramine staining (15–20 minutes) and duration of quenching from 0.5–3 minutes had no effect on microscopy results, thus the shorter staining and quenching durations may be used to increase convenience and test speed.

### PD-838-31 To assess the workload of designated microscopy centers (DMC) under national tuberculosis programme, India

S Dhawan,<sup>1</sup> S Mannan,<sup>2</sup> P Patel,<sup>3</sup> KS Sachdeva.<sup>4</sup> <sup>1</sup>Ministry of Health & Family Welfare, Government of India, PATH, Central TB Division, New Delhi, <sup>2</sup>Central TB Division, Ministry of Health and Family Welfare, Government of India, World Health Organization, Country Office for India, New Delhi, <sup>3</sup>State Government, Family Welfare, Gujarat, Intermediate Reference Laboratory, Ahmedabad, Ahmedabad, <sup>4</sup>Directorate General of Health Services, Ministry of Health and Family Welfare, Government of India, Central TB Division, New Delhi, India. e-mail: alitangni@gmail.com

**Background:** India's Revised National Tuberculosis Control Programme adopted the DOTS strategy as the most systematic and cost-effective approach for tuberculosis control and sputum smear microscopy for reliable diagnosis in the general health system. The laboratory network in India is the world's largest with more than 13000 DMCs. We undertook this study to assess the daily workload of these DMCs.

**Design/Methods:** The monthly laboratory abstracts were compiled for 6 consecutive months (Jan-Jun 2013) from 13048 DMCs doing ZN sputum smear microscopy. This covers 100% population of India under NTP. All these DMCs are under the ambit of External Quality Assurance. The daily slide volume at these microscopy centers was calculated. We assessed the impact of various policy options on laboratory workload and for optimally utilizing the available laboratory services.

**Results:** The analysis of workload at DMCs across India showed that 29% (3820) were examining two or less than two slides a day, 55% (7189) were examining 3–10 slides, 12% (1625) were examining 11–24 in a day while only 3% (414) had high workload and were examining more than 25 slides a day. The laboratories which have high work load are in the district headquarters and at sub-district level.

**Conclusion:** We believe the NTP in India should reconsider the criteria for establishing the DMCs at one per 100,000 population. For high workload DMCs, deployment of human resource to maintain quality of services or increasing DMCs in area can be considered. Low workload DMCs maybe linked with collection centers and efforts should be made to increase referral from health facilities by sensitizing doctors, paramedics and community level workers. Moreover, further study can be conducted to understand usefulness of such DMCs in terms of improving access to services and workload of other laboratory investigations at such low workload DMCs.

### 30. WHAT DO SINGERS, FOOTBALL AND MAPS HAVE IN COMMON: NEW HORIZONS IN TB COMMUNITY ENGAGEMENT

#### PD-839-31 Participation de la communauté dans la prise en charge de la tuberculose au Sénégal

M T Mbodji.<sup>1</sup> <sup>1</sup>Projet GF, Plan Sénégal, Dakar, Senegal. Fax: (+221) 338 247 359. e-mail: mortalla4@yahoo.fr

**Contexte / Justifications :** Au Sénégal, la tuberculose demeure toujours un problème de santé publique. Selon les estimations de l'OMS la mortalité était estimée en 2012 à 20 cas pour 100000 habitants. Des avancées notables sont notés dans la détection des cas de TB toutes formes confondues qui est passé de 48% à 65% entre 1990 et 2012, tandis que le taux de succès au traitement des nouveaux cas est passé de 44% à 85%. Cependant malgré les efforts faits depuis la mise en place de ce programme, la morbidité et la mortalité attribuable à cette maladie restent toujours d'actualité. Pour y faire face, le recours à la participation communautaire a été identifié comme pouvant permettre d'accélérer la lutte conformément aux recommandations du Partenariat mondial Halte à la tuberculose.

**Interventions :** Plan Sénégal en collaboration en collaboration avec 7 ONG ont mis en œuvre un projet consistant à confier à des membres de la communauté formés le déroulement de 2 paquets d'activités de plaidoyer, communication et mobilisation sociale d'une part et de soins communautaires TB d'autre part. Le paquet de soins consiste à l'identification et à la référence des cas avec présomption de tuberculose qui sont dans la communauté vers les structures sanitaires pour y bénéficier d'un diagnostic et d'une prise en charge.

**Résultats et leçons apprises** Après 2 années de mise en œuvre du projet, 6,118 relais communautaires ont été formés sur la tuberculose à l'échelle nationale. Ces relais regroupés au sein de 442 organisations communautaires de base ont déroulé les 2 paquets. Les résultats principaux obtenus en 2013 ont été l'identification de 1,162 nouveaux cas confirmés de tuberculose à partir des 10,658 cas avec présomption de tuberculose référés par les acteurs communautaires soit un taux de positivité de 11%. Ce nombre de cas détectés par les acteurs communautaires représentait en 2013 une proportion de 12% de l'ensemble des cas de tuberculose à frottis positifs dépistés dans le pays. La notification nationale des cas de tuberculose a connu une hausse dépassant plus de 9,000 nouveaux cas de tuberculose à frottis positifs.

**Conclusion :** La mise en œuvre de ce projet a révélé le potentiel de la communauté à contribuer dans la lutte contre la tuberculose au Sénégal et ainsi dans l'atteinte des OMD. L'utilisation de la communauté ne nécessitant pas des coûts élevés a montré son efficacité et son efficience dans la détection des cas incidents de TB.

### PD-840-31 Measuring community involvement and engagement in TB care and control: experience from the GF supported TB projects of World Vision India and partners

S Mukhopadhyay,<sup>1</sup> S Cornelius,<sup>1</sup> V K Edward.<sup>1</sup> <sup>1</sup>Health, World Vision India, New Delhi, India.  
e-mail: sugata64@gmail.com

**Background and challenges to implementation:** World Vision India (WV India) and 6 partners have been implementing GF-supported Project Axshya since Apr'10. The project covers difficult-to-reach areas, conflict zones and high-risk population in 74 districts of 7 states of India to improve their access to TB services. During first phase (Apr'10 – Mar'13) WV India & partners sensitized 27,434 villages on TB (out of total 48,978 villages of project universe) but couldn't measure impact of such sensitization. In second phase (Mar'13 – Sept'15; ongoing) the project focused on high-impact & follow-up activities and intensified monitoring and aimed to measure impact of TB sensitization of the villages.

**Intervention or response:** To bring standard in project implementation WV India and its partners developed and rolled out a Standard Operational Procedure guideline. Like other activities of the project, TB sensitization of the villages was implemented to achieve objectives like, 1) To cover at least 14,800 villages in the second phase, 2) To assist at least 10% of those villages in preparing their TB action plan as part of village health plan, 3) To help villages in implementing their TB action plan by their internal funds, 4) To help villagers in detection of TB cases in their villages. The activities and their outcomes were meticulously documented and analyzed by the project staff.

**Results and lessons learnt:** Between Apr'13 – Dec'13, the project helped residents of 3944 villages to know about TB. Of those 500 villages developed their TB action plan and implemented activities like TB wall-writing, school-children's TB awareness rally, observance of WTD by their own funds. The villagers identified 2193 TB presumptive cases with help of the project, of which 940 screened for TB, 94 TB cases detected (positivity rate 10%) and put under DOT. 346 samples of sputum collected from those villages by community volunteers, 310 samples tested and 79 cases detected (positivity rate 25%) and put under DOT. Lost to follow-up during referral (57%) is a concern. Difference in positivity rate (15%) between physical referral and sputum collection is an important observation.

**Conclusions:** The interventions were able to measure community involvement& engagement in terms of facilitating village action plan to respond to local TB crisis and mobilizing identification of TB presumptive cases of the villages and their testing demonstrating that community involvement is key in TB control.

### PD-841-31 Factors associated with tuberculosis stigma: a systematic review

J Crispim,<sup>1</sup> L Silva,<sup>1</sup> M Yamamura,<sup>1</sup> I Freitas,<sup>1</sup>

TRS Silveira,<sup>1</sup> ACV Ramos,<sup>1</sup> IC Pinto,<sup>1</sup> RA Arcêncio.<sup>1</sup>

<sup>1</sup>Maternal-Infant Nursing and Public Health, Ribeirão Preto School of Nursing, University of São Paulo, Ribeirão Preto, SP, Brazil. e-mail: julianecrisp@gmail.com

**Background:** The relevance of the tuberculosis (TB) stigma has been widely discussed in the planning of disease control actions due to the impact on the diagnosis and treatment outcome. The study aimed to look for available evidences, in the scientific literature, about the associated factors to the TB stigma, in different contexts.

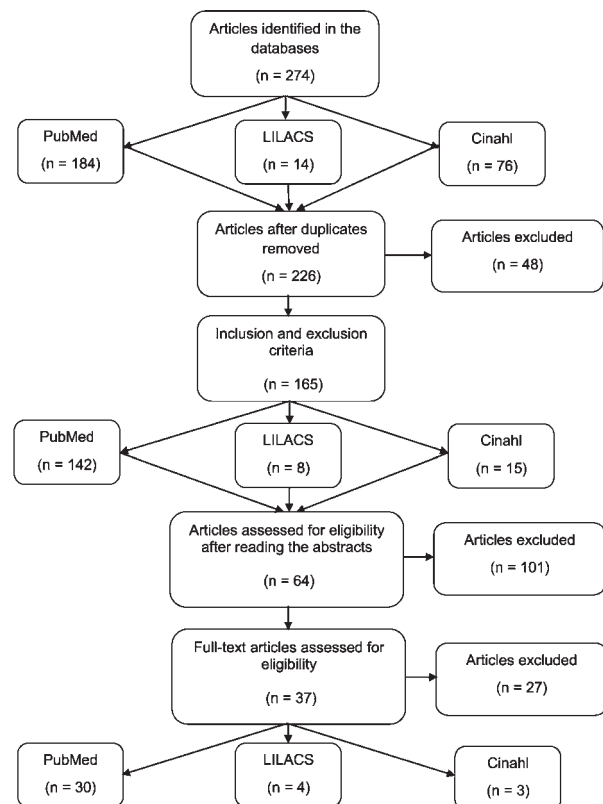


Figura 1. Flow diagram of the studies selected for the systematic review about TB stigma and factors associated.

**Design/Methods:** It is a systematic review of the literature bounded by the steps of problem identification, selection of articles, information definition to be extracted from papers, results discussion and synthesis of the produced knowledge. It was possible to define, by taking into consideration the presented issue, the following question: "What scientific knowledge is produced about the factors associated with the TB stigma, in different contexts?". Several articles, which presented as a central focus the TB stigma, were selected in English, Spanish and Portuguese languages, published between 2000 and 2014, with abstracts available online and indexed in PubMed, CINAHL and LILACS data-bases. The publications and review studies that were not in a scientific paper format were excluded. It was adopted as descriptors "tuberculosis" and "prejudice"

and, as a keyword, "stigma." In relation to data analysis, it was used the meta-summarization that corresponds to the extraction of results and distribution of frequencies. Thus, it was possible to point out the most prevalent ones in order to validate them.

**Results:** Thirty seven items were selected with the predominance of publications in English (89.2%), and studies with a qualitative approach performed in Africa and Asia (37.8%). Among the populations, it is possible to highlight TB patients (62.1%), community members (51.3%) and health professionals (24.3%). It is observed as significant factors related to the TB stigma the disease concealment associated to the social exclusion (40.5%), fear of contagion (29.7%), lack of knowledge about TB (24.3%), beliefs (21.6%), the association with HIV/AIDS (16.2%), poverty (10.8%), low education (10.8%), the stigma in public services and the search for private services (8.1%).

**Conclusion:** Data indicate the heterogeneity of factors related to the TB stigma in investigations conducted, predominantly, in countries of Africa and Asia. The review evidences point to the need for conducting educational actions on health and guidance about the disease, in different contexts, in order to reduce the TB stigma.

#### **PD-842-31 Pension schemes for tuberculosis patients: an advocacy effort from TB forum members of Kerala, India**

S Gadala,<sup>1</sup> C Joltin,<sup>1</sup> RV Jinesh Lal,<sup>1</sup> T Thomas,<sup>1</sup> M Krithika,<sup>1</sup> P Banuru Muralidhara.<sup>2</sup> <sup>1</sup>Project Axshya, Catholic Health Association of India, Hyderabad, <sup>2</sup>Project Axshya, Union Against Tuberculosis & Lung Diseases, New Delhi, India. Fax: (+91)40-27811982. e-mail: srinivasa-rao@chai-india.org

**Background:** Civil Society participation in advocacy for TB has increased in India through continued effort of Project Axshya and support from Global Fund. Locally established Tuberculosis Forum (TB Forums) has set an example and model across the World. TB forum members constitute stakeholders like health care workers, opinion leaders, media personnel, bureaucrats and most importantly cured TB patients with a mandate of patient centric and community centric perspective in TB care and control. This is an experience of advocacy effort from a TB forum in Kerala for revisions in revenue guide of government of Kerala to nutritional support for TB patients.

**Intervention:** Kerala was one among the states to introduce financial support scheme for TB patients in 1963. The utilization of scheme was abysmally low due to lack of information. The pension scheme was therefore revised in 2010 to Rs 300 per month (USD 4.8) and same was revised to Rs 525 per month in 2012 and to Rs 800 in 2013 (USD 13). Despite the continuous revision in the amount of pension, there was no revision regarding the eligibility criteria (annual income below Rs 2400 i.e., USD 39) for availing the schemes which was identified by the TB Forums in Kerala. As a result none of the TB patients were able to avail the service. TB forum

members from Kerala, through various forums (government-community) advocated for TB pensions schemes.

**Result:** Advocacy efforts led to consideration by government for revisions in the TB pension schemes. The government proposed decision for revisions in the local assembly proposing for revisions: eligibility on annual income from Rs 2400 to Rs 100,000 (USD 1613), increase in the amount to Rs 1000 (USD 16). Both the proposals were up-hold and about Rs 1,651,000 (USD 26630) for the current financial year have been earmarked. For the period April 2013 to January 2014 a sum of Rs 1,651,000 (USD 26630) has reached around 300 patients from 26 Taluks (sub-divisions of the district)

**Conclusion:** Thousands of Tuberculosis patients in the state of Kerala will now be supported financially through TB pensions schemes through continued advocacy by TB forum members and Project Axshya. Other TB forum members across the country are now sensitized and are operating on similar lines for support of TB patients. Global fund and other donors need to take cognizance of these additional indicators while considering value for money.

#### **PD-843-31 How to develop a patient advocacy association**

O Rucsineanu.<sup>1</sup> <sup>1</sup>TB, SMIT TB Patient Association, Balti, Moldova. e-mail: oxana\_rucs@yahoo.com

**Background and challenges to implementation:** AIM: Build the capacities of the TB affected population

**Intervention or response:** METHODS; Personal experience of TB surviving has revealed the necessity of starting a patient organisation. The lack of literacy treatment, efficient communication between partners and low involvement of the TB affected communities in the process of decision making at different levels lead to the development of a patient association.

**Results and lessons learnt:** RESULTS; A patient advocacy association has been developed in the Republic of Moldova in order to develop activities in the benefit of the people and communities affected by tuberculosis. Advocating for partnership between TB patients, medical staff and authorities, making the treatment process more efficient, make the voices of the TB affected populations heard – this all has laid at the basis of the organization. The team of the organization focuses the efforts on issues related to human rights, public awareness, care and support for people affected by all forms of TB. A TB association is meant to dig out the existing problems in TB approach in a country as well as to represent the TB affected communities at public levels. Through conducted activities, SMIT builds TB patients capacity on issues related to treatment literacy, following the treatment, contributing to the health of their community. During all the possible dialogues with decision makers SMIT speaks publicly about the necessity of developing social, material, psychological and legal support to people with tuberculosis.

**Conclusions and key recommendations:** CONCLUSION; A patient advocacy association in hand with all



interested partners should get involved in all the activities that would benefit national as well as global community in regard to Classic and DR Tuberculosis.

### PD-844-31 Increasing TB treatment success by engaging community volunteers; Mapping method in Cimahi City, West Java Indonesia

I Tochija,<sup>1</sup> F Manan,<sup>1</sup> M Reksoprodjo,<sup>1</sup> H Diatmo.<sup>1</sup>

<sup>1</sup>National Board, Indonesian Association Against Tuberculosis, Jakarta, Indonesia. Fax: (+621)7397494. e-mail: henry.ppti@gmail.com

**BACKGROUND:** Cimahi city is one municipality in West Java Province Indonesia with population 559,608 (2013). Before 2010, many TB patients were lost to follow up due to lack of human resources to track defaulters. PPTI collaborate with Family Welfare Empowerment Organization to empower volunteers/cadres who have high commitment for supporting community outreach.

**INTERVENTION:** Community cadres were trained to develop the map of TB patients in sub villages. The cadres acted as the coordinator of treatment observers (family observers) of TB patients. They reminded family observers on adherence and conducted active contact tracing around TB patients, according to the maps. The cadres had targets of TB suspects and TB smear positive numbers based on local incidence and were responsible for TB treatment success in their areas. PPTI facilitated monthly monitoring to update the maps in collaboration with primary health centers. All activities were evaluated annually by District Health Office and PPTI.

**RESULT:** Each year, around 1.200 TB Cases were notified in these areas. Among them, TB treatment success rates increased from 83% (2010) to 99% (2011) and 86% (2012). The defaulter rate decreased from 5.6% to 1.8%. Around 200 close contacts were detected and investigated per year. Childhood TB cases increased from 186 to 205. The use of maps helped PPTI to look for the future TB cases.

**CONCLUSION:** Mapping method is very useful for the works of community volunteers. They used maps for following up patients, for close contact tracing and for looking for future TB cases. The maps helped them to identify several cases of childhood TB and for early treatment.

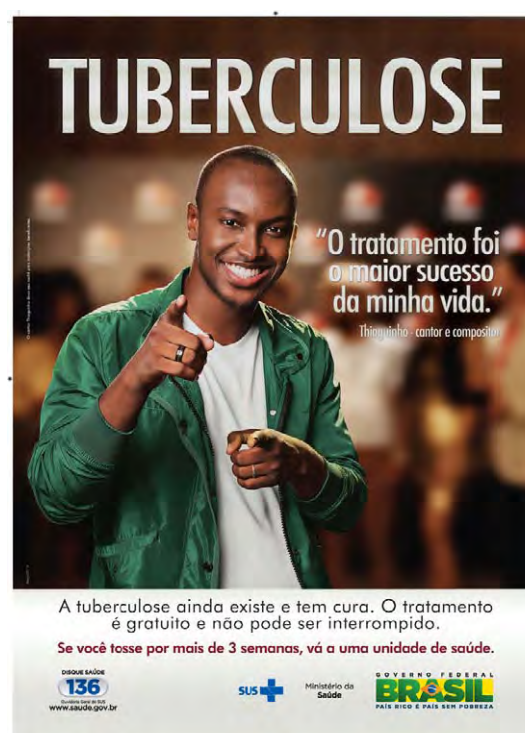
### PD-845-31 2014 Brazilian TB campaign: a collective revolution

A Paranagua Fraga,<sup>1</sup> D Barreira,<sup>1</sup> C Oliveira Dantas,<sup>1</sup> P Werlang,<sup>1</sup> L Seara,<sup>1</sup> V Camargo Da Costa.<sup>1</sup> <sup>1</sup>National Tuberculosis Programme (NTP), Ministry of Health, Brasília, DF, Brazil. Fax: (+55) 613 213 8047. e-mail: ana.fraga@saude.gov.br

**Background and challenges to implementation:** Despite of being a priority for the Federal Government since 2003, tuberculosis (TB) is not recognized in the Brazilian society. A research conducted by the Federal Fluminense

University in 2010 showed that half of the population (49%) have little or no knowledge about the disease. This demonstrates that the lack of information is still a major challenge when it comes to TB control in Brazil. According to an article from the Oswaldo Cruz Foundation, published in 2011, for 100 years the TB campaigns produced by the Ministry of Health are basically the same, with a few changes of language and image. The campaigns did not address the different aspects involved in the disease, and remained restricted to symptoms such as cough.

**Intervention and response:** The National Tuberculosis Programme (NTP) decided to change the campaigns' creation process, involving key players in elaborating a briefing addressed to advertising agencies. Thus, the 2014 campaign was conceived through meetings with health professionals, governments, activists, service users and representatives of academia, in which national and international campaigns were analyzed. The discussions indicated the key message to be used in the new campaign, as well as the best tone for the written, verbal and visual messages to achieve a better response and absorption of information from people.



**Results:** The briefing indicated the need to show that TB still exists, it is curable and the diagnosis and treatment are free in Brazil. It also showed that the invisibility of the disease and the crystallization of old concepts are responsible for the myths that reinforce stigma and prejudice. In this sense, the briefing suggested inviting the Brazilian singer and songwriter "Thiaguinho" as the new campaign's face. In addition to being ranked one of the most influent people in Brazil in 2013, the artist has made his TB diagnosis public, sharing his experience in the media. Accordingly, the slogan of the campaign was

built as the singer's revelation: "The TB treatment was the biggest success of my life".

**Conclusion and recommendations:** On March 24, the NTP released the new campaign with the singer. The campaign is being transmitted on TV during prime time, reaching millions of people. Besides the TV intersection, graphic pieces such as posters and brochures, radio spot and materials for emails, websites, social networks and viral internet videos have been developed.

#### **PD-846-31 Increasing TB knowledge and action: lessons from "We Beat TB" campaign!**

L Legoabe,<sup>1</sup> J Benkie.<sup>1</sup> <sup>1</sup>USAID TB Program, University of Research Co., LLC (URC), Pretoria, South Africa. e-mail: lerato.legoabe@gmail.com

**Background:** South Africa faces a severe dual epidemic with 12.2% of the population being infected with HIV and TB incidence of 1003/100,000 (WHO 2013), with 65% of people infected with TB co-infected with HIV. Previous research found low levels of TB/HIV co-infection knowledge.

**Intervention:** 'We Beat TB' is a national mass media campaign of the USAID TB Program, which aims to improve health-seeking behaviour among South African communities by increasing knowledge on TB prevention, encouraging early presentation for diagnosis and treatment adherence. Messages around TB and TB/HIV co-infection were broadcast on national television and radio channels between year 2009 and 2012. Key message delivered include: 'Open your windows and cover your cough', 'Take 180 doses to be number one ok! (TB can cured)' and 'TB is curable - even if you have HIV'. 'We Beat TB' campaign included community level interventions using a communication for participatory development approach, developed by the Johns Hopkins - Center for Communication Programmes. This approach involves building partnerships with communities to raise awareness on symptoms of TB and HIV, the use of IEC materials (pamphlets in local language and billboards) as well as forming a community of care and support for TB and HIV patients. The campaign was evaluated using a cross-sectional study; data collected from a sample of 10 034 males and females aged 16–55 years. Multivariate regression analysis was used to determine significant factors contributing to the impact.

**Results:** 13.6 million or 48.3% of South Africans aged 16–55 knew about the campaign (51% of females and 46% of males). 84% of respondents knew that people living with HIV (PLHIV) were more likely to get TB (86% of females and 82% of males). 78% knew that it was possible to cure TB in PLHIV (82% of females and 74% of males). Controlling for other factors, those with high exposure to 'We Beat TB' were twice as likely to have high knowledge of TB/HIV co-infection (AOR: 2.06; 95% CI 1.79 – 2.37). Those exposed to the campaign were 1.3 times more likely to have tested for HIV in the past 12 months (AOR: 1.32, 95% CI 1.15 – 1.51).

**Conclusions:** 'We Beat TB' successfully increased knowledge of TB/HIV co-infection and promoted HIV counseling and testing. Effective communication campaigns can reach large numbers of people in the population, impact on key health knowledge and health seeking behavior for better population health outcomes.

#### **PD-847-31 Kick TB: from South Africa to Brazil - a TB campaign for the FIFA World Cup momentum**

C Oliveira Dantas,<sup>1</sup> A De Paula Lobo,<sup>1</sup> P Werlang,<sup>1</sup> J Brandao,<sup>2</sup> E Ishimoto,<sup>3</sup> A Paranagua Fraga,<sup>1</sup> D Barreira.<sup>1</sup> <sup>1</sup>National TB Programme, Ministry of Health, Brasilia, DF, <sup>2</sup>Civil Society, Stop TB Brazil, Recife, PE, <sup>3</sup>Municipal TB Programme, Sao Paulo Health Secretary, Sao Paulo, SP, Brazil. e-mail: cintia.dantas@saude.gov.br

**Background and challenges to implementation:** Since November 2013, the National Tuberculosis Programme (NTP) started to articulate with the South African Health Department the implementation of a project for the World Cup that was firstly implemented in that country for the 2010 World Championship: the Kick TB. Stakeholders representing civil society and government worked together to adapt the project in order to fit the Brazilian reality. The project is a tuberculosis (TB) awareness campaign in schools, taking advantage of the mobilization that evolves around the championship. The main tool of the project is a soccer ball that is given to all students from selected schools with TB messages. Along with the ball, children receive a Health Passport to screen their households based on the information passed to them by the educators through all activities predicted.

**Intervention and response:** A pilot version was developed to be implemented in the city hosting the opening ceremony for the Cup: Sao Paulo. All activities were developed in partnership with the state and municipality's health secretary and with the Health in School Programme – a partnership among health and education from both ministries. The idea is to implement this pilot project, gather the results and impacts, and reproduce it in all priority areas of the country for the following years.

**Results:** Once the project was adapted to the Brazilian reality, there was an intense participation of stakeholders at local level. Local governments representing health, education and sports managed to organize all activities predicted in the project, as well as a launching event.

**Conclusion and recommendations:** The pilot version of the project is being launched in order not to lose the World Cup momentum as the initiation of intersectorial activities. Once this project is duly implemented and impacts are measured, the flow to expand it for the rest of the country is established. We expect to strengthen articulations with the different sectors of government and civil society, and use the Brazilian passion for soccer to spread the TB Kick TB campaign.

### PD-848-31 Understanding tuberculosis stigma in Dar es Salaam, Tanzania

C Miller,<sup>1</sup> L Samu,<sup>2</sup> S G Mfinanga,<sup>2</sup> P Hopewell,<sup>1</sup> E Fair.<sup>1</sup>

<sup>1</sup>Curry International Tuberculosis Center, University of California San Francisco, San Francisco, CA, USA; <sup>2</sup>Research, National Institute of Medical Research, Dar es Salaam, United Republic of Tanzania. e-mail: cecily.miller@ucsf.edu

**Background:** Stigma expressed towards those with tuberculosis (TB) thwart control and eradication efforts by discouraging health-seeking behavior and treatment compliance, leading to worse health outcomes and continued transmission. Due to inequitable traditional gender roles in this society, as well as the feminization of the HIV epidemic in this region, stigma related to infectious disease often disproportionately affects women. Efforts to reduce TB-related stigma require in-depth knowledge of how stigma works and is expressed in a given context.

**Design/Methods:** We sought describe the current state of TB-related stigma in Dar es Salaam, Tanzania, and to understand how it differs by gender, in order to inform the further development and implementation of interventions to reduce TB burden. We held focus group discussions with 1) current TB patients, and 2) patients' household members in order to elucidate: the current level of TB-related stigma operating in this setting, the interaction of gender and TB stigma, and the consequences of gendered TB stigma on knowledge of TB and health-seeking behaviors. The focus group participants were enrolled from a larger parent study of contact investigation being conducted in Dar es Salaam, Tanzania.

**Results:** In July 2013 we performed 8 focus group discussions with TB patients and their household members, 2 each with female and male index patients and household contacts, with 6 participants each (see table) to elicit each group's unique perspectives on the current state of TB-related stigma. Similar key themes emerged from all focus groups: fear of the disease and other associated conditions (most prominently HIV), were discussed in all focus groups, as well as isolation that accompanied diagnosis of TB. Participants discussed the difficulties the disease caused their personal relationships, and the current state of TB-related stigma in their communities, highlighting the changes in the community's thoughts and attitudes towards TB in the recent past. Participants described the current manifestations of stigma in their community, specifically stigma from the health providers, as a prominent barrier to accessing and utilizing care.

Table. Focus group discussions

	Women	Men
<b>TB Patients</b>	2 focus groups of 6 members each	2 focus groups of 6 members each
<b>Household members</b>	2 focus groups of 6 members each	2 focus groups of 6 members each

**Conclusions:** Understanding stigma as a barrier to care is critical for planning and designing appropriate and effective active case-finding interventions for TB, and for tailoring such interventions to be targeted to the weakest points in the patient pathway to care.

### PD-849-31 Reaching the unreached by involving religious forum

M Ubaid,<sup>1</sup> P Varghese,<sup>1</sup> G Singh,<sup>1</sup>

B Entoor Ramachandran.<sup>2</sup> <sup>1</sup>Catholic Bishops Conference of India Coalition for AIDS and Related Diseases, New Delhi, <sup>2</sup>International Union Against Tuberculosis and Lung Disease, New Delhi, India. e-mail: ubaidcbci@gmail.com

**Introduction/Background:** As per the census of 2011, 68% of populations in India live in rural areas and mostly they visit religious place to get rid of their diseases. The Tuberculosis Control Programme had adopted a strategy of passive case finding over a decade. In rural areas where there is lack of government health facilities, often the people opt for traditional methods of treatment which are imparted by local religious leaders. **Intervention:** Catholic Bishops Conference of India Coalition for AIDS and Related Diseases (CBCI CARD) a sub recipient of Global Fund round 9 is implementing an ACSM project under The UNION. The project is being implemented in 29 districts across 4 states of India. The evidence has been gathered from district Varanasi, which is considered as mythological place. Matridham is a religious center managed by faith based organization, here people from all creed come for weekly mass prayer. At the weekly mass prayer there is gathering of around 2500—3000 people and these people have a strong belief of getting their disease cured after visiting the place and participated in the mass prayer. CBCI CARD identified this centre as focal point for intervening and sensitizing people about TB. After conducting advocacy with Matridham management, CBCI CARD in partnership with local partner NGOs organized camps for sensitizing people on TB symptoms, diagnosis and treatment. In the process of conducting camps, TB chest symptomatic were identified screened and were referred for Sputum testing in nearby Designated Microscopic centre.

**Result:** During Sept 2012 to Dec 2013, CBCI CARD organized 68 sensitization meetings where people were given complete knowledge about TB. Around 150,000 people from marginalized and vulnerable areas were reached and got informed about TB. Through this 1545 TB symptomatic were identified, 1062 TB symptomatic were referred for sputum diagnosis and rest 342 TB symptomatic their sputum was collected and transported (SC&T) for diagnosis. From both approach of referrals and SC&T, 134 TB patients were identified and were linked to Directly Observed Treatment Short course treatment.

**Conclusion:** In developing countries, like India where large number of people have strong belief on religious institution for their well being and cure of illness, tapping this type of institution or centers for any public health program can be a very effective strategy for reaching out to large number of people.



### 31. INEXTRICABLY LINKED: INTEGRATING TB AND HIV CARE

#### PD-850-31 Intensified TB case finding (ICF) in HIV high risk groups with the help of GF-supported civil society organisations. TB project in India

S Mukhopadhyay,<sup>1</sup> AK Kandukuri,<sup>2</sup> S Cornelius,<sup>1</sup> B Samuel,<sup>1</sup> V K Edward,<sup>1</sup> J Banavaliker,<sup>2</sup> U Ramakrishna,<sup>3</sup> T Kailashditya.<sup>3</sup> <sup>1</sup>Health, World Vision India, New Delhi, <sup>2</sup>Health, TB Alert, Hyderabad, <sup>3</sup>Targeted Intervention, State AIDS Control Society, Andhra Pradesh, Hyderabad, India. e-mail: sugata64@gmail.com

**Background and challenges to implementation:** India has adopted Universal Access to TB care in RNTCP (Revised National TB Control Program) where all TB cases are targeted to be brought under standardized care. But the major challenge is gradual decline of incident TB case notification rate of the country since last 5- 6 years (current rate 91 per 100,000 against estimated incidence 176 per 100,000). There is an urgent need to improve case notification in RNTCP. World Vision India (WV India) and TB Alert have been jointly implementing GF-supported Project Axshya in Andhra Pradesh, India to support the State TB Program in improving TB case notification in high-risk groups. One of such group is HIV high risk communities (migrants, sex workers, IDUs, MSM, Transgender) whom Stop TB/WHO have already identified as high risk for TB. WVI & TB Alert engaged 194 HIV prevention projects of AP (covering around 250,000 high risk population) in TB control program through Project Axshya in collaboration with State AIDS Control Society (SACS) and State TB Cell (STC).

**Intervention or response:** WV India & TB Alert facilitated TB & ICF training of the Managers of 194 HIV prevention projects in collaboration with SACS and STC of AP and by using a specially designed training module. The Project Managers learnt to develop TB action plan for their respective HIV projects. The TB action plans were implemented through identification of TB presumptive cases within HIV projects through ICF by their project staff and referral and screening of those cases in RNTCP-labs. The cases were line-listed and followed-up meticulously. There was no additional cost for this programmatic collaboration.

**Results and lessons learnt:** ICF of TB presumptive cases in HIV prevention projects and their referral to RNTCP increased from 1879 of 2011 & 1630 of 2012 to 12316 in 2013, especially after TB sensitization of the HIV project managers. Out of 12316 referrals mentioned earlier, 10089 cases tested for TB, 645 cases were detected with active TB (positivity rate 6.4%) & put on TB treatment within 7 days of diagnosis, 150 TB patients cured so far and results of others are under follow-up. The intervention was highly cost-effective (10 USD/one detected TB case).

**Conclusions:** If replicated across 2500 such HIV prevention projects of the country the intervention can

detect large number of TB cases from HIV high risk groups in cost-effective way to support Universal Access strategy and improve notification rate.

#### PD-851-31 Successful decentralisation of TB care but high mortality among HIV co-infected patients in the rural Shiselweni region, Swaziland

B Kerschberger,<sup>1</sup> A Telnov,<sup>2</sup> A Mafukidze,<sup>1</sup> S M Kabore.<sup>1</sup> <sup>1</sup>Medical, Medecins Sans Frontieres, Mbabane, Swaziland; <sup>2</sup>Medical, Medecins Sans Frontieres, Geneva, Switzerland. e-mail: benadi11@yahoo.de

**Background:** Tuberculosis is the main cause of mortality in HIV infected individuals. Swaziland has one of the highest HIV prevalence (31%) and TB incidence (1,380/100,000) in the world. Since 2009 TB care was decentralized in the rural Shiselweni region (Swaziland) and coinciding with increasing anti-retroviral-therapy (ART) coverage reaching 80% in 2012. This retrospective cohort analysis describes risk factors of adverse treatment outcomes in the context of HIV/TB care scale-up.

**Design/Methods:** Study eligibility was defined as all  $\geq 16$  year old TB cases initiating category I/II TB treatment at 3 secondary and 22 primary care facilities (01/2009-12/2012). For HIV co-infected TB patients, we used logistic regression to describe associations between baseline factors and the composite endpoint LTFU/death/treatment failure.

**Results:** In total, 6,795 TB cases were reported. Annual notifications declined from 2,369 in 2009 to 1,101 in 2012, but increased proportionally at primary care level (4% in 2009 to 54% in 2011) and sustained thereafter. Median age was 35 (IQR 28-47) years, 50% (n=3420) were females and 73% were (n=4,979) HIV co-infected. Being on ART before commencement of TB treatment increased from 25% (n=438) in 2009 to 36% (n=290) in 2012. Treatment success for bacteriologically confirmed (BK+) and unconfirmed (BK-) pulmonary TB increased from 68 to 77% and 69 to 75%. Death remained high at 8% for BK+ and 15% for BK- pulmonary TB in 2012; 84% of all deaths occurred in HIV co-infected patients. In multivariate analysis for HIV co-infected TB cases, treatment initiation at primary care (adjusted Odds Ratios [aOR] 0.66, [95%CI] 0.56-0.77) and BK- TB (0.60, 0.51-0.7) had decreased probability of an unfavourable outcome. It was increased for re-treatment (1.56, 1.30-1.88) and extra-pulmonary (1.24, 1.02-1.52) TB cases, and also for lower CD4 count strata in comparison to CD4  $\geq 351$  cells/ $\mu$ L (CD4 0-49: 2.64, 1.78-3.91; CD4 50-99: 1.96, 1.3-2.95). No associations were detected for calendar year, age, gender and ART status at TB diagnosis.

**Conclusion:** Although TB burden decreased and treatment outcomes improved during decentralization of TB/HIV services, mortality in HIV co-infected patients remained high. This study indicates that TB care at primary care level and better baseline immunological

status may be essential to further improve treatment outcomes in a high HIV prevalence setting.

### PD-852-31 Survey of the level of HIV-TB service integration in health facilities in 4 districts in Malawi: towards implementation of the national framework

D Garone,<sup>1</sup> O Jalon,<sup>1</sup> T Beyene,<sup>2</sup> M Van Lettow,<sup>2,3</sup> J Van Oosterhout,<sup>2</sup> F Cataldo,<sup>2</sup> M Matchaya,<sup>4</sup> M Murowa.<sup>5</sup> <sup>1</sup>Medical and Research Department, Médecins Sans Frontières-Belgium, Thyolo, <sup>2</sup>Medical and Research Department, Dignitas International, Zomba, Malawi; <sup>3</sup>Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada; <sup>4</sup>Nsanje District Hospital, Ministry of Health Malawi, Nsanje, <sup>5</sup>Thyolo District Hospital, Ministry of Health Malawi, Thyolo, Malawi.  
e-mail: msfocb-blantyre-opr@brussels.msf.org

**Background:** HIV and TB control programs have traditionally functioned as separate entities, with distinct delivery structures, funding sources and little coordination of services for patients. Integration of TB and HIV services has been associated with optimized health care delivery and potentially improved patient outcomes. While the 2012/13 Malawian HIV/TB operational framework provides guidance, it fails to identify barriers and address the practical aspects of service integration at health facility level.

**Design/Methods:** A cross-sectional survey of HIV and TB services was conducted in 95 health facilities in 4 districts in Malawi. An evaluation tool based on HIV and TB national guidelines was developed to determine the level of service integration in the HIV/TB prevention and treatment domain. A total of 559 health workers who were present on the survey day were interviewed to identify the training they received and their HIV/TB clinical practices. Services were considered as 'integrated' if a "one-stop-service" was provided, 'collaborative' if cross-referrals occurred between HIV and TB services, and 'partially integrated' if any TB or HIV screening or care was provided in the other service.

**Results:** Different models of integration coexisted in the majority of the sites suggesting the delivery of "one-stop-service" for HIV/TB patients is inconsistent. Overall, 80% and 95% of the health facilities were partially integrated in HIV/TB prevention and treatment services respectively. Only 5% of the clinics provided integrated HIV/TB treatment as a "one-stop-service". 22% of the facilities performed HIV testing in the TB rooms. Among the HIV staff 11% (24/218) was trained on TB management and 20% received TB infection control training. Among the TB staff 34% (21/61) was trained on HIV management. A greater proportion of clinicians were trained on TB management compared with nurses (34% vs. 8%). Overall 4% of the nurses were trained to initiate TB patients on TB treatment.

**Conclusion:** Our study shows that despite the commitment at the national level and an existing operational framework, full integration of HIV and TB services has not yet occurred in Malawi. HIV and TB services in most of the health facilities surveyed function with varying

levels of collaboration. Addressing barriers like the lack of integrated HIV/TB trainings and limited TB infection control is crucial for further services integration.

### PD-853-31 Exploring patients' perspective on HIV and TB service integration in the southern regions of Malawi

F Cataldo,<sup>1</sup> M Van Lettow,<sup>1,2</sup> O Jalon,<sup>3</sup> T Beyene,<sup>1</sup> J Van Oosterhout,<sup>1</sup> L Trivino,<sup>3</sup> D Garone.<sup>3</sup> <sup>1</sup>Medical, Dignitas International, Zomba, Malawi; <sup>2</sup>Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada; <sup>3</sup>Medical, Médecins Sans Frontières-Belgium, Thyolo, Malawi. e-mail: msfocb-blantyre-opr@brussels.msf.org

**Background:** TB is one of the leading causes of morbidity and mortality among HIV-infected patients. Integration of TB and HIV treatment and prevention programmes has been promoted to improve the diagnosis, treatment and outcomes for patients affected by both HIV and TB. Evidence to date suggests that closer integration of services is linked to better health outcomes, however little is known about the experience of patients who access integrated TB/HIV services.

**Design/Methods:** As part of a cross sectional study aiming to measure and analyse the level of HIV and TB service integration in healthcare facilities (HF) in Malawi, the perspective of patients was explored through a qualitative approach. Semi-structured questionnaires were conducted with 125 patients accessing care for TB and HIV in 30 HFs across Thyolo, Nsanje, Zomba and Balaka districts, Malawi, between January and April 2014.

**Results:** Patients (42% male; 58% female), median age 36 years (IQR 29:42) had few years of education (11% with no education, 74% primary level). 46% had been diagnosed with HIV for more than 12 months, and most (71%) had been accessing the HF for more than 6 months. Each patient's visit to the HF lasted on average 1h.20min., during which they were mainly attended by Health Surveillance Assistants (44%). All but one patients were on ART and 86% of co-infected patients were diagnosed with TB within the past 6 months. Patients expressed favorable views regarding integrated TB/HIV care. Their positive perception of service integration was mainly articulated in relation to their interaction with the HF staff, their access to ART and TB treatment within the same HF, the potential to reduce the number of visits to the HF, as well the rapidity and reliability of services. Some deplored, however, the lack of drugs in some HFs, the late morning start of some services, and the lack of food assistance for co-infected patients. The lack of services integration was perceived in some HFs as a barrier to accessing HIV care free of stigma.

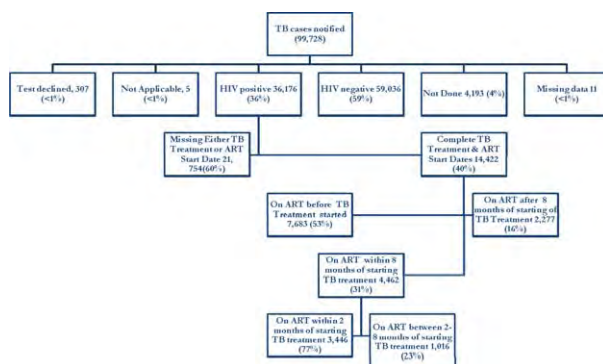
**Conclusion:** Patients expressed largely positive views in relation to their access to integrated TB and HIV services within HFs. Continuing efforts to support the integration of TB and HIV care as 'one stop services' is expected to improve patients' experience of accessing health services in Malawi.

### PD-854-31 Timing of ART initiation among HIV-infected TB patients in Kenya: going behind service coverage

E Masini,<sup>1</sup> J Kioko,<sup>1</sup> G Kasera,<sup>1</sup> M Mwakala,<sup>1</sup> H Weyenga,<sup>1</sup> R Muthoka.<sup>1</sup> <sup>1</sup>National Tuberculosis, Leprosy and Lung Disease, Ministry of Health, Nairobi, Kenya. Fax: (+254)6824003. e-mail: emasini32@gmail.com

**Background:** Tuberculosis (TB) is the leading cause of mortality in HIV-infected patients. Optimal combination of TB and HIV care interventions is critical in improving TB outcomes. Early initiation of Highly Active Antiretroviral Therapy (HAART) among HIV TB patients has a demonstrated mortality benefit. Kenya has a high TB and HIV burden, with TB case notification of 338/100,000 (2012) and an HIV prevalence of 5.6% among adolescents and adults aged 15–49 years and has successfully implemented TB-HIV collaboration. Kenya recommends initiation of HAART in all people living with HIV and active TB, and that TB treatment should be started first, followed by HAART, within the first 2 months. While there is near universal HAART uptake among HIV infected TB patients, the timing of the initiation in Kenya has not been systematically evaluated in Kenya. We analyzed the national case based TBHIV data to describe the timing of ART among TB HIV patients enrolled 2012.

**Design/Methods** Kenya national TB data for 2012 was imported from the national web-based TB surveillance system (TIBU), personal identifiers removed and descriptive analysis done using Epi Info™ 7. Initiation of ART within 2 months of start of anti-TB treatment was considered early initiation while death was defined as mortality from any cause during the course of treatment.



**Results:** A total of 99,728 TB patients were notified in Kenya in 2012, 94% of them were tested for HIV and 36,176 (36.3%) found to be HIV infected. Of the TB HIV co-infected, 88.7% (32094) were on HAART by the end of TB treatment. Among these, 14,422 (39.9%) patients had complete records to determine the timing of ART initiation. Of these 7683 (53.3%) were on HAART before initiation of TB treatment while, 4462 (30.9%) and 2276 (15.8%) respectively were initiated HAART within and after 8 months of TB treatment. Of the TBHIV co-infected patients started on HAART after TB

treatment was initiated, only 3446 (49.7%) received HAART within the first 2 months of start of TB treatment. Mortality was lower among those receiving early HAART (within 2 months) at 4.7% compared to those receiving late (8.4%).

**Conclusion:** Despite the high uptake of HAART among TBHIV co-infected patients in Kenya, more than half of the patients are initiated beyond the recommended 2 months after the start of TB treatment. Further operational research is required to identify the constraints to early HAART initiation and measures established to address them.

### PD-855-31 Linkage between TB and HIV programmes: provider-initiated HIV testing and counseling for tuberculosis patients in 26 provinces in Viet Nam, 2007–2013

K Do,<sup>1</sup> T Vu,<sup>1</sup> Nhan Do,<sup>1</sup> Khan Vu,<sup>1</sup> V N Nguyen.<sup>2</sup> <sup>1</sup>TB-HIV, Viet Nam-US Collaboration HIV Project on Prevention and Care, Hanoi, <sup>2</sup>Program Management, National Hospital of Lung Disease, Hanoi, Viet Nam. e-mail: tuankimdo@gmail.com

**Background:** The WHO recommends provider-initiated HIV testing and counseling (PITC) for all TB patients. In Viet Nam, PITC has been implemented since 2007 under VAAC-US.CDC project and expanded to 26 provinces in 2013, with counseling and serological testing offered by TB program staffs.

**Methods:** HIV testing and referral data from routine quarterly reports of 26 provinces from 2007 – 2013 were analyzed.

**Results:** Among 182,435 registered TB patients, 6,390 (3.5%) were already known to be HIV-infected. Of 175,324 TB patients with unknown HIV status, 161,944 (92.4%) received HIV counseling and 158,982 (98.2%) of these agreed to testing. A total of 3,731 patients were newly diagnosed with HIV infection for an overall HIV prevalence in TB patients of 5.6%. Of the 9,754 known HIV-infected TB patients, 67.3% were successfully referred to HIV care facilities (59.1% in 2008, 51% in 2009, 63% in 2010, 66.4% in 2011, 69.2% in 2012, 71% in 2013), 39.4% had a documented CD4 cell count, 76.5% received cotrimoxazole preventive therapy, and 42.7% received antiretroviral therapy (ART) during TB treatment (27% in 2008, 17% in 2009, 33% in 2010, 43% in 2011, 53% in 2012 and 57% in 2013). There was an increase in proportions of successful referral and ART over time.

**Conclusion:** These findings demonstrate the practicality and acceptance of PITC and support the need to expand PITC to TB settings in Viet Nam as a routine program. Despite improvement in proportion trends over time, low rates of successful referral and ART indicate that barriers still remain and more efforts are needed to provide integrated care to HIV-infected TB patients such as the development of standard operating procedures of referral between TB and HIV settings as well as providing ART for TB patients at TB settings.



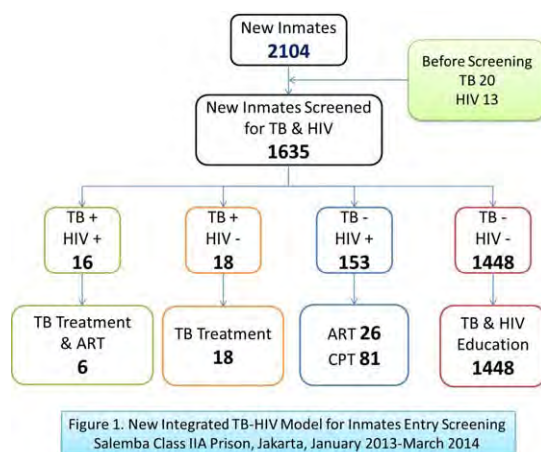
### PD-856-31 New integrated TB-HIV model in prison: Salemba Prison, Jakarta

A Murni,<sup>1</sup> ET Putri,<sup>1</sup> L Nurhidayaty,<sup>1</sup> LD Khristianti,<sup>1</sup> M Andeska,<sup>1</sup> M Ibrahim,<sup>1</sup> C Natpratan,<sup>2</sup> M Samsuri.<sup>2</sup>

<sup>1</sup>Policlinic, Salemba Prison, Central Jakarta, <sup>2</sup>Clinical Services Unit, FHI360 Indonesia, DKI Jakarta, Indonesia.  
e-mail: msamsuri@fhi360.org

**Background and challenges to implementation:** Salemba prison Jakarta has been implementing TB comprehensive screenings since 2011. All new inmates were screened for TB, mass TB screening for all inmates once a year and active case finding via symptoms. All TB patients were tested for HIV and received treatment accordingly, including ART and CPT. Recently, MoH has issued the policy of Test and Treat (HIV test and ART) among TB patients and IPT. Salemba prison has adjusted the TB-HIV screening in a more integrated way and implemented the new treatment strategy.

**Intervention or response:** All new inmates were screened for both TB and HIV after the group counseling. TB diagnosis used sputum examination and later when GeneXpert was available, some were diagnosed by Xpert. HIV tests were done according to the national algorithm. Inmates who had both TB and HIV were provided TB DOT and ART/CPT, inmates who had TB but not HIV received TB DOT, inmates who had HIV but not TB were considered to get ART and will be given IPT in near future. For those who had no HIV and TB were educated and would be assessed in the next TB screening. TB infection control interventions were conducted. Post-released follow up was planned with CSO (Partisan). All screenings and activities were supported by inmate volunteers.



**Results and lessons learnt:** With new integrated TB-HIV model at entry screening, we manage to have early detection of TB and HIV cases. Previously only TB cases being found early at new inmates screening, and now, we also have HIV cases being found earlier. This made proper management of TB and/or HIV started earlier. From 16 inmates with TB & HIV, 8 already released before being treated. From 153 inmates with HIV, 59 already released before being on ART and 42 already

released before being on CPT. All of inmates with only HIV, who are still in prison will be considered for IPT.

**Conclusions and key recommendations:** The new integrated model of TB-HIV provided early detection of two fatal diseases among prison's inmates. The comprehensive packages of services are up to date according to the national policy of MoH. Collaboration with facilities of MoH nearby is indispensable. Technical assistance from TB CARE I/USAID is needed.

### PD-857-31 Integration of "One-Stop" TB-HIV services at a methadone site in Dushanbe, Tajikistan

O Bobokhojaev,<sup>1</sup> d Iskandarov,<sup>1</sup> R Adilbekova,<sup>2</sup>

B Babamuradov,<sup>2</sup> T Mohr.<sup>2</sup> <sup>1</sup>National Republican TB Center, Ministry of Health, Dushanbe, <sup>2</sup>Global Health, Project HOPE, Dushanbe, Tajikistan. Fax: (+7)727 264 63 64.  
e-mail: tmohr@projecthope.org

**Background:** People living with HIV are vulnerable to TB infection due to weakened immune systems. In Dushanbe, Tajikistan, they often experience difficulties in TB diagnosis due to atypical picture and, in part, due to high TB stigma. The Republican Narcology center, with Global Fund financial support, provides substitution therapy for 160 drug addicts who are co-infected with TB-HIV. These patients receive ART and Methadone at one treatment site and TB treatment at other sites in PHC facilities. This creates challenges for patients to adhere to TB treatment and a risk for development of MDR-TB.

**Methods:** The USAID /Quality Health Care Project (Quality Project) piloted outpatient treatment for TB/HIV co-infected patients at a Methadone therapy site with support of the Republican Narcology Center in Dushanbe, Tajikistan in 2013. Short trainings were conducted for doctors and nurses at the Narcology center to introduce "One-Stop" services for methadone patients who were also co-infected with TB/HIV. Doctors and nurses were trained in TB control, including TB case finding, treatment, MDR-TB case management, and consequences of inadequate TB case management. In addition, the Quality Project supported TB doctors to provide weekly consulting and screening at this site for former and current TB patients with HIV infection including those who receive ARV therapy.

**Results:** Out of the 160 Methadone site clients there were 42 TB suspects (26%). All of them passed through the TB diagnostic algorithm. Of 42 screened TB suspects there were two TB patients diagnosed, 4.76% (one is a MDR-TB patient). They were enrolled in TB treatment immediately after GeneXpert testing; the MDR TB patient was started on a SLD course according to the National rules.

**Conclusion:** The "One-Stop" treatment at the Methadone site in Dushanbe provides clients consultations, ARV therapy and Methadone therapy utilizes a more convenient and patient centered approach. This facilitates TB detection and treatment among PLVH. Anecdotal evidence indicates that the "One-Stop" approach for provision of services should be expanded to facilitate

this patient centered approach and to improve earlier detection of TB and initiation of treatment.

### PD-858-31 Improving TB-HIV linkages through integration of services in Northern Uganda

E Nyamugisa,<sup>1</sup> F Ocom.<sup>1</sup> <sup>1</sup>Health Services Delivery, USAID/NU-HITES Project, Plan International - Uganda, Gulu, Uganda. e-mail: estheraloyo@gmail.com

**Background and challenges to implementation:** The Northern Uganda-Health Integration for Enhanced Services (NU-HITES) is a United States Agency for International Development (USAID) funded project that aims to strengthen health systems and increase the use of quality health services in Northern Uganda. The regional HIV prevalence is 8.3% (national average is 7.3%), and TB case detection rate stands at 83.2% (National averages 69%[1]). The regional TB-HIV co-infection rate is at 53%. Health worker competence gaps in TB-HIV co-management at TB clinics and poor integration of TB-HIV activities were identified as obstacles to TB-HIV collaboration during a baseline assessment conducted by the project. [1] WHO 2012

**Intervention or response:** Over a period of one year (October 1, 2012 – September 31, 2013) interventions targeting 121 TB Diagnostic-and-Treatment Units (DTUs) in 15 districts were rolled out. Health care workers in-charge of TB clinics at 23 large volume DTUs were trained in Provider-Initiated-Testing-and-Counseling (PITC). TB-HIV co-management training and quarterly mentorships were conducted for providers at 121 DTUs to build TB-HIV co-treatment competences. Sixty five DTUs not offering ART were assessed and accredited for ART provision to increase ART coverage. Three hundred fifty one linkage facilitators and 136 community Workers were oriented and supported to establish and/or strengthen TB-HIV linkages. Thirty District TB Supervisors and health workers from 9 large volume DTUs were oriented on the principles of Continuous Quality Improvement (CQI) with TB-HIV indicators prioritized as the first CQI projects. Data collected and aggregated using the MoH Quarterly TB reporting form for all districts; quarterly data quality assurance was conducted by the Zonal TB supervisor for each district.

**Results and lessons learnt:** Collaboration among trained providers from HIV and TB clinics as well as community workers harnessed application of CQI approaches to TB-HIV indicators at the 9 DTUs; PITC was integrated at TB clinics following PITC training while competent linkage facilitators operationalized TB-HIV linkages. These resulted in improvements in HTC, CPT and ART coverage amongst TB-HIV co-infected patients from 80%, 94% and 34% one year before project inception to 97%, 100% and 81% respectively after the interventions.

**Conclusions and key recommendations:** Facility led integration of TB-HIV services improves and sustains recommended TB-HIV linkages.

### PD-859-31 Factors associated with successful treatment outcomes for new TB-HIV co-infected cases in the Free State Province (South Africa)

M Engelbrecht,<sup>1</sup> G Kigozi,<sup>1</sup> P Chikobvu,<sup>2</sup> S Van Der Merwe,<sup>3</sup> HCJ Van Rensburg.<sup>1</sup> <sup>1</sup>Centre for Health Systems Research & Development, University of the Free State, Bloemfontein, <sup>2</sup>Department of Community Health, University of the Free State, Bloemfontein, <sup>3</sup>TB Directorate, Free State Department of Health, Bloemfontein, South Africa. Fax: (+27) 444 5011. e-mail: engelm@ufs.ac.za

**Background:** TB is the most common opportunistic infection and a leading cause of death in persons with HIV/AIDS. In South Africa, which has the worst TB epidemic in the world (TB incidence 1 003/100 000 population) and an adult (15–49 years) HIV prevalence rate of 17.3% (65% co-infection), the reciprocal benefits for integrating TB and HIV/AIDS management is evident. Adequate TB control contributes to HIV/AIDS care, and the prevention of HIV transmission leads to improved TB control. This paper seeks to describe the factors associated with successful treatment outcomes for new TB-HIV co-infected cases in the Free State Province, South Africa.

**Design/Methods:** This was a retrospective record review of routinely collected data in the Electronic TB Register (ETR.net) from 2009 to 2012. The study population was defined as all new TB-HIV co-infected cases. Treatment success was defined as cases who had completed the TB regimen successfully or who were cured. Unsuccessful treatment was defined as cases who had died, defaulted or failed treatment. Data was described using frequencies and percentages. Associations were established using  $\chi^2$  tests. Logistic regression analysis was used to determine which factors were significantly associated with successful treatment outcomes for TB-HIV co-infected cases.

**Results:** During 2009–2012 there were 99 805 new TB cases of which 55 306 (55%) were co-infected with HIV/AIDS. The average age was  $34.19 \pm 6.25$  years. In almost a quarter of the cases HIV status was unknown ( $n=24\ 000$ ; 24.05%). Almost half of the co-infected patients were on ART ( $n=27\ 438$ ; 49.6%). The successful treatment rate was 76.03% among the TB-HIV co-infected patients. After adjusting for other variables, having a CD4 count of more than 350 (AOR: 2.57; CI: 2.31–2.85); and being on antiretroviral treatment (ART) (AOR: 1.94; CI: 1.80–2.09) were the highest predictors of successful treatment outcome. Females were more likely than males to have a successful treatment outcome (AOR: 1.06; CI: 0.99–1.29). However, treatment success reduced with increasing age; compared to age group 0–4 years, patients older than 75 years were 0.30 (AOR: 0.30; CI: 0.12–0.72) times less likely to have a successful treatment outcome.

**Conclusion:** The importance of TB/HIV/AIDS integration is evident as patients with higher CD4 counts and those on ART are more likely to have a successful TB outcome. Co-infected patients who require more programmatic attention are males and older people.

### PD-860-31 Missed opportunities for tuberculosis screening among patients in pre-ART care in Nigeria

EK Dokubo,<sup>1</sup> S Agolory,<sup>1</sup> R Shiraishi,<sup>1</sup> S Odafe,<sup>2</sup> D Onotu,<sup>2</sup> I Dalhatu,<sup>2</sup> M Swaminathan,<sup>1</sup> A Bashorun.<sup>3</sup>

<sup>1</sup>Division of Global HIV/AIDS, US Centers for Disease Control & Prevention (CDC), Atlanta, GA, USA; <sup>2</sup>Division of Global HIV/AIDS, CDC, Abuja, <sup>3</sup>National AIDS and STI Control Program, Federal Ministry of Health, Abuja, Nigeria.  
e-mail: vic8@cdc.gov

**Background:** Tuberculosis (TB) is the leading cause of mortality among persons living with HIV (PLHIV) globally and often goes undiagnosed. The World Health Organization (WHO) recommends routine TB screening of all adult PLHIV at every clinical encounter using a four-symptom screen. HIV-positive adults who screen negative for TB should be provided Isoniazid preventive therapy to reduce the risk of developing TB, and HIV-positive patients with a positive TB-symptom screen should undergo further diagnostic evaluation and be initiated on TB treatment and subsequently started on ART if diagnosed with active TB. We assessed TB screening among adult patients enrolled in care but not yet started on ART (pre-ART patients) in Nigeria to identify missed opportunities for TB screening.

**Methods:** A retrospective study was conducted among a nationally representative sample of HIV-positive adults enrolled in U.S. President's Emergency Plan for AIDS Relief (PEPFAR)-supported care and treatment programs from January 2004 to December 2012. Data were abstracted from medical records of pre-ART patients from 35 sites selected using probability-proportional-to-size sampling. TB screening at clinic visits was assessed among PLHIV enrolled in care but not yet initiated on ART.

**Results:** Among 2415 pre-ART patients, 78.7% (95% confidence interval [CI] 69.9–85.4%) were screened for TB at time of initial enrollment into care, of which 8.6% (95% CI 5.8–12.7%) had a positive TB symptom screen. At the most recent clinical visit, only 60.3% (95% CI 46.8–72.4%) of the pre-ART patients were screened for TB, of which 7.6% (95% CI 4.3–13.0%) had a positive TB symptom screen. Year of enrollment in care was not associated with the likelihood of being screened for TB at baseline ( $p = 0.118$ ) or at the most recent clinic visit ( $p = 0.905$ ).

**Conclusion:** A substantial proportion of pre-ART patients are not being screened for TB at clinical visits. The gap in screening HIV-positive patients for TB limits identification of PLHIV who may be infected with TB and may result in missed opportunities to initiate HIV-positive TB patients on TB treatment and ART. Efforts need to be intensified to screen and detect TB among PLHIV, in order to ensure appropriate treatment to decrease TB and HIV morbidity among co-infected patients.

### PD-861-31 Roll-out of TB-HIV activities in Democratic Republic of Congo: major outcomes and drawn lessons

G Kabuya,<sup>1</sup> S Bisuta Fueza,<sup>1</sup> F Teto Mamona,<sup>1</sup> JL Matala,<sup>2</sup> F Fwamba,<sup>2</sup> G Bakaswa.<sup>1</sup>

<sup>1</sup>Programme National de lutte contre la TB, Ministère de la Santé Publique, Kinshasa, <sup>2</sup>Programme National de lutte contre le VIH, Ministère de la Santé Publique, Kinshasa, Democratic Republic of Congo.  
e-mail: kmutala@yahoo.fr

**Background:** During 2013, collaborative TB/HIV activities were being rolled out in 660 TB clinics throughout DRC. Currently integrated TB/HIV services cover 43 % of TB clinics in DRC (660/1522). The aim of the study was to evaluate the outcomes after the rolling-out TB/HIV activities from 207 TB clinics to 660 in DRC and to draw lessons for future scaling –up.

**Methods:** We did a retrospective review of all records reported by the provincial TB coordination (CPLT) in 2013. From cases notification gathered in TB registers, we determine the major outcomes/indicators of the implementation of collaborative TB/HIV activities in DRC.

**Results:** Among the 113 797 TB cases notified in 2013, 64 118 TB (56%) patients did get access to VCT services in TB clinics within the country. Preliminary data shows that 43,7% (49 816 ) have been tested for HIV. Overall 14 % (6 984) of TB patients, who were tested, are found to be HIV positive. Of 6 984 co-infected patients, 70 % (4 866) got access to Cotrimoxazole prevention and 48 % (3 371) to ARV treatment.

**Conclusion:** Implementation of TB/HIV activities services coverage is still limited due to the lack of adequate provisions of supply and funds. Collaborative activities TB/HIV should continue to be strengthened to ensure that all TB patients have access to HIV testing and treatment.

## 32. BEST PRACTICES IN SUPPORTING CLIENTS TO COMPLETE TB TREATMENT

### PD-862-31 Tuberculosis patients under treatment: pathway in a municipality of southeastern Brazil, 2013

ME Brunello,<sup>1</sup> MF Simiele,<sup>1</sup> NH Orfao,<sup>1</sup> A Wysocki,<sup>1</sup> G Magnabosco,<sup>1</sup> R Andrade,<sup>1</sup> T Arakawa,<sup>1</sup> TC Scatena Villa.<sup>1</sup> <sup>1</sup>Maternal Infant and Public Health, University of Sao Paulo, Ribeirão Preto, SP, Brazil.  
e-mail: mefb\_usp@yahoo.com.br

**Background:** Local experiences can be useful to comprehend how different health services provide care for tuberculosis (TB) treatment and the pathway done by patients suggest evidences to comprehend this panorama. **AIM:** to describe the health services utilized by TB patient during treatment.

**Design/Methods:** descriptive study, survey type, conducted in Ribeirão Preto, Sao Paulo, Brazil in 2013. TB patients who had already finished treatment during the period of June 2012-June 2013, resident in Ribeirão



Preto who already finished treatment, outside the prison system, as well as that had not local transference and change of diagnosis as outcome formed a sample of 109 TB patients. Data about TB patients pathway, number of medical appointments, type of care provided, exams performed and health professionals that conducted care were collected from an online computerized electronic medical record system (Hygia WEB). For data analysis, health services were classified into three categories: Primary Health Care (PHC), Emergency Services (ES) and Specialized Services (SS). Data were analyzed using descriptive statistics.

**Results:** 100% of TB patients were followed by SS, had an average 54 attendances ([IQR] 1–161) during 6 months of treatment in these services ([IQR] 3–11), considering medical appointments and nursing home visits to monitor TB supervised treatment. 76.1% sought care at another health service, in addition to health services they were followed, during treatment, 61.5% sought ES and 33.9% sought PHC, before any complication during the treatment period. An average of 4 return visits for medical appointments ([IQR] 0–12) were recorded and 19 eventual appointments (without scheduling) ([IQR] 0–69).

**Conclusion:** The study shows the centralization of TB treatment by specialized teams that operate in SS and preference for searching for ES in case of any complication to the detriment PHC, perhaps because of the easier access for 24 hours every day of the week.

#### **PD-863-31 Role of financial support in identifying different types of TB cases from community and their management: BRAC experience**

S Munim,<sup>1</sup> S Islam,<sup>1</sup> M Akramul Islam,<sup>1</sup> S Alam,<sup>1</sup> K Fatema,<sup>1</sup> A Husain,<sup>2</sup> V Begum.<sup>3</sup> <sup>1</sup>HNPP, BRAC, Dhaka, <sup>2</sup>TB, NTP, Dhaka, <sup>3</sup>TB, WHO, Dhaka, Bangladesh.  
e-mail: shayla.dhaka@gmail.com

**Background and challenges to implementation:** Since 1984, BRAC has been working for addressing TB problem and became major partners of National Tuberculosis Program (NTP) in 1994, and Principal Recipient of Global Fund grant since 2004 along with NTP. Currently it is serving 93 million populations countrywide. To improve case notification and overcome unfavorable treatment outcome, the organization introduced financial support in TB control program.

**Intervention or response:** BRAC has been providing financial support for TB control in many ways to different target groups it includes diagnostic, transportation and nutritional support. It introduced incentive system for the Shasthya Shebikas (Frontline Community Health Worker) who mobilize community, organizing outreach sputum collection centers, identify suspect and provide DOT to TB patients. All MDR-TB and TB-HIV co-infected patients get nutritional and investigation support (including transport cost) to enhance better treatment outcome. Diagnostics supports (X-ray, FNAC, MT, X-pert etc.) has been providing to poor TB symptomatic and TB patients from ultra-poor family

are getting nutritional support during the course of treatment.

**Results and lessons learnt:** The case notification rate has been increased to 130 in 2013 which was 99 in 2011 and 111 in 2012 in BRAC supported areas. The program has already observed improved treatment adherence as well as treatment success rate increased over the years up to 94% among the new smear positive patients registered in 2012. In hard to reach and coastal areas, all case notification has been increased from 90 to 118 during 2010 to 2013 respectively. In 2013, 173,568 TB symptomatic got diagnostic support from BRAC, and a total of 30,141 Smear negative and 18,181 extra-pulmonary TB cases were identified which were significantly higher than 2012 (13,481 smear negative and 15,209 extra-pulmonary cases). A total of 1,802 MDR-TB and 107 TB-HIV patients got nutritional support up to December 2013.

**Conclusions and key recommendations:** Planned and effective utilization of financial support could improve the program performances as well as reduce the country's disease burden.

#### **PD-864-31 Modify Directly Observed Treatment Short-course (DOTS) for tuberculosis control programme in Hualien and Nantou mountain areas of Taiwan**

Y-W Huang,<sup>1,2</sup> J-J Lee,<sup>3</sup> Y-C Chen,<sup>2</sup> C-Y Tsao.<sup>1</sup> <sup>1</sup>Chung Shan Medical University, Institute of Medicine, Taichung, <sup>2</sup>Changhua Hospital, Department of Health, Pulmonary and Critical Care Unit, Changhua, <sup>3</sup>Buddhist Tzu Chi General Hospital, Hualien and Tzu Chi University, Department of Internal Medicine, Hualien, Taiwan. Fax: (+886) 4 828 3275. e-mail: hiwen1533@yahoo.com.tw

**Background:** Tuberculosis (TB) has a high incident rate in mountain areas of Taiwan. The aim of this study was to assess the impact of Modify-DOTs in screening tuberculosis and treatment outcome in Hualien and Nantou mountain areas of Taiwan from Jan 2011 up to Dec 2013.

**Design/Methods:** A component of the Modify-DOTs strategy was employed Taiwanese native case managers to help screening close contacts using chest x-ray and ensure patients' compliance to treatment.

**Results:** Incidence rate in Hualien was reduced from 393.3 to 235.7 per 100 000 population and it was reduced from 338 to 235.5 in Nantou mountain area. Furthermore, the rate of active case finding was increased from 17.4% to 33.8% as compared to an average value 6.5 % of CDC, Taiwan, for the specified years. This data show that enhanced active case finding of close contacts reduced TB incidence, and the Modify-DOTs strategy was applicable for controlling tuberculosis in the Taiwan's mountain areas.

**Conclusion:** The study employed Taiwanese native case managers to enhance DOTs and improve the compliance of tuberculosis patients and control epidemic tuberculosis. The Modify-DOTs strategy has higher active case finding and results in a lower incidence compared with the DOTS program. This study also provided further

insight into the implementation of hospital-to-community level case management using Modify-DOTs by TB control policy.

### **PD-865-31 Community volunteers as messengers of tuberculosis control: a study from Faridkot, India**

S Gadala,<sup>1</sup> A Kumar,<sup>1</sup> T Thomas,<sup>1</sup> M Krithika,<sup>1</sup> P Banuru Muralidhara.<sup>2</sup> <sup>1</sup>Project Axshya, Catholic Health Association of India, Hyderabad, <sup>2</sup>Project Axshya, Union against Tuberculosis & Lung Diseases, New Delhi, India. Fax: (+91) 40-2781 1982. e-mail: srinivasa-rao@chai-india.org

**Background:** Tuberculosis a global public health issue characterized with limited access to health services is one of the bigger challenges faced by India where the incidence is around one-fifth of the global cases reported. In view of this, the need for community participation is a pivotal measure in combating the global burden of tuberculosis. Project Axshya, a civil society initiative for TB care and control recognizes the importance of community participation through the involvement of community volunteers. Volunteers are the first point of contact and are identified and trained from within the community.

**Intervention:** The community volunteers were identified within the communities and trained in aspects such as identification of TB symptomatic, sputum collection and transportation, referral, intensive outreach activities and also on engaging them as community DOTS providers from Faridkot district of Punjab.

**Results:** Around 30% of TB symptomatics registered at the District Microscopy Centre (DMC) were identified by the community volunteers for the year 2013-14. Of which, 74% have been identified through sputum collection and transportation (SCT) while 26% through referrals. Out of the TB symptomatics tested for TB 10% were found positive. The community volunteers ensured that all those who were tested positive, were put on DOTS treatment.

**Conclusion:** Community volunteers are able to reach to marginalized and vulnerable areas of the district. Engaging these volunteers is an essential link in service delivery. Through this process a community system strengthening is being established for TB care and control.

### **PD-866-31 Overcoming access barriers to DOTS in Nigeria: the case of distance**

T Ensor,<sup>1</sup> O Chukwuogo.<sup>2</sup> <sup>1</sup>Nuffield Centre for International Health and Development, Leeds Institute of Health Sciences, Leeds, UK; <sup>2</sup>Community Medicine, University of Nigeria Teaching Hospital, Enugu, Nigeria. e-mail: ogoamakai@yahoo.com

**Background:** African Union (AU) Member States during the Special Summit of the AU on HIV/AIDS, Tuberculosis (TB) and Malaria (Abuja +12) recommended among other things that 'no one is left behind'. However access to health care remains a major health system problem.

This is because access derives only from the favourable interplay of factors between health system and the individuals /community that consume services provided. Using TB control in Nigeria as a case study, this paper demonstrates how physical distance constitutes an access barrier to effective uptake of Directly Observed Treatment Short-course (DOTS) for TB

**Design/Methods:** This combines in depth interviews with TB program managers and DOTS providers and a comprehensive review of literature to explore the dimensions of distance as an access barrier to DOTS in Nigeria and current best practices in other low and middle income countries to mitigate the effect of distance. The source of data includes electronic and non electronic sources. Using a conceptual framework the different dimensions through which distance portends an access barrier and the different strategies that can overcome these are discussed. An appraisal of the feasibility of the identified strategies is done using specified criteria.

**Results:** The analysis shows that distance constituted an access barrier not just by physical distance but by travel cost incurred, availability of transport and opportunity costs. These are factors outside the health system. These dimensions are more prevalent in the rural areas and among the low Socio Economic Status (SES) groups in the community. Different strategies are identified which have been used singly but mostly in combination to address these various dimensions. However an appraisal of these strategies reveals that community TB care, community outreach, establishment of new health facilities, health equity funds, vouchers, and engagement of other sectors like transport are feasible in Nigeria.

**Conclusion:** Some of the dimensions of distance are not direct health system factors but interventions can be routed through the health system and by involvement of other sectors. It is recommended that the above listed strategies be adopted in combination and implemented using a phased approach taking into consideration the geopolitical and cultural diversity in Nigeria.

### **PD-867-31 Delay in treatment initiation among the TB patients: findings from a knowledge, attitude and practice survey conducted in 30 districts in India**

K Sagili,<sup>1</sup> S Srinath,<sup>2</sup> N Wilson,<sup>3</sup> S Chadha.<sup>4</sup> <sup>1</sup>Research, The Union, New Delhi, <sup>2</sup>Centre for Operational Research, The Union, New Delhi, <sup>3</sup>Public Health, Independent Consultant, New Delhi, <sup>4</sup>TB Control Unit, The Union, New Delhi, India. Fax: (+91)011 4605 4430. e-mail: ksagili@theunion.org

**Background:** Early diagnosis of Tuberculosis (TB) and immediate treatment initiation are key in controlling TB transmission and ensuring favourable treatment outcomes. Patient-related delays include casual attitude, fear of death, loss of wages, lack of finances, visiting multiple providers for quality treatment, free treatment, confidentiality or accessibility & fear of discrimination and TB-related stigma in the community. Provider-related delays include lack of knowledge at provider's end, non-

availability of qualified providers, non-availability of technicians or lab facility in a given location, non-availability of drugs or DOT provider.

**Design/Methods:** A community-based knowledge, attitude and practice survey was conducted in 30 districts covering 15 states. 496 TB patients (patients who were currently undergoing treatment or had finished treatment in the past one year) (M: 302, F: 194; urban: 127, rural: 369) were identified using household listing process. Using a pre-tested questionnaire, TB patients were interviewed regarding their knowledge about TB, their diagnosis and treatment details.

**Results:** This survey includes not only those patients who are registered with the national TB control program but also those who take treatment from private sector. Of the 496, 401 (81%) were diagnosed within one month of the onset of symptoms. Of these, about 53% were diagnosed in about 20 days. 337 (68%) got diagnosed at a government facility. However, only 233 (47%) were initiated on treatment within one week of diagnosis, about 26% were initiated between 1–3 weeks, about 17% were initiated on treatment only after 3 weeks and about 10% could not respond to this question. About 253 (51%) were taking treatment at the government centres. There is no statistical difference between those started treatment at government centre and those who started treatment in private sector.

**Conclusion:** About 43% do not start their treatment as soon as they are diagnosed. This group is a risk factor for TB transmission in the community. On an average, it takes at least 20 days to one month to diagnose most TB patients from the time of on-set of symptoms. Treatment initiation takes anywhere from less than a week to 3 weeks for most of the patients. Delay in treatment initiation facilitates continued TB transmission. A systematic gap analysis of delay at different stages is essential to reduce or eliminate this delay, which directly contributes to TB control.

#### **PD-868-31 Delay in diagnosis and treatment of tuberculosis in different agro-ecological zones in Oromia region, Ethiopia**

B Girma,<sup>1</sup> Z Habtamu,<sup>2</sup> HA Worku,<sup>3</sup> E Zemene,<sup>1</sup> S Negash,<sup>1</sup> Y Haile,<sup>4</sup> M Melese,<sup>1</sup> P Suarez.<sup>4</sup> <sup>1</sup>Help Ethiopia Address the Low TB Performance (HEAL TB) project, Management Sciences (MSH), Addis Ababa, <sup>2</sup>Oromia Regional Health Bureau, Department of Oromia Regional Health Bureau, Addis Ababa, <sup>3</sup>MHS, TB Care I, Addis Ababa, Ethiopia; <sup>4</sup>MSH, Centre for Health Services, Arlington, VA, USA. e-mail: bgirma@msh.org

**Background:** In Ethiopia, 30% of TB cases at a point in time are undiagnosed. The delay in diagnosis and treatment results in increasing the risk of transmitting the disease to contacts. In Ethiopia, median patient delay ranges from 21 days to 30 days and median duration of total delays were reported as high as 97 days. Understanding the magnitude of and factors contributing to delay in diagnosis and treatment among TB patients is crucial in designing TB implementation strategies.

**Methods:** A health facility based cross sectional study design was used to assess the delay in diagnosis and treatment of TB patients. A stratified sampling approach was used. The first stratum was urban, rural dichotomy. The rural is again stratified by 2 agrarian and one pastoralist zones. From each zone 3 districts were selected randomly and one town making a total of 10 districts for the study. Two health facilities were selected randomly from each district. The sample was allocated to the health facilities proportional to the number of cases notified in the previous year. Pulmonary TB Patients (PTB) in intensive period of treatment were enrolled for the study. Patient's delay was defined as the time from the appearance of the first symptom of disease (TB) to the first consultation with a health care provider and a health care systems delay was defined as time from the first consultation with a health care provider to initiation of anti TB drugs. The data was entered into EPI info 3.5.4 software.

**Results:** A total of 538 new smear positive PTB patients and smear negative tuberculosis patients participated in the study. The median total delay was 39 days. The median patient delay and health system delay were 30 and 9 days, respectively. The patient delay ranges from 20–30 days ( $P=0.001$ ) and the median delay from first consultation to diagnosis varies from 2–20 days (Kruskal-Wallis test  $P=0.0001$ ). The total delay in pastoralist zone was high (56 days). The health system delay contributes to larger variation among zones.

**Conclusion:** Patient delay was high in all zones and the health system delayed was higher for pastoralist zone of Guji.

**Interventions:** to overcome barriers towards service access including rapid point of care diagnostics for pastoralist areas and health seeking behavior need to be strengthened. In addition to this, targeted interventions are indicated to improve health system factor that contributes to additional delays in pastoralist areas.

#### **PD-869-31 Gender matters: innovative approaches to TB prevention and care using gender integration to improve patient care**

T Faramand,<sup>1</sup> M Ivankovich.<sup>1</sup> <sup>1</sup>Gender Integration, WI-HER LLC, Vienna, VA, USA. e-mail: mivankovich@wi-her.org

**Background and challenges to implementation:** World-wide, tuberculosis disproportionately impacts women in their most productive years. Risk factors include malnutrition and overcrowding. TB is more aggressive in women of reproductive age and is associated with infertility, morbidity, and low birth weight. Gender also impacts detection: women often delay presenting to clinics and are diagnosed later; men are more likely to be newly diagnosed but less likely to adhere to treatment. Addressing the different needs, behaviors, and preferences of women, men, boys, and girls is critical to optimize TB services, efficiently use resources, and ensure quality care. Under the USAID Applying Science to Strengthen and Improve Systems (ASSIST) Project,



WI-HER has developed and implemented an innovative, practical, and holistic approach to integrate gender to improve health outcomes.

**Intervention or response:** The WI-HER gender integration approach builds local capacity to identify, routinely examine, and address gender-related gaps and issues that can affect access to and utilization of care. It actively identifies and responds to these issues by developing and testing changes in conjunction with other interventions to achieve higher quality care. The USAID ASSIST Project in Uganda and Swaziland works to expand coverage and quality of integrated TB/HIV services and improve outcomes using modern quality improvement approaches. Data is disaggregated by sex, routinely monitored, and programs adjusted accordingly to close identified gaps.

**Results and lessons learnt:** Our unique gender integration approach results in locally-developed solutions, improved country leadership, links to other sectors, institutionalized gender integration at all levels, and improved health outcomes. The approach has built the capacity of healthcare providers to seamlessly address gender issues in programming and enhanced their skills in monitoring and evaluating programs by disaggregating data by sex and age and developing gender-sensitive indicators. We observed increased enrolment in care among MDR TB male patients in Swaziland from 38% to 50% in twelve months. We also observed improvement in completing treatment of HIV/TB co-infections from 47% to 62% among men and from 67% to 81% among women.

**Conclusions and key recommendations:** Innovation in gender integration using the science of improvement in TB programs leads to improved program effectiveness and better outcomes among women, men, boys, and girls.

#### **PD-870-31 Views of district health managers (DHMs) on barriers to effective implementation of community TB care (CTBC) approaches in Botswana**

T Katlholo,<sup>1,2</sup> J Cuervo-rojas,<sup>3</sup> M Seretse,<sup>1,4</sup> F Mwangemi,<sup>3</sup> L Busang,<sup>3</sup> B Kgwaadira,<sup>1,4</sup> O Bahemuka,<sup>2</sup> I Halldorsdottir.<sup>5</sup> <sup>1</sup>Public Health, Ministry of health, Gaborone, <sup>2</sup>Global Health, Afya Bora Consortium Fellowship, Gaborone, <sup>3</sup>Public Health, Africa Comprehensive HIV/AIDS Partnerships, Gaborone, <sup>4</sup>Global Health, International Training and Education Centre for Health, Gaborone, <sup>5</sup>Public Health, Research 4 Results (PTY) Ltd, Gaborone, Botswana. Fax: (+267)3910327. e-mail: thkatlholo@gmail.com

**Background and challenges to implementation:** Community Tuberculosis Care (CTBC) was introduced in 2004 to engage communities in the care of TB patients to improve treatment outcomes. Patients are empowered to opt to take their medication from several CTBC approaches including families, institutions and community Volunteers managed by Civil Society Organizations (CSOs) or Government. In December 2013, the CSOs CTBC programs stopped functioning due to diminished

external funding. This may have resulted in non-adherence which could negatively impact treatment outcomes.

**Response:** Despite diminished funding and efforts to scale up CTBC, evidence on CTBC barriers is scarce. Therefore we sought to elucidate the expert views of DHMs regarding key barriers to CTBC implementation to lay the basis for greater ownership and facilitate decision making on the most appropriate CTBC approach to be adopted for Botswana. This abstract originates from a national CTBC approaches evaluation study carried out in 9 districts of Botswana. The evaluation used mixed methods. A Retrospective Cohort Study and in-depth interviews and focus group discussions were carried out. This abstract concentrates on the experiences and views of DHMs.

**Results and lessons learnt:** Identified barriers were non-adherence due to poor relationships with providers and volunteers; competing priorities such as alcohol abuse; poor monitoring due to high mobility of patients, staff shortage, poor infection control practices; inadequate knowledge of TB for patients and the community, which we associate with lack of community participation and stigma. All approaches were acceptable and deemed effective. CTBC approaches managed by CSOs were noted to be significantly effective despite poor sustainability. CTBC success was shown to be associated with availability of volunteer incentives.

**Conclusion and key recommendations:** This evaluation suggests incentive provision for all volunteers and social and livelihood support to patients must be considered if treatment objectives are to be achieved. Regardless of approach, training for volunteers needs to be ensured as with the need to address the knowledge gap among the community regarding infection control and TB. The evaluation supports the promotion of the Patient's Charter for TB Care to reduce stigma and recommend assessment of the effectiveness of current measures for monitoring volunteers by health facilities is essential

#### **PD-871-31 Revisiting DOTS strategy in view of TB recurrence in Delhi, India**

Ashw Khanna,<sup>1</sup> RK Mehra,<sup>1</sup> R Nagar,<sup>1</sup> S Chandra,<sup>2</sup> N Sharma,<sup>3</sup> M Hanif,<sup>4</sup> D Kundu.<sup>2</sup> <sup>1</sup>State TB Control Office, Directorate of Health Services, New Delhi, <sup>2</sup>Revised National Tuberculosis Control Program, WHO Country Office for India, New Delhi, <sup>3</sup>Community Medicine, Maulana Azad Medical College, New Delhi, <sup>4</sup>Intermediate Reference Lab (TB), New Delhi TB Centre, New Delhi, India. e-mail: chandras@rntcp.org

**Background and challenges to implementation:** Despite commendable advancements towards disease containment efforts for tuberculosis (TB) control, a sizeable number of treated patients report recurrence suggesting an urgent need to reassess the program conditions on which the principles of DOTS is pivoted. Apart from the polemics of regimen efficacy, there are several factors which determine successful treatment outcomes and in turn recurrent TB episodes. This study is an attempt to understand the need to revisit the conventional DOTS

strategy for declaring treatment completion based on sputum microscopy in light of disease progression leading to relapse within the framework of treatment adherence.

**Intervention or response:** The longitudinal study was conducted in two districts (from North and East Delhi) which reported more than the State proportion of relapses out of the total previously treated TB case notifications for the year 2012. Registered relapses were interviewed by field supervisors using a semi-structured questionnaire. In addition, internal evaluation records were checked for both the districts regarding data validation, lab quality assurance, and patient interview records taken during evaluation for past history, treatment interruptions, health service accessibility and follow up sputum examination at the end of treatment.

**Results and lessons learnt:** Preliminary analysis has shown that out of the 335 total relapses notified in the two districts in 2012, 27% (92) patients have reported back within the first year of DOTS treatment. Individual district analysis revealed that from the cohort of relapse under review, 25 successfully treated new infectious TB patients and 5 previously treated patients reported back as relapse; 96% (28/30) reported back in less than one year while 47% (11/23 new infectious successfully treated) reported back within the first 6 months of being declared cured ( $p < 0.01$ ). Similarly, in the other District 42% (62) relapses were those who reported back with symptoms in less than one year of treatment under DOTS program. No significant lapses were found in the internal evaluation records checked for patient compliance. Samples of patients who reported back in less than 6 months were subjected to liquid culture for bacteriological confirmation.

**Conclusions and key recommendations:** In view of the findings mentioned above, efficacy of the DOTS strategy whereby treatment completion is declared based on sputum microscopy remains debatable especially in light of disease progression to relapse. As recurrent TB episodes can be due to reactivation or reinfection, it is time that TB program revisits the conventional strategy of treatment completion with deployment of liquid culture techniques at the end of treatment for TB control in high burden settings.

### 33. TUBERCULOSIS AND DIABETES: LOOK OUT FOR BOTH

#### PD-872-31 Impact of diabetes mellitus on epidemiological rates of pulmonary tuberculosis

V Punga,<sup>1</sup> M Yakimova,<sup>1</sup> L Rusakova.<sup>1</sup> <sup>1</sup>TB epidemiology, statistics and information technologies, Central TB Research Institute, Moscow, Russian Federation.  
e-mail: marina-air@mail.ru

**Background:** A rapid increase in the number of cases with diabetes mellitus (DM) in general population is

being observed in the Russian Federation. Over the period of 2011–2012 the incidence rate of insulin-independent diabetes increased from 2,372.3 to 2,514.5 cases per 100,000 population, while the rate of insulin-dependent diabetes over the same time period increased from 214.9 to 220.1. Purpose of the study: To study the TB incidence in patients with DM and its impact on TB epidemiology in general in the Russian Federation.

**Design/Methods:** The forms of official statistics with data on new cases of diabetes mellitus and TB notified in five regions of the Russian Federation were analyzed over the period of 2010–2011. For each new case of TB and DM a questionnaire was filled in with the following information: method of TB detection (active – at the time of referral, passive – during preventive fluorography screening); clinical form of TB at the moment of registration (cavitation of lung tissues, bacterial status); range of MbT drug resistance to the first- and second-line drugs, treatment success. The total number of patients was 104.

**Results:** The DM incidence rate in the study sites varied from 447.2 to 694.8 per 100,000 DM patients. The proportion of patients with TB and DM co-morbidity among all new cases was not high – 2.0–3.8%. In the majority of DM patients tuberculosis was detected at the referral, although DM patients belong to TB risk group and should undergo annual fluorography examination. In 86.5% of cases cavitation of lung tissues was diagnosed, 90.4% of cases had MbT+, including 22.6% cases with MDR MbT. When indicating therapy to patients with TB and DM, compensation of diabetes and specifics of TB treatment were taken into consideration. Treatment success based on bacterial conversion in those patients was not high – 57.8% (while in TB patients with no DM the rate was 68.7%).

**Conclusion:** The DM incidence has a negative impact on TB epidemiology. Patients with DM are being diagnosed with severe, disseminated forms of TB with cavities of lung tissues and bacterial excretion. Every fifth patient has MDR-TB which complicates treatment. Treatment is often ineffective which leads to development of chronic cases.

#### PD-873-31 Diabetic tuberculosis cases characteristics in Baghdad

M Abdulrazaq,<sup>1</sup> Lyat Salihi,<sup>1</sup> A Alfarttoosi.<sup>2</sup> <sup>1</sup>General Health, Specialized Center for Chest and Respiratory Disease, Baghdad, <sup>2</sup>Baghdad University, Baghdad Medical College, Baghdad, Iraq. e-mail: myahyasz@hotmail.com

**Background:** The link between diabetes mellitus and tuberculosis has been recognized for centuries. Diabetes mellitus was a known risk factor for tuberculosis. Now, with the current global increase in cases of type 2 diabetes mellitus, the association between tuberculosis and diabetes mellitus is re-emerging. It is estimated that the number of individuals with both tuberculosis and diabetes mellitus will increase dramatically. The WHO has identified diabetes mellitus as a global epidemic.

Simultaneously, tuberculosis continues to be a major cause of death worldwide. The current pandemic of type 2 diabetes mellitus is accelerating in a world where approximately one third of the population is latently infected with *Mycobacterium tuberculosis*

**Objectives:** identify diabetic tuberculosis cases characteristics

**Methods :** A case-control study ,was done in the specialized center for chest and respiratory disease in Baghdad during the period 1<sup>st</sup> of August 2010 - 31<sup>st</sup> of July 2011 , in this study diabetic tuberculosis cases enrolled as cases and non-diabetic tuberculosis cases as control. A total number of 218 tuberculosis patients older than 14 were enrolled in this study. 77 diabetic and 141 non diabetic. A full medical history, physical examination and Blood sugar tests were done for all. Statistical Package for Social Sciences version 20 used for data input and analysis.

**Results:** 218 tuberculosis patients were enrolled in this study. 59.7% of diabetic group were male while for non diabetic group the percentage was 53.2% male. Dominant age group was 45–64 year in diabetic patients and 15–44 year in non-diabetic patients. The mean age of diabetic group was 50.2 year while for non diabetic group the mean was 42.2 year. In the diabetic group 54.5% were married ,while In the non diabetic group 61.7% were married. Diabetic tuberculosis patients more likely to be of lower education level than non-diabetic tuberculosis patients. There was no significant difference in mean body mass index between the groups. Diabetic group less likely to have extrapulmonary tuberculosis. And more likely to have associated medical disease and this disease is more likely to be hypertension. There was no significant difference in smoking and contact history between the groups.

**Conclusions:** Diabetic tuberculosis patients were older and more likely to be of lower education level than non-diabetic tuberculosis patients.

#### PD-874-31 Efficacy of MDR-tuberculosis in patients with different types of diabetes mellitus

O.G Komissarova,<sup>1</sup> o.o. Konyayeva,<sup>1</sup> R Abdullaev,<sup>1</sup> I Vasilyeva.<sup>1</sup> <sup>1</sup>Therapeutic, Central TB Research Institute, Moscow, Russian Federation. e-mail: rizalla@mail.ru

**Aim:** Comparison of clinical manifestations and efficacy of treatment patients with MDR/XDR tuberculosis and different types of diabetes mellitus.

**Materials and Methods:** we investigated 53 patients with MDR/XDR tuberculosis (TB) in the age from 18 till 59 years (male - 38 and female - 15). In 30 patients were detected diabetes types 1 and in 23 patients - diabetes type 2. All patients were treated by individualized regimen. The efficacy of chemotherapy was estimated by the frequency and time of negativation of sputum and by reducing of cavity in lung.

**Results:** It was established that the age of patients with diabetes type 1 was 18–39 years, and patients with diabetes type 2 - 40–59 years. Among patients both

group more frequently observed infiltrative TB, fibro-cavernous TB and tuberculome. Severe TB intoxication frequently was detected among patients with diabetes type 1. Destruction in the lung was observed in all patients. The cavity with diameter of 2 cm were more frequently in patients with diabetes type 1, and 2–4 cm - in patients with diabetes type 2. *M. tuberculosis* (MTB) was detected in sputum of all patients. Quantity of MTB in sputum of patients with diabetes type 1 was few and in patients with diabetes type 2 - much. Conversion of sputum after 6 months of chemotherapy was detected in 78,5% and patients with diabetes type 1 and in 65,2% - with diabetes type 2. The frequency of closing cavities at 6 months of treatment was observed in 53,3% patients with diabetes type 1 and in 47,8% - with diabetes type 2. **Conclusion.** Clinical manifestations and efficacy of MDR/XDR TB in patients with type 1 and type 2 diabetes mellitus are different.

#### PD-875-31 Comparison of anti- tuberculosis drug susceptibility in new cases of tuberculosis patients with and without diabetes mellitus

P Baghaei Shiva,<sup>1</sup> P Tabarsi,<sup>1</sup> M Marjani,<sup>1</sup> A Moniri,<sup>1</sup> MR Masjedi.<sup>1</sup> <sup>1</sup>National Research Institute of Tuberculosis and Lung Diseases, Clinical Tuberculosis and Epidemiology Research Center, Tehran, Islamic Republic of Iran. Fax: (+98) 21 261 09590. e-mail: baghaei\_gp@yahoo.com

**Background:** To determine the impact of diabetes mellitus (DM) on anti-tuberculosis (TB) drug resistance in new cases of TB patients.

**Design/Methods:** A prospective study was conducted on all adult newly pulmonary TB patients with DM as cases and without DM as controls treated at National Research Institute of Tuberculosis and Lung Disease from May 2013 to Oct 2013. A rapid nucleic acid amplification test (PCR) and a molecular resistance test for rapid detection of resistance to isoniazid and rifampin were done for all positive smear TB patients. A multivariate analysis was performed to determine the impact of DM on any anti-TB drug resistance.

**Results:** 45 TB cases with DM and 45 TB cases without DM were included. TB cases with DM were more likely to be older (61 vs. 47 years,  $p=0.001$ ). Two TB-DM patients had multidrug-resistant TB (MDR-TB) (4.4%) compared to no MDR-TB in control group and TB-DM cases were resistant at least one drug (11.1% vs. 4.4%,  $p=0.43$ ). DM remained significantly associated with any drug resistant (OR: 6.32, 95% CI: 1- 40.72) in multivariate analysis.

**Conclusion:** SNew TB patients with DM are at increased risk of any drug resistant. More other studies need to prove these results.



**PD-876-31 Multidrug-resistant tuberculosis (MDR-TB) and diabetes mellitus in Brazil, 2007-2011: a descriptive study**

F. Dockhorn,<sup>1</sup> H Barroso Bernal,<sup>1</sup> J Toledo,<sup>1</sup> O Rodrigues,<sup>1</sup> C David,<sup>1</sup> D Barreira,<sup>1</sup> J N Lima.<sup>1</sup> <sup>1</sup>National Tuberculosis Control Programme, Brazilian Ministry of Health (MoH), Brasília, DF, Brazil.  
e-mail: fernanda.dockhorn@saude.gov.br

**Background** Tuberculosis (TB) is an infectious disease with high cure rates when is treated with the basic scheme. Resistance to rifampicin and isoniazid is called multidrug resistance tuberculosis (MDRTB), which is public health challenge. Comorbidities such as HIV / AIDS, smoking, alcoholism and diabetes mellitus (DM) modify the natural history of TB, and especially of MDRTB, increasing the number of treatment failure and death. This study aims to evaluate the cases of MDR-TB associated with DM in Brazil in the period 2007–2011. **Design / Methods:** MDR-TB Surveillance is recorded in a specific databank system (SITE-TB). This databank contains information about all special cases of TB notification and tracking. This study is based on a cohort of new cases of MDRTB and self-reported DM, registered in the SITE-TB from 2007 to 2011. It describes association between TB and DM, as well as outcome (cure, complete treatment, treatment failure, abandon, death). HIV serological status was also evaluated.

**Results:** From 2007 to 2011, a total of 2016 new MDR-TB cases were reported in SITE-TB. Of these, 11.5% (232) mentioned DM. The rate cure of TB and DM comorbidity was 40% (93) and complete treatment was 29.3% (68), a treatment success of 69.3%, higher than the national average for the same period (63%). In the same period loss to follow up outcome was observed in 9.5% (10 cases) and 11.2% died. 6.9% of these deaths were due to TB and 4.3% deaths from other causes. In the same period the abandon rate of MDRTB population was 14.2% (287) and 11.9% (241) died. When analyzed the “HIV testing status” variable, 100% were examined, with positive results observed in 5.1% (12) of the cases. In the same period, the national average for this association (MDRTB/HIV) was of 8.5%.

**Conclusions:** The results show that despite all efforts, control of MDRTB/DM control in Brazil remains a challenge. The association MDRTB/DM presented better success cure rates when compared to the general population and might be due to better access to health services. The association MDRTB/DM has high rates of abandon and death, over the targets set by the World Health Organization. Further studies should be conducted to analyze the risk factors related to the outcomes of this group.

**PD-877-31 Prevalence of diabetes among TB patients attending DOTS clinics in South-South Nigeria: the need for comprehensive TB patient care**

V Obot,<sup>1</sup> V Adams,<sup>2</sup> M Gidado,<sup>3</sup> A Ekpeudom.<sup>4</sup> <sup>1</sup>Public Health, Ministry of Health, Uyo, <sup>2</sup>Community Health, University of Benin, Benin, <sup>3</sup>TB, KNCV/TBCARE 1, Abuja, <sup>4</sup>Community Health, University of Uyo Teaching Hospital, Uyo, Nigeria. Fax: (+234)424 52 311.  
e-mail: valerie\_\_obot@yahoo.com

**Background:** People with diabetes have an approximately 3-fold risk of developing active TB. The prevalence of diabetes in developing countries is on the increase and considering the prevalence of TB in Nigeria 322/100,000, this is a major concern to the TB control program. We sought to determine the prevalence of DM among TB patients registered in DOTS clinics in Uyo, Nigeria in order to make an informed decision for screening of DM in DOTS clinics as an entry point of care for both diseases.

**Methodology:** A descriptive cross sectional study among diagnosed TB cases using both semi- structured interviewer administered questionnaire and fasting blood sugar test for all TB patients registered in DOTS clinics in Uyo, Nigeria in 2013. Patients were assessed for symptoms of DM. Data analyzed using stata 10.

**Result:** A total of 172 TB patients from three DOTS clinics in Uyo Local Government Area were enrolled for the study. The mean age was  $35.8 \pm 11.5$  years, more than half of the respondents were males 100 (58.0%). One fifth of the total patients 35(20.0%) had symptoms of DM (polyphagia & polydipsia) and 70(41.0%) had symptoms of weight loss. One tenth 18(10%) of the patients were existing cases of DM, 4(2.3%) were newly diagnosed. The prevalence of DM among TB patients was 22 (12.7%) {95% CI(7.7– 17.7%)}; compared to DM prevalence of 5.8% {95%, CI 3.7 – 7.8%} in the general population of Uyo (  $p=0.003$ ). Only gender was statistically significant after adjusting for age and occupation, as a risk factor for DM. The male gender had an Odds ratio of 0.29 (71% reduced risk) of having DM,  $p = 0.016$ .

**Conclusion:** The prevalence of DM among TB patients was 12.7%. Considering the growing prevalence of DM in Nigeria and developing countries; and the high prevalence of DM among TB patients, it will be recommended to integrate TB screening among all DM patients and vise-versa in order to mitigate the complications that could arise from both diseases. All TB Patients should be offered comprehensive patient care. Further research needed to investigate the impact of DM on TB presentation and treatment outcomes.

**PD-878-31 Diabetes in a cohort of tuberculosis patients in Rome, Italy**E Caraffa,<sup>1</sup> M Sane Schepisi,<sup>1</sup> A Gualano,<sup>2</sup> A Rianda,<sup>2</sup> V Galati,<sup>2</sup> C Pinnetti,<sup>2</sup> F Palmieri,<sup>2</sup> E Girardi.<sup>1</sup><sup>1</sup>Epidemiology and Pre-clinical research, National Institute for Infectious Diseases "L.Spallanzani", Rome, <sup>2</sup>Clinical Department, National Institute for Infectious Diseases "L.Spallanzani", Rome, Italy. e-mail: saneschepisi@inmi.it

**Background.** The rising worldwide diabetes mellitus burden poses a threat to global TB control. The convergence of these two epidemics is expected to increase markedly in the coming decades. **Objective.** The aim of the study is to describe the socio-demographic and clinical characteristics of a cohort of TB patients in Italy - a low DM prevalence country (5.1%).

**Methods.** We performed a retrospective study of all cases of TB diagnosed at a tertiary TB referral center in Rome, Italy, that included a high proportion (74.4%) of foreign born patients during the period January 2007-December 2012.

**Results.** Among 980 TB patients of which 729 foreign born, 63 (6.4%) had diabetes mellitus (type2 in 49/63 and type1 in 8/63 patients). Of the 63 TB - DM patients 40 (63.5%) were foreign born, most frequently from Africa and Asian countries. Compared to the TB only cohort, TB-DM patients were older (median 55.7 yrs compared to 38.2); male gender (77.8% vs. 64.4%) and Italian nationality (36.5% vs. 24.9%) were more represented ( $p < 0.05$ ). TB - DM patients were more likely to be born in a country with DM prevalence  $\geq 7\%$ . Foreign born TB-DM patients were younger and male were more represented than among Italian TB-DM patients. Diabetes was more frequently identified at the time of TB diagnosis in foreign born than in Italian born patients (27.5% vs. 8.7%) ( $p = 0.07$ ). Poor glycemic control (HbA1c  $\geq 8\%$  or FBG  $\geq 200$  mg/dl) was found in 32/63 (50.8%) TB-DM patients, in similar proportions among foreign and Italian born (52.5% and 47.87%). Among 729 foreign born, TB - DM patients, compared to only TB patients, were older and more frequently male, and their countries of origin had higher TB incidence rates.

**Conclusion.** The results of this study show how in our hospital diabetes and tuberculosis may represent a public health problem, especially in people originating from countries at high risk for both diseases, in which prevention policies including bi-directional TB-DM screening could be recommended.

**Table** Characteristics of 63 TB - DM patients

	Foreign born (n. 40)	Italian born (n.23)	p
Age (median, yrs)	47.5	69.9	<0.001
Male gender	33 (82.5%)	16 (69.6%)	
DM diagnosis at the time of TB diagnosis (data available for 59/ 63 TB-DM patients)	11 (27.5%)	2 (8.7%)	0.07
Poor glycemic control	21 (52.5%)	11 (47.8%)	

**PD-879-31 Risk stratification for diabetes screening at a tuberculosis referral hospital in Tanzania**M Sariko,<sup>1</sup> G Kibiki,<sup>1</sup> J Gratz,<sup>2</sup> E Houpt,<sup>2</sup> S Mpagama,<sup>1,3</sup> S Heysell.<sup>2</sup> <sup>1</sup>Biotechnology Laboratory, Kilimanjaro Clinical Research Institute, Moshi, United Republic of Tanzania; <sup>2</sup>Infectious Diseases and International Health, University of Virginia, Charlottesville, VA, USA; <sup>3</sup>Research, Kibong'oto National TB Hospital, Kilimanjaro, United Republic of Tanzania. e-mail: scott.heysell@gmail.com

**Background:** Recommendations by the World Health Organization to study implementation strategies of bidirectional screening for tuberculosis (TB) and diabetes have been met with varying levels of uptake by national TB programs in resource-limited settings. In Tanzania, the National TB and Leprosy Program remains undecided on how to screen for diabetes among TB patients.

**Design/Methods:** Kibong'oto National TB Hospital (KNTH) is a regional referral hospital for TB cases from Northern Tanzania, and the national referral hospital for multidrug-resistant (MDR)-TB. We therefore sought to perform point-of-care glycated hemoglobin (HgbA1c) testing among all patients admitted to KNTH to determine the point prevalence of diabetes (HgbA1c  $\geq 6.5\%$ ) and prediabetes (HgbA1c 5.7-6.4%).

**Results:** All patients hospitalized at KNTH over a single week (starting on World TB Day 2014) were enrolled. Of 148 patients, 107 (72%) were men. Fifty-nine (38%) cases had no prior TB treatment, 22 (15%) were retreatment and 69 (47%) were being treated for MDR-TB. Only 3 (2%) had a known history of diabetes. 110 (77%) had a Hgb A1c  $\leq 5.6$  (normal), 28 (19%) had Hgb A1c  $\geq 5.7 < 6.5$  (prediabetes), and 6 (4%) with Hgb A1c  $\geq 6.5$  (diabetes). Patients with diabetes were older and had significantly higher mean body-mass index ( $25.8 \pm 4.9$ ) compared to patients with normal HgbA1c ( $19.6 \pm 3.3$ ) ( $p = 0.01$ ). Among patients with A1c  $\geq 5.7\%$  (prediabetes or diabetes) compared to those with normal A1c levels, retreatment patients were significantly more likely have a A1c  $\geq 5.7\%$  [adjusted odds ratio 3.2 (95% CI 1.2-9.0) and  $p = 0.02$ ] compared to those without prior TB treatment, which was not the case for multidrug-resistant TB patients [adjusted odds ratio 0.67 (95% CI 0.27-1.7) and  $p = 0.39$ ]. No retreatment case was a known diabetic, thus the number needed to screen to diagnose one new case of diabetes among retreatment cases was 11.

**Conclusion:** Diabetes prevalence by HgbA1c testing was less common than expected, but significantly more frequent among retreatment cases, allowing for a rationale, resource-conscious screening approach.

### PD-880-31 Implementación de Estrategia Nacional para la atención integral de la comorbilidad tuberculosis-diabetes mellitus en México

M A Garcia,<sup>1</sup> Y Dávila,<sup>1</sup> Mart Castellanos.<sup>1</sup> <sup>1</sup>Programa Nacional de Tuberculosis, Secretaría de Salud, México DF, Mexico. Fax: (+55) 2614 6433. e-mail: novimarta@hotmail.com

**Antecedentes:** La tuberculosis y la Diabetes Mellitus representan dos serios problemas de salud pública, cada uno constituye un desafío para su abordaje y control. En México 20% de los casos de Tuberculosis están asociados a la Diabetes Mellitus. Del 2000 al 2011 se registró incremento de 159%. Durante el 2014 se identificaron 4,529 casos nuevos de TB-DM con tasa de  $3.8 \times 100,000$  hab. Proceso Durante el 2011 se realizó reunión con expertos clínicos en el manejo de la tuberculosis y la diabetes y se definió el protocolo de atención integral que se basa en tres pilares fundamentales: A) Coordinación interprogramática; B) Diagnóstico: detección de TB en personas con DM y de DM en personas con TB; C) Tratamiento y seguimiento; tratamiento de TB en personas con DM-tratamiento de la DM en personas con TB, seguimiento bacteriológico-glicémico. En 2013 se modifica la Norma Oficial Mexicana para la atención de la tuberculosis que incorpora este modelo de atención integral para la comorbilidad TB-DM. Resultados Aumento en la cobertura de detección de DM en personas con TB: 75%; aumento en éxito terapéutico TB-DM: 85.5%. Mejora de adherencia terapéutica para ambos padecimientos; efectiva coordinación clínico-programático. Atención integral de la comorbilidad Tb-DM. Seguimiento bacteriológico y glicémico de los casos Inclusión de Indicadores de evaluación de detección de DM en personas con TB en el Sector Salud. Modificación de la NOM para incorporar el capítulo de atención y control de TB-DM **Conclusiones:** La atención integral clínico-programática de la comorbilidad TB-DM favorece la detección oportuna de ambos padecimientos, así como la adherencia terapéutica para lograr la curación de la Tb y el control de la DM.

## 34. TB IN SPECIAL POPULATIONS

### PD-881-31 Alteraciones respiratorias en pacientes que han padecido tuberculosis pulmonar en el Hospital Nacional San Rafael y Hospital Nacional Zacamil

M R Soto Villalta.<sup>1</sup> <sup>1</sup>NTP Ministry of Health, San Salvador, El Salvador. e-mail: mariosotodr@gmail.com

**Background and challenges to implementation:** ¿cuáles son las alteraciones respiratorias residuales (clínicas, radiológicas y funcionales) en pacientes que han padecido tuberculosis pulmonar que han finalizado tratamiento? en el periodo comprendido de junio 2009 a junio de 2013

**Intervention or response:** Estudio de tipo descriptivo de tipo transversal.

#### Población en estudio

- 100% de pacientes que han padecido de tuberculosis en el pasado (58 hombres y 74 mujeres)

#### Objetivos

- Determinar las alteraciones Rx más frecuentemente descritas
- Conocer el patrón de limitación al flujo aéreo por espirometría más frecuente.
- Conocer la alteración gasométrica más frecuente.
- Describir los síntomas respiratorios residuales más frecuentes luego de haber padecido tuberculosis pulmonar.
- Conocer la frecuencia de hospitalización por causas respiratorias y el tiempo de estancia hospitalaria promedio de pacientes con antecedente de tuberculosis pulmonar.
- Describir los diagnósticos de alta con que son egresados de hospitalización.

#### Results and lessons learnt:

- La alteración radiológica más frecuentemente descrita en los expedientes de pacientes con secuelas de tuberculosis es la bronquiectasia, siendo mencionadas en 65% de lecturas de Rx.
- El tipo de limitación al flujo aéreo por espirometría más frecuentemente consignado en los expedientes de los pacientes con secuelas de tuberculosis es el patrón mixto, lo cual equivale al 38% de la población en estudio.
- La alteración gasométrica más frecuentemente (46%) observada en la población en estudio es la hipoxemia.
- El síntoma respiratorio residual más frecuente luego de haber padecido tuberculosis pulmonar es la disnea de esfuerzo, esta fue observada en 65% de pacientes.
- El diagnóstico de alta más frecuente, con el cual es egresado de hospitalización el paciente con secuelas de tuberculosis es EPOC, el cual se repite en 60 ocasiones en los expedientes clínicos.
- La frecuencia de hospitalización promedio por causas respiratorias en el paciente con secuelas de tuberculosis es de uno a dos ingresos por año en los últimos 5 años de vida.
- El tiempo de EIH promedio de pacientes con antecedente de tuberculosis pulmonar es de dos a cuatro días, con un costo aproximado de \$ 1500 por ingreso por paciente.

### PD-882-31 La adherencia al tratamiento de la tuberculosis: vulnerabilidades grupo inmigrante en São Paulo, Brasil

R Biagolini,<sup>1,2</sup> M Bertolozzi,<sup>1</sup> T Figueiredo,<sup>1</sup> K Ferreira.<sup>1</sup>

<sup>1</sup>Escola de Enfermagem, Universidade de São Paulo, São Paulo, SP, <sup>2</sup>Secretaria da Saúde, Prefeitura do Município de São Paulo, São Paulo, SP, Brazil. e-mail: romineo@ig.com.br

La tuberculosis (TB) es problema importante de salud pública en Brasil, asociada a la exclusión social. En São Paulo, el Coeficiente de Incidencia (CI) en 2013 fue de 49,1 casos/100.000 habitantes, donde grupos de bolivi-



anos en busca de mejores condiciones de trabajo y de vida, se ha concentrado en algunas regiones, con impacto en lo CI. Por tanto, es esencial para identificar las vulnerabilidades que intervienen en la enfermedad y mejorar las políticas de control de la tuberculosis con el fin de satisfacer las necesidades de salud de este grupo y tratar de aumentar la adherencia al tratamiento. **Objetivo:** Identificar las vulnerabilidades en relación a la enfermedad y el tratamiento de la tuberculosis entre los inmigrantes bolivianos, asistió en una región de salud de São Paulo. **Método:** Estudio cualitativo basado en la hermenéutica, realizado con 23 pacientes tratados en los servicios de salud en esta región, a través de entrevistas semiestructuradas. Las entrevistas fueron grabadas, transcritas y analizadas de acuerdo con la Teoría del Curso Generativo del Significado. **Resultados:** Eran frecuentes: varones (60,9%), con edades entre 20–29 años (78,3 %), la educación 8 a 11 años (60,9%), 87,0% eran sastres; 60,9% fueron descubiertos en unidades de urgencia/emergencia; 8,7% había abandonado previamente el tratamiento y la TB pulmonar fue prevalente (87,0 %); 80,0% inició tratamiento DOTS. Los discursos surgieron las categorías: 1. Conceção sobre la enfermedad y la enfermedad: la preponderancia de la falta de signos y síntomas de la TB y el retraso en el inicio del tratamiento; 2 Ruta del diagnóstico: un promedio de 3 servicios de salud; profesionales no establecen como primer diagnóstico de la tuberculosis; 3. Reação antes del diagnóstico: Los sentimientos negativos con respecto a la transmisión de la enfermedad; 4. Conceção sobre el tratamiento: no hay dificultades para acceder al servicio, el cumplimiento del tratamiento se produce cuando el paciente presenta un proyecto de vida, para lo cual se requiere el tratamiento; 5. Acolhimento/Vínculo en la Unidad de Salud: es eficaz cuando los profesionales de la salud demuestran, la atención, la preparación y la escucha; por lo general es a las enfermeras profesionales de referencia. **Conclusión:** Hay ventajas y desventajas en relación con el cumplimiento del tratamiento. Escuchar al paciente y apoyar la identificación de un proyecto de vida puede aumentar la adherencia al tratamiento.

#### **PD-883-31 Acciones volcadas al control de la tuberculosis en población en situación de calle**

L Sá,<sup>1</sup> KRS Moura,<sup>1</sup> KKS Barbosa,<sup>2</sup> RPF De Queir,<sup>2</sup> A A Romera,<sup>1</sup> T Romão,<sup>1</sup> LA Lima,<sup>3</sup> CLA Lima.<sup>3</sup> <sup>1</sup>Programa de Pós-Graduação em Enfermagem, Universidade Federal da Paraíba, João Pessoa, PB, <sup>2</sup>Departamento de Enfermagem, Universidade Federal de Campina Grande, Campina Grande, PB, <sup>3</sup>Serviço de Atenção Básica, Secretaria de Saúde do Município de João Pessoa, João Pessoa, PB, Brazil. Fax: (+55) 3216 7216. e-mail: sa.lenilde@gmail.com

**Background and challenges to implementation:** La incidencia de la tuberculosis en moradores de calle es cerca de 70 veces mayor al que en la población en general. Este estudio trata de un relato de experiencia a partir de un Proyecto de Extensión de la Universidad Federal de Paraíba (UFPB), el cual tuvo como objetivo presentar la vivencia de estudiante de enfermería en acciones de cuidado a la población en situación de calle,

realizadas junto al trabajo de los profesionales del “Consultorio en la Calle” de la Secretaría de Salud del Municipio João Pessoa, Paraíba, Brasil.

**Intervention or response:** Participaron de la experiencia estudiantes del curso de enfermería que junto con el equipo de “Consultorio de Calle”, desarrollaron acciones semanales volcadas a la identificación sintomáticos respiratorios y el encaminamiento a los servicios de salud. Las actividades fueron realizadas en el período de mayo a diciembre de 2012 bajo una perspectiva pedagógica problemática, proporcionando condiciones para el desarrollo del censo crítico y reflexivo sobre la enfermedad y el enfermo. Posterior a cada abordaje en la calle, sobre las vivencias eran elaboradas narrativas, asociando a la vulnerabilidad de la TB a los determinantes sociales de la salud.

**Results and lessons learnt:** Las narrativas muestran que las personas en situación de calle son encontradas generalmente en grupos, abrigadas en lugares insalubres, expuestas a violencia e intemperies de la naturaleza, lo que justificaba la identificación de significativo número de sintomáticos respiratorios. Los identificados como enfermos de TB, generalmente abandonan el tratamiento. Para estos la enfermedad no es vista como un problema grave. En su escala de valores, su forma de vida es más grave que la propia enfermedad y sufren prejuicio cuando buscan los servicios de salud.

**Conclusions and key recommendations:** La experiencia fue positiva en dos sentidos: por proporcionar una formación ampliada a los estudiantes en el área de salud pública, segundo; el enfoque de los determinantes sociales de la salud y por permitir identificar singularidades relacionadas a las personas con TB o vulnerables a la enfermedad en personas en situación de calle. Los resultados encontrados fundamentan la innovación de abordajes en salud a esa población.

#### **PD-884-31 Impacto de búsqueda de casos de tuberculosis en personas privadas de la libertad en México**

D Arana,<sup>1</sup> M Castellanos,<sup>1</sup> M A Garcia.<sup>1</sup> <sup>1</sup>Tuberculosis, Secretaria de Salud, Mexico, Mexico. e-mail: aranasaldae@yahoo.com.mx

**Objetivo:** Diagnosticar y curar los casos de tuberculosis pulmonar en personas privadas de la libertad.

**Método:** En coordinación con autoridades de las prisiones en las 31 entidades federativas de México, personal médico de los reclusorios y personal de Salud de los Servicios de Salud estatal, se realizó búsqueda de sintomáticos respiratorios en 180 prisiones durante el primer semestre del 2013, para realizar exámenes de laboratorio y diagnosticar casos de tuberculosis pulmonar e ingresarlos a tratamiento, seguimiento y curación.

**Resultados:** Se realizó búsqueda en una población de 171,959 personas privadas de la libertad, se estudiaron 11,298 sintomáticos respiratorios, se identificaron 182 casos con tuberculosis pulmonar, de los cuales 135 curaron (74%), 18 terminaron tratamiento (10%), 4 fracasaron (2%), 1 defunción por tuberculosis (0.5%),

11 abandono (6%), 1 traslado (0.5%), 7 continúan en tratamiento (4%) También se realizó detección de VIH a 6,152 personas privadas de la libertad, se encontraron 41 casos con binomio TB-VIH.

**Conclusiones:** El trabajo coordinado con el personal de salud y autoridades de los reclusorios permitió la búsqueda de casos de tuberculosis pulmonar en personas privadas de la libertad que constituyen un grupo vulnerable para el desarrollo de la enfermedad. El diagnóstico, ingreso a tratamiento estrictamente supervisado (DOTS), seguimiento y curación de los casos, contribuyó a romper con la cadena de transmisión en esta población en el periodo establecido.

### PD-885-31 Seguimiento de las Referencias Binacionales EU-México de pacientes migrantes con tuberculosis de 2007-2013

A Muñoz,<sup>1</sup> M Castellanos,<sup>1</sup> M A García,<sup>1</sup> L Salazar,<sup>1</sup> A Cruz Salgado.<sup>1</sup> <sup>1</sup>Tuberculosis, Secretaría de Salud, México, Mexico. e-mail: tuberculosis@live.com.mx

**Introducción:** La migración de México a EUA, presenta carencias sociales y de salud, que generan daños a la salud de millones de personas que cruzan anualmente la frontera norte del país, por el que en el 2000 la Comisión Nacional de Salud dictaminó diversas intervenciones para su atención.

**Background:** En México en el 2003, inicio la operación de un Sistema de Seguimiento que actualmente funciona en ambos países **Objetivo:** Realizar el seguimiento de los casos de tuberculosis bi-nacionales, a través del registro en la Plataforma Única de Información Módulo Tuberculosis (PUI) de los migrantes que inician tratamiento antituberculosis en EU y regresan a México a concluirlo.

**Material y métodos:** La referencia es notificada en formatos específicos vía electrónica por los programas Cure-TB y TBNet al Programa Nacional de Tuberculosis (PNTB), a los Servicios de Salud Estatal, Jurisdicciones Sanitarias (J.S) y a los centros de salud (C.S), donde recibirán la atención. En el nivel local, si el paciente es localizado el personal lo incorpora al PNTB, le da continuidad al tratamiento prescrito en EU y lo notifica a la jurisdicción correspondiente. La Jurisdicción Sanitaria lo registra en la PUI, analiza los resultados bacteriológicos mensualmente y toma decisiones oportunas en caso de inasistencia al laboratorio o al C.S Informa trimestralmente al Nivel Estatal el estatus de los pacientes Los Servicios de Salud Estatales concentran, analizan y cotejan mensualmente la información con el nivel nacional para retroalimentar a las J.S. Trimestralmente el PNTB, realiza reuniones con los socios Cure TB y TBNet para validar o descartar la información Anualmente entrega un informe final por entidad federativa a los programas Cure-TB y TBNet

**Resultados:** En el periodo de 2007-2013 se registraron 664 referencias EU-México, de las cuales 43.67% curó, 15.66% terminó tratamiento (Tx), 3.91% continúa TX, 0.60% fueron trasladados a otras unidades, el 4.51% fueron defunciones, 4.06% abandonos, el 20.18% se

clasificaron como casos perdidos, el 6.47% no son casos TB y 0.90% correspondió a referencias México-E.U.

**Conclusión:** Esta estrategia de referencias binacionales, ha permitido el seguimiento y control de más de 500 pacientes con tuberculosis, la detección oportuna de probables casos y ha evitado gastos innecesarios en para ambos países. 1 Programa Nacional de Tuberculosis. Centro Nacional de programas preventivos y Control de Enfermedades

### PD-886-31 Búsqueda activa de casos de TB, con perspectiva de género (población masculina) indígena mediante charlas comunitarias en localidades del Municipio

M A Clavel,<sup>1</sup> R E Huicochea,<sup>1</sup> V Leyva.<sup>1</sup> <sup>1</sup>Tuberculosis, Servicios de Salud del Estado de Guerrero, Chilpancingo, Guerrero, Mexico. Fax: (+52) 55 261 46 438. e-mail: arceliaavena@yahoo.com.mx

**Objetivo.** Detectar casos de Tuberculosis en población masculina mediante charlas comunitarias de TB, en localidades del Municipio de Azoyu, Guerrero.

**Justificación.** Ante la escasa participación de los hombres campesinos que por su labor y accesibilidad no demandan servicios de salud y con riesgo de ser casos no detectados, se hace necesario realizar actividades para el empoderamiento de esta población sobre TB, ya que el municipio de Azoyu, anualmente registra 10 casos de TBP, el 63.6% en el sexo masculino, y 36.4% en el femenino.

**Metodología.** Previo a la impartición de pláticas de TB, se seleccionaron 9 localidades, se presentó el Plan de Trabajo a las autoridades comunitarias, se promovió en cada localidad día y hora de las pláticas dirigidas a hombres campesinos, con la estrategia "Aprender Haciendo", se procedió a localizar Sintomáticos Respiratorios, identificados por la misma población capacitada, para toma de baciloscopias.

**Resultados:** De abril-agosto del 2013, se impartieron 16 talleres con 640 asistentes, se identificaron 68 Sintomáticos Respiratorios, se diagnosticaron 6 casos de TBP, el rango edad fue de 24 a 71 años, 67.3 % fueron hombres y el 33.3 % mujeres, el intervalo de positividad fue de 2 a 9 bacilos (83.3%) y el 16.7% (+), la curación fue del 100% de los casos sometidos a TAES.

**Conclusiones.** La estrategia de capacitación en TB para el empoderamiento, demostró oportunidad en el diagnóstico de TB, disminuyendo la transmisión de *Mycobacterium tuberculosis* en la comunidad; los hombres campesinos no demandantes de servicios de salud tienen 3 veces más de riesgo a TB, con relación a las mujeres.

### PD-887-31 La tuberculosis en pueblos indígenas de Rondônia Brasil: caracterización de acceso a servicios de salud

J Malacarne,<sup>1</sup> P Basta.<sup>1</sup> <sup>1</sup>Oswaldo Cruz Foundation, Rio de Janeiro, RJ, Brazil. e-mail: jocielimlc@gmail.com

**Background:** A pesar de la tuberculosis (TB) se mantener como uno de los más importantes problemas de salud

pública en Brasil, sobre todo entre los pueblos indígenas, se sabe poco acerca de las dificultades que enfrentan los pacientes indígenas para el acceso a los servicios de salud y obtener el tratamiento adecuado, de acuerdo con las recomendaciones por las directrices nacionales. Este estudio tiene como objetivo investigar el acceso de los sospechosos indígenas y los enfermos de tuberculosis a servicios de salud en el Estado de Rondônia (RO) Brasil.

**Design/Methods:** Se realizó un estudio descriptivo que ocurrió el período comprendido entre 2009–2011, en el que se entrevistó a los indios con síntomas respiratorios (SR) y tratamiento de la tuberculosis en cuatro casas de Salud Indígena (CASAI) en Rondonia.

**Results:** En el contexto de CASAI, 76 indígenas fueron entrevistados con SR y/o sospecha de TB. Se observó predominio de la etnia Surui (40,8%), Wari' (19,7%) y Karitiana (11,8%). Se observó que el 34,2% de los indios informó haber alcanzado por sí mismos CASAI, 31,6% informó haber sido enviado por el agente de salud de los indígenas (AIS). Desde el inicio de los primeros síntomas, el 34,2% de los entrevistados tardó más de 30 días en llegar a CASAI. La falta de transporte fue la mayor dificultad para llegar a la clínica, y el 32,9% informó que se llevó más de 5 semanas para obtener un diagnóstico. Entre los entrevistados, 52 comenzaron tratamiento para la TB y el tiempo desde la primera consulta hasta el inicio del tratamiento fue de más de 30 días en el 61,5% de los indígenas, y supervisado el tratamiento no se realizó en el 34,6% de los casos.

**Discusión:** Nuestros resultados revelaron los problemas que enfrentan las personas indígenas a obtener acceso a servicios de salud, recibir un diagnóstico correcto e iniciar el tratamiento adecuado para la tuberculosis.

**Conclusion:** los servicios de salud en Rondônia en relación con la detección de acciones, diagnóstico, tratamiento y seguimiento de los casos de tuberculosis entre los indígenas están en desacuerdo con las normas establecidas por las Directrices para el Control de la Tuberculosis en Brasil. Por lo tanto, se sugiere que las autoridades de salud para revisar las estrategias actualmente para el control de la enfermedad en esas poblaciones y tratan de dar prioridad a la detección y el tratamiento de los casos.

#### **PD-888-31 Búsqueda activa de casos de TB, en población indígena mediante promotores comunitarios, en el municipio de Chilapa de Álvarez Guerrero-México.**

R E Huicochea,<sup>1</sup> V Leyva,<sup>1</sup> ME Guerrero.<sup>1</sup> <sup>1</sup>Tuberculosis, Servicios de Salud del Estado de Guerrero, Chilpancingo, Guerrero, Mexico. Fax: (+52) 55 261 46 438. e-mail: arceliaavena@yahoo.com.mx

**Objetivo:** Detectar casos de TB en población indígena, en localidades marginadas del municipio de Chilapa del Estado de Guerrero, México.

**Justificación:** El 70% de la incidencia de TB registrada en el municipio de Chilapa, que anualmente registra 15 casos, reside en comunidades indígenas de alta marginación que habla idioma náhuatl, aunado la asociación

TB/Desnutrición en 33.3%, 27.8% a la Diabetes Mellitus y 11% al alcoholismo, por lo que se hace necesario focalizar estas áreas con promotores de la región para la detección de casos de tuberculosis.

**Metodología:** Se gestionaron incentivos para promotores comunitarios, autorizados por el Régimen de Seguridad Social en Salud (Seguro Popular), dos en un primer período de 3 meses, posteriormente 5 por semestre. Previa selección de localidades, se capacitó en tuberculosis a los promotores seleccionados, las actividades fueron coordinadas por la enfermera de la Red TAES, se realizaron pesquisas de Sintomáticos Respiratorios, casa a casa e impartición de pláticas con la pancarta "Mi Tos es seca o con Flemas", realizando toma de baciloscopias.

**Resultados:** De marzo a noviembre del 2013, se recorrieron 45 localidades, impartiendo 4,321 pláticas por los promotores, 6016 vistas domiciliarias; se examinaron 650 Sintomáticos Respiratorios, se diagnosticaron 11 casos de TBP, el rango edad fue de 34 a 74 años de edad, 54.5% fueron hombres y 45.5% mujeres, asociándose TB/Desnutrición en 36.4%, Diabetes Mellitus en 27% y alcoholismo en 9.0%; la positividad fue de 63.4% (+), 27.3% (+++) y 9.1% por Rx. El 90.9% curó y 9.1% falleció durante el Tratamiento.

**Conclusiones:** La estrategia basada en la contratación de promotores comunitarios logró ampliar la cobertura de diagnóstico oportuno en población indígena con mayor riesgo de TB asociada a la desnutrición y a la Diabetes Mellitus, en áreas altamente marginadas.

#### **PD-889-31 Tuberculosis en población migrante Haitiana en la República Dominicana: investigación cualitativa**

FV Villanueva F,<sup>1</sup> M Guzman,<sup>1</sup> R Adames,<sup>1</sup> R Cruz Ferreira,<sup>2</sup> B Marcelino,<sup>3</sup> J Medina,<sup>1</sup> M Dilerme,<sup>3</sup> J Heredia. <sup>1</sup>Unidad Ejecutora Proyecto Fondo Mundial, Ministerio de Salud Pública, Distrito Nacional, <sup>2</sup>Viceministerio Garantía de la Calidad, Ministerio Salud Pública, Distrito Nacional, <sup>3</sup>Programa Nacional de Control de la tuberculosis, Ministerio de Salud Pública, Distrito Nacional, Dominican Republic. e-mail: belkys\_tb@yahoo.es

**Background and challenges to implementation:** En el marco de los acuerdos entre el Programa Nacional de Control de la TB de República Dominicana (PNCT) y el Programa Nacional de Lucha Contra la Tuberculosis de Haití (PNLT), tomando como base los resultados de los estudios realizados, la experiencia de las actividades de ACMS en Haití y República Dominicana. Es este contexto se desarrolló esta investigación, como herramienta importante que aportará información relevante en cuanto a las percepciones, actitudes, prácticas sobre la tuberculosis en la población haitiana que transita y reside en el país. **Objetivo:** determinar los conocimientos, actitudes y prácticas sobre la tuberculosis en población migrante.

**Intervention or response:** Se diseñó y aplicó una investigación cualitativa, de tipo descriptiva y transversal. También identificamos información base sobre comportamiento de la población que nos permitieron establecer en qué etapa están los procesos educativos.



Entrevistas semi-estructuradas a informantes claves y grupos focales, con guías de discusión previamente elaboradas a la población objeto de estudio y personal de salud de referencia y/o de acceso de esta población.

**Results and lessons learnt:** La Población Migrante Haitiana consultada está en la etapa de **Pre contemplación**: “No se es consciente del problema de la TB, por lo que no es una preocupación el cambio”. El personal de salud vinculado al programa de TB y de ONG consultado, están en la etapa de Contemplación, “esta consciente del problema de la TB y entienden la necesidad del cambio en el futuro cercano”.

**Conclusions and key recommendations:** En función de la etapa en que se encuentra esta población, las estrategias de comunicación para el cambio de comportamiento deben estar basadas en ofrecer información básica que permita a los sujetos aumentar su percepción de riesgo, tener un conocimiento preciso sobre la TB, forma de transmisión y la existencia del programa y la estrategia que ofrece oportunidad de curarse a las personas que contraigan la condición de TB.

## 35. SOCIAL DETERMINANTS AND QUALITY OF TB CARE

### PD-890-31 The impact of the implementation of integrated pharmaceutical logistic system in reducing anti-TB drug stock outs in two vast regions of Ethiopia

Y Zegioris,<sup>1</sup> M Legesse,<sup>2</sup> D Jerene,<sup>2</sup> M Melese,<sup>2</sup> S Negash,<sup>2</sup> Y Kassie,<sup>2</sup> B Girma,<sup>2</sup> P Suarez.<sup>3</sup>

<sup>1</sup>Pharmaceuticals Fund and Supply Agency, Department of Forecasting and Capacity Building Directorate, Addis Ababa,

<sup>2</sup>Help Ethiopia Address the Low TB Performance (HEAL TB) project, Management Sciences for Health (MSH), Addis Ababa, <sup>3</sup>MSH, Centre for Health Services, Arlington, VA, USA. e-mail: mlegesse@msh.org

**Background:** Frequent stock outs of anti-tuberculosis (TB) drugs impedes effective implementation of national TB programs. In Ethiopia, such stock outs are usually attributed to poor pharmaceutical inventory control and weak logistics management information systems. In the Amhara and Oromia regions, the USAID supported project, HEAL TB baseline assessment showed that 22 percent of the 691 health facilities experienced anti-TB drug stock outs between October and December of 2011. Furthermore, during this quarter, just 11 percent were using drug reporting and requisition forms and only 25 percent had up-to-date drug stock cards.

**Intervention:** To improve the facilities' drug management systems, the HEAL TB project supported the Pharmaceuticals Fund and Supply Agency (PFSA), the Amhara and Oromia RHBs, and all lower health structures in implementing an integrated pharmaceutical logistics system (IPLS) between December of 2011 and April of 2013. IPLS improves drug supply chains by integrating drug requisition, distribution, and reporting into a single mechanism. As part of the implementation process, 691

health facility health professionals were trained on IPLS operations, 355 and 691 health facilities were provided with lockable drug cabinets and recording & reporting tools respectively. The pharmaceutical logistics personnel were supported through joint supportive supervision visits, regular regional review meetings, and quarterly mentorship using standard-of-care indicators.

**Results and lessons learnt:** After implementing IPLS, a follow-up assessment conducted between April and June of 2013 showed that only 0.2 percent of the 691 health facilities experienced anti-TB drug stock outs. The assessment also revealed a 49 percent improvement in updating drug stock cards and a 64 percent improvement in the use of reporting and requisition forms.

**Conclusions:** Implementation of IPLS through trainings, equipment provision, use of recording and reporting tools, supportive supervision, review meetings, and mentorship support contributed to a significant reduction in the anti-TB drug stock out rates in Amhara and Oromia Regions of Ethiopia. This intervention should be expanded and replicated in other areas with weak drug supply management systems.

Table: Status of IPLS Implementation Indicator	Baseline, %	End line, %	% increment
Stock out adult anti-TB drugs	22	0.2	21.8
Updated stock cards	25	74	49
RRF use	11	75	64

### PD-891-31 Improving TB cure rate of new TB SS + cases through strengthening local implementation capacity in Amhara and Oromia regions, Ethiopia 2011–2013

S Negash,<sup>1</sup> Y Kassie,<sup>1</sup> M Melese,<sup>1</sup> Z Habtamu,<sup>2</sup>

W Gebrekiros,<sup>3</sup> B Girma,<sup>1</sup> P Suarez,<sup>4</sup> <sup>1</sup>Help Ethiopia

Address Low TB Performance (HEAL TB) project, Management Sciences for Health (MSH), Addis Ababa,

<sup>2</sup>Oromia Regional Health Bureau, Addis Ababa, <sup>3</sup>Amhara Regional Health Bureau, Bahr Dar, Ethiopia; <sup>4</sup>MSH, Centre for Health Services, Arlington, VA, USA.

e-mail: bgirma@msh.org

**Background:** In Amhara and Oromia regions, although a commendable achievement was made in treatment success rate of sputum smear positive tuberculosis patient, the progress for cure rate was relatively low. Only 70% of sputum smear positive(SS+) tuberculosis patients had complete microscopic evaluation to determine the cure rate. Limited capacity of health workers, poor capacity in monitoring and evaluation and limited coverage of microscopic service were important contributing factors for low performance in determining cure rate.

**Intervention/ Response:** Amhara and Oromia regional health bureaus with the support of the USAID funded project MSH/Heal TB conducted a baseline assessment on the cure rate and bottlenecks to conduct microscopic confirmation at the end of the treatment between October –December 2011. Following the baseline

findings training was given to lab professionals on Acid Fast bacilli sputum microscopy, health workers on TB diagnosis, treatment and follow up. During the trainings the frontline health workers were trained on how to apply the standard patient follow up practice and implementation of DOT practice. Facility level multi-disciplinary teams were strengthening to review performance and take timely action. District and zonal technical supervisors were capacitated to provide assistance to the health workers. The health facilities were provided regular supportive supervision.

**Results:** At baseline only 65% of health facilities were providing TB microscopic service. The coverage at the end of 2013 has reached 93.6%. As indicated in the table below the baseline cure rate was 70.6% and has reached 85.6% by the end of December, 2013. The treatment success rate has also increased from 88% to 93.6%. Undesired treatment outcomes like death, and lost to follow up have also declined. Contribution of patients who were not evaluated has declined from 5.1 % to 1.8%. The same holds true for lost to follow up cases (4.05% vs 1.05%). The differences were statistically significant ( $p < 0.001$ )

Indicator	2011	2012	2013
Number of TB SS + cases notified in the previous year	11415	10848	10363
Number SS+ TB cases evaluated during the cohort period	11415	10823	10363
Cured %	70.64	81.47	85.67
TSR%	88.05	11.92	93.6
Died%	3.07	2.86	2.31
Failure %	0.24	1.17	0.78
Lost to follow up%	4.05	1.35	1.05
Not evaluated during the cohort period%	5.1	4.28	1.82

**Conclusion:** The TSR and cure rate has improved in two years' time. Enhanced implementation of standard TB control activities through training, equipping TB diagnostic units, and on-site supportive supervisions were critical to improve patient follow up and cure rate.

#### PD-892-31 Déterminants des résultats de traitement des nouveaux cas de tuberculose pulmonaire à microscopie positive au Bénin

A Makpenon,<sup>1</sup> S Anagonou,<sup>1</sup> V Schwoebel,<sup>2</sup> A Trébucq.<sup>2</sup>  
<sup>1</sup>Statistics, National Tuberculosis Programme, Cotonou, Benin ; <sup>2</sup>Technical Assistance, The Union, Paris, France.  
 e-mail: amakpenon@gmail.com

**Background:** Le programme national contre la tuberculose (PNT) du Bénin met en œuvre le traitement directement observé et dépasse 90% de succès thérapeutique. Cette étude avait pour but d'identifier les facteurs déterminant la guérison entre 2006 et 2012.

**Design/Methods:** Les données individuelles ont été saisies pour tous les patients enregistrés dans les registres de tuberculose du PNT en 2006, 2009 et 2012. Les facteurs associés au résultat du traitement (guéri, traitement terminé, échec, perdu de vue ou décès) ont été

analysés par régression logistique multinomiale parmi tous les patients adultes atteints de tuberculose pulmonaire à microscopie positive (TPM+), à l'exclusion des patients transférés dont on ne connaît pas le résultat final.

**Results:** 96% de l'ensemble des données ont été saisies et on a pu analyser les données de 8 500 adultes nouveaux cas TPM+. Le taux de guérison est passé de 75,2% en 2006 à 82,4% en 2012. Les taux de décès et d'échec sont restés stables respectivement autour de 5,6% et de 2,7% au cours de la période. Le taux de traitement terminé est 11,5% en 2006 à 8,5% et le taux de perdu de vue de 4,7% à 0,6%. Le risque de décès était lié à l'âge avancé (OR=2,36, 95% IC : 1,75-3,17), à la non conversion du frottis après 2 mois de traitement (OR=1,69, 95% IC : 1,16-2,47) et à la séropositivité VIH (OR=6,52, 95%IC : 4,65-9,16). Le taux de traitement terminé était plus élevé chez les hommes (OR=1,85, 95%IC : 1,56-2,20), chez les étrangers (OR=2,03, 95%IC : 1,59-2,60) et chez les patients résidents en milieu urbain (OR=1,43, IC95% : 1,22-1,68). Le risque d'échec était élevé chez les hommes, les séropositifs à VIH et en cas de non conversion après 2 mois de traitement (OR=5,32, 95%IC : 4,06-6,97). Les hommes, les étrangers et les patients résidents en milieu urbain avaient un risque plus grand d'être perdu de vue.

**Conclusion:** Le taux de non guérison est très faible mais peut-être augmenté pour certains patients plus à risque de décès, d'échec ou d'abandon, pour lesquels il faut concentrer des efforts particuliers.

#### PD-893-31 Social determinants of health and access to healthcare for TB patients in Republic of Macedonia

D Gudeva Nikovska,<sup>1,2</sup> F Tozija.<sup>1,3</sup> <sup>1</sup>Social Medicine, University Ss Cyril and Methodius, Faculty of Medicine, Skopje, Macedonia, <sup>2</sup>Unit for implementation of GFATM funded TB program, Ministry of Health, Skopje, Macedonia, <sup>3</sup>Social Medicine, National Institute of Public Health, Skopje, Macedonia, Yugoslav Republic. Fax: (+389)23177983. e-mail: dgnikovska@gmail.com

**Background** Health is a complex phenomenon and equity as a basic human right an integral part of constitutions in almost all countries in the world, including Republic of Macedonia (RM). Although with declining incidence of 17.2/100000 in 2013 compared to 24/100000 in 2010, tuberculosis (TB) is still clustered regionally and in certain ethnic groups, being 20 and 5 times higher in Albanian and Roma minorities, respectively.

**Objective** Survey of this type has never been conducted in RM and the gap in the health status among poor and wealthier population strata has never been systematically studied, leading to policies and programs that are targeting entire population, rather than vulnerable groups. The main objective is to analyze social determinants of health (SDH) and access to health care services for TB patients in RM, aimed at complex analysis of all factors that are causing inequities in access to health care.

**Methods** Nested case-control study was conducted on a representative sample of 567 households (HH) in the

period Jan – Sep, 2013, with selected modules of WHO World Health Survey questionnaire. “Cases” are HH of patients diagnosed with TB in the period Jul, 2012 – Jun, 2013 and controls are HH with no TB patients in their immediate vicinity.

**Results** Analysis of SDH show that TB cases are less educated, are three times more likely to be unemployed or cannot work because they feel too sick and are of lower socio-economic status. These SDH in turn influence TB patients’ access to health care, the main reasons being lack of health insurance, lack of funds or means of transport and inability to pay for health services. Percentage of TB patients who did not receive care when in need is higher (71.4%), compared to controls (28.6%),  $p=0.027$ ; controlled for place of residence, education and ethnicity, statistically significant difference on access to healthcare have income, ethnicity, employment and educational status in cases (TB patients), and only educational status in controls.

**Conclusion** Our survey has identified the main SDH of TB patients and as existence of regional differences in availability and access to health services, associated with both material (inability to pay for service, lack of transport) and non-material factors (lack of knowledge where to seek healthcare), all of which require further research to identify underlying factors and provide recommendations for bridging the gap between different socio-economic strata in society

#### PD-894-31 Quality of tuberculosis care in India: a systematic review

S Srinath,<sup>1</sup> R Subbaraman,<sup>2,3</sup> P Shete,<sup>4</sup> J Das,<sup>5</sup> A Cattamanchi,<sup>4</sup> K Mayer,<sup>6</sup> P Hopewell,<sup>4</sup> M Pai.<sup>1</sup>

<sup>1</sup>Epidemiology and Biostatistics, McGill University, Montreal, QC, Canada; <sup>2</sup>Infectious Diseases, Brigham and Women’s Hospital and Harvard Medical School, Boston, MA, USA; <sup>3</sup>Research, Partners for Urban Knowledge, Action, and Research, Mumbai, India; <sup>4</sup>Curry International Tuberculosis Center, University of California San Francisco, San Francisco, CA; <sup>5</sup>Development Economics Research Group, World Bank, Washington, DC; <sup>6</sup>The Fenway Institute and Beth Israel Deaconess Medical Center, Boston, MA, USA.  
e-mail: ssrinath@theunion.org

**Background** India accounts for 25% of estimated TB burden worldwide and 30% of the ‘missing cases’. Although India’s national TB program provides free TB care in public sector health facilities, nearly 50% of the TB cases seek care in the private sector. Understanding the quality of care across these sectors provide key insights into treatment choices and potential pathways for improvements in care for TB patients. We report findings from the first systematic review of studies assessing the quality of TB care in India.

**Methods** Using pre-specified terms, we searched multiple databases to identify articles published between 2000 and 2013 that reported on providers’ knowledge and practice related to TB care. We used the ISTC to benchmark providers’ knowledge and practice, and generated forest plots for each Standard with data from five or more studies.

**Results** The literature search yielded 754 non-duplicate citations of which 43 articles met predefined inclusion criteria. Thirty-one studies obtained information using questionnaires and 12 used chart abstraction. All studies were localized to a few geographical areas. Heterogeneity in the findings precluded meta-analysis for most of the standards. Nine of 20 studies evaluating provider knowledge about using a sputum smear for diagnosis found that less than half of providers had correct information; studies assessing provider practices found that less than one-fourth correctly ordered a sputum smear for chest symptomatics. Ten of 13 studies that assessed treatment, found that less than one-third of providers knew the standard treatment regimen for drug susceptible TB. Similar deficits were identified for 18 of the 21 ISTC standards for which findings were available. Adherence to guidelines in actual practice was generally lower than correct knowledge of those guidelines. Eleven studies evaluated both public and private sector providers. Across a variety of ISTC standards, nearly all of these studies found substantially higher levels of appropriate and/or practice in the public sector.

**Conclusions** The available evidence highlights poor quality of TB care, especially in the private sector. Inappropriate care may be contributing to delays in TB diagnosis, poor patient outcomes, and drug resistance. To improve quality of TB care, strategies should be developed to disseminate guidelines like the ISTC and measure the impact of implementation on public health.

#### PD-895-31 An analytical perspective on gender participation in access to NTP (RNTCP) services in India

L Reza,<sup>1</sup> A Das,<sup>1</sup> K Sagili,<sup>1</sup> S Chadha,<sup>1</sup> S Warsi.<sup>2</sup>

<sup>1</sup>Tuberculosis, International Union Against Tuberculosis and Lung Disease, New Delhi, <sup>2</sup>Political Sciences, Jamia Millia Islamia, New Delhi, India. e-mail: lwreza@theunion.org

**Background:** The social discrimination based on gender is prevalent in Indian societies and women is neglected all front. The Indian Patriarchal society is subjugating and suppressing the other counterpart i.e women and which leads to poor accessibility of women in health services as well. This problem is more serious in rural areas, where access to the health facility by female patient is limited because gender discrimination is embedded in India as a “part and parcel” of life. If we take a look at the historical perspective of gender discrimination in INDIA the study can be done on numbers of issues including access of health services by women. The NTP is not different but having same problem and number of women patient is less at TB clinics. The objective of the study is to understand whether proportion of women have more tuberculosis as compared to men.

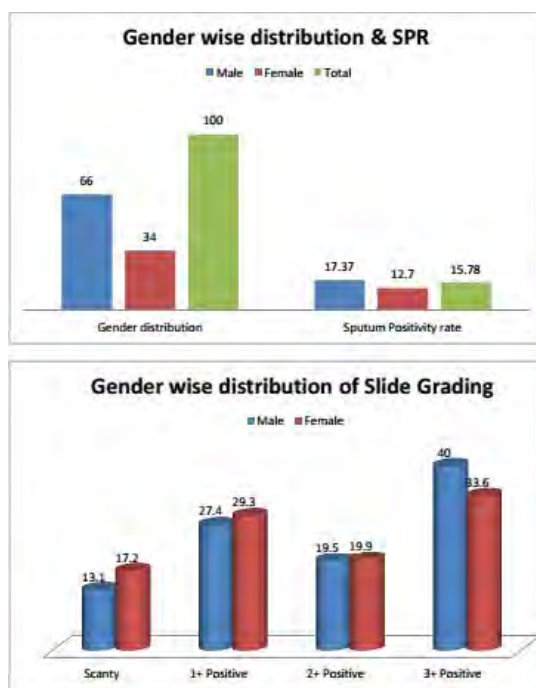
**Design/Methods:** Study population consisted of TB symptomatic who underwent sputum smear examination during July-December, 2011 and July-December, 2012 in 30 medical colleges of India as project sites. The same periods of 2011 and 2012 were chosen to minimize the effect of seasonal variation on the number of TB



symptomatics examined and smear positive TB cases diagnosed. It is also assumed that the external factors were similar in these project sites. The data is collected from laboratory register on routine basis and verified by project staffs from centres on their field visits. The smear positivity of male patient and their grading has been compared with female patient.

**Results:** The sputum positivity rate of male group is significantly related to female group ( $P < 0.01$ ). The SPR of male and female is 17% and 13% respectively (Fig 1). The SPR of Female in agegroup 0–14 and 15–24 is significantly higher as compared to their male subgroup. Of total 40% of male patient as compared to female 33% are 3+.

**Conclusion:** The study result shows that male patients are facing constraint in access to TB care services and coming late to service centre. The result also is concluded that female go for early diagnosis and disease progression is less among them. The constraint in access of services by male should be studied further.



#### PD-896-31 Lessons learned from TB patients evaluation of programme performance in Kazakhstan

I Leimane,<sup>1</sup> B Temerbekova,<sup>2</sup> G Raimova,<sup>3</sup> G Kaliakbarova,<sup>4</sup> A Tursynbaeva,<sup>4</sup> S Van Den Hof.<sup>1</sup> <sup>1</sup>Unit ACALA, KNCV TB Foundation, The Hague, Netherlands; <sup>2</sup>TB, Oskemen Oblast TB dispensary, Oskemen, <sup>3</sup>TB, Semei Regional TB dispensary, Semei, <sup>4</sup>Representative Office for Central Asia, KNCV Tuberculosis Foundation, Almaty, Kazakhstan. Fax: (+31) 70 358 4004. e-mail: ieva.leimane@kncvtbc.org

**Background:** Treatment success rate for new bacteriologically confirmed tuberculosis (TB) patients in Kazakhstan in 2011 was 61%, far below the international target of 85%. Although default rates are low (2%), treatment

interruptions regularly occur. Psycho-social support (PSS) program to improve treatment adherence was initiated in East Kazakhstan Oblast (EKO) in 2010. Method: We used the tool "QUOTE-TB Light" to evaluate patients' appreciation of the TB services including PSS. Importance score was measured by ranking nine quality dimensions of TB services and structured questions on the performance score of TB services were added. 173 TB patients ( $\geq 18$  years) who were on treatment and were receiving PSS in 2012 in Oskemen and Semei cities in EKO participated in this study. Interviews were carried out by interviewers, not involved in direct TB service delivery.

**Results:** Importance scores by ranking nine quality dimensions were measured: availability of services, information, inter-personal communication, TB/ HIV relationship, infrastructure, professional competence, stigma, affordability and PSS. TB/HIV was ranked as the most important area (median score 9). Other areas scored high were: infrastructure, information/ communication and stigma (median scores 7, 6 and 6 respectively). Related to TB/HIV, 87% of patients were informed about TB/ HIV, 90% were advised to take an HIV-test after TB diagnosis was confirmed and 80% were informed on HIV infection prevention. In relation to information, 99% of patients were informed about importance of DOT and 94% of them were informed about TB prevention. In relation to communication, 94% indicated that information was presented based on health literacy principles, 7% experienced language problems. 97% felt they were always or usually treated with dignity and respect, 61% never felt discriminated and 94% said that privacy was usually or always respected. In relation to infrastructure, for 86% of patients TB services were usually available, 21% would prefer other service hours. **Conclusions:** Regardless low HIV prevalence in Kazakhstan (2% co-infection among TB patients), TB/HIV was scored as the most important care dimension. In some cases patients still felt discriminated, waiting time was not always convenient and some experienced language barriers. While planning TB services it would be necessary to address all these factors to improve treatment adherence and reduce interruptions.

#### PD-897-31 Tuberculosis y su asociacion con los determinantes sociales de salud

T Figueiredo,<sup>1</sup> M.L. Pinto,<sup>1</sup> TC Silva,<sup>1</sup> E Silva,<sup>2</sup> M Bertolozzi,<sup>3</sup> LCF Gomes,<sup>4</sup> ML Pinto,<sup>5</sup> TB Freire.<sup>5</sup>

<sup>1</sup>Programa de Pós Graduação em Saúde Pública, Universidade Estadual da Paraíba, Campina Grande, PB, <sup>2</sup>Departamento de Estatística, Universidade Estadual da Paraíba, Campina Grande, PB, <sup>3</sup>Departamento de Saúde Coletiva da Escola de Enfermagem da USP, Universidade de São Paulo, São Paulo, SP, <sup>4</sup>Programa de Pós Graduação em Geografia Física, Universidade Federal do Ceará, Fortaleza, CE, <sup>5</sup>Departamento de Enfermagem, Universidade Estadual da Paraíba, Campina Grande, PB, Brazil. e-mail: taniaribeiro\_2@hotmail.com

**Fondo:** A pesar de los esfuerzos empleados en un intento por controlar la tuberculosis (TB), la enfermedad

continúa merecer una atención especial, puesto que todavía configura como problema de salud pública mundial. En 2012, Brasil registró incidencia por cada 100.000 habitantes de 36,7. El objetivo es construir un indicador de la determinación social de la tuberculosis y asociarlo con la ocurrencia de nuevos casos de la enfermedad en el municipio de Crato/CE/Brasil. La pregunta que realizó la encuesta era: la ocurrencia de casos de tuberculosis se relaciona con los determinantes sociales de la salud en el municipio de Crato, estado de Ceará?

**Método:** Estudio ecológico, temporal con enfoque cuantitativo. Se construyó un indicador para la determinación de la tuberculosis, a través del análisis factorial, utilizando datos del censo 2010. Las variables seleccionadas fueron: hombres residentes en el sector de censo de 20–59 años; Residentes de los hogares en el sector de censo sin escolaridad; Renta per cápita de menor o igual al 01 salario mínimo y los residentes promedio por hogar. Para identificar a tres distintos estratos con índice de características similares fue sometido a la técnica de la agrupación “hierarchical cluster analysis”. Un mapa temático fue creado y esto indica la determinación social alta, intermedia y baja por la enfermedad, que fue comparada con el mapa de la concentración de casos nuevos de tuberculosis mediante la estimación del núcleo.

**Resultados:** Fue identificado que las regiones con el mayor número de casos coincidían con las zonas de concentración de la pobreza y la determinación social intermedio. Las áreas identificadas como ser de determinación social alta para la ocurrencia de la enfermedad presentan densidad de población significativa, algunos de estos son hogar de “bolsones de pobreza”, con la presencia de grandes favelas y asentamientos, así como la explotación local fuerte del narcotráfico, sin embargo, en estas localidades la densidad de los casos es baja, lo que sugiere posible registro.

**Conclusiones:** La distribución de la TB en el espacio geográfico no es el mismo en todos los grupos de la población y factores socioeconómicos, presentados relación con la ocurrencia de la enfermedad. Es necesario el sistema de salud reconocer y tratar específicamente con las características de cada región y dar prioridad a aquellos que presentan una mayor determinación social y, por tanto, casos de la enfermedad.

#### PD-898-31 Standard of care indicators as a capacity building and TB programme improvement tool: an innovative approach

B Girma,<sup>1</sup> S Hamusse Daba,<sup>2</sup> S Negash,<sup>1</sup> Y Kassie,<sup>1</sup> Z Zewdie,<sup>3</sup> D Jerene,<sup>1</sup> M Melese,<sup>1</sup> P Suarez.<sup>4</sup> <sup>1</sup>Help Ethiopia Address the Low TB Performance (HEAL TB) project, Management Sciences for Health (MSH), Addis Ababa, <sup>2</sup>Oromia Regional Health Bureau, Addis Ababa, <sup>3</sup>Amhara Regional Health Bureau, Bahr Dar, Ethiopia; <sup>4</sup>MSH, Centre for Health Services, Arlington, VA, USA. e-mail: bgirma@msh.org

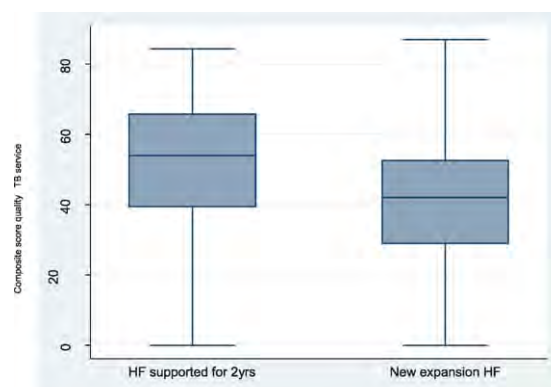
**Background:** There is limited experience of using quality indicators to assist decision making on training, continuing medical educations, technical and logistic support needs of TB program at facility level. To address this

gap, Amhara and Oromia Regional Health Bureaus (RHBs) developed and implemented standard of care (SoC) TB indicators, with assistance from the USAID-funded project, Help Ethiopia Address the Low TB Performance (HEAL TB). These indicators were based on international standards of TB care.

**Intervention:** A team of clinical and laboratory officers from the RHBs and HEAL TB developed SoC TB indicators on case detection, patient treatment outcomes, TB/HIV collaboration, drug supply and availability, laboratory services, and data quality. The team assigned each indicator a minimum performance score and decided that facilities that did not meet these performance scores would be placed on a performance improvement plan and closely monitored to ensure progress. For analysis each indicator was given 2 scores for excellent performance and 0 points for poor performance. After establishing this system, the RHBs and HEAL TB implemented it at 688 health facilities in the Amhara and Oromia regions. The team assessed the impact of this intervention by evaluating service quality at the 688 facilities after they had used the SoC indicators for two years and compared it to baseline data on service quality at 515 facilities that had not supported by the project. For analysis a Mann Whitney test was used to determine the statistical significance.

**Results:** After two years of implementation health facilities with the intervention had a median composite score of 53.9(interquartile range of (39.4, 65.7)) from a baseline score of 28. The 515 health facilities that had never used the SoC indicators had a median score of 42(with IQR of (28, 52)). There was statistically significant difference between their median composite scores ( $\chi^2=106$ ,  $p=0.0001$ ).

**Conclusion:** Health facilities using SoC indicators and a performance improvement system showed a higher level of TB service quality than health facilities not using the performance improvement system. Supportive supervision, trainings, and mentoring guided by SoC indicators are useful tools for measuring TB service delivery quality and performance. These indicators and the performance improvement system can be tailored for other aspects of service delivery and be expanded to improve TB service delivery in Ethiopia.



Impact of a performance improvement system on TB service delivery quality at health facilities after two years of implementation

### PD-899-31 The impact of social determinants of health on MDR-TB patients in Swaziland

N Mdluli,<sup>1</sup> W Mthetwa,<sup>1</sup> S Haumba.<sup>1</sup> <sup>1</sup>ASSIST, URC, MBABANE, Swaziland. e-mail: NokuthulaM@urc-sa.com

**Introduction:** Multi Drug resistant TB is a significant problem in Swaziland in 7.9% of new patients and 33.3% of previously treatment patients. Additionally, HIV co-infection exists in 83% of these patients.

**Situation** Most of the patients have challenges with transport; some cannot afford bus fare due to poverty for their daily injections (DOT), medical review and refill of medication. DR TB patients have to suffer at work as the treatments have side effects like loss of hearing which compromises their working capabilities. This results to patient being replaced or getting unpaid sick leave. The majority of the patients lose their jobs thus; most patients may end up defaulting or stopping treatment just to save their daily income. The living conditions of these are very poor as evidenced by home assessments done in 2012, where 274 (48%) homesteads were visited and only 129 had favorable home assessment. Lack of social and food support also impacts negatively on patient care in the communities.

**Intervention** Transport system for the two MDR-TB management sites (Piggs Peak and The National TB hospital) was availed from 2012. This transport system is being used for home visits, home assessment, mapping of patients, tracking of defaulters and also screening of contacts from the family members. The community MDR-TB team which includes nurses and adherence officers visit communities four times a week. The national TB program has ensured that the patients also receive food parcels every month and patient support from the trained community treatment supporters who also part of the community team. Audiology services have also been availed for patients in both sites where patients are seen pre-treatment and followed up during treatment for early identification of pending hearing loss for prompt treatment adjustment.

**Conclusion:** In order for us to stop the spread of DR TB in the country we need to reach out to the communities to improve living conditions and understanding of the disease pattern.

**Recommendations** Growing awareness of the importance of social determinants of health in other areas, particularly in MDR-TB has seen other countries like Lesotho having half way homes for patients who live in unreachable areas and have no social support, thus this may also benefit our patients and the control of MDR-TB if the same was done in Swaziland.

### PD-900-31 Desigualdades étnicas raciales en lo acompañamiento de casos de la tuberculosis en Brasil

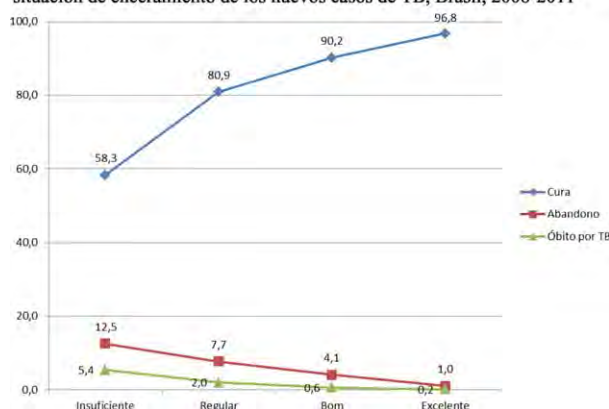
P Viana,<sup>1</sup> M Gonçalves,<sup>2,3</sup> P Basta.<sup>1</sup> <sup>1</sup>Endemias Samuel Pessoa, Escola Nacional de Saúde Pública Sérgio Arouca-ENSP/FIOCRUZ, Rio de Janeiro, RJ, <sup>2</sup>Sociodiversidade em Saúde, Instituto Leônidas e Maria Deane - Fiocruz Amazônia, Manaus, AM, <sup>3</sup>Enfermagem em Saúde Pública, Escola de Enfermagem de Manaus- UFAM, Manaus, AM, Brazil. e-mail: paulovictorsviana@gmail.com

**Background:** Analizar los aspectos operacionales de la vigilancia de nuevos casos de tuberculosis en Brasil, por regiones y categorías de raza/color, en el período 2008–2011.

**Design/Methods:** Estudio epidemiológico descriptivo, retrospectivo de casos nuevos de tuberculosis notificados en Sinan entre 01/01/2008 y 31/12/2011. Las variables estudiadas fueron la raza/color, región, situación de encerramiento, baciloscopias de controles del segundo, cuarto y sexto mes de tratamiento y tratamiento supervisado (TS).

**Results:** Durante el período de estudio se notificaron 278674 casos nuevos en Brasil, lo que corresponde a un promedio de incidencia de 36,7/100.000. En más del 40 % de los casos no se realizaron baciloscopias del 2°, 4° y 6° mes. El porcentaje de tratamiento supervisado fue del 40,2%, mientras que el porcentaje fue mayor entre los indígenas (68,6%) y la más baja entre los blancos (37,2%). Cuando estratificamos el porcentaje de TS entre regiones y raza/color el porcentaje más alto se observó entre los indígenas de la región del Centro-Oeste (91,1%) y más baja entre los negros del sur (68%). Para el indicador para el seguimiento de los casos en contra de la situación de encerramiento y estratificada por raza/color se observó que la tasa de cura más bajo cuando la vigilancia se calificó como insuficiente indígena (49,5%) y el mayor porcentaje de cura en los casos clasificados como excelente también entre los indígenas (97,7%). En el abandono de tratamiento, los individuos negros clasificados como insuficientes tuvieron la tasa de abandono más alta (15,2%).

**Gráfico 1:** Análisis comparativo de indicadores de acompañamiento y la situación de encerramiento de los nuevos casos de TB, Brasil, 2008-2011



**Conclusion:** Estos resultados ayudan a entender las disparidades en las tasas de TB activa, según la



clasificación racial que prevalece en Brasil. Por lo tanto, creemos que para el desarrollo de estrategias efectivas, las autoridades brasileñas deben desarrollar estrategias específicas para el control de la tuberculosis, teniendo en cuenta las diferencias de cada grupo específico, centrado en los pacientes de raza/color negro y indígena abordando los determinantes sociales de la salud de estos grupos.

#### **PD-901-31 Análisis de varianza aplicada en nuevos casos de tuberculosis en los principales municipios reportados en los estados de la región Nordeste de Brasil**

E Silva,<sup>1</sup> T Figueiredo,<sup>2</sup> Ramó Sánchez,<sup>3</sup> A Carmona,<sup>3</sup> M Bertolozzi,<sup>4</sup> DC Aguiar.<sup>1</sup> <sup>1</sup>Departamento de Estatística, Universidade Estadual da Paraíba, Campina Grande, PB, <sup>2</sup>Mestrado em Saúde Pública, Universidade Estadual da Paraíba, Campina Grande, PB, Brazil; <sup>3</sup>Departamento de Estadística e I.O. Universidad de Granada, Universidad de Granada, Granada, Spain; <sup>4</sup>Escola de enfermagem, Universidade de São Paulo, São Paulo, SP, Brazil. Fax: (+55) 8333 153459. e-mail: edwirde@uepb.edu.br

**Background:** identificar y analizar la vulnerabilidad de nuevos casos reportados de tuberculosis en los nueve estados de la región Nordeste de Brasil, representados por los siete principales municipios con mayor tasa de tuberculosis, en el período de 2011 a 2013.

**Design/Methods:** El análisis de varianza es uno de los métodos más usados para contrastar la homogeneidad de las variable. Intentaremos determinar si a pesar de las diferencias en el muestreo de las poblaciones, existe diferencias en el número de casos de tuberculosis entre los municipios de diferentes estados cumpliendo los supuestos de verificar si las variaciones son debidas al azar como consecuencia de la aleatoriedad del número casos en cada estado y sus respectivos municipios. La variable dependiente son los casos de tuberculosis y los factores son los estados y posteriormente los municipios.

**Results:** Las dispersiones muestran un ritmo creciente en el tiempo y también diferencias importantes de nuevos casos de tuberculosis entre los municipios en estudio. Para los estados hubo una diferencia un poco menor. Los estados Sergipe, Piauí e Alagoas tienen un número pequeño de casos tuberculosis, mientras que la mayor concentración de los casos de enfermos con tuberculosis se sitúan en los Estados de Bahía, Pernambuco y Ceará. Considerando que estos estados son grandes centros industriales del nordeste brasileño, que se destacan por lo desarrollo económico y culturales, al mismo tiempo que es perceptible grandes bolsas de pobreza y la exclusión social, lo que favorece a proliferación de la enfermedad. En los municipios se destacaron Salvador, Recife e Fortaleza.

**Conclusion:** por encima de la relevancia de los resultados obtenidos en la presente investigación es de gran importancia, entender las diferentes circunstancias en los casos de tuberculosis entre los estados y/o municipios para el control y aplicación de una política de salud inclinada para el control de la tuberculosis y las reales necesidades de cada localidad.

#### **PD-902-31 Social determinants of tuberculosis: the need for international standardised definitions**

J Hall,<sup>1</sup> P Windish,<sup>1</sup> Y Appleby,<sup>1</sup> A Story.<sup>1</sup> <sup>1</sup>Find&Treat, University College London Hospitals, London, UK. Fax: (+44) 203 447 9938. e-mail: joehall@nhs.net

**Background:** The epidemiology of tuberculosis (TB) in low incidence countries is characterised by a concentration of disease among socially excluded populations in major urban centres. This has prompted efforts to capture patient characteristics relevant to TB social determinants in national surveillance and scientific studies. While informing understanding of TB epidemiology and the targeting of specific interventions, of standardised definitions for key social determinants has limited opportunities to compare data both within and between countries and inform the development of supra-national TB control policies and more effective control interventions.

**Methods:** We reviewed published national TB guidance reporting surveillance definitions for social risk factors for TB routinely collected in low incidence settings and scientific papers reporting case definitions for TB social risk factors.

**Results** were classified according to the sub-population groups covered and whether the risk factor was relevant to either having ever occurred, having occurred within a specified timeframe or at time of diagnosis or treatment episode.

**Results:** The key population groups identified as relevant to social determinants were Homeless Populations-street populations/rough sleepers, people using night shelters and hostels providing temporary residence, people alternating between multiple residences (sofa-surfing/squatting); Incarcerated Populations and people with a history of incarceration; Substance Misusers-People Who Inject Drug (PWID), Alcohol dependent persons, other illicit drug users; Itinerant Communities - gypsies, travellers and Roma populations; Indigenous/Aboriginal Populations-First Nation Communities. Definitions for these key groups varied considerably as did the time frame relevant to the occurrence of risk factors. Many socially excluded TB patients have multiple social risk factors but considerable variation exists in the way these overlapping social determinants are reported.

**Conclusion:** Eradication strategies for TB require implementation of cost-effective and innovative targeted interventions to improve early case detection and treatment outcomes among socially excluded populations. Many low incidence countries systematically collect data on TB social determinants but lack of standardised definitions hamper efforts for meaningful comparison between countries and monitor trends

### 36. COMORBIDITY AND DEADLY TB

#### PD-903-31 Underreporting of tuberculosis cases that resulted in death: probabilistic record linkage between databases

JA Nogueira,<sup>1</sup> ROG Romero,<sup>2</sup> L Sá,<sup>3</sup> TC Scatena Villa,<sup>4</sup> CMC Ribeiro.<sup>5</sup> <sup>1</sup>Clinical Nursing, Federal University of Paraíba, João Pessoa, PB, <sup>2</sup>Epidemiology, Health Secretary of Joao Pessoa, João Pessoa, PB, <sup>3</sup>Public Health, Federal University of Paraíba, João Pessoa, PB, <sup>4</sup>School of Nursing at Ribeirao Preto, University of Sao Paulo, Ribeirão Preto, SP, <sup>5</sup>Epidemiology, Health Secretary of Joao Pessoa, João Pessoa, PB, Brazil. e-mail: jalnogueira31@gmail.com

**Background:** Routine recording and reporting of the numbers of tuberculosis cases diagnosed and treated by Tuberculosis Control Program and monitoring of treatment outcomes is a core element of Stop TB Strategy. The occurrence of tuberculosis deaths underreported in the information system may suggest barriers in access to health services and flaws in the system. In this way, this abstract aims to verify if patients that died of tuberculosis were underreported in the Information System for Notifiable Diseases

**Design/Methods:** Cases with tuberculosis cause of death were selected from the Brazilian Mortality Information System (SIM), enrolled in a northeastern Brazilian city. Probabilistic record linkage was carried out between the SIM database and the Information System for Notifiable Diseases (SINAN), for the years 2007 to 2011. The odds ratio of individuals who died with TB not reported in the Information System of Disease Notifications was calculated according to sociodemographic characteristics.

**Results:** Out of the 147 deaths from tuberculosis in the period, 107 (72.8%) were not registered in the SINAN. Women were 2.60 times less likely to be reported than men, and younger patients were 1.86 times less likely to be reported when compared to the elderly. Show fewer than eight years of study represented 4.42 times the odds of not being reported for eight or more years of study (p-value <0.05). Not having formal education was a protective factor for notification (OR = 0.40). The deaths were lower in individuals of white ethnicity (27.8%), although showing greater chance of not being notified (OR = 2.36).

**Conclusions:** The outcomes demonstrate that tuberculosis cases that resulted in death were underreported in the SINAN. Data suggest problems in the detection of cases, failure in clinical management and obstacles in adequate and timely treatment, as well as to quality flaws in the information system

#### PD-904-31 A tuberculosis mortality register study in municipalities of the department of Chocó, Colombia, 2012

J M Hernández,<sup>1,2</sup> H Andrade,<sup>3</sup> L Murillo,<sup>4</sup> L Velasquez,<sup>3</sup> M Mejia,<sup>1</sup> A Gomez,<sup>1</sup> J Robledo.<sup>1,2</sup> <sup>1</sup>Antioquia, Corporación para Investigaciones Biológicas, Medellín, <sup>2</sup>Antioquia, Universidad Pontificia Bolivariana, Medellín, Colombia, Medellín, <sup>3</sup>Chocó, IPS Erchichijay, Quibdó, <sup>4</sup>Chocó, Dirección Seccional de Salud del Chocó, Quibdó, Colombia. Fax: (+574)4415514. e-mail: jrobledo@cib.org.co

**Background:** The number of deaths related to tuberculosis is one of the indicators that allow analysis of the impact of activities of the tuberculosis control programs. In addition it is the base to adjust activities, assignation of resources and improvement of the tuberculosis control program. Consequently, the accuracy of this register is crucial to understand how well is functioning a tuberculosis control program.

**Objective:** to identify death related to tuberculosis in the Department of Chocó, Colombia, during year 2012 and to compare the data according to the different register sources.

**Design/Methods:** A descriptive, retrospective study with a quantitative analytical approach was performed. The study population consisted of all cases of mortality associated to tuberculosis in 30 municipalities of the department of Chocó (Colombia pacific coast) during the year 2012. Data collection was carried out through oral interviews with relatives (indigenous communities), consulting clinical charts and data from community health workers and local tuberculosis program in each municipality.

**Results:** A total of 31 deaths related to tuberculosis were identified during the year 2012. Gender distribution was similar being slightly higher for women (52%), the indigenous population showed the higher mortality records (67%). We verified the consistency between mortality records data at the national and local levels. By 2012, We found that DANE (National Administrative Department of Statistics) reported six deaths caused by tuberculosis in the department, while at the local level, the tuberculosis program and SIVIGILA had 21 registries of deaths due this cause.

**Conclusion:** In the Chocó Department there was an underreporting of cases of tuberculosis mortality for the year 2012. Taking into account the data of the departmental program, underreporting was 31% and 80% when compared to data from national level (DANE). An effort should be made to adjust the mortality register of tuberculosis deaths according to the different sources of the data.

### PD-905-31 Antibiotic prescriptions in tuberculous pneumonia associated with hemodynamic instability and toxicity to first-line drugs

R Martinez,<sup>1</sup> C Jimenez,<sup>1</sup> C Bueno,<sup>1</sup> A Valencia.<sup>1</sup>

<sup>1</sup>Enfermedades Infecciosas, Clinica Comfamiliar Risaralda, Pereira, Colombia. e-mail: ricardoamartinezg@hotmail.com

**Background:** TB pneumonia may be associated with hemodynamic instability in 10% of cases being needed urgently initiate TB therapy once the diagnosis is made, however the situation can be complicated by the presence of drug-induced liver toxicity, unable to establish which of the drugs of first line is the cause of the situation. The aim of this study is to describe in these patients, the clinical behavior and smear findings after the first month of treatment with pharmacological unconventional schemes.

**Design/Methods:** Information of 36 patients admitted to intensive care in western Colombia between January 2003 and December 2013 due TB pneumonia and drug toxicity to first-line drugs is collected.

**Results:** Following the initiation of conventional therapy 90% of patients presented elevation of more than 5 times the normal value in the level of liver enzymes, the remaining 10% the value was between 3 and 5 times, hyperbilirubinemia document in all cases; the time to onset of toxicity was 8 days on average and in all cases the tests normalized after the withdrawal of the scheme ; the combination of moxifloxacin, aminoglycoside and ethambutol was used in 32 cases, in the remaining 2 ethambutol was excluded ; the average prescription time while hemodynamic stability was achieved and the cause of drug toxicity was established replacement was 28 days ; toxicity was secondary to pyrazinamide in 55%, whereas isoniazid and rifampicin in 30 and 15% respectively ; the time of mechanical ventilation had a mean of 9 days; 2 patients died ;the smear was positive in 4 patients after the term of unconventional scheme;in all patients conventional scheme is restart once were in hemodynamic stability and removing the causative drug toxicity.

**Conclusion:** The severity of hemodynamic and respiratory compromise in patients following TB pneumonia requires drug alternatives in situations in which drug toxicity appears to conventional antituberculosis drugs , this is based on the impact may cause the delay of antibiotic therapy in patients with critical condition. The combination of moxifloxacin, aminoglycoside, ethambutol is presented as a therapeutic alternative in patients whose condition can not tolerate delays in initiation of treatment.

### PD-906-31 The causes of death among patients with tuberculosis in institute for lung diseases and tuberculosis, Skopje, Macedonia

L J Simonovska,<sup>1</sup> M Trajcevska,<sup>1</sup> V Mitreski,<sup>1</sup>

I Simonovska.<sup>1</sup> <sup>1</sup>Lung diseases, Institute for lung diseases and tuberculosis, Skopje, Macedonia, Yugoslav Republic. e-mail: damjanovska25@hotmail.com

**Introduction** Tuberculosis is one of the main causes of morbidity and mortality in different societies. In 2010,

there were an estimated 12 million people living with active TB, including 8.8 million new cases and there were an estimated 1.4 million deaths. Identifying causes for death following diagnosis of TB is important for planning effective interventions to reduce death rates. The aim of this study was to assess and determinate main causes of death in TB patients in our Institute.

**Materials and methods** It is a retrospective descriptive study conducted in Institute for lung diseases and tuberculosis, Skopje, Macedonia, from 2010 to 2013. Medical records of died tuberculosis patients over 4 – year period were reviewed and death data were analyzed. **Results** Twenty two deaths ( 15% from all hospitalized patients ) with mean age of 58+/- 10.3 years were detected, 69.6% were male and 30.4% were female. The frequency rate for cigarette smoking, alcoholism, diabetes, intravenous drug usage, as risk factors were 54.5%, 22.7%, 4.5% and 4.5% respectively. 12 deaths ( 54.5%) were directly attributed to tuberculosis, among them overwhelming TB disease with respiratory failure, massive hemoptysis and MDR-TB accounted as the cause of death in 75%, 8.3% and 16.6% respectively. 10 deaths (45.5%) were due to other medical problems, which included, COPD, cardiovascular diseases, high blood pressure, cirrhosis, dementia i.e. 18.2%, 31.8%, 18.2%, 4.5% and 4.5% respectively. The median time of survival was 28 days. 77.2% of patients died during the initial-2- month intensive phase of anti - TB treatment. 36.4% died in the first 10 days of treatment. Those who died of tuberculosis had statistically significant (p< 0.001) a shorter median survival ( 14,9 ) days in comparison with group who had other medical problems ( 27days ).

**Conclusion** This study showed that overwhelming TB disease, with respiratory failure, haemoptysis, cardiovascular diseases, COPD, cirrhosis are main causes of death. Smoking, alcoholisms, diabetes, intravenous drug usage are frequent risk factors for TB mortality.

### PD-907-31 Increased mortality risk in HIV-infected patients is limited to those with low CD4 counts in the stride study

S Swindells,<sup>1</sup> M Kendall,<sup>2</sup> L Chinula,<sup>3</sup> R Escada,<sup>4</sup>

R Mngqibisa,<sup>5</sup> D Havlir.<sup>6</sup> <sup>1</sup>Internal Medicine, University of Nebraska Medical Center, Omaha, NE, <sup>2</sup>SDAC, Harvard School of Public Health, Boston, MA, USA; <sup>3</sup>UNC Project, University of North Carolina Lilongwe CRS, Lilongwe, Malawi; <sup>4</sup>CRS, Instituto de Pesquisa Clinica Evandro Chagas CRS, Rio de Janeiro, RJ, Brazil; <sup>5</sup>Enhancing Care Foundation, Durban International CRS, Durban, South Africa; <sup>6</sup>Positive Health Program, University of California San Francisco, San Francisco, CA, USA. e-mail: sswindells@unmc.edu

**Background:** Tuberculosis (TB) control is complicated by the interaction of the TB and human immunodeficiency virus (HIV) epidemics, yet participation of HIV-infected patients in TB treatment trials is often limited. Reasons for this include drug-drug interactions amongst antiretroviral and antituberculous agents, overlapping drug toxicities, and concerns about increased morbidity and mortality from the HIV disease, all of which may



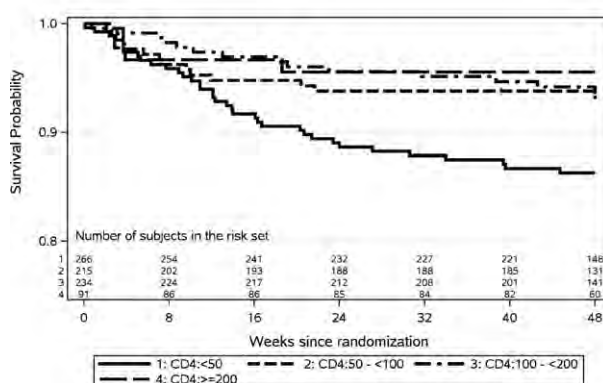
confound the analyses of study results. We report here an analysis of mortality in an HIV/TB treatment strategy trial.

**Methods:** The STRIDE study was a multi-country randomized trial comparing earlier antiretroviral therapy (ART), within 2 weeks after TB treatment initiation, versus later ART at 8–12 weeks after TB treatment initiation in 806 HIV-infected patients starting rifampicin-based TB treatment. In a post-hoc analysis, time to death from randomization was calculated by baseline CD4 count strata of  $<50$ ,  $50-<100$ ,  $100-<200$  and  $\geq 200$  cells/mm<sup>3</sup> using Kaplan-Meier survival plots. Proportions survived were calculated using Kaplan-Meier estimators at week 48 with 95% Greenwood confidence intervals (CIs).

**Results:** In the 806 participants, 68/806 (8%) died. With respect to overall survival, 230/266 participants with baseline CD4  $<50$  cells/mm<sup>3</sup> survived, compared to 508/540 with baseline CD4  $\geq 50$  cells/mm<sup>3</sup>. Among those with baseline CD4  $<50$ , 86.3% (95% CI = 82.1, 90.4) survived in contrast to 93.8% (90.5, 97.1), 94.2% (91.1, 97.2), and 95.5% (91.3, 99.8) surviving in the three upper CD4 strata, respectively; see Figure. In the earlier ART arm, 222/246 participants with CD4  $<100$  survived versus 7/159 with CD4  $\geq 100$ : 90.0% (86.2, 93.8) survival versus 96.1% (93.0, 99.2). With later ART, 105/126 participants with CD4  $<50$  survived versus 259/275 with CD4  $\geq 50$ : 83.1% (76.5, 89.7) versus 94.4% (91.6, 97.1).

**Conclusions:** Inclusion of HIV-infected patients into TB treatment trials is critical, particularly with novel agents and regimens. While the absolute mortality rate in our study was higher than commonly observed in TB treatment trials in HIV-uninfected participants, we report here that most of the deaths occurred in participants with very low CD4 counts at initiation of TB treatment. Earlier initiation of ART ameliorated this difference. These data may reassure researchers and developers in the field, and facilitate access for a large majority of HIV-infected participants in future clinical trials of novel strategies and TB drugs.

Figure: Kaplan-Meier Survival Plot by Baseline CD4 Count Strata



## PD-908-31 Etude des facteurs associés au décès chez les patients tuberculeux mis sous traitement au Centre national de lutte antituberculeuse, Burkina Faso

E Zoungrana,<sup>1</sup> M Drabo,<sup>2</sup> J-F Tessier,<sup>3</sup> Y Moyenga,<sup>1</sup>

A Zigani,<sup>4</sup> B Kaboré.<sup>4</sup> <sup>1</sup>Programme National de Lutte

Contre la Tuberculose, Ministère de la Santé, Ouagadougou,

<sup>2</sup>Département Biomédical et Santé Publique, Institut de Recherche en Sciences de la Santé, Ouagadougou, Burkina Faso;

<sup>3</sup>Institut de Santé Publique, d'Epidémiologie et de Développement, Université de Bordeaux, Bordeaux, France ;

<sup>4</sup>Centre National de Lutte Antituberculeuse, Ministère de la Santé, Ouagadougou, Burkina Faso.

e-mail: ezoungrana@gmail.com

**Contexte:** Au Burkina Faso, la tuberculose représente un problème de santé publique. La létalité de la tuberculose a oscillé entre 8,6% et 14,4% ces dix dernières années pour une norme de moins de 5% préconisée par l'Organisation mondiale de la santé (OMS). Notre étude avait pour objectif de déterminer la mortalité des patients tuberculeux en cours de traitement au Centre national de lutte antituberculeuse (CNLAT) sur la période du 1er janvier 2011 au 30 juin 2012 ainsi que les facteurs qui lui sont associés.

**Méthodes:** Il s'agissait d'une étude de cohorte rétrospective de tous les cas de tuberculose toutes formes enregistrés au CNLAT sur la période du 1er janvier 2011 au 30 juin 2012, âgés d'au moins 15 ans et dont le dossier était disponible.

**Résultats:** De janvier 2011 à juin 2012, sur les 330 patients qui ont été enregistrés et mis sous traitement, 60 sont décédés en cours de traitement (18,2%). Ces derniers étaient constitués de 51,7% (31) de femmes et de 48,3% (29) d'hommes avec un sex-ratio de 0,93. La tranche d'âge la plus représentée était celle de 35 à 44 ans (31,7%). La majorité des patients décédés étaient atteints de tuberculose extrapulmonaire (43,3%). Trente quatre patients (56,7 %) décédés pesaient moins de 50 kg. Plus des 2/3 des décès (73,4 %) sont survenus au cours des 2 premiers mois de traitement. Plus de la moitié (56,7%) des patients sont décédés moins de 30 jours après avoir débuté le traitement antituberculeux dont 23,3% (14 cas) au cours de la 1ère semaine. Dans près de la moitié des cas (48,3%), les résultats de lecture des frottis sont revenus négatifs. Près de la moitié des patients décédés avaient une sérologie VIH positive (45%). L'analyse multivariée a permis d'identifier les facteurs associés à la survenue des cas de décès. Il s'agissait de l'âge avancé  $\geq 60$  ans (OR : 3,71 ; IC à 95% : 1,28–10,69), de la tuberculose pulmonaire à microscopie négative (OR : 3,81 ; IC à 95% : 1,12–12,92), du faible poids à l'initiation du traitement antituberculeux (OR : 4,49 ; IC à 95% : 1,86–10,83) et du VIH (OR : 3,48 ; IC à 95% : 1,42–8,51).

**Conclusion:** Au Burkina Faso, réduire les taux élevés de létalité au cours du traitement antituberculeux reste un défi majeur. Le dépistage précoce des cas de tuberculose, le renforcement de la prise en charge des malades co-infectés TB/VIH et un soutien nutritionnel aux patients

pourraient permettre d'obtenir de meilleurs résultats cliniques et de traitement.

### PD-909-31 Who are the patients that died with tuberculosis in 2012 in the northern region of Portugal

A Franco Spinola,<sup>1</sup> Ana Correia,<sup>2</sup> M Gomes,<sup>3</sup> R Duarte.<sup>3,4</sup>

<sup>1</sup>Faculty of Medicine of Porto University, Faculty of Medicine of Porto University, Porto, <sup>2</sup>Public Health Dept, Portuguese Northern Health Administration, Porto, <sup>3</sup>Dept of Clinical Epidemiology, Predictive Medicine and Public Health, Institute of Public Health University of Porto, Porto, <sup>4</sup>Portuguese Reference Centre for M/XDR-TB, Centro Hospitalar de Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal. e-mail: acspinola@gmail.com

**Background:** Portugal is a country of intermediate Tuberculosis (TB) incidence (24 per 100,000 people) with a declining mortality rate over the last years. As epidemic reverses worst clinical cases may rise as issues to future clinical approach. Understanding of the deaths from TB can help to identify additional risk factors and prognosis indicators. This study aims to investigate the demographic and clinical characteristics of the TB-treated patients that died in 2012 in the northern region of Portugal.

**Design/Methods:** A case control study was designed using the records from the national surveillance system for TB, SVIG-TB. TB-treated patients in the northern region of Portugal which died in 2012 were defined as cases, and controls were randomly selected from the TB-treated patients that did not die in the same year. A logistic regression model was applied to evaluate factors potentially associated with death as well as to calculate the odds ratios (OR).

**Results:** 1736 patients finished the TB treatment in 2012 in the northern region of Portugal. From these 92 died; mostly males (80%) living in Porto (75%) with older age (57%  $\geq 65$  years old) with pulmonary (30.4%) and hepatic (11%) co morbidities prior to TB treatment. Gender (OR 0.3, 95%CI 0.16-0.53), co morbidities prior to treatment (other than HIV) (OR 3.19 95%CI 1.86-5.49) and number of drugs used during TB-treatment (OR 8.2 95% 4-16.8) were associated with increased risk of death.

**Conclusion:** Results from this study identifies what can be the most vulnerable patient groups and its clinical characteristics when comes to treat TB. Poor functional status, indicated by co morbidities prior to TB treatment, greatly influences the outcome of TB-treatment. Clinical data on this variable should be further characterized and a more detailed study developed in order to draw future strategies.

### PD-910-31 Resultados de los tratamientos antituberculosos instaurados en Galidia en período 2008–2012

E Cruz-ferro,<sup>1</sup> MI Ursúa-Díaz,<sup>1</sup> X Hervada-Vidal,<sup>1</sup>

JA Taboada-Rodríguez,<sup>1</sup> . Grupo de Trabajo del

Programa Galle.<sup>1</sup> <sup>1</sup>Programa Galego de Prevención e

Control da Tuberculose, Consellería de Sanidade, Dirección

Xeral de Innovación e Xestión da Saúde Pública, Santiago de Compostela, Spain. Fax: (+34) 8815 42971.

e-mail: elena.cruz.ferro@sergas.es

**Antecedentes:** El Programa Gallego de Prevención y Control de Tuberculosis fue establecido en 1995. Su principal objetivo es registrar todos los casos nuevos de tuberculosis (TB) y asegurar que todos los pacientes se adhieran al tratamiento para conseguir su curación y así disminuir la morbi-mortalidad de esta enfermedad en la región de Galicia. Objetivo: describir la situación final de los tratamientos de TB instaurados en Galicia en el período 2008–2012.

**Métodos:** Estudio observacional descriptivo retrospectivo. Fuente: Sistema de Información de Tuberculosis. Período: 1996–2012. Ámbito: Galicia. Variables: tratamientos supervisados (DOT) y situación final del tratamiento, clasificada en: curación, tratamiento completo, fracaso terapéutico, traslado, abandono, muerte, otro (no evaluado o todavía en tratamiento), desconocido. Se considera resultado satisfactorio la suma de curaciones y tratamientos completos.

**Resultados:** El número de casos nuevos de TB registrados en el período 2008–2012 fue: 909; 862; 786; 691 y 669, respectivamente. En estos años se instauraron los siguientes tratamientos supervisados (entre paréntesis el porcentaje sobre el total de casos): 231 (25,4%); 308 (35,7%); 297 (37,8%); 295 (42,7%); 287 (42,9%). Los resultados de todos los casos fueron satisfactorios en el siguiente número (y porcentaje): 820 (90,1%); 773 (89,7%); 687 (87,4%); 615 (89,0%); 592 (88,5%). En la tabla se presenta, con más detalle, la situación final de todos los casos del período 2008–2012.

	2008		2009		2010		2011		2012	
	n	%	n	%	n	%	n	%	n	%
Curación	185	20,3	155	18,0	141	17,9	113	16,4	97	14,5
Tratamiento completo	635	69,8	618	71,7	546	69,5	502	72,6	495	74,4
Resultados satisfactorios	820	90,1	773	89,7	687	87,4	615	89,0	592	88,5
Sin tratamiento: refusa por indicación médica	3	0,3	2	0,2	0	0,0	2	0,3	3	0,5
Abandono	11	1,2	19	2,2	10	1,3	7	1,0	9	1,3
Fracaso terapéutico	0	0,0	0	0,0	0	0,0	0	0,0	0	0,0
Traslado	13	1,4	7	0,8	14	1,8	9	1,3	12	1,8
Muerte	61	6,7	60	7,0	63	8,1	58	8,4	46	6,9
Otro (no evaluado, o todavía en tratamiento)	0	0,0	0	0,0	0	0,0	0	0,0	0	0,0
Desconocido	2	0,2	0	0,0	4	0,5	0	0,0	3	0,4
Total de casos nuevos de TB	910		862		786		691		669	

**Conclusiones:** El porcentaje de tratamientos supervisados instaurados en Galicia en el período 2008–2012 aumenta de forma progresiva, lo que puede indicar que, aunque cada vez tenemos menos casos, estos son más complicados. Seguramente la supervisión directa de los tratamientos (DOT) contribuya a la consecución de unos altos porcentajes de resultados satisfactorios, que están entorno al 90% en los 5 años analizados.

Grupo de Trabajo del Programa Gallego de Prevención y Control de la Tuberculosis: Abdelkader Hasan A, Anibarro García L, Castro-Paz Álvarez-Buylla MA, Cruz Ferro E, Ferreiro Fernández L, Hervada Vidal X, Otero Santiago M, Penas Truque A, Rodríguez Canal A, Taboada Rodríguez JA, Ursúa Díaz I, Valiño López P, Vázquez Gallardo R, Vázquez García-Serrano E

### PD-911-31 Control of TB death structure in the Moscow city, Russia

E Belilovsky,<sup>1</sup> P Seltsovsky,<sup>1</sup> L Rybka,<sup>1</sup> O Chizhova,<sup>1</sup> S Borisov.<sup>1</sup> <sup>1</sup>Public Health in Moscow, Moscow Scientific and Practical Center for Tuberculosis, Moscow, Russian Federation. Fax: (+7) 495 964 86 37.  
e-mail: belilovsky@gmail.com

**Background:** Moscow has one of the lowest levels of TB mortality rate in Russia (3.2 per 100K, 2013) which is decreasing annually. Further decreasing of indicator can be provided by separate control of different factors influenced on TB mortality indicator. Study analyzed two factors, which have essential influences on TB mortality: - status of inhabitancy of TB cases before death: permanent residents (PR) or who had not a permanent address of inhabitancy, - status of TB death registration relative to time of TB case notification: postmortem TB cases (never been registered before death, PM), cases of death less 1 month after TB notification (D1M), and who died later 1 month after notification (M1M). It permits to extract: (1) difficult controlled part of TB deaths - PM and D1M, which can be decreased by improvement of case-finding process and (2) M1M cases, which can be controlled by enhancement of effectiveness of treatment control.

**Methods:** Data about 800 TB death cases, registered in 2012–2013 in Moscow were analyzed based on death certificates data saved in the mortality register. Status of inhabitation (including PR, homeless (HL), who arrived from other Russian regions before death (RF) and migrants (MG)), time between TB case registration and TB death, socio-demographic and death registration data were used in analysis.

**Results:** Data showed 367 PM&D1M cases (45.9%), which included 292 (36.5%) PM. 345 TB death cases (43.1%) had not permanent address of inhabitancy, including 13.4% RF cases, 24.3% HL and 5.5% MG. Log-regression multivariate model demonstrated that difficult controlled part of TB deaths (PM&D1M), contrary to M1M cases, showed less proportion of PR (41.1% vs. 70.2%, OR=0.4, 95% CI 0.3-0.6), and larger proportion of women (24.8% vs. 17.3%; OR=2.0; 1.4-3.9), place of death at home (21.3% vs. 13.5% at hospital, OR=2.5; 1.6-3.9) and homeless (38.4% vs. 12.2%, OR=2.4; 1.5 –3.8). TB deaths among PR, contrary to other cases, had higher proportion of women (23.7% vs. 16.8%,  $p<0.05$ ), of place of death at home (23.9% vs. 6.4%,  $p<0.01$ ), and lower proportion cases with age younger 35 (17.9% vs. 25.2%,  $p<0.05$ ) and PM&D1M. Age median, which was equivalent 51.2, was older for PR then for other cases: 55 vs. 44 ( $p<0.05$ ). **Conclusion:** Activities directed to decrease of TB mortality have to be specified according to particularities of TB mortality components, defined by time between TB registration and TB death and by status of inhabitancy before TB death.

### PD-912-31 Intestinal helminth co-infections among smear-positive tuberculosis patients in Dar es Salaam, Tanzania

F Mhimbira,<sup>1</sup> J Hella,<sup>1</sup> N Kapalata,<sup>2</sup> M Sasamalo,<sup>1</sup> L Fenner.<sup>3,4</sup> <sup>1</sup>TB Research, Ifakara Health Institute, Dar es Salaam, <sup>2</sup>Temeke district, National Tuberculosis and Leprosy Programme, Dar es Salaam, United Republic of Tanzania; <sup>3</sup>Medical Parasitology and Infection Biology, Swiss Tropical and Public Health Institute, Base, <sup>4</sup>University of Basel, University of Basel, Basel, Switzerland.  
e-mail: fmhimbira@gmail.com

**Background:** The dual tuberculosis (TB) and HIV epidemic is associated with a high morbidity and mortality. HIV is a known risk factor for developing TB. However, there is only limited information on the burden of intestinal helminths co-infections and the significance on clinical presentation among TB patients in low-income countries.

**Objective:** We aimed to describe the epidemiology of intestinal helminth co-infections in TB patients in the densely populated Temeke district in the city of Dar es Salaam (Tanzania), and to compare patients with and without helminth co-infections.

**Methods:** Sputum smear-positive TB patients aged 18 and older were prospectively recruited in two sub-districts in Temeke from December 1, 2013 to March 15, 2014. TB and HIV diagnosis were done as per national guidelines. Stool and urine were examined for helminth infections using Kato-Katz (in triplicates), FLOTAC, Baermann, and urine filtration methods. Detailed clinical and laboratory data were captured using electronic questionnaires.

**Results:** A total of 102 TB patients were enrolled with a median age of 33 years (interquartile range [IQR] 25–39); 63 (62%) were males and 28 (27.5%) were HIV co-infected (Table). The median body mass index (BMI) was 23 kg/m<sup>2</sup> (IQR 21–25), and 6 (6%) had underweight (<18.5 kg/m<sup>2</sup>). Median blood haemoglobin was 11.2 g/dl (IQR 9.8–12.8g/dl). The overall prevalence of intestinal helminth co-infections was 27.5% (28 patients). Strongyloides stercoralis was the most frequently detected helminth infection (13 patients, 12.8%), followed by Schistosoma mansoni in 11 (12.75%) and A. duodenale in 9 (9.3%) TB patients. Dual helminth co-infections of S. stercoralis and A. duodenale was found in 5 (17.9%) TB patients. Helminth co-infections were found to be less common in HIV-infected compared to HIV-negative TB patients (7.1% vs 35.1%,  $p=0.003$ ). There was no evidence for an association of helminth co-infection with age, sex, anaemia and BMI (Table).

**Conclusion:** Intestinal helminth co-infections were frequent among TB patients, but less frequent among HIV co-infected TB patients, possibly due the local practice of regular anti-helminth treatments in HIV-infected patients. Screening for intestinal helminths at time of TB diagnosis or regular anti-helminth treatment may need to be considered in settings with a high prevalence of helminth infections. Future study prospects should include the impact of helminth infections on clinical outcomes.



**Table.** Patient characteristics of tuberculosis (TB) patients, comparing patients with and without intestinal helminth co-infections.

Characteristic	Intestinal helminth co-infection		P value
	Yes	No	
Age, years, median (IQR)	29 (23-34)	34 (27-39)	0.18 <sup>1</sup>
Sex, n (%)			0.9 <sup>2</sup>
Female	11 (28.1)	28 (84.2)	
Male	17 (15)	46(85)	
Haemoglobin (g/dl), median (IQR)	11.4 (10-12.6)	11.2 (9.6-13.2)	0.8 <sup>1</sup>
BMI, kg/m <sup>2</sup> , median (IQR)	22 (21-23.6)	23 (21.1-25.7)	0.3 <sup>1</sup>
HIV infection, n (%)	2 (7.14)	26 (35.1)	0.005 <sup>3</sup>
Total	28	74	

<sup>1</sup> Wilcoxon ranksum test; <sup>2</sup> Chi-square; <sup>3</sup> 2-sided Fisher's exact test

BMI, body mass index; IQR, interquartile range

### PD-913-31 Performance of clinicians in identifying tuberculosis as cause of death using verbal autopsy questionnaires in Siaya County, Kenya

S Murithi,<sup>1</sup> H Kipruto,<sup>2</sup> E Amukoye,<sup>3</sup> Y Kombe,<sup>3</sup> E Mitchell,<sup>4</sup> C Muturi,<sup>5</sup> B Langat.<sup>1</sup> <sup>1</sup>Disease Prevention and control, National TB control Program/MoH, Nairobi, <sup>2</sup>Research, National TB Control Program/WHO, Nairobi, <sup>3</sup>Research, KEMRI, Nairobi, Kenya; <sup>4</sup>Epidemiology, KNCV Tuberculosis Foundation, Hague, Netherlands; <sup>5</sup>Pathology, Jaramogi Oginga Odinga Training and Referral Hospital, Kisumu, Kenya. e-mail: sgacheri@nltp.co.ke

**Background:** African countries lack complete vital registration systems. Cause of Death (COD) is often derived from Verbal autopsy (VA). This study assessed performance of clinicians in identifying tuberculosis as COD. Concordance among clinicians was also measured against Post Mortem (PM).

**Methodology:** Study was done among deceased persons aged 1 year and above, who died of respiratory related symptoms in a rural Kenyan setting with a high TB/HIV prevalence within a Demographic Surveillance Site in Siaya between 2012 and 2013. PM complemented by Culture and GeneXpert were done at a public referral hospital by pathologist. VA questionnaires were each reviewed by 2 clinicians trained in VA interpretation and ICD-10 coding. Concordance among clinician in identifying TB as COD was calculated using Kappa statistics. Sensitivity and specificity tests were measured.

**Results:** 156 eligible cases were enrolled 78 (50%) in the study and 76 of them had complete data. PM results detected 11 TB deaths of which only 3 (27%) (Sensitivity: 27% [95% CI 10%, 57%]) had concordant results with the ClinicalVA interpretation. Concordance among clinicians regarding presence of TB with Cohen's Kappa was 0.56 (95%CI 0.34 - 0.78). Among the 65 patients with non-TB COD by PM, clinicians identified 8 (specificity: 72.3% [95%CI 65%, 86%]).

**Conclusions:** Results demonstrated moderate agreement among clinicians regarding presence of TB at death. Concordance between clinician and PM was significantly low. Identification of TB related deaths by clinicians

using VA questionnaires appear inadequate in providing accurate estimates of TB mortality in a setting with high HIV prevalence.

### PD-914-31 Patient characteristics and determinants of tuberculosis mortality in the Free State Province, South Africa: 2003–2012

S Van Der Merwe,<sup>1</sup> G Kigozi,<sup>2</sup> P Chikobvu,<sup>3</sup> J Heunis.<sup>2</sup>

<sup>1</sup>Provincial Tuberculosis Management, Free State Department of Health, Bloemfontein, <sup>2</sup>Centre for Health Systems Research & Development, University of the Free State, Bloemfontein, <sup>3</sup>Department of Community Health, University of the Free State, Bloemfontein, South Africa. Fax: (+27) 514 019 694. e-mail: heunisj@ufs.ac.za

**Background:** For more than two decades, South Africa has been faced with increasing TB mortality. Indeed, the rate of mortality (excluding HIV) soared from 42/100 000 population in 1990 to 59/100 000 in 2012. In 2009, the Free State registered the highest proportion of deaths among TB patients, at 10.4% with mortality of 178/100 000 (excluding HIV). This study ascertained patient characteristics and other factors associated with TB mortality in the province.

**Design/Methods:** The study followed a retrospective record review of routinely collected data between 2003 and 2012 in the Free State electronic TB database (ETR.net). The study population was defined as TB cases registered from 2003 to 2012. Data was cleaned and analysed using Stata v. 12. Data was described using percentages for categorical variables and mean for continuous variables. Pearson's X<sup>2</sup> test was used to establish any association between independent variables and the outcome variable death (patients who died before TB treatment completion)/treatment success (patients who were cured or completed treatment). Multivariate logistic regression analysis was used to identify the factors influencing death of TB patients.

**Results:** Out of the 208 256 records reviewed, 31 197 (15.7%) patients had died while the remainder had received a successful (cured/treatment completed) treatment outcome. The average age of patients who died was 39.0 years (SD: 13.9). Close to one-third (30.8%) of the patients who died were aged between 35 and 44 years. More than half of the patients were male (55.3%), had died within the first two months of TB treatment (50.2%) and had unknown HIV status (59.2%), while just over two-thirds (79.4%) were newly diagnosed with TB. Old age was the leading independent predictor of death; patients aged 75 years and older were 9.8 times more likely to have died than those aged 0–4 years. Patients with missing/unknown HIV status and HIV positive status were respectively 2.8 (CI: 2.6-2.9) and 2.2 (CI: 2.1–2.4) times more likely to have died than those with HIV negative status. Undergoing cotrimoxazole therapy was protective against death (OR: 0.73; CI: 0.6-0.9).

**Conclusion:** Patient demographics and HIV infection played a significant role in the deaths of TB patients in the Free State. It is therefore disconcerting that HIV status was unknown/missing for most of these patients.

This study confirms the need for intensified HIV testing for TB patients to facilitate care of co-infected patients.

### PD-915-31 Comparison of lipid profiles between pulmonary tuberculosis and community acquired pneumonia

J He,<sup>1</sup> Yu Wang,<sup>1</sup> Wei Mao,<sup>1,2</sup> G Ji,<sup>1</sup> J Wu.<sup>1</sup> <sup>1</sup>Respiratory, West China Hospital, Chengdu, <sup>2</sup>Internal Medicine, Chengdu Sifa Jingguan general Hospital, Chengdu, China.  
e-mail: 18980602293@qq.com

**Background:** It has been reported that patients with pulmonary tuberculosis (PTB) have lower total cholesterol levels than the general population. We aimed to compare lipid profiles between patients with PTB and patients with community-acquired pneumonia (CAP).

**Design/Methods:** One hundred patients with PTB, 100 patients with CAP were included in this analytic study. Serum total cholesterol (TC), triglyceride (TG), high density lipoprotein-cholesterol (HDL-C), and low density lipoprotein-cholesterol (LDL-C) concentrations were determined in all subjects. Differences between groups were analyzed by using a two-tailed t-test and  $p < 0.05$  was considered significant.

**Results:** There were significantly lower TC ( $3.76 \pm 0.10$  vs.  $4.03 \pm 0.10$ ,  $p = 0.036$ ), TG ( $1.12 \pm 0.10$  vs.  $1.51 \pm 0.10$ ,  $p = 0.006$ ) and LDL-C ( $2.23 \pm 0.07$  vs.  $2.44 \pm 0.07$ ,  $p = 0.031$ ) values in the PTB group than the CAP group. There was no significantly difference in HDL-C levels between the PTB group and the CAP group ( $1.09 \pm 0.04$  vs.  $1.10 \pm 0.04$ ,  $p = 0.886$ ).

**Conclusion:** We conclude that lipid profile differed between pulmonary tuberculosis patients and community-acquired pneumonia patients. Serum TC, TG, and LDL-C concentrations are generally lower in patients with PTB than those with CAP. The clinical significance of this finding needs further investigation in studies with larger sample size and more clinical data available.

## 37. TB ACTIVE CASE FINDING

### PD-916-31 Need for public-private mix approach as priority to reduce under-reporting in the country

R K Fatima,<sup>1</sup> E Qadeer,<sup>1</sup> Enar Donald,<sup>2</sup> S Gudmund Hinderaker.<sup>3</sup> <sup>1</sup>Research, National Tuberculosis Control Program Pakistan, Islamabad, Pakistan; <sup>2</sup>Research, International Union Against Tuberculosis and Lung Disease and University of Stellenbosch, Western Cape, South Africa; <sup>3</sup>Research, HSLP UK, London, UK. Fax: (+92) 51 8438 081. e-mail: drrazia\_fatima@yahoo.com

**Background:** The National Tuberculosis Control Programme (NTP) in Pakistan has officially achieved a tuberculosis (TB) case detection rate of 64% in 2011, with an estimated incidence rate of 230 per 100000 populations, but is likely to be missing an unknown number of patients, particularly in the private sector.

**Design/Methods:** A surveillance system was established among all eligible non-NTP providers in selected districts

from January to March 2012. Record linkage and capture re-capture analysis was conducted. All public and private sector providers in 12 randomly selected districts of Pakistan were included. **OBJECTIVE:** To estimate TB incidence and TB notification rates in Pakistan in 2012.

**Results:** Of 8346 TB cases identified after record linkage, 6061 were registered with the NTP. The estimated number of unobserved TB cases was 10 030 (95%CI 7800–12 910), which meant that the proportion of notified cases was 32% (95%CI 17–49). The calculated annual incidence was 878 000 cases (95%CI 573 000–1 675 000), corresponding to a rate of 497/ 100 000 (95%CI 324–948) annually in the population.

**Conclusion:** The study estimated that the proportion of cases notified to the NTP was low, with actual incidence rates being higher than official estimates. TB surveillance should be strengthened to reduce under-reporting.

### PD-917-31 Increasing access to slum populations in Abuja, Nigeria

S T Abdurrahman,<sup>1</sup> O Oladimeji,<sup>2</sup> L Lawson,<sup>2</sup> J O Obasanya,<sup>3</sup> S Adeshina,<sup>3</sup> R Dacombe,<sup>4</sup> L Cuevas.<sup>4</sup> <sup>1</sup>FCT Tuberculosis and Leprosy Control Programme (TBLCP), FCT Ministry of Health, FCT-Abuja, <sup>2</sup>Tuberculosis Research Unit, Zankli Medical Centre, FCT-Abuja, <sup>3</sup>National Tuberculosis and Leprosy Control Programme (NTBLCP), Federal Ministry of Health, FCT-Abuja, Nigeria; <sup>4</sup>Tropical Medicine, Liverpool School of Tropical Medicine, Pembroke place, Liverpool, UK. e-mail: droladfb@gmail.com

**Background:** Abuja, the new capital of Nigeria is one of the fastest growing Metropolises in Africa. The plan metropolitan area is surrounded by large slum populations who have recently migrated in search for employment. Medical services in these areas are limited and access to TB diagnosis is limited, with many cases likely to go undetected by health services.

**Design/Methods:** This was a prospective study to assess whether community health extension workers visiting the slums and canvassing households to identify adults with chronic cough would increase the detection of cases. Participants were screened by collecting two sputum specimens on the spot and specimens were screened using smear-microscopy. Smear-negative specimens were further screened with Xpert. Data was compared with surveillance data before the intervention and with a neighbouring State where the intervention was not implemented.

**Results:** A total of 163,007 households and 6,537 symptomatic individuals were screened in one year of implementation. A total of 968 (15%) bacteriologically confirmed cases were identified, of which 670 (69%) were smear positive. The systematic screening of smear-negative patients with Xpert resulted in 298 (31%) additional cases. The number of cases reported to the TBLCP the year of implementation was 4,131 compared to 2,038 a year before.

**Conclusion:** The implementation of outreach activities in slum populations significantly increased case detection. The systematic screening of smear-negative cases with Xpert provided an additional 31% of bacteriologically

confirmed cases, but at a much higher cost than smear microscopy.

### PD-918-31 Active case finding of tuberculosis among marginalised and vulnerable population from two districts in India: a retrospective cohort study

T Soni,<sup>1</sup> K Sagili,<sup>1</sup> B Thapa,<sup>1</sup> S Chadha,<sup>1</sup> N Wilson.<sup>1</sup>

<sup>1</sup>Tuberculosis, International Union against Tuberculosis and Lung Diseases, New Delhi, India.  
e-mail: tanusoni.86@gmail.com

**Background:** India has the highest number of TB cases (~2.5 million) in the world. It is estimated that about 1 million cases are missed by the public health system in India annually, indicating a large potential infectious pool leading to continued transmission of TB in the community. Many of these people belong to marginalised community with limited access to diagnostic and treatment services. Active case finding (ACF) along with enhancing access to TB services could be an appropriate strategy to identify the missing TB cases.

**Objectives:** To identify TB symptomatics and TB positive cases among marginalized and vulnerable population through Active Case Finding in two districts of India.

**Intervention and Methodology:** Active case finding strategy was designed under Project Axshya, a Global fund supported project being implemented in 300 districts in India with focus on enhancing accessibility to TB services among households. Trained community volunteers visit households to sensitize about TB symptoms followed by identification of TB symptomatic individuals (having cough over 2 weeks) in these households. Identified symptomatics are either referred to the nearest designated microscopy centres or if required organise the sputum collection and transportation indirectly linking them with TB services. The details of the households, symptomatics, sputum test results have been documented in standardised formats. A retrospective analysis of these records for the duration October- December 2013 in two districts – Sonapat (Haryana) and Banda (Uttar Pradesh) was carried out.

**Results:** A total of 6088 households were visited through ACF and a total of 718 TB symptomatics were identified. Of these, sputum samples of 383 (53%) were examined for TB. A total of 31 were found TB positive (including smear positive and negative). About 8% of the TB symptomatics identified and tested through ACF were TB positive.

**Conclusion:** Total number of 8 households need to be visited to identify one TB symptomatic and about 12 TB symptomatics need to be tested to identify 1 TB positive. This suggests that active case finding is an effective strategy to detect a substantial yield of TB cases among the marginalised and vulnerable groups. There is an urgent need to introduce ACF by national TB program to identify TB cases in high risk groups and link them to TB services. This also contributes in reduction of TB transmission in the community.

### PD-919-31 Improving TB case finding among HIV-positive patients in Northwest Cameroon

F Sauter,<sup>1</sup> S Mboli,<sup>2</sup> E Mbu,<sup>1</sup> A Zoufaly,<sup>3</sup> J Jochum,<sup>3</sup>

J Noeske,<sup>4</sup> J-L Abena Foe,<sup>4</sup> M Sander.<sup>2,5</sup> <sup>1</sup>Day Hospital,

Northwest Regional Hospital, Bamenda, <sup>2</sup>Tuberculosis Reference Laboratory Bamenda, Bamenda, Cameroon;

<sup>3</sup>Infectious Diseases/ Medicine 1, University Medical Center Hamburg-Eppendorf, Hamburg, Germany; <sup>4</sup>National Tuberculosis Program, Yaounde, <sup>5</sup>GIZ, Yaounde, Cameroon.

e-mail: flo2311@gmx.de

**Background:** Detection of tuberculosis in HIV-positive patients is difficult but can be significantly improved by a combination of intensified case finding and laboratory testing using sensitive diagnostics. In many TB prevalent settings, additional information is needed to maximize TB case detection while simultaneously making the best use of limited laboratory resources.

**Design/Methods:** We performed a cross-sectional study of all adults newly diagnosed with HIV at the Regional Hospital Bamenda in Northwest Cameroon. Participants were screened for TB using the current WHO TB symptom screening algorithm (cough, fever, night sweats, and/or weight loss) and sputum culture using an automated liquid culture system.

**Results:** In total, 1169 patients were enrolled from August 2012 to August 2013, and 983 (84%) produced sputum for laboratory testing. Of those tested for TB, 68% were women, the median age was 35 (28–42) years, and the median CD4 count was 291 (114–496) cells/mL. In this population, 86% of patients reported at least one symptom of TB, including 48% with current cough, 24% with fever, 41% with night sweats, and 63% with weight loss. A comparison of the number of patients, cases detected, TB prevalence, and tests needed per case detected for several patient categories is shown in the Table.

**Table** Comparison of different TB case detection approaches

Patients for TB testing	Number (%) of patients tested	Number (%) of TB cases detected	TB prevalence	Number of cultures performed per case detected
All newly diagnosed				
HIV positive	983 (100%)	137 (100%)	13,9%	7,2
All HIV+ with symptoms (current cough, fever, night sweats, weight loss)	847 (86%)	127 (93%)	15,0%	6,7
All HIV+ with CD4 <500 cells/mL or WHO stage 3/4	769 (78%)	121 (88%)	15,7%	6,4
All HIV+ with CD4 <500 cells/mL or WHO stage 3/4	626 (64%)	116 (85%)	18,5%	6,0
All HIV+ with CD4 <500 cells/mL or WHO stage 3/4	466 (47%)	104 (76%)	22,3%	4,5

**Conclusion:** In similar settings with a high prevalence of HIV and TB, systematic laboratory TB screening of all newly diagnosed HIV-positive patients may be warranted. This approach would not significantly increase the number of laboratory tests needed as compared to testing



all symptomatic patients, and it would enable detection of a relatively large number of asymptomatic TB cases.

### PD-920-31 Estudio de contactos de tuberculosis, Galicia, 2008–2012

MI Ursúa-díaz,<sup>1</sup> E Cruz-Ferro,<sup>1</sup> X Hervada-Vidal,<sup>1</sup> JA Taboada-Rodríguez,<sup>1</sup> . Grupo de Trabajo del Programa Galle.<sup>1</sup> <sup>1</sup>Programa Galego de Prevención e Control da Tuberculose, Consellería de Sanidade, Dirección Xeral de Innovación e Xestión da Saúde Pública, Santiago de Compostela, Spain. Fax: (+34) 881542971. e-mail: elena.cruz.ferro@sergas.es

**Introducción:** El estudio de contactos (EC) de tuberculosis (TB) es una importante herramienta para el control de la TB. Permite diagnosticar precozmente nuevos enfermos y prevenir nuevos casos en contactos infectados. Objetivo: conocer el porcentaje de transmisión de la TB respiratoria (TBR) según la bacteriología del caso índice, grupo de edad y ámbito de transmisión de los EC realizados en Galicia entre 2008–2012.

**Material y Métodos:** Estudio observacional descriptivo retrospectivo. Fuente: Sistema de Información de Tuberculosis. Ámbito: Galicia. Período: año 2008–2012. TBR: incluye pulmón, árbol traqueobronquial y laringe. Brote: aparición de uno o más casos de TB relacionados con el primer caso detectado.

**Resultados:** En el período 2008–2012 se diagnosticaron 2.511 casos de TBR: - 1.326 TBR bacilífera: consta el EC en 1.155 (87,1%), estudiándose un total de 19.065 contactos (16,5 contactos por caso índice), resultando 236 (1,2%) enfermos y 6.587 (34,6%) infectados. - 795 TBR no bacilífera: tienen EC 461 (58,0%), estudiándose un total 3.333 contactos (7,2 contactos por caso índice): 32 (1,0%) enfermos y 1.066 (32,0%) infectados. - 390 TBR sin confirmación bacteriológica: de ellas 157 (40,3%) tiene EC; siendo un total de 1.072 los contactos estudiados (6,9 contactos por caso índice): 8 (0,7%) enfermos y 307 (28,6%) infectados. En los <5 años se observó el mayor porcentaje de enfermedad (92 enfermos de 1.429 contactos estudiados; 6,4%). En la tabla se presenta la distribución de los resultados del EC en función del ámbito de transmisión. Se declararon 180 brotes de TB (133 de 2 casos, 31 de 3, 13 de 4, 1 de 5, 1 de 6 y 1 de 34), detectándose el 58,9% entre los convivientes. Se indicó tratamiento de infección tuberculosa (TIT) a 4.124 (51,8%) de los infectados, rechazándolo el 3,4%. Cumplimentación correcta: 77,1%. Conclusiones: De los contactos estudiados entre 2008–2012, un tercio resultaron infectados y 1,2% enfermos, siendo el colectivo de convivientes y <5 años los más afectados. Del 15,6% de contactos desconocemos el resultado del estudio, lo que podría indicar que no se concluyó o una infradeclaración de los datos. La aparición de brotes de TB podría indicar retraso diagnóstico. Es preciso mejorar el seguimiento de los TIT, asegurando su correcta cumplimentación. Deben potenciarse los EC en aquellos casos de TBR no bacilífera y sin confirmación bacteriológica. Diseñar estrategias para un mejor control de los contactos contribuirá a disminuir la endemia TB.

Diagnóstico	Enfermos		Infectados		No infectados		No consta		Total
	n	%	n	%	n	%	n	%	
Convivientes	128	46,4	2.207	27,7	1.468	12,7	426	11,6	4.229
No convivientes	73	26,4	2.264	28,4	2.394	20,7	870	23,7	5.601
Escolar	59	21,4	1.030	12,9	4.461	38,6	1.383	37,7	6.933
Laboral	15	5,4	2.431	30,5	3.220	27,9	978	26,6	6.644
No consta	1	0,4	28	0,4	18	0,2	16	0,4	63
Total	276	1,2	7.960	33,9	11.561	49,3	3.673	15,6	23.470

### PD-921-31 Contribution of TB infection control (TBIC) implementation to the TB case detection trend in Afghanistan

A Momand,<sup>1</sup> GQ Qader,<sup>1</sup> M Rashidi,<sup>1</sup> A Zarabi,<sup>2</sup> SM Sayedi,<sup>1</sup> M Seddiq,<sup>2</sup> Mr Sadri,<sup>2</sup> P Suarez.<sup>3</sup> <sup>1</sup>TB CARE I, Management Sciences for Health (MSH), Kabul, <sup>2</sup>National TB Program, Ministry of Public Health of Afghanistan, Kabul, Afghanistan; <sup>3</sup>TB CARE I, Management Sciences for Health, Arlington, VA, USA. e-mail: amomand@msh.org

**Background** In 2010, TB control indicators were very poor at health facilities in Afghanistan. For example, the TB suspect rate was 1.1%, the suspect testing rate was 77%, and new sputum smear positive (NSS+) case detection rate was 6.1%. To improve these indicators, the national TB program (NTP) has been working to implement TB infection control (TB IC) measures at 120 health facilities, with support from the USAID-funded TB Control Activity Project (TB CAP), and its follow-on, TB CARE I.

**Interventions** TB CARE I helped the NTP develop standard operational procedures (SOPs) for TB IC and trained 1,200 frontline health workers to use these SOPs. The partners also developed and disseminate 23,000 TB IC educational brochures, established 90 TB IC committees at the health facility level, integrated TB IC into health facilities' general infection prevention plans, renovated 70 health facilities to improve their TB IC capacity, and established 430 safe sputum collection sites. TB CARE I and the NTP monitored the trained staff through close supervision and feedback systems to ensure they were correctly and consistently conducting all TB IC activities. In 2014, the NTP and TB CARE I conducted an assessment to determine if their TB IC interventions had contributed to improved TB suspect identification, testing, and TB case detection. The partners' analyzed data recorded between 2010 and 2013 at 55 of the 90 health facilities where they had implemented TB IC activities.

**Results** From 2010 to 2013, the number of TB suspects identified at the 55 facilities increased by 75.8% (from 23,120 in 2010 to 40,642 in 2013). Among those identified as TB suspects, the number tested for TB increased by 111.7% (from 19,125 in 2010 to 40,489 in 2013). Similarly, the number of newly identified TB sputum smear positive cases increased by 147.7% (from 1,328 in 2010 to 3,290 in 2013).

**Conclusion** TB IC activities contributed to improved TB suspect identification, testing, and TB case detection. These TB IC measures should be maintained at the 90 health facilities and expanded to additional health facilities to further improve TB control in Afghanistan.

**Table 1: Contribution of TB IC interventions to TB suspect identification and testing and TB case detection at 55 facilities in Afghanistan, 2010-2013**

Indicators	2010	2011	2012	2013	% improvement (2010-2013)
No. of TB suspects identified	23,120	30,050	31,024	40,642	75.8%
No. of identified TB suspects tested for TB	19,125	29,087	30,354	40,489	111.7%
No. of new sputum smear positive cases notified	1,328	2,755	2,855	3,290	147.7%

### PD-922-31 Where might 6–8-year-olds be exposed to tuberculosis in northern KwaZulu-Natal? Preliminary results from a large social contact pattern survey

T Yates,<sup>1,2</sup> F Tanser,<sup>1</sup> I Abubakar.<sup>2</sup> <sup>1</sup>Epidemiology and Population Studies, Africa Centre for Health and Population Studies, nr Somkhele, South Africa; <sup>2</sup>Infection and Population Health, University College London, London, UK.  
e-mail: t.yates@ucl.ac.uk

**Background** Molecular epidemiology suggests much tuberculosis (TB) transmission in high burden settings occurs between members of different households. Here we quantify children's social contact patterns in such a setting. These data were collected by the Africa Centre demographic and health household surveillance programme, in a largely rural area north of Durban. **Methods** Data on contact patterns were collected from a key informant during a household surveillance visit in 2013. The survey asked how many times in the last 7 days the child had visited a commercial building, a social venue or a church or had taken public transport; how many times in the last month the child had visited clinic or hospital; the number of visitors to the household and the number of other households the child had visited in the last week. This analysis is restricted to resident children, born in 2005 or 2006, registered in the surveillance programme, on whom we have complete data for these variables. Estimates of number of contacts and of time spent in each setting were obtained as a product of the number of visits, obtained from the survey, and estimates for each setting of typical occupancy and visit duration. Here, 'contact' means being in the same indoor space.

**Results** We obtained complete data on 2713 (73%) of 3699 resident children. 1192 (44%) of these children had visited none of the settings we asked about. The mean number of weekly contacts with other people in non-school congregate settings was estimated at 76 contacts per child, with 2 hours 34 minutes per week the mean time spent in such settings. Most contacts were made in commercial buildings, on public transport and in church, contributing a mean of 28, 23 and 19 contacts per child per week respectively. Most time was spent on public transport and in church – a mean of 46 and 75 minutes per child per week. Nine percent of children had been to a clinic or hospital in the preceding month. Twenty-five percent of households had had visitors in the last week and 32% of children had visited other households.

**Conclusions** Children's encounters with non-household members are concentrated in a limited number of congregate settings in this community, with commercial settings, public transport, church, and (not directly measured) school dominating. Further research should assess risk of TB exposure in these settings and in less frequented potentially high risk places, such as clinics and hospitals.

### PD-923-31 Higher yield for tuberculosis cases using enhanced case finding compared to passive case finding in Cambodia

S Ahuja,<sup>1</sup> S Batra,<sup>1</sup> J Chen.<sup>1</sup> <sup>1</sup>Management, Operation ASHA, Phnom Penh, Cambodia.  
e-mail: jacqueline.chen@opasha.org

**Introduction:** Cambodia has been scaling up active case finding activities since 2005. In 2010, Operation ASHA supplemented national efforts by conducting enhanced case finding in 5 Operational Districts (estimated population of 1.1m) in Cambodia to improve access to TB care.

**Method:** Field supervisors (locals who live in the area) act as the TB care coordinators for an assigned geographical area in the community. Each day, the field supervisors identify TB suspects thorough door-to-door screening for TB symptoms and collect sputum samples from TB suspects. They then deliver the sputum samples to designated laboratories under the National Tuberculosis Program. Field supervisors inform TB suspects when the results are out. Patients tested positive for TB are enrolled for TB treatment. When needy TB suspects require further tests, the field supervisor transports them to health facilities for chest X-ray screening.

**Results:** In 2013, 234,554 households were given counseling on TB in interventions Operational Districts (ODs). Of these, 12,170 individuals were found to have TB symptoms on screening. Among those screened, 3,093 (25.4%) were diagnosed to have all forms of TB and 1,176 (9.7%) had smear-positive TB. We used control ODs that had only passive case finding (i.e. symptomatic individuals approached health centres for consultation). Compared to them, the intervention ODs diagnosed 1,324 (30%) more cases, year-on-year.

**Conclusion:** The yield for TB cases is far greater for enhanced case finding. Hence, we suggest that national TB programs of high TB burden countries should consider adopting community-based door-to-door screening on a regular basis.

### PD-924-31 Characteristics of smear-positive tuberculosis persons identified by active contact tracing in Port-au-Prince, Haiti, November 2012-June 2013

S Galbaud,<sup>1</sup> S Koenig,<sup>2</sup> L Hashiguchi,<sup>1,3</sup> P Julma,<sup>1</sup> J.W. Pape.<sup>1,4</sup> <sup>1</sup>Les Centres GHESKIO, Les Centres GHESKIO, Port-Au-Prince, Haiti; <sup>2</sup>Division of Global Health Equity, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, <sup>3</sup>Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, <sup>4</sup>Division of Infectious Diseases, Center for Global Health, Weill Medical College of Cornell University, New York, NY, USA. e-mail: sgalbaud@gheskio.org

**Background** Haiti has the highest rate of tuberculosis (TB) in the Western Hemisphere, with an estimated prevalence of 296/100,000 population. Based in Port-au-Prince (PAP), GHESKIO-INLR is the largest provider of TB services in the Caribbean. Though contact tracing is a cornerstone of an effective TB program, these activities are rarely conducted in resource-poor settings, due to financial limitations. We present the outcomes of an active contact tracing project we conducted at GHESKIO.

**Design** The GHESKIO model of active contact tracing included active identification of household members and close contacts of persons with sputum smear-positive TB. TB contacts with respiratory symptoms were screened for TB with smear microscopy and chest radiographs. Contacts diagnosed with active TB were placed on same-day treatment and offered HIV testing. GHESKIO staff obtained consent to go to the home of the TB index case to invite household members for screening. All services were provided free of charge, and patients were also provided a subsidy for transportation. Screening at the TB clinic also included an education session using videos and pamphlets.

**Results** From November 2012 to June 2013, downtown PAP GHESKIO treated 1,035 patients for TB. Of these, 445 (43%) patients had smear-positive TB (41% female; median age 33 years). Following TB education sessions, 176 (40%) of these smear-positive index cases brought 404 household contacts to GHESKIO for TB evaluation (65% female, median age 24 years, 17% HIV-positive). Among contacts, 297 (67%) lived on <\$US 3/day and 150 (37%) were unemployed. From contact tracing, 15 (3.7%) patients were identified with smear-positive TB (67% female; median age 35 years, 17% HIV-positive). In multivariable analysis (including age, gender, income, education, residence zone, marital status, and HIV status), positive HIV status was not associated with a contact developing TB. However, marital status was significantly associated, with contacts who were cohabitating or widowed having a greater odds of developing TB when compared to married contacts (cohabitating OR 6.7,  $p=0.05$ ; widowed OR 34.8,  $p=0.01$ ).

**Conclusion** Active contact tracing yields additional diagnoses of smear-positive TB, breaking the chain of transmission. However, compliance with contact tracing was low, even with the provision of free care and transportation subsidies. Additional strategies will be

necessary to increase the proportion of contacts who are screened for TB.

### PD-925-31 Characteristics of undiagnosed tuberculosis cases identified through periodic intensified case finding in Blantyre, Malawi

A Choko,<sup>1</sup> L Corbett.<sup>1,2</sup> <sup>1</sup>TB/HIV, Malawi Liverpool Wellcome Trust Clinical Research Programme, Blantyre, Malawi; <sup>2</sup>Faculty of Infectious and Tropical Diseases, London School of Hygiene & Tropical Medicine, London, UK. e-mail: augutc@gmail.com

**Background** Despite global progress, tuberculosis (TB) remains a leading cause of death in Southern Africa. Intensified case-finding provides early diagnosis, with potential individual and community-level benefits that remain poorly defined. Here we describe participants in periodic intensified case finding in Blantyre, Malawi.

**Methods** A total adult population of 114,450 was covered by periodic screening activities including leafletting, megaphone messages and door-to-door enquiry for TB symptoms (with a focus on prolonged cough). Two sputum specimens (both spot) for fluorescent microscopy were collected from individuals reporting TB symptoms, with culture confirmation if positive. HIV testing and counselling (HTC) was provided to all smear+ve individuals. Data from participants in 5 rounds of intervention (April 2011 to December 2013) were analysed.

**Results** 6,053 participants (5.3% of the total adult population) reported symptoms and provided sputum during the period under analysis. Among 118 (1.9%) smear+ve participants, mean age was 34.4 years (SD: 11.6 years), 57 (48.3%) were HIV positive, and 61 (55.5%) were men. All but 6 (95.4%) registered for treatment. Including pre-registration events, 6 month TB outcomes in 93 patients (25 still on treatment) were: death in 4 (4.3%), default in 9 (9.7%), with cure/completion in 80 (86.0%). Symptoms included cough for  $\geq 2$  weeks for 104/118 (94.6%) smear-positive patients. Significant risk factors for undiagnosed smear positive TB were: prolonged cough (aOR 3.23, 95% CI: 1.40, 7.44), male gender aOR 2.11 (95% CI: 1.42, 3.13); being on antiretroviral therapy (ART) aOR 2.00 (95% CI: 1.26, 3.18); self-rated fair/poor compared to good/excellent general health aOR 2.00 (95% CI: 1.34, 2.97); previous consultation for their TB symptoms (aOR 2.23, 95% CI: 1.44, 3.46). Compared to individuals in the 16–25 age group, only participants aged  $\geq 45$  years had significantly decreased odds of undiagnosed TB aOR 0.39 (95% CI: 0.20, 0.77).

**Conclusions** Patients identified through intensified case-finding in the community had low mortality, despite high HIV prevalence. Very few declined full treatment, resulting in high cure rates. A better understanding of the characteristics of patients with undiagnosed TB may help to provide more effective health messaging, and targeting. Long term follow-up of communities is required to assess the benefit to communities from this type of systematic TB screening.



### PD-926-31 A theory-informed approach to identifying barriers to routine implementation of household TB contact investigation in Kampala, Uganda

I Ayakaka,<sup>1</sup> A Cattamanchi,<sup>2</sup> P Kajubi,<sup>1</sup> M Handley,<sup>2</sup> E Fair,<sup>2</sup> S Ackerman,<sup>2</sup> A Katamba,<sup>1</sup> L Davis.<sup>2</sup> <sup>1</sup>MU-UCSF Research Collaboration, Makerere University, Kampala, Uganda; <sup>2</sup>Medicine - San Francisco General Hospital, UCSF, San Francisco, CA, USA. Fax: (+1) 415 695 1551. e-mail: lucian.davis@ucsf.edu

**Background** TB contact investigation has a high yield (range 1–10%) for identifying active TB and WHO has recently recommended implementation in high-burden countries. Unfortunately, there are few data on how to promote uptake of contact investigation into routine practice. We sought to develop a systematic, theory-informed approach to this process.

**Methods:** We organized focus groups of clinic and community health workers to characterize barriers to contact investigation in 7 public health clinics in Kampala, Uganda. We developed a focus group guide using the “Behavioural Change Wheel,” an evidence-based framework for identifying barriers and linking them to appropriate interventions. Discussions were designed to elicit capabilities, opportunities, and motivations that might influence health worker behaviours related to 3 key processes of contact investigation: identifying index patients, screening contacts in households, and evaluating symptomatic contacts who present to clinic. A Ugandan social scientist and a Ugandan TB epidemiologist led discussions.

**Results:** We held 7 focus group discussions of 1–2 hours involving 73 staff and community workers. Participants knew of the high risk of TB in household contacts and believed in screening them. The main barrier related to capability was limited knowledge about pediatric TB evaluation. Barriers related to opportunity included heavy workloads of clinic staff, limited space to ensure patient privacy, patients’ severity of illness, and a perception that patients do not provide accurate household information because of fear of stigma. Staff suggested contact investigation may be more effective if initiated once patients feel better and by community health workers, who have better rapport with patients. Finally, clinic staff indicated they would be more motivated to participate in contact investigation if at a minimum funds were provided for phone communications with patients and if health workers visiting households were given allowances for transport and lunch.

**Conclusions:** An implementation strategy for contact investigation should include rehearsing relevant skills, such as evaluating child contacts, to enhance beliefs about capabilities. Also, assigning these duties to community health workers would avoid overburdening clinic staff and better engage TB patients and contacts. Further evaluation is needed to determine if a theory-informed implementation strategy yields better outcomes than standard guideline training.

### PD-927-31 Active case finding in urban slums: experience from a pilot under Axshya project in India

S Muhammed,<sup>1,2</sup> C Joltin,<sup>3</sup> P Banuru Muralidhara,<sup>4</sup> A Nair.<sup>2</sup> <sup>1</sup>Department of Public Health, Global Institute of Public Health, Thiruvananthapuram, <sup>2</sup>Axshya Project, Health Systems Research India Initiative, Thiruvananthapuram, <sup>3</sup>Axshya Project, The Catholic Health Association of India, Hyderabad, <sup>4</sup>Project Axshya, The Global Fund Round 9 Project, The Union South-East Asia Office, New Delhi, India. e-mail: fmshaffi@gmail.com

**Background and challenges to implementation:** Active case search is relevant in urban slums going by the high risk of TB in slum dwellers, relatively lower level of awareness and less accessibility to TB diagnostic and treatment services. Thiruvananthapuram city, Kerala has 182 enlisted slums with a population of 66483. An urban slum based house-to-house active case search campaign was formulated as a pilot under Axshya project in selected four urban slums in Thiruvananthapuram in February 2014.

**Intervention or response:** A 2-member team goes from house to house with a questionnaire. The team enlists all members of the household, with name, age and gender including children. Anyone who reports a cough of 2 weeks or more, or blood in sputum was identified as ‘probable TB’. They were then given sputum cups and explained how to collect a good sputum sample. The volunteers transported the sample to the nearest microscopy centre under NTP and the report was communicated back. To gain the confidence of the community, meetings were conducted every week with community members especially the women’s’ help groups, wherein symptoms suggestive of TB gets explained and the details of the nearest diagnostic facility. The house-to-house survey was done after the meetings.

**Results and lessons learnt:** In the first month of pilot, 1707 people were screened from 364 households, given a family size of 4.8, which is quite high compared to average family size in Kerala. Close to nine percentage households had TB symptomatics (2.34% of total household members). More females reported to be symptomatic but all the three positives were males-giving a sputum positivity rate of 21% among males (see summary table). The survey is on going and all the households in the selected four slums will be covered in coming 11 months. With a proper background setting by an awareness program, house-to-house screening in urban slums will help to identify TB symptomatics and will help to diagnose cases at the earliest. Sputum collection and transportation system should be in place to facilitate testing, else may lead to drop-outs.

**Conclusions and key recommendations:** Active case finding in urban slums is an important area to be prioritized in TB control efforts. Not only that the community is receptive to such interventions; the results are promising to help detect cases hitherto undiagnosed case. The NTP should involve more agencies and undertake similar active case finding efforts in the entire slum.

	No screened	TB Symptomatics	No Diagnosed as TB
Total households	364	32(8.79%)	3
Total members	1707	40(2.34%)	3(7.5%)
Males	652	14(2.15%)	3(21.43%)
Females	729	25(3.43%)	0
Children	326	25(7.67%)	0

### 38. TUBERCULOSIS: A CONTACT SPORT

#### PD-928-31 Concordancia entre la prueba de la tuberculina (PT) y QuantiFERON TB Gold in tube en contactos de pacientes con tuberculosis pulmonar.

X Martinez Lacasa,<sup>1</sup> R Font,<sup>1</sup> A Jaen,<sup>1</sup> E Cuchi,<sup>2</sup> J Lite.<sup>2</sup>

<sup>1</sup>Tuberculosis control Unit, Hospital Universitari Mutua Terrassa, Terrassa, <sup>2</sup>Microbiology, Cat Lab laboratories, Terrassa, Spain. Fax: (+34) 937 835 577.

e-mail: xmartinez@mutuaterrassa.es

**Introducción:** Hasta hace pocos años la prueba principal en la diagnóstico de la infección latente tuberculosa (ILT) era la PT. Los métodos diagnósticos basados en la detección de interferón gamma específico en sangre (IGRAs) han permitido, eliminar algunos inconvenientes de la PT como la interferencia con antígenos vacunales o derivados de otras micobacterias no tuberculosas.

**Material y métodos:** Estudio comparativo realizado entre septiembre de 2010 y octubre de 2011. Se estudiaron todos los contactos de pacientes con tuberculosis pulmonar confirmada. Se les realizó el PT y QuantiFERON-TB Gold In-Tube (QF-G-IT). Se descartó enfermedad activa. Se recogió la intensidad del contacto y si eran convivientes. Se consideró positivo la PT con  $> 5$ mm en convivientes y  $\geq 10$ mm en el caso de pacientes no convivientes. El análisis de la concordancia entre pruebas se realizó mediante el coeficiente kappa. Se realizó un estudio de coste efectividad entre las dos estrategias basadas en la PT o en QF-G-IT.

**Resultados:** Se estudiaron 101 contactos, 80 (79,2%) fueron contactos de pacientes bacilíferos. La media de edad fue de 38,9 (DE: 12,4) y 51,5% fueron varones. Un total de 40(39,6%) estaban vacunados con BCG. En 61(60,3%) contactos la PT fue positiva en algún momento del estudio, y en 42 (41,5%) el QF fue positivo. Un 31,1% presentaron un QF negativo y la PT positiva y solo hubo en caso en el que el QF fue positivo y la PT negativa. La concordancia entre la PT y el QF fue del 79,8%% con una kappa de 0,61. En el grupo de vacunados la concordancia fue del 75% con una kappa de 0,42 y entre los no vacunados fue del 87,8% con una kappa de 0,73. En el grupo con BCG, 10 contactos con PT positiva presentaron QF negativo y ningún contacto de QF positivo con PT negativa. En el grupo de no vacunados 4 contactos presentaron QF negativo con PT positiva, y un caso de QF positivo con PT negativa. La estrategia diagnóstica basada en QF fue más costo efectiva que la basada en la PT.

**Conclusiones:** Los resultados del QF tienen una buena correlación con la PT en los contactos de pacientes con

tuberculosis pulmonar, sobre todo en no vacunados. En el grupo de no vacunados la concordancia mejora de forma notable. EL QF-G-IT debería ser considerada la prueba esencial para el estudio de contactos de enfermos con tuberculosis pulmonar. Además ha demostrado ser más costo-efectiva que la PT en el estudio de contactos inmunocompetentes.

#### PD-929-31 Size and growth of molecular strain typing clusters in the UK: 2010–2012

M Lalor,<sup>1</sup> L Anderson,<sup>1</sup> L Thomas,<sup>1</sup> I Abubakar.<sup>1</sup>

<sup>1</sup>Tuberculosis Section, Respiratory Disease Department, Centre for Infectious Disease Surveillance and Control, Public Health England, London, UK.

e-mail: maeve.lalor@phe.gov.uk

**Background:** In the UK, since 2010, the first isolate of each culture confirmed tuberculosis case was prospectively typed using 24-loci Mycobacterial Interspersed Repetitive Unit Variable Tandem Repeats (MIRU-VNTR). Molecular clusters which met certain criteria were investigated to try to identify transmission settings and inform public health action. To help refine the criteria to identify clusters warranting investigation, the characteristics of cases within molecular clusters between 2010 and 2012 to determine risk factors for being part of a large and fast growing molecular cluster were analysed. **Methods:** Notified tuberculosis cases from England, Wales and Northern Ireland were linked to laboratory results. Molecular clusters were defined as a cluster of two or more cases with indistinguishable MIRU-VNTR profiles. Clusters were categorised as either, large and fast growing vs small or large slow growing clusters. Potential risk factors, including demographic, clinical and social characteristics, and strain lineage were explored using multivariable logistic regression modelling.

**Results:** 6,113 cases were in 1,401 molecular clusters, with a median cluster size of 3 cases (range 2–121). 6% (87) of clusters were classified as large fast growing clusters. 34% of clustered cases (2,047) were in large fast growing clusters. Risk factors for cases being part of a large fast growing cluster compared to a small and large slow growing cluster included being male (aOR 1.15,  $P=0.029$ ), born in the UK (aOR 1.74,  $P<0.001$ ), of Black Caribbean (aOR 1.61,  $P=0.008$ ) or Black African (aOR 1.50,  $P<0.001$ ) ethnic group (compared to White ethnicity), having a strain type of Beijing lineage (aOR 3.10,  $P<0.001$ ), CAS lineage (aOR 1.68,  $P<0.001$ ) (compared to EAI lineage), being a drug user (aOR 1.45,  $P=0.026$ ), or imprisonment (aOR 1.61,  $P=0.005$ ). Factors inversely associated with cases being in a large fast growing cluster included having a Bangladeshi ethnicity (aOR 0.37,  $P<0.001$ ) and having a strain type with EA lineage (aOR 0.77,  $P=0.041$ ) (compared to EAI).

**Conclusion:** This analysis identified factors which were associated with being in large fast growing molecular clusters. The outputs of this analysis will be used to develop alerts to identify cases and clusters which are most likely at high risk of transmitting to further individuals. This will allow prioritisation of resources

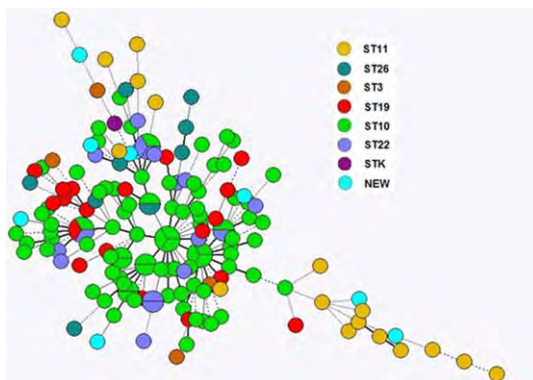
to the investigation of cases and clusters which would most benefit from rapid public health interventions.

### PD-930-31 Spatial Clustering of *Mycobacterium tuberculosis* in Eastern China

W Wang.<sup>1</sup> <sup>1</sup>Epidemiology, Fudan University, Shanghai, China. e-mail: ww@fudan.edu.cn

**Background:** China is one of 22 countries with the highest TB burden, having the second largest total TB cases and being one of the world's 27 highest TB drug resistant burden countries. Due to the characteristics of latent infection, the traditional methods of epidemiological study cannot meet the needs to trace TB infection sources and clarify the route of transmission, while the molecular epidemiology have advantages to tackle the above epidemiological questions. The combination of spatial epidemiology and molecular epidemiology provides a new idea for studying TB.

**Design/Methods:** During the study period, there were 680 and 445 active pulmonary TB patients reported in Funing and Yinzhou respectively. Geographic information system (GIS) was used to conduct spatial autocorrelation analysis, with SaTScan (version 8) for spatial scan statistic analysis. Respectively 199 and 179 Mtb stains from Funing and Yinzhou were collected during the study period, and genotyped by 15 loci VNTR-MIRU. Mtb Beijing family strains were identified by the region of difference (RD) and further classified into subtypes by SNP typing.



**Results:** Purely spatial scan statistic analysis showed Guoshu town as the only one cluster area (RR=1.89, P=0.036) in Funing county, while Yizhou District had three clusters including Xiaying street, Shiqi street and Wuxiang town. A total of 359 strains out of 378 strains showed unique genotype and 32 strains belonged to 14 clusters. As a result, the proportion of clustering was 8.47%, and the proportion of cases due to recent transmission was estimated at 4.76%. TB patients in clusters were significantly different from the patient owning unique genotype in the aspect of household registration ( $\chi^2=11.458$ , P=0.001). Most of TB patients in clusters were the local residents. Comparing the genotype of Funing with other studies conducted in Chongming, Taiwan and Japan, we found that the

genetic distance of Funing strains and Chongming strains were relatively close, while it is far between Funing strains, Taiwan strains and Japan strains.

**Conclusion:** The incidence of TB in rural areas of Eastern China has positive local spatial autocorrelation. Sporadic transmission of TB may have played an important role in the transmission of TB in rural areas of eastern China. Recent transmission did not explain most of the geospatial clustering, suggesting that geospatial clustering largely depend on environment factors and social determinants.

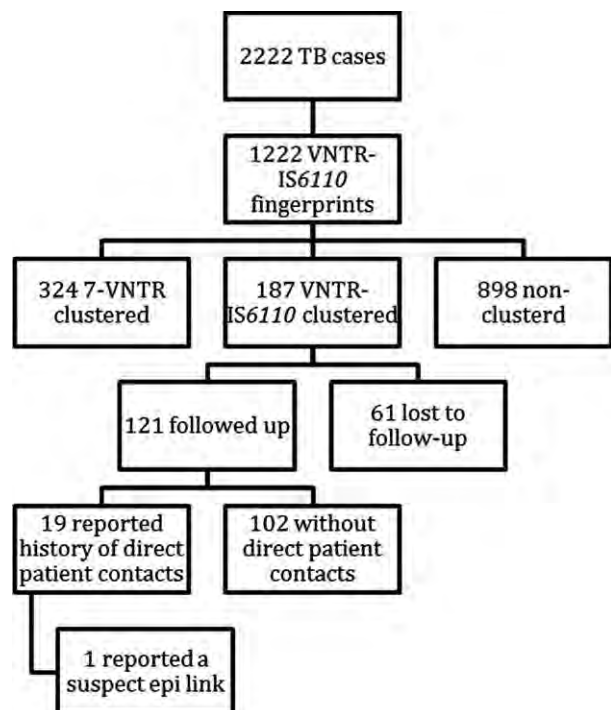
### PD-931-31 Role of casual contacts in the recent transmission of tuberculosis in settings with high disease burden

W Wang,<sup>1</sup> Yi Hu,<sup>1</sup> Q Zhao,<sup>1</sup> B Xu,<sup>1</sup> W Jiang.<sup>1</sup>

<sup>1</sup>Epidemiology, Fudan University, Shanghai, China. e-mail: ww@fudan.edu.cn

**Background:** Tuberculosis (TB) remains a major cause of morbidity and mortality worldwide. It is expected that combining multiple molecular methods will further help in focusing contact investigations.

**Design/Methods:** We performed a population-based molecular epidemiologic study in 6 sites in China between 1 June 2009 and 31 December 2010. A genotyping combining 7-loci MIRU-VNTR and IS6110-based RFLP was employed to determine predictors of recent transmission. A second interview was performed with the clustered patients to identify potential epidemiological links.



**Results:** The molecular clustering analysis revealed that 187 isolates (15.3%) shared the VNTR-IS6110 pattern, with an estimated recent transmission index being 8.9%.



None of these patients reported having contacts with other members within the same cluster. Nineteen of 121 reported having a history of contact to a TB case within 2 years before the current TB diagnosis. Additionally, geographic correlation was established for 19 cases in 9 clusters, while only one possible epidemiological link was established in secondary interview.

**Conclusion:** The result underscored the role of causal contact as a driving factor maintaining the current endemicity in rural China with high disease burdens of tuberculosis.

### PD-932-31 Is early tuberculosis death associated with increased TB transmission? A case-control study in Canada

A Parhar,<sup>1</sup> Z Gao,<sup>1</sup> C Heffernan,<sup>1</sup> R Ahmed,<sup>1</sup> R Long.<sup>1</sup> <sup>1</sup>TB Program Evaluation and Research Unit, University of Alberta, Edmonton, AB, Canada. e-mail: aparhar@ualberta.ca

**Background:** Tuberculosis (TB) is now an uncommon disease in high income countries. As such, its diagnosis may be missed or delayed resulting in death before or shortly after the introduction of treatment. Whether early TB death (an indication of delayed diagnosis) is associated with increased TB transmission is unknown. To determine the transmission risk attached to early TB death we undertook a case-control study.

**Methods:** All adults (age >14 years) diagnosed in the Province of Alberta, Canada between 1996 and 2012, with culture-confirmed pulmonary TB that died before or within 60 days of the start date of treatment were identified. In these “cases”, TB was a primary or contributory cause of death. Two “controls” for each “case” were then randomly selected from amongst adult culture-confirmed pulmonary TB cases that survived beyond 60 days of treatment. Two different matching criteria were used. First, “controls” were matched by age ( $\pm 3$  years), sex, and population group; second “controls” were matched by age, sex, population group and smear status. The contact lists of the “cases” and “controls” were then assessed using conventional and molecular methods to determine the number of secondary cases. Transmission windows lasted from 6 months before to 24 months after the date of diagnosis. Conditional logistic regression was used to find associations in both univariate and multivariate analysis.

**Results:** Amongst 65 “cases”, there were four that gave rise to 6 secondary cases. Amongst 130 “controls” matched by age, sex and population group, there were four that gave rise to 5 secondary cases; amongst 130 “controls” matched by age, population group and smear status, there were two that gave rise to 2 secondary cases. “Cases” were no more likely than “controls” to have secondary cases. (OR=1.6, 95% CI=0.43, 5.96,  $p=0.48$  and OR not available respectively).

**Conclusions:** Early TB death is not associated with increased transmission as measured by secondary cases at contact tracing, perhaps because both “cases” and “controls” were older and foreign-born: a demographic with a relatively low transmission risk.

### PD-933-31 Yield of household contact tracing for tuberculosis in rural South Africa

K Little,<sup>1</sup> R Msandiwa,<sup>2</sup> N Martinson,<sup>2</sup> J Golub,<sup>1</sup> R E Chaisson,<sup>1</sup> D Dowdy.<sup>1</sup> <sup>1</sup>Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA; <sup>2</sup>Perinatal HIV Research Unit, University of the Witwatersrand, Soweto, South Africa. e-mail: klittle@jhsph.edu

**Background:** If the global community is to meet aggressive tuberculosis (TB) control targets in the next decade, efficient and high-yield approaches for active TB case finding must be identified. However, research into the comparative yield and cost-effectiveness of active case finding strategies in high-burden settings is sparse. We replicated a campaign of household contact tracing performed in a South African city and deployed it in a rural, lower-incidence South African district to assess the comparative performance of contact tracing across the 2 settings.

**Design/Methods:** We established routine household contact tracing for all people presenting with active TB (“index cases”) in a rural district of northeastern South Africa with relatively low annual TB incidence rate (Approximately 350 per 100,000/year). All members of an index case’s household were tested for TB using sputum smear microscopy and culture through the South African national laboratory service. All participants completed surveys including TB symptom history, TB & HIV infection and treatment history, and demographic information. The yield of contact tracing was defined as the number of new TB cases identified per index case traced. A log-binomial regression model was constructed to examine risk factors for new TB infections among household contacts.

**Results:** To date, 160 household contacts of 80 index cases have been enrolled. Index cases were recruited from 61 different villages at an average rate of 18 cases per month. Index cases averaged 40.5 years of age (IQR: 30.4–50.9), were predominantly male (60%), and 46% were HIV-positive. By contrast, household contacts were younger (mean age 28.4 years, IQR: 16.8–48.6), mostly female (73%), and less likely to be HIV infected (18/76, 24%). Of the 72 household contacts (representing 33 households) with laboratory results completed, 13 (18%) had cultures positive for *M. tuberculosis* – a yield of 0.39 cases identified per index patient (Poisson 95% CI: 0.21–0.67). None had a positive sputum smear, and contacts with culture positive TB had no greater probability of reporting TB symptoms than those without TB (38.5% vs. 44.8%, RR=0.86,  $p=0.68$ ).

**Conclusion:** Household contact tracing using culture for active TB in rural South Africa more challenging and resource-intensive than in urban settings, but results in an exceptionally high yield. Sputum smear microscopy and symptom screening are ineffective tools for screening in this population.

### PD-934-31 Rates, timing and risk factors for tuberculosis among children in close contact with infectious tuberculosis patients

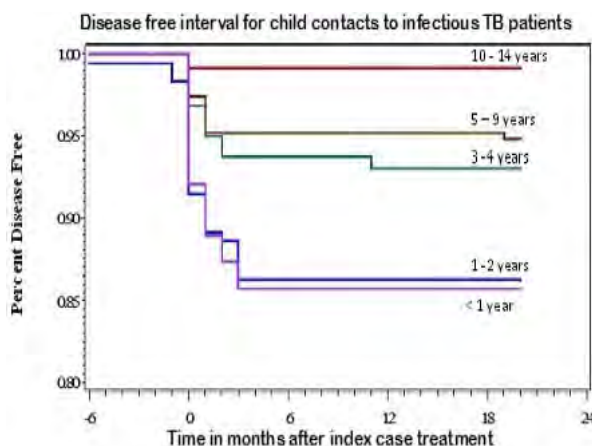
M Reichler,<sup>1</sup> B Chen,<sup>1</sup> J McAuley,<sup>2</sup> J Moran,<sup>3</sup> B T Mangura.<sup>4</sup> <sup>1</sup>Division of Tuberculosis Elimination, Centers for Disease Control and Prevention, Atlanta, GA, <sup>2</sup>Pediatrics, Rush University, Chicago, IL, <sup>3</sup>Public Health, Columbia University, New York City, NY, <sup>4</sup>New Jersey Medical School, Rutgers University, Newark, NJ, USA. Fax: (+1) 404 639 8961. e-mail: mrr3@cdc.gov

**Background and challenges to implementation:** The proportion of young children who develop tuberculosis (TB) following exposure to an infectious TB patient is not well established. We sought to determine rates, timing, and risk factors for TB among children with recent exposure to an infectious TB patient.

**Intervention or response:** Adult culture-positive pulmonary TB patients and their close contacts < 15 years of age were enrolled at 9 sites in the United States and Canada. Clinical and epidemiologic data were collected through interview and medical record review, contacts underwent tuberculin skin test and chest radiograph screening. TB registry matches were performed 2 years after final enrollment. Analysis of risk factors for TB was performed comparing characteristics of contacts with and without TB.

**Results and lessons learnt:** TB was diagnosed in 59 (6%) of 956 child contacts. TB rates were 13%, 13%, 9%, 9%, 3%, and 1%, respectively, among children < 1, 1, 2–3, 4–5, 6–9, and 10–14 years of age. Fifty-three (90%) contacts with TB were identified during contact investigation and 6 (10%) by registry match. Risk factors for TB in univariate analysis included age < 6 years ( $P < 0.001$ ), passive cigarette smoke exposure ( $P = .03$ ), and index case with positive sputum smear ( $P = .02$ ), cough ( $P < 0.001$ ), weight loss ( $P < 0.001$ ), bilateral disease ( $P < 0.001$ ), or cavitary radiograph ( $P < 0.01$ ).

**Conclusions and key recommendations:** Children in close contact with infectious TB patients are at high risk of developing TB, and contact investigation is an important means of identifying childhood TB. Risk factors for TB identified in this study may be useful to TB control programs for prioritizing contact investigations.



### PD-935-31 Comparison of the yield from contact screening among smear positive versus smear negative tuberculosis patient in north western Ethiopia

Y Kassie,<sup>1</sup> M Melese,<sup>1</sup> M Demissie,<sup>2</sup> B Girma,<sup>1</sup> A Mekonnen,<sup>1</sup> Z Zewdie,<sup>3</sup> D Jerene,<sup>1</sup> P Suarez.<sup>4</sup> <sup>1</sup>HEAL TB, Help Ethiopia Address the Low TB Performance (HEAL TB) Project, Management Science for Health (MSH), Addis Ababa, <sup>2</sup>Addis Continental Institute of Public Health, Department of Public Health, Addis Ababa, <sup>3</sup>Amhara National Regional Health Bureau, Department of Management, Bahir Dar, Ethiopia; <sup>4</sup>MSH, Centre for Health Services, Arlington, VA, USA. e-mail: ykassie@msh.org

**Background and challenges to implementation:** TB is a major cause of morbidity and mortality in Ethiopia with a significant proportion of active cases often left undiagnosed. The World Health Organization (WHO) recommends that countries focus on TB screening to increase TB case notification rates (CNR). Little research has been conducted to determine the yield of TB cases through contact screening among sputum smear negative (SSN) TB patients

**Intervention or response:** In 2013, Ethiopia's National TB Program (NTP) and USAID-funded Help Ethiopia Address the Low TB Performance (HEAL TB) project conducted a cross-sectional study on contact screening in Bahir Dar city of Amhara Region. The study involved all SS+ and SSN TB patients who were on treatment during the study period and their contacts. The nurses referred those with TB symptoms to health facilities for TB diagnosis. The study team entered the contacts' TB diagnosis results into EPI-Info and calculated rates with 95% CI using SPSS software

**Results and lessons learnt:** Out of the 135 index cases included in the study, 63 had SS+ TB and 72 had SSN TB. In 3 of the index cases (2.2%), household contacts were not screened due to refusal. The remaining 132 index cases had 447 household contacts and 428 of these (95.7%) consented to be screened for TB. Out of these, 53 (12.4%) had TB symptoms. Among those with TB symptoms, 14 (26.4%) had active TB of all forms. The prevalence of active TB among household contacts of SS+ TB cases was 4.3% (95% CI 1.8- 8.4) and among SSN TB cases was 2.5% (95% CI .91-5.41). This translates to an adjusted CNR of 4,300 per 100,000 population for contacts of SS+ TB cases and 2,500 per 100,000 population for contacts of SSN TB cases. The result shows that there are more than ten times TB cases among SSN TB contacts and 20 times among SS+ contacts as compared to the routine CNR of 247 per 100,000 in the general population

**Conclusions and key recommendations:** TB screening among household contacts of SS+ and SSN TB patients resulted in a high CNR, compared to the CNR in Ethiopia's general population. Household contacts of both SS+ and SSN TB patients should be considered "high risk" groups for TB and systematic, active TB screening should be conducted in this population. This study should be conducted at a larger scale to determine

the yield, feasibility, and cost-effectiveness of a TB screening system among household contacts in Ethiopia.

### PD-936-31 Early results from a large scale implementation of health facility-based contact investigation in Amhara and Oromia regions of Ethiopia, 2013–2014

B Girma,<sup>1</sup> Y Kassie,<sup>1</sup> Z Zewdie,<sup>2</sup> S Hamusse Daba,<sup>3</sup> D Jerene,<sup>1</sup> M Melese,<sup>1</sup> P Suarez.<sup>4</sup> <sup>1</sup>Help Ethiopia Address the Low TB Performance (HEAL TB) project, Management Sciences for Health (MSH), Addis Ababa, <sup>2</sup>Amhara Regional Health Bureau, Bahr Dar, <sup>3</sup>Oromia Regional Bureau, Addis Ababa, Ethiopia; <sup>4</sup>MSH, Centre for Health Services, Arlington, VA, USA. e-mail: bgirma@msh.org

**Background:** Although Ethiopia's national TB guidelines provide a policy framework for contact investigation implementation, this strategy has not been regularly implemented. This is partly due to a lack of operational guidance for standardizing TB contact screening. To fill this gap, the national TB program, with support from the USAID-funded Help Ethiopia Address the Low TB Performance (HEAL TB) project, implemented contact investigation in two regions of Ethiopia.

**Interventions:** We initiated the implementation of regular contact screening by developing standard operational reporting mechanisms. We then oriented health facility staff and trained zonal and district TB personnel on how to provide mentoring and follow up to the health facility staff. The health workers registered the close contacts of smear positive pulmonary TB index cases in a contact register. The index cases were then advised to bring their close contacts for screening. The procedure involved symptom screening followed by sputum microscopy for presumptive pulmonary TB cases, and other diagnostic methods including X-ray, fine needle aspiration and histology as per the national algorithm. Participating facilities attended regular quarterly at zonal and sub-national levels to review staff performance, identify gaps, and develop corresponding action plans.

**Results:** Between April and December of 2013, 659 health facilities registered 1,883 smear positive pulmonary TB index cases and 4,905 of their family members. All in all 4,454 of the family contacts (90.8%) were screened and 294 (6.6%) of these had presumptive TB symptoms. Out of these presumptive TB cases, 89 (30.2%) were diagnosed with all forms of TB, which corresponds to 1998 cases per 100,000 population. In 2012, the case notification rate for all forms of TB in the two regions was 141/100,000. The contact screening case notification rate was 14 times higher than the case notification rate in the routine system.

Indicator	Performance
SS+ index cases	1883
Number family contacts	4905
% presumptive TB	6.6
% TB among presumptive TB case	30.2
% Yield among contacts	1.9

**Conclusions:** If TB index cases are properly counseled and better informed about TB transmission, they can

educate and bring their close contacts for screening. The yield following this strategy was high. Clear implementation guidelines, adequate orientation, continuous staff support is necessary for effective implementation of contact screening at larger scale.

### PD-937-31 Profile of tuberculosis among household contacts of MDR-TB patients in Delhi, India

R Singla,<sup>1</sup> N Singla,<sup>2</sup> Vith Myneedu,<sup>3</sup> D Behera,<sup>4</sup> R Sarin,<sup>1</sup> A Kumar.<sup>1</sup> <sup>1</sup>Tuberculosis and Respiratory Diseases, National Institute of Tuberculosis and Respiratory Diseases, New Delhi, <sup>2</sup>Epidemiology and Public Health, National Institute of Tuberculosis and Respiratory Diseases, New Delhi, <sup>3</sup>Microbiology, National Institute of Tuberculosis and Respiratory Diseases, New Delhi, <sup>4</sup>Respiratory Diseases, Post Graduate Institute of Medical Education and Research, Chandigarh, India. Fax: (+91)1 126 517 834. e-mail: drrupaksingla@yahoo.com

**Background:** The occurrence of tuberculosis (TB) among House Hold Contacts (HHCs) of MDR-TB patients is largely unknown in India. The objective of the current study was to study the prevalence of tuberculosis (TB) among HHCs of MDR-TB patients put on treatment under Programmatic Management of Drug-resistant TB programme (PMDT). Secondary objectives were to study the spoligotyping pattern and the drug resistance profile of active TB (if any) among HHCs and comparing it with their respective index cases.

**Design/Methods:** It was a prospective cohort study. All consenting MDR-TB patients enrolled under PMDT program at a national tertiary referral institute from Jan 2012 to Dec 2012 were enrolled in the study and their sputum cultures were stored for spoligotyping study. All their consenting house hold contacts (HHCs) were also enrolled. HHCs were evaluated for presence of symptoms suggestive of TB and their sputum examination were done for AFB smear, culture and drug susceptibility tests (DST). All HHCs were contacted at least once every 3 months for one year and were also counseled to report passively if any time they developed symptoms suggestive of TB.

**Results:** A total of 294 index cases and 836 contacts were enrolled. Out of 836 contacts, 45 (5.4%) developed tuberculosis: 39 (86.7%) developed pulmonary TB (PTB) and 6 (13.3%) developed extra-pulmonary TB. In 28 of 39 PTB HHCs, whose culture and DST were available, 23 (82.1%) had MDR-TB. In 16 cases the spoligotyping reports were available for index well as the respective HHCs. In 13 out of these 16 pairs (81.2%) the spoligotyping was of same pattern while in rest 3 (18.8%) it was different indicating that these 3 HHC could have required infection from the community rather than from their index case in the same house. In two index cases 2 HHCs developed PTB; both showing same spoligotyping pattern. Another index case had 3 HHCs developing PTB; two HHCs showed same spoligotyping pattern while one had different pattern again indicating different transmission dynamics within the same family.



**Conclusion:** Around 5% of HHCs of MDR-TB patients treated under national program in India develop TB in 1 year of follow up period and almost four fifth among them develop MDR-TB. Significant number of HHCs may acquire infection from the community rather than from their respective index cases in the house. There is a need for active follow up of HHCs of MDR-TB patients under national program.

#### PD-938-31 Four years tuberculosis case contact tracing among contacts of MDR-TB cases in Paris

A Fournier,<sup>1</sup> C Bernard,<sup>2,3,4</sup> W Sougakoff,<sup>2,3,4</sup> S Quelet,<sup>1</sup> F Antoun,<sup>1</sup> I Dormant,<sup>1</sup> MO Dufour,<sup>1</sup> N Veziris.<sup>2,3,4</sup>

<sup>1</sup>Centre de Lutte Antituberculeuse, Mairie de Paris, Paris, <sup>2</sup>Centre National de Référence des Mycobactéries, Laboratoire de Bactériologie-Hygiène, Assistance Publique Hôpitaux de Paris, Paris, <sup>3</sup>U1135, Centre d'Immunologie et des Maladies Infectieuses, Team E13, INSERM, Paris, <sup>4</sup>Centre d'Immunologie et des Maladies Infectieuses, Team E13, Sorbonne Universités, UPMC, Paris, France. Fax: (+33)142162127. e-mail: nicolas.veziris@upmc.fr

**Background:** Active case tracing around tuberculosis cases is the main screening strategy for tuberculosis in low-incidence countries. The objective of this study was to evaluate the outcome of active case tracing of contacts of index multidrug resistant tuberculosis cases (MDR TB). Design and

**Methods:** We conducted a prospective study of active case finding of contacts of MDR TB cases in Paris between 2010 and 2013. Contact cases underwent clinical evaluation, chest X-ray and QuantiFERON® testing. Strains of *M. tuberculosis* isolated from contact cases were compared to that of index case with MIRU VNTR genotyping and drug resistance mutations analysis.

**Results:** 68 index MDR TB cases were identified, 46 (69%) were smear positive. Among the 66 cases born outside France, 40 (59%) were in France for less than one year. 68 surveys identified 84 contacts. Twenty-four contacts (33%) were born in France and 39 (46%) were close contacts living in the same house as the index case. Among the contacts, 25 (32%) had latent TB infection (LTBI). Six contacts had tuberculosis (6/84, 7%). Of these, four (4/6, 66%) had a strain sharing same MIRU VNTR and drug resistance genotype as the index case. All were close contacts of index case. Half of these 4 cases were probably infected in France. Among close contacts, 10% had secondary TB whereas no secondary TB was identified among occasional contacts. Interestingly among occasional contacts, 2 tuberculosis cases did not share the same genotype as the index case.

**Conclusion:** The population of contacts of MDR TB cases is different from that of susceptible TB cases: more often born abroad, more often belonging to a narrow (family, friends) circle, more LTBI (32% versus 15% among contacts of susceptible cases during the same period) and more secondary tuberculosis cases (7 % vs 1 %). Interestingly, genotyping identified that one third of

tuberculosis cases identified among contacts was not related to index case.

#### PD-939-31 Factores asociados a la subnotificación de la tuberculosis en España

C Morales García,<sup>1</sup> t Rodrigo,<sup>2</sup> F Casas,<sup>3</sup> P Bermudez,<sup>4</sup> M García-clemente,<sup>5</sup> S Maria,<sup>6</sup> M Casals,<sup>7</sup> J A Cayla.<sup>7</sup>

<sup>1</sup>Neumología, Hospital Universitario Virgen de las Nieves, Granada, <sup>2</sup>Programa Integrado de Investigación de Tuberculosis, Fundación Respira de Separ, Barcelona, <sup>3</sup>Neumología, Hospital Universitario Clínico San Cecilio, Granada, <sup>4</sup>Microbiología, Hospital Universitario Carlos Haya, Málaga, <sup>5</sup>Neumología, Hospital Central de Asturias, Oviedo, <sup>6</sup>Neumología, Consorcio Sanitario de Tarrasa, Barcelona, <sup>7</sup>Epidemiología, Agencia de Salud Pública, Barcelona, Spain. e-mail: concepcionmorales@telefonica.net

**Background:** No existen estudios recientes sobre la subnotificación de la tuberculosis (TB) en España pero parece probable que sea importante. Objetivo: Conocer la subnotificación de los casos de TB en los centros sanitarios de diversas Comunidades Autónomas y analizar los factores asociados a la misma.

**Design/Methods:** Estudio multicéntrico, retrospectivo. Se han incluido los casos de TB diagnosticados en cada uno de los centros participantes, desde el 1 de enero de 2011 hasta el 31 de diciembre de 2012. Se han contrastado los registros de cada centro con los registros de casos notificados a los Servicios de Salud Pública correspondientes. Se analizó si diversas variables demográficas, microbiológicas y clínicas se asociaban a la falta de notificación. Se calculó el número y porcentaje de casos no notificados. Los factores asociados a la no notificación se analizaron a nivel bivariado mediante tablas de 2 × 2, calculándose las Odds ratio (OR) y sus intervalos de confianza del 95% (IC). A nivel multivariado se utilizó regresión logística calculándose también las OR y sus IC.

**Results:** Se incluyeron datos de 16 centros sanitarios que aportaron 586 casos, 85 de los cuales (14,5%) no habían sido notificados. En los centros que aportaron más de 25 casos por año el porcentaje de casos no notificados osciló entre 0% y 45,2%. A nivel bivariado las categorías de las variables asociadas a la no notificación fueron: edad > 51 años, ser jubilado, exfumador, pacientes nacidos en España, caso atendido por especialista de zona, radiografía de tórax normal o con alteración no cavitaria, no bacilífero, y enfermedad extrapulmonar. A nivel multivariado las categorías de las variables asociadas a la no notificación fueron: sexo femenino (OR= 1,68 IC 0,96–2,95), casos atendidos por especialista de zona (OR=2,10 IC 1,03–4,31), caso no bacilífero (OR=1,73 IC 0,93–3,22) y enfermedad extrapulmonar (OR=2,85 IC 1,15–7,05).

**Conclusion:** El porcentaje de subnotificación detectado es importante. Algunas variables clínico-epidemiológicas se asocian discretamente a la no notificación pero se estima que el factor más determinante es la diferencia entre los centros sanitarios en la práctica de notificar sistemáticamente los casos de TB.

### PD-940-31 Providing sustainable household contact tracing and screening in TB patients and families: a cluster randomised trial in Blantyre, Malawi

K Kaswaswa,<sup>1</sup> M Mukaka,<sup>2</sup> B Ngwira,<sup>2</sup> J Mpunga,<sup>3</sup> H Maheswaran,<sup>2</sup> L Corbett.<sup>2</sup> <sup>1</sup>HNTI, University of Malawi, College of Medicine, Blantyre, <sup>2</sup>TB/HIV, Malawi Liverpool Wellcome Trust Clinical Research Programme, Blantyre, <sup>3</sup>Malawi National TB Programme, Ministry of Health, Lilongwe, Malawi. e-mail: kkaswaswa@yahoo.com

**Background** Household contact tracing provides TB screening and isoniazid preventive therapy (IPT) to contacts at high risk of TB disease. However, it is resource intensive, inconvenient, and often poorly implemented. We investigated a novel model aiming to improve uptake. **Methods** A pragmatic household-randomized trial (ISRCTN81659509) in Blantyre, Malawi. Consenting TB patients in 2 sites during May-December 2013 were randomized to either standard of care (SOC) or intervention (PACTS). PACTS patients received one screening/triage tool and sputum pots for each reported contact (sharing meals), adapted from WHO syndromic management (IMAI) guidelines. The tool guided participants through symptom screening; IPT eligibility; sputum collection; and served as a referral slip for contacts identified for further management. SOC used national guidelines (verbal instruction on who to bring for investigation/IPT). The primary outcome compared between arms the cumulative incidence among contacts of TB treatment before a 3 month home visit for outcome ascertainment. The secondary outcome was IPT initiation among U5Y children. An additional secondary outcome (IPT completion) is awaited. Individual record analysis used Stata 10.3 (Stata Corporation, Timberland, Tx, USA), with random effects to adjust for household clustering.

**Results:** 213 TB patients were block-randomized from 2 sites (106 PACTS and 107 SOC) of whom 62.8% were HIV-positive and 52.1% were culture-positive. 247 otherwise eligible patients declined participation. 19 households (14 PACTS, 5 SOC) lost to follow-up are not included in analysis. Of 831 contacts, 407 (49.0%) were in PACTS with 424 (51.0%) in SOC arms. 4 contacts (2 in PACTS and 2 in SOC arm) had TB diagnosed before home visit: adjusted odds ratio 1.03 (95%CI 0.09–11.2). 2 further cases (both PACTS) were diagnosed at home visit. Children in the PACTS arm (48/71 U5Y, 67.6%) were significantly more likely to have initiated IPT before the 3 month visit than those in the SOC arm (37/87 [42.5%] arm: aOR 2.31, (95% CI 1.05-5.06).

**Conclusion** An alternative patient-delivered symptom screen and IPT eligibility tool significantly increased timely IPT uptake among U5Y children in Blantyre, Malawi. This promising model needs to be optimised for acceptability and investigated in other low resource settings, with a view to scale-up if reproducibility is confirmed.

### PD-941-31 New smear-positive tuberculosis among household contacts in Lima, Peru

L Otero,<sup>1,2</sup> F Barletta,<sup>1,3</sup> F Gehre,<sup>3</sup> T Battaglioli,<sup>2</sup> B De Jong,<sup>3</sup> C Seas,<sup>1</sup> L Rigouts,<sup>3</sup> P Van Der Stuyft.<sup>2</sup>

<sup>1</sup>Instituto de Medicina Tropical Alexander von Humboldt, Universidad Peruana Cayetano Heredia, Lima, Peru;

<sup>2</sup>Department of Public Health, Institute of Tropical Medicine, Antwerp, <sup>3</sup>Department of Biomedical Sciences, Institute of Tropical Medicine, Antwerp, Belgium.

e-mail: larissaotero@gmail.com

**Background:** Investigation of household contacts of smear-positive tuberculosis (TB) cases is a priority to control transmission. In areas where there is ongoing transmission, contacts can be at high risk of TB infection also outside the household. We determined the contribution of intra and extra household transmission of recent smear-positive pulmonary TB in a high incidence district in Lima, Peru, through strain genotyping.

**Methods:** From April 2008 to December 2012, adults with a first episode of smear-positive pulmonary TB were enrolled. The names of their household contacts were registered. A secondary case was defined as a person listed as a household contact by a study participant (index case) that subsequently developed new smear-positive TB. Sputum samples of study participants were obtained at diagnosis and cultured in Löwenstein-Jensen medium. Cultures of index and secondary cases were fingerprinted with spoligotyping to determine phylogenetic lineages. When the same lineage was found, samples were further analysed by mycobacterial interspersed repetitive unit-variable number tandem repeat 15-loci typing (MIRU15). If more than two MIRU15 loci were different between the strains of the index and secondary case, they were considered to have been infected from different sources.

**Results:** During the study period, 2112 patients were enrolled and a secondary case occurred in 51 household contacts. We obtained paired DNA samples from 25 of them, of which 8 had different patterns of spoligotyping. Among the 17 with the same lineage: 2 did not have a result with MIRU15, 9 had a different pattern and 6 had the same pattern. Therefore, among 23 household pairs with complete results, in 17 (74%) pairs, index and secondary cases were infected with different strains and in 6 (26%) pairs they were infected with the same strain, reflecting likely intra household transmission. Eight pairs with different strains and two pairs with the same strain were diagnosed with TB within six months of each other.

**Conclusions:** Transmission outside the household was very frequent among our study population. Early case detection and treatment of infectious cases in the community, besides contact investigation, are a priority to reduce TB transmission in the community in this setting.

### 39. MDR-TB: OUTCOMES OF TREATMENT

#### PD-942-31 Risk factors associated with default among multidrug and extensively drug resistant tuberculosis patients in Georgia, 2013

M Gegia,<sup>1</sup> I Kachkachishvili,<sup>2</sup> N Korinteli,<sup>2</sup> T Gabunia.<sup>1</sup>

<sup>1</sup>URC, USAID Georgia Tuberculosis Prevention Project, Tbilisi, <sup>2</sup>ISSA, Institute of Social Studies and Analysis, Tbilisi, Georgia. e-mail: mgegia@gmail.com

**Background:** Default from treatment among multidrug and extensively drug resistant tuberculosis (M/XDR TB) patients remains a serious public health concern in Georgia. In the 2010 cohort, the loss to follow-up rate among M/XDR TB patients was 26%. Georgia has high rates of M/XDR TB and has pushed to expanded access to treatment in recent years. USAID Georgia Tuberculosis Prevention Project organized the survey of M/XDR TB patients defaulted from treatment in 2008–2013 years. The purpose of this study was to identify the risk factors associated with default and to determine the long-term outcomes of treatment default

**Design/Methods:** The study was conducted by using the social research methods including focus group discussion with policy experts and face-to-face interviews with M/XDR TB patients identified as defaulters by the National TB Program. The data were derived from the medical records of all MDR/XDR TB patients with laboratory-confirmed M/XDR-TB TB who initiated treatment at any TB clinic in Georgia. One hundred sixty three respondents were selected through multistage cluster sampling out of 258 full cohort of patients registered during 2008–2013

**Results:** The survey found that a vast majority of patients loss to follow up (85%; 139) were male; 59.5% were of working age; 64% (104) were unemployed. The multivariate analysis indicated that independent risk factors for default were side effects (OR 4.08, CI 1.15–14.69), depression (OR 12.00, 95% CI 2.94–69.53) and financial constraints (OR 7.94, CI 2.45–30.17). Almost one out of five patients (19%) reported self-treatment or receiving treatment from traditional healers. The existence of social support was found to be an important factor contributing towards positive adherence behavior. The high levels of stigma, geographic access barriers, fear of loss job, and substance abuse were also discussed but these factors were not statistically significant.

**Conclusion:** Multiple factors influence MDR TB patients' treatment adherence behavior. The National Tuberculosis Program in Georgia, which provides universal access to second line TB treatment medications for all in need, can achieve better clinical outcomes through improved management of TB drug side effects and promoting psychological and social support initiatives including financial incentive schemes while on treatment. .

#### PD-943-31 An evaluation of tuberculosis retreatment in Brazil, 2007–2011

M.S. Evangelista,<sup>1</sup> F. Dockhorn,<sup>1</sup> R Maia,<sup>1</sup> J Toledo,<sup>1</sup> J N Lima,<sup>1</sup> F Moherdau,<sup>1</sup> D Barreira.<sup>1</sup> <sup>1</sup>National Tuberculosis Control Program, Brazilian Ministry of Health (MoH), Brasilia, DF, Brazil.

e-mail: maria.evangelista@saude.gov.br

**Background:** Tuberculosis retreatment in Brazil constitutes a public health challenge because of its impact on the burden of MDR tuberculosis, including its diagnosis and treatment. In addition to that, patients under retreatment are the major risk group to develop MDR-TB. Thus, tuberculosis retreatment is a priority for the Brazilian Ministry of Health (MoH). The objective of this study was to evaluate tuberculosis retreatment in Brazil, from 2007 to 2011.

**Design/Methods:** A cross sectional study was performed with data from the Brazilian National Epidemiologic Surveillance System (SINAM), 2007 to 2011. Sociodemographic variables, HIV serological status, tuberculosis clinical presentation, smear-sputum results, culture results and clinical endpoint (cure, treatment abandon, relapse)

**Results:** From 2007 to 2011, a total of 429.692 tuberculosis cases were notified, of which 12.3% (52.852) were of tuberculosis retreatment. 50% of cases aged 20–39 years, 72.4% male, 55.5% afrodescendent and 93.7% with pulmonary presentation. 50.3% were treatment abandon, 49.7% relapsing cases. 81.5% had smear-sputum exams, of which 59.3% had positive results. Of these, 63.4% were pulmonary forms. Of the patients on retreatment, 28.5% had culture results. According to the clinical outcome, 44.2% had unfavourable results, 25.1% abandoned and 63.1% relapsed. Death cases represented 4.3% of cases and 1.7% were MDR-TB. The retreatment rate increased 23.5% during the period.

**Conclusion:** Results show that tuberculosis retreatment cases have an unfavourable clinical outcome and increasing trends during the period evaluated. There is a need to implement healthcare measures and cases follow up, as well as strategies to strength tuberculosis control and its epidemiological surveillance.

#### PD-944-31 Loss to follow up and acquired drug-resistance during treatment of multidrug-resistant tuberculosis

E Kurbatova,<sup>1</sup> J Ershova,<sup>1</sup> T Dalton,<sup>1</sup> P Cegielski,<sup>1</sup> and Global Petts Investigators. <sup>1</sup>Division of TB Elimination, CDC, Atlanta, GA, USA. Fax: (+1) 404-639-1566. e-mail: ies3@cdc.gov

**Background.** Loss to follow up from multidrug-resistant tuberculosis (MDR-TB) treatment prevents programs from reaching their targets for treatment success. We describe the rates of acquired resistance (AR) to second-line drugs among patients that were lost to follow up from MDR-TB treatment.

**Methods.** In the "Preserving Effective TB Treatment Study," consecutive adults with locally confirmed,



pulmonary MDR-TB starting treatment 2005–2008 in nine countries were prospectively enrolled, and followed for two years. AR was defined as drug-susceptibility tests (DST) of the baseline isolate showing susceptibility, of the last available isolate showing resistance to the same drug, and genetic analysis (MIRU-24) showing the same strain. Time to event was estimated using survival analysis techniques.

**Results:** A total of 1,607 patients were enrolled per protocol and had known treatment outcomes. Overall, 19.2% (309/1,607) patients were lost to follow up. The treatment success rate was 60.6%, 14.1% died, and in 6.1% treatment failed. Proportion of patients lost to follow up varied between countries, 0% to 35.6%. Median time on treatment before loss to follow up was 13.3 months (95% confidence interval 11.9–13.9). At the time of loss to follow up, 31.6% of patients remained culture-positive. Of 1,607 patients, 799 (49.7%) had follow up isolates. Of these, 165 (20.7%) were lost to follow up. Among patients who were lost to follow up, 47 (28.5%) had extensive drug resistance (XDR) or pre-XDR at the start of treatment. Ten (6.1%) had XDR TB, 19 (11.5%) had any fluoroquinolone [FQ] resistance, and 38 (23.0%) had any second-line injectable [SLI] drug resistance. During treatment 18 (11.6%) of 155 at risk for AR (for respective drugs) acquired pre-XDR or XDR. Of 146 at risk for AR to FQ, 13 (8.9%) acquired resistance, 9/127 (7.1%) had AR to any second-line injectable (SLI) agent, and 13/155 (8.4%) became XDR. In contrast, rates of AR among patients with successful outcome, respectively, were 3.0% (11/371), 3.9% (15/390) and 1.8% (7/398).

**Conclusion:** Of MDR-TB patients lost to follow, almost 1/3 started treatment with pre-XDR or XDR and an additional 12% acquired drug resistance while on treatment. In addition, 1/3 of those lost to follow up remained culture positive at last contact, which could lead to community transmission of strains with more extensive resistance.

#### PD-945-31 Risks of multi and extensively drug-resistant tuberculosis in patients with multiple previous treatments in rural China

B Xu,<sup>1</sup> Q Zhao,<sup>1</sup> Yi Hu,<sup>1</sup> Y Shi,<sup>1,2</sup> W Wang,<sup>1</sup> V Diwan.<sup>3</sup>

<sup>1</sup>Epidemiology, School of Public Health, Fudan University, Shanghai, <sup>2</sup>Tuberculosis prevention and control, Ministry of Health, Beijing, China; <sup>3</sup>Public Health Sciences, Centre for Global Health, Karolinska Institutet, Stockholm, Sweden. Fax: (+86)2154237710. e-mail: catherinexu61@yahoo.com

**Background:** Tuberculosis (TB) patients with a history of multiple anti-TB treatments are the “neglected” group to the free anti-TB treatment policy in China. This study aimed to understand what patients with multiple previous treatments had experienced on their TB medical care with regard to bacteriologic diagnosis, treatment regimen and treatment completion, and how this might influence the risks of multidrug and extensively drug-resistant TB (M/XDR-TB).

**Design/Methods:** A cross-sectional study was conducted in 10 county/district TB clinics in 5 provinces of China.

The study participants were TB patients having at least two longer-than-one-month treatment episodes previously. Face-to-face interviews and drug susceptibility testing (DST) were given to the consented participants.

**Results:** A total of 328 TB patients were recruited. The proportion of MDR-TB was 58.2% in the 287 DST confirmed patients. Forty-two percent of the patients did not complete their first treatment course. About 23.8% of the participants had a history of taking second-line drugs, and more than 77.8% of them were treated in county TB dispensaries where only sputum microscopy was applied. Multivariate analysis found that the use of second-line drugs was significantly associated with frequency of previous treatments ( $p < 0.01$ ), but not with drug resistance profiles of patients.

**Conclusion:** Patients with multiple previous treatments are at extremely high risk of MDR-TB in China. The unregulated use of second-line drugs bring about the threat of XDR-TB epidemic. Drug susceptibility testing guided treatment and strict regulations of anti-TB treatment should be assured for the high risk TB patients for the prevention and control of M/XDR-TB.

#### PD-946-31 Monitoring of MDR-TB treatment outcomes in the Russian Federation

V Testov,<sup>1</sup> I Vasilieva,<sup>1</sup> Serg Sterlikov,<sup>2</sup> V Erokhin,<sup>1</sup>

T Kasaeva.<sup>3</sup> <sup>1</sup>Epidemiology, Central TB Research Institute RAMN, Moscow, <sup>2</sup>TB Monitoring, Federal Research Institute for Health Organization and Informatics, Moscow, <sup>3</sup>Health Care Organization, Ministry of Health Russian Federation (MoH), Moscow, Russian Federation. Fax: (+7) 49974 83026. e-mail: testov.vadim@mail.ru

**Background:** WHO recommended 24–36 months’ report of MDR-TB treatment result doesn’t present accurate treatment success rate because part of MDR-TB patients remain on treatment beyond the reporting period. Calculation of real treatment results in MDR-TB cohort is important task due to high-cost of MDR-TB case management. The objective of the research is to define final treatment outcomes for annual MDR-TB cohorts.

**Design/Methods:** Treatment outcomes in annual Russian civilian MDR-TB cohorts 2008, 2009 and 2010 were collected by standard 24–36 months’ and additional – 36–42 months’, 42–48 months’ and 48–52 months’ reports. Total number of MDR-TB patients is 7.504. Cohort 2008 included 1.074, cohort 2009 – 2.664, cohort 2010 – 3.766 MDR-TB patients.

**Results:** Standard 24–36 months’ report showed treatment success rate in cohort 2008 as 49.6%; in cohort 2009– 44.9% and in cohort 2010– 42.8%. Part of patients who were still on treatment comprised 5.3–6.2%. 36–42 months’ report showed treatment success rate in cohort 2008 as 52.6%, in cohort 2009– 47.1%, in cohort 2010– 44.9% and 1.7–3.6% patients were still on treatment. 42–48 months’ report showed treatment success rate in cohort 2008 as 53.8%, in cohort 2009– 48.7%. 01–0.8% MDR-TB patients were still on treatment. In cohort 2010– 0.7% patients were on treatment after 39<sup>th</sup> month. Only 48–52 months’ report

presented final treatment outcomes – 53.9% in cohort 2008 and 49.4% in cohort 2009.

**Conclusion:** Accurate result of treatment intervention for MDR-TB patients can be defined only in 48–52 months past the closing date of year of treatment. Standard WHO recommended 24–36 months' report presented treatment success rate for Russian MDR-TB cohorts in 4.3–4.5% less than it is real effectiveness of treatment intervention.

#### PD-947-31 Amplified drug resistance and association with poor outcomes among patients with multidrug-resistant tuberculosis

R Kempker,<sup>1</sup> M Kipiani,<sup>2</sup> V Mirtskhulava,<sup>3</sup> N Tukvadze,<sup>2</sup> M Magee,<sup>4</sup> H Blumberg.<sup>1,4</sup> <sup>1</sup>Division of Infectious Diseases, Emory University School of Medicine, Atlanta, GA, USA; <sup>2</sup>Tuberculosis, National Center for Tuberculosis and Lung Diseases, Tbilisi, <sup>3</sup>Public Health and Epidemiology, Davit Tvildiani Medical University, Tbilisi, Georgia; <sup>4</sup>Epidemiology, Emory University Rollins School of Public Health, Atlanta, GA, USA. e-mail: rkempke@emory.edu

**Background:** Amplified drug resistance (ADR) during tuberculosis (TB) treatment increases the risk of treatment failure; however, little is known about ADR among patients with multidrug-resistant (MDR) TB. We sought to measure the risk and predictors of ADR and the association of ADR with poor outcomes among patients being treated for MDR-TB in the country of Georgia.

**Methods:** A retrospective study of patients receiving treatment for culture-confirmed pulmonary MDR-TB through the National Center for TB and Lung Diseases in Tbilisi, Georgia. Drug susceptibility testing (DST) for second-line drugs (SLDs) was performed at baseline and after three and six months and every third month thereafter if cultures were positive. ADR was defined by any SLD that went from susceptible on baseline DST to resistant on follow-up DST. Logistic regression was utilized to assess risk factors for ADR and the association of ADR with poor outcomes (default, treatment failure, and death).

**Results:** A total of 135 of 152 patients followed during the study period were included in this analysis (11 excluded with XDR and 6 with  $\leq$  three months follow-up). Among the 135 patients, 17 (13%) developed ADR at a mean of 215 days after starting MDR-TB treatment. ADR was seen similarly to ofloxacin (10/123, 9%) and the injectable drugs capreomycin or kanamycin (11/105, 10%). In multivariate analysis, the presence of cavitary disease at baseline (aOR 5.1, 95% CI 1.5–16.9), resistance to  $\geq$  6 drugs at baseline (aOR 4.8, 95% CI 1.4–16.7), and a four-month positive acid-fast bacillus (AFB) sputum smear (aOR 7.5, 95% CI 1.4–39.2) were significantly associated with ADR. Risk of poor treatment outcome was significantly higher among patients with ADR (87%, 3 death, 4 failure, 6 default) compared to patients without ADR (37%, 4 death, 1 failure, 36 default),  $p < 0.01$ . Both ADR (aOR 5.7, 95% CI 1.11–29.4) and a six-month positive AFB sputum smear (aOR 2.8, 95% CI 1.1–6.9) were significantly associ-

ated with a poor treatment outcome in multivariate analysis.

**Conclusions:** Risk of ADR was high among patients being treated for MDR-TB and ADR was significantly associated with poor treatment outcomes. Patients with baseline cavitary disease and persistent AFB sputum smear positivity are at increased risk of ADR. A better understanding of mechanisms of ADR and identifying patients at increased risk of ADR may help improve MDR-TB treatment.

#### PD-948-31 Extensive drug resistance acquired during treatment of multidrug-resistant tuberculosis

P Cegielski,<sup>1</sup> T Dalton,<sup>1</sup> J Campos Caoili,<sup>2</sup> C C Contreras,<sup>3</sup> J Ershova,<sup>1</sup> E Kurbatova,<sup>1</sup> C Kvasnovsky,<sup>1</sup> and Global Petts Investigators. <sup>1</sup>Division of TB Elimination, CDC, Atlanta, GA, USA; <sup>2</sup>TB, Tropical Disease Foundation, Manila, Philippines; <sup>3</sup>TB, Socios en Salud Sucursal, Lima, Peru. Fax: (+1) 404-639-1566. e-mail: ies3@cdc.gov

**Introduction:** Increasing access to drugs for the treatment of multidrug-resistant (MDR) tuberculosis (TB) is crucial but could lead to increasing resistance to these same drugs. In 2000, the international Green Light Committee (GLC) initiative began to increase access while attempting to prevent acquired resistance.

**Subjects and Methods:** To assess the GLC's impact, we followed adults with pulmonary MDRTB from the start to the end of treatment with monthly sputum cultures, drug susceptibility testing, and genotyping. We compared the frequency and predictors of acquired resistance (AR) to second-line drugs (SLD) in nine countries that volunteered to participate, five countries that met GLC criteria and four countries that did not apply to the GLC.

**Results:** In total, 832 subjects were enrolled. Of those without baseline resistance to specific SLDs, 68 (8.9%) acquired extensively drug-resistant (XDR) TB, 79 (11.2%) acquired fluoroquinolone (FQ) resistance, and 56 (7.8%) acquired resistance to second-line injectable drugs (SLI). The relative risk (95% confidence interval) of AR was lower at GLC-approved sites: 0.27 (0.16,0.47) for XDRTB, 0.28 (0.17,0.45) for FQ, and 0.15 (0.06,0.39) to 0.60 (0.34,1.05) for three different SLI. The risk increased as the number of potentially effective drugs decreased. Controlling for baseline drug resistance and differences between sites, the odds ratios were 0.21 (0.07,0.62) for acquired XDRTB and 0.23 (0.09,0.59) for acquired FQ resistance.

**Conclusions:** Treatment of MDRTB involves substantial risk of developing AR to SLD, increasing as resistance to baseline drugs increase. The risk was significantly lower in programs documented by the GLC to meet specific standards.

### PD-949-31 Impact of acquired drug resistance on treatment outcomes among patients treated for multidrug-resistant tuberculosis

P Cegielski,<sup>1</sup> E Kurbatova,<sup>1</sup> J Campos Caoili,<sup>2</sup> C C Contreras,<sup>3</sup> T Dalton,<sup>1</sup> J Ershova,<sup>1</sup> C Kvasnovsky,<sup>1</sup> and Global Petts Investigators. <sup>1</sup>Division of TB Elimination, CDC, Atlanta, GA, USA; <sup>2</sup>TB, Tropical Disease Foundation, Manila, Philippines; <sup>3</sup>TB, Socios en Salud Sucursal, Lima, Peru. Fax: (+1) 404-639-1566. e-mail: ies3@cdc.gov

**Background:** Treatment of multidrug-resistant (MDR) tuberculosis (TB) includes a substantial risk of additional acquired drug resistance (AR), but the impact of AR on MDR TB treatment outcomes is unknown.

**Methods:** Preserving Effective TB Treatment Study (PETTS) is a prospective cohort study of consecutive adults with locally confirmed, pulmonary MDR TB who started treatment with second line drugs (SLDs) between 01/2005 and 12/2008 in nine countries and were followed for two years. AR was defined as drug-susceptibility test (DST) results of baseline isolate showing susceptibility but DST of the last available isolate showing resistance to the same drug with genetic analysis showing the same strain.

**Results:** Among 832 patients, 52 (6.3%) had resistance to a fluoroquinolone at the start of MDR TB treatment, 89 (10.7%) to second-line injectable drug (SLI) and 66 (7.9%) to both (i.e., extensively drug-resistant (XDR) TB). Of 766 non-XDR TB cases, 20 (2.6%) acquired resistance to fluoroquinolones only, 26 (3.4%) to SLI only, and 69 (9.0%) to both. Patients with AR had worse treatment outcomes than patients who started with resistance to the same drug(s) at baseline. Acquired resistance to SLI was associated with failure or death in 50.0% of cases compared with 20.2% among those with baseline SLI resistance ( $P=0.02$ ). For FQ, failure or death was 60.0% versus 32.7%, respectively ( $P=0.03$ ). Failure or death was approximately 10% more frequent among pre-XDR patients who acquired XDR TB than patients with baseline XDR TB.

**Conclusion:** Poor outcomes increased with greater initial drug resistance, increasing even more with acquired drug resistance.

### PD-950-31 Ability of early sputum culture conversion to predict long-term outcomes in an MDR-TB clinical trial

P Meyvisch,<sup>1</sup> A Gaddah,<sup>1</sup> B Dannemann,<sup>2</sup> K Andries,<sup>1</sup> C Kambili,<sup>3</sup> M Haxaire-theeuwes.<sup>1</sup> <sup>1</sup>Infectious Diseases - Diagnostics BVBA, Janssen, Beerse, Belgium; <sup>2</sup>Research & Development LLC, Janssen, Titusville, NJ, <sup>3</sup>Global Services LLC, Janssen, Raritan, NJ, USA. e-mail: pmeyvisc@its.jnj.com

**Background:** Sputum culture status at 2 or 3 months after treatment initiation has been suggested as a predictor of efficacy in drug-sensitive tuberculosis trials. In multi-drug resistant tuberculosis (MDR-TB) trials, culture conversion at time points later than 2–3 months has been proposed. Using data from a recently completed phase 2 bedaquiline clinical trial (C208 Stage 2; NCT00449644), we evaluated the ability of sputum

culture conversion at various time points to predict long-term treatment outcome, and using a model, we investigated the time to sputum culture conversion (or reversion).

**Design/Methods:** This was a multicenter clinical study in patients with newly-diagnosed sputum smear-positive pulmonary MDR-TB randomized to receive 24 weeks of bedaquiline or placebo with a standardized background regimen. After 24 weeks, patients continued on a background regimen for an additional 48 to 72 weeks. The sensitivity (i.e. fraction of patients with positive cultures among those in whom treatment failed) and the specificity (i.e. fraction of patients with negative cultures among those with successful outcome) for a range of early time points were calculated to identify the optimal time for using sputum culture conversion as a biomarker for treatment response in MDR-TB drug trials. A multi-state model was applied to simultaneously estimate the time-to-event (sputum culture conversion or reversion).

**Results:** Of the 160 enrolled patients, 139 (bedaquiline: 69; placebo: 70) had positive culture at baseline and were thus evaluable. For predicting treatment outcome, sputum cultures at week 8 of MDR-TB treatment had 80% sensitivity and 48% specificity. At week 24, it was 37% sensitivity and 93% specificity after which values stabilized. This translates to a positive likelihood ratio (i.e. sensitivity/(1-specificity)) which is  $> 3$  times higher at 24 weeks than at 8 weeks. On the time-to-event analysis, patients who received bedaquiline were more likely to convert than those who received placebo, and once converted those in the bedaquiline group had lower tendency to revert sputum to positive.

**Conclusions:** Our analysis suggests that the biomarker of sputum culture conversion at month 6 is more reliable to predict long-term treatment outcomes in MDR-TB than earlier time points. However, given the low sensitivity of sputum conversion at 24 weeks to predict cure, concurrent modeling of time to culture conversion and time to reversion may provide valuable information.

### PD-951-31 Time of sputum culture conversion of MDR-TB-HIV co-infected patients on second-line anti-tuberculosis drugs

N N Nwokoye,<sup>1</sup> C C Onubogu,<sup>1</sup> A Bowale,<sup>2</sup> N Tochukwu,<sup>1</sup> S Adesasen,<sup>1</sup> O Idigbe.<sup>1</sup> <sup>1</sup>National TB Reference Laboratory, Microbiology, Nigerian Institute of Medical Research, Lagos, <sup>2</sup>DR-TB Treatment Center, Mainland Hospital, Lagos, Nigeria. e-mail: negene21@yahoo.com

**Background:** Multi-drug resistant tuberculosis (MDR-TB) is treated with 2<sup>nd</sup>-line TB drugs. This treatment is monitored for efficacy and adverse side effects. Monitoring with culture is an intermediate outcome used in predicting treatment success. This study evaluates the effect of human immunodeficiency virus (HIV) infection on time to sputum culture conversion of MDR-TB patients on treatment

**Design/Methods:** Forty patients receiving 2<sup>nd</sup>-line anti-TB drugs were followed up for a period of not less than 8 months with clinical and laboratory investigations.



Smear microscopy, TB culture and drug susceptibility test (DST) were done at baseline. Subsequently, culture and smear microscopy were carried out monthly for a period of 8 months. HIV status, CD4 count and other tests were also done. Sputum culture conversion was defined as 2 negative cultures taken at least one month apart

**Results:** There were 12(30%) females and 28(70%) males with mean age of 37.7years. Among these, 9(22.5%) and 31(77.5%) were HIV-positive and negative respectively. DST results demonstrated 19 MDR and 21 mono-resistance to rifampicin. In general, 10(25%) patients achieved culture conversion at month 2, 20(50%) at month 3, 6(15%) at month 4 and 3(7.5%) at month 5. A patient (HIV-negative) was confirmed extensively- drug resistant TB (pre-XDR-TB) after 5 months of positive culture by 2<sup>nd</sup> -line DST. Stratifying by HIV status, At month 2, 8(25.8%) HIV-negative patients attained culture conversion as against 2(22.2%) HIV-positive patients. At month 3, rates of culture conversion were 15(48.2%) for HIV-negative and 5(55.6%) for HIV-positive patients, while rates of conversion at 4<sup>th</sup> month were 4(12.9%) and 2(22.2%) for the HIV-negative and positive patients respectively. Seven HIV-positive patients had CD4 counts of >300cells/mm<sup>3</sup>.

**Conclusion:** Time to culture conversion between the HIV-positive and negative patients were comparable. Similarity in conversion time may be due to the high CD4 counts of the co-infected patients. Early initiation of anti-retroviral therapy may improve MDR-TB treatment success in HIV co-infected patients.

#### **PD-952-31 Good treatment outcomes among prisoners with drug-resistant tuberculosis: hope from Baku, Azerbaijan and a challenge to the TB world**

R Mekhdiyev,<sup>1</sup> C Auer,<sup>2,3</sup> E Gurbanova,<sup>4</sup> F Huseynov,<sup>1</sup> N. Rakhmanov,<sup>4</sup> N. Karimova,<sup>1</sup> R Tahirli,<sup>4</sup> G B Migliori.<sup>5</sup>

<sup>1</sup>Main Medical Department, Ministry of Justice, Baku, Azerbaijan; <sup>2</sup>Swiss Centre for International Health, Swiss Tropical and Public Health Institute, Basel, <sup>3</sup>University of Basel, Basel, Switzerland; <sup>4</sup>Prison TB Hospital, Baku, Azerbaijan; <sup>5</sup>Fondazione S. Maugeri, Care and Research Institute, WHO Collaborating Centre for TB and Lung Diseases, Tradate, Italy. Fax: (+41) 61 2848103. e-mail: christian.auer@unibas.ch

**Background:** In 2012, there were an estimated 2810 MDR-TB cases among the 7138 notified pulmonary TB cases in Azerbaijan. Treatment of drug-resistant tuberculosis (DR-TB) started in the TB prison hospital in 2007. Objectives: To document treatment outcome of the first 250 DR-TB cases receiving treatment in the penitentiary system of Azerbaijan and to describe factors predicting poor outcome.

**Methods:** Cohort analysis of 250 DR-TB patients, enrolled for treatment between 28 April 2007 and 1 April 2010, focussing on treatment outcome and predictors of poor treatment outcome. Data collection was based on standard medical records. Data entry was with EpiInfo; data analysis with STATA.

**Results:** Description: Among the 250 cases, 20.8% had a body mass index below 17.5 kg/m<sup>2</sup>, 47.2% had bilateral cavities, 5.2% were HIV-positive and 90.4% were re-treatment cases. The mean number of drugs to which the cases were resistant was 5.1. 8.4% had pre-XDR-TB and 0.8% had XDR-TB. After four months of treatment, 21% of the cases were still culture-positive. Treatment outcome: 76.8% got cured (72.8% had cure and no re-occurrence of DR-TB), 6.4% died, 7.6% defaulted and 9.2% failed treatment. Multivariate analysis found that the following baseline characteristics were significant risk factors for poor treatment outcome (i.e. 'death' or 'treatment failure' or 're-occurrence of DR-TB after cure'): - Low body mass index - Bilateral cavities - Low body mass index and bilateral cavities - Age below 31 years - Harboring pre-XDR-TB or XDR-TB. The likelihood of cure without re-occurrence of DR-TB was 94.5% for the 76 cases with neither low body mass index nor bilateral cavities while it was only 46.3% for the 42 cases with low body mass index and bilateral cavities. Being culture-positive after two months of treatment was a risk factor for poor treatment outcome (odds ratio of 4.4; 95% confidence interval: 1.7 – 11.2). The chance of cure decreased the longer patients remained sputum positive, especially for patients with bilateral cavities.

**Conclusion:** Despite the difficult setting (high levels of drug resistance, advanced stage of TB in many patients, co-morbidities) this DR-TB control programme in Azerbaijan's penitentiary system achieved a high cure rate (77%). The overall figures hide high-risk sub-populations: certain baseline features (such as low body mass index and bilateral cavities) and culture positivity after two months of treatment are strongly associated with poor treatment outcome.

#### **PD-953-31 Trend of the drug-resistance surveillance in Thailand, 199-2012**

S Rienthong,<sup>1</sup> D Rienthong,<sup>1</sup> C Boonin,<sup>1</sup> N Phothong,<sup>1</sup> C Namwat.<sup>1</sup> <sup>1</sup>Disease Control, National TB Reference Laboratory, Bureau of Tuberculosis, Bangkok, Thailand. Fax: (+662)212 5935. e-mail: dhanida2547@yahoo.com

**Background:** Survey of randomly selected cluster of patients on an ongoing basis in countrywide in 2012 covering 100 clusters in 63 of 77 provinces of Thailand. To observe the trend of anti-tuberculosis drug resistance in Thailand 2012 and to compare the findings with those of the previous three surveys

**Design/Methods:** *Mycobacterium tuberculosis* isolates from smear-positive pulmonary TB (PTB) cases, 1622 newly treated cases and 196 previously treated cases were subjected to susceptibility testing against 4 anti-tuberculosis drugs. The drug resistance levels were compared with the result of DRS in Thailand in 1997 - 2012, and the trend of MDR was observed.

**Results:** Of 1622 isolated newly treated cases, 237 (16.83%) were resistant to any drug, 198 (12.21%) had any INH resistance, 36 (2.22%) had any R resistance and MDR-TB was found in 33 (2.03%). Of 196 isolates

from previously treated patients, 77 (39.29%) were resistant to any drug, 58 (29.59%) had any INH resistance, 47 (23.98%) had any R resistance and MDR-TB was found in 37 (18.88%).

**Conclusion:** MDR-TB prevalence remains low among new TB patients in Thailand, but is more common among previously treated patients. If it is assumed that the sampling process reflects the distribution of new patients and previously treated patients in the study areas, the amount of combined drug resistance (any resistance) in the community of smear-positive patients is approximately 19%. To further monitor programme performance the NTP will embark on a nationwide survey again in 2018.

#### 40. MDR-TB MANAGEMENT

##### PD-954-31 "I'm fed up": Experiences of prior tuberculosis treatment in patients with drug-resistant tuberculosis and HIV

J Furin,<sup>1</sup> P Isaakidis,<sup>2</sup> T Reid,<sup>3</sup> K Kielmann.<sup>4</sup> <sup>1</sup>Case Western Reserve University, TB Research Unit, Cleveland, OH, USA; <sup>2</sup>Epidemiology, Médecins Sans Frontières, Mumbai, India; <sup>3</sup>Operational Research Unit, Médecins Sans Frontières, Luxembourg; <sup>4</sup>Institute of International Health & Development, Queen Margaret University, Edinburgh, UK. e-mail: jff38@case.edu

**Objectives:** The aim of this study was to understand the impact on past tuberculosis (TB) treatment experiences of patients co-infected with HIV and MDR-TB on their current perceptions and attitudes towards treatment.

**Methods:** Qualitative study using in-depth interviews with 12 HIV/MDR-TB co-infected patients in Mumbai, India.

**Findings:** Patients reported unnecessarily long pathways to care and a high burden of fatigue with diagnostic and treatment procedures. In particular, they expressed concerns over the lack of efficacy of their current treatment regimen based on their experiences with TB treatment regimens in the past.

**Conclusion:** Patients reported negative experiences with previous HIV and TB treatment. Access to early diagnosis and rapid initiation of integrated care for HIV/MDR-TB co-infected patients with a strong, patient-centered support system could help to combat the low morale and lack of faith in treatment described in this group of patients.

##### PD-955-31 Epidemic levels of drug-resistant tuberculosis in HIV-infected patients in metropolitan Mumbai, India

P Isaakidis,<sup>1</sup> A Kumar,<sup>2</sup> M Khetarpal,<sup>3</sup> B Adsul,<sup>4</sup> A Bhamne,<sup>4,5</sup> M Manglani,<sup>6</sup> A Kanchar,<sup>7</sup> A Deshpande.<sup>8</sup> <sup>1</sup>OCB, Médecins Sans Frontières, Mumbai, <sup>2</sup>South-East Asian Regional Office, International Union Against Tuberculosis and Lung Disease (The Union), New Delhi, <sup>3</sup>BawalaWadi, Chinckpokli, City TB Office, Mumbai, <sup>4</sup>(MDACS), Mumbai Districts AIDS Control Society, Mumbai, <sup>5</sup>BMC, Brihanmumbai Municipal Corporation, Mumbai, <sup>6</sup>L.T.M. Medical College & General Hospital, Sion, Pediatric Centre of Excellence for HIV Care, Mumbai, <sup>7</sup>National AIDS Control Organisation, Department of AIDS Control, New Delhi, <sup>8</sup>ID Department, MGM Institute of Health Sciences, Navi Mumbai, India. e-mail: msfocb-asia-epidemio@brussels.msf.org

**Aim** Drug-resistant tuberculosis (DR-TB) is emerging as a major threat to tuberculosis control in India, however, no country-wide prevalence and incidence data are available. Similarly, the burden of DR-TB in patients co-infected with HIV is unknown. We conducted a survey to assess the DR-TB burden in HIV-infected patients attending the public antiretroviral treatment (ART) centers in the greater metropolitan Mumbai, India.

**Methods** A cross-sectional survey was conducted among adult and children ART-center attendees with presumptive tuberculosis. Culture and drug susceptibility testing (DST), for all first and second-line TB drugs, were used for bacteriological confirmation and for identifying resistance patterns at the patient and population levels.

**Results** Between March 2013 and January 2014, 1724 patients with presumptive TB were screened and included. Of these 72 (4%) were smear positive and 202 (12%) had a positive culture for tuberculosis. Overall DR-TB was diagnosed in 34% of culture positive TB patients. The proportions of DR-TB were 25% and 44% among new and previously treated cases respectively. The patterns of DR-TB were: 16% mono-resistant, 12% poly-resistant, 38% multidrug-resistant, 21% pre-extensively-drug-resistant, 6% extensively-drug-resistance and 2% extremely-drug-resistant TB. Bivariate and multivariate models showed elderly age, Pre-ART status, CD4 count less than 200 cells/ $\mu$ L at their last visit and previous episode of TB associated with culture-positive TB. None of the factors other than previous history of TB among patients were associated with drug-resistant TB and multi-drug resistant TB.

**Conclusion** The burden of DR-TB among HIV-infected patients attending public ART-centers in Mumbai is alarmingly high, likely representing ongoing transmission in the community and hospital settings. These data highlight the need to promptly diagnose drug-resistance among all TB cases and promptly treat all patients diagnosed. Moreover, in settings like Mumbai with varied resistance patterns, access to first and second line DST or molecular testing should be systematically offered to all patients with presumptive TB and especially in HIV co-infected.

### PD-956-31 Impact of decentralisation of treatment services on management of drug-resistant tuberculosis

S Balakrishnan,<sup>1</sup> DSA Karthickeyan,<sup>1</sup> A Kumar,<sup>2</sup> A Sreenivas,<sup>1</sup> S Mrithunjayan,<sup>3</sup> J Subramoniyapillai.<sup>3</sup>

<sup>1</sup>Tuberculosis, WHO India, New Delhi, <sup>2</sup>Research, The Union South East Asia Office, New Delhi, <sup>3</sup>Tuberculosis, Directorate of Health Services, Kerala, Thiruvananthapuram, India.  
e-mail: balakrishnans@rntcp.org

**Background:** Clinical management of Drug Resistant tuberculosis (DRTB) in India is tertiary care hospital based at start of treatment, in contrast to the complete domiciliary management of drug sensitive TB. In a resource limited setting, this causes significant out of pocket expenditure for patients' travel, loss of income of attendees and waiting for treatment due to wide patient to bed ratio, in addition to transmission of drug resistant tuberculosis infection in transit and in health facility. We assessed the impact of decentralization of treatment services on management of drug resistant tuberculosis.

**Methodology:** In Kerala, the southernmost state of India, half of the 14 districts initiate the Multi-Drug Resistant (MDRTB) patients on treatment at the district level health facilities, whereas the other half send their patients to the provincial DRTB centre. NTP records of all MDRTB patients diagnosed during May 2012 to April 2013 in both settings were reviewed, and demographic, laboratory and clinical data were abstracted and compared.

**Results:** A total of 226 MDR-TB patients were diagnosed and 218 (97%) started treatment during the study period; 173 (77.7%) were male and 53 (22.3%) were female. The median age was 47 years (IQR: 35–56) among treatment initiated. Most of the (66%) patients were below poverty line. The median time to initiation of treatment was 19 days (IQR: 14–27) for centralized treatment initiation and 21 days (IQR: 15–29) for decentralized treatment initiation ( $p=0.856$ ). In either model, there were no serious adverse drug reactions like liver failure, renal failure, suicidal tendency etc. during the early phase of treatment that warranted mandatory hospitalization. Sex, age group, living below the poverty-line, duration between diagnosis and treatment were not associated with treatment initiation site. Distance from patient's residence to treatment initiation site ( $P < 0.001$ ), cost of travel to treatment initiation site ( $P=0.015$ ) and duration of hospital stay ( $P < 0.001$ ) were significantly reduced in the decentralised MDR-TB care model. Most importantly, when 7 of the 105 diagnosed MDRTB cases were lost to treatment in the centralized model, only one of the 121 was lost to treatment in the decentralized model.

**Conclusion:** NTPs may consider implementing decentralized care for DRTB cases to reduce loss to treatment, travel; out of pocket expenditure and hospital stay of patients in resource limited settings.

### PD-957-31 Ambulatory /Community MDR-TB management in Oyo State of Nigeria

S Okewoye,<sup>1</sup> O Lawal,<sup>2</sup> B.O. Okewoye,<sup>3</sup> A. Adekola,<sup>4</sup> S. Olopade.<sup>5</sup> <sup>1</sup>MDR-TB, Movement Against TB, HIV/AIDS and Malaria in Nigeria (MATHAMAN), Ibadan, Oyo State, <sup>2</sup>TB and Leprosy, Oyo State Tuberculosis and Leprosy Control Program (STBLCP), Ibadan, Oyo State, <sup>3</sup>TB-HIV, Community Development Alliance (CDA), Ibadan, Oyo State, <sup>4</sup>MDR-TB, Damien Foundation Belgium (DFB), Ibadan, Oyo State, <sup>5</sup>MDR-TB, Community Development Voluntary Workers Initiative (CODEVOWIN), Ibadan, Oyo State, Nigeria.  
e-mail: stoptboy@yahoo.com

**Background/challenge:** Increasing cases of untreated MDR-TB were discovered in Oyo State of Nigeria. These posed public health problems and threats to lives of downtrodden masses at urban and rural communities needed urgent intervention. Passionate efforts in combating this life-threatening epidemic started with Ambulatory/Community MDR-TB Care in Oyo State in Oct 2013.

**Intervention/response :** 2 Community-Based Organizations - Movement Against TB, HIV/AIDS and Malaria in Nigeria (MATHAMAN) and Community Development Voluntary Workers Initiative (CODEVOWIN) were trained on "Ambulatory/Community MDR-TB Care" under the Global Fund Project jointly organized by Institute of Human Virology of Nigeria (IHVN) and Health Alive Foundation (HAF). The CBOs swung into action and took charge of Ambulatory/Community MDR-TB Management in collaboration with Tuberculosis Supervisors (TBLS) in LGAs where MDR-TB are prevalent. At first stage intervention, 25 MDR-TB Clients were identified in Oyo State. 5 of them were placed on Ambulatory MDR-TB Care (Intensive Phase drug and injection for first 8 months) while 20 on Continuation Phase (after completing 8 months in MDR-TB Clinic) were placed on Community MDR-TB Management (drugs for 12 months). 25 Treatment Supporters were trained by the 2 CBOs. Treatment Supporter attached to 1 MDR-TB client to ensure Directly Observed Therapy Short-course (DOTS) daily right inside their homes. CBOs are doing proper monitoring and follow-up to Treatment Supporters and MDR-TB clients to ensure Drug Adherence. The MDR-TB clients are attached to DOTS Centers in 17 LGAs of Oyo State and TBLS in LGAs are attending to them regularly.

**Results/lessons learnt :** In 6 months -Oct 2013–Mar 2014, 5 of 20 MDR-TB clients on Continuation Phase had successfully completed treatment and cured of TB. Remaining 15 on Continuation Phase and 5 on Intensive Phase are responding positively to treatments. They feel comfortable to receiving treatment at their homes by efforts of TS, TBLS and CBOs. This life-saving intervention proved that as Tuberculosis is curable, MDR-TB can be cured, it takes 20 months regimen.

**Conclusion:** More MDR-TB cases need be detected in communities to avoid infecting others. More CBOs need be trained to cope with increasing cases of untreated MDR-TB. Efficacy of 2<sup>nd</sup> line drugs for MDR-TB need be



improved to reduce fearful and most common side-effects such as partial deafness and irrational behavior.

### PD-958-31 eHealth for multidrug-resistant tuberculosis management and care

A Vladzimirsky, <sup>1</sup> T A Tsyganok, <sup>1</sup> V V Mozgovoy, <sup>2</sup> A G Kovaleva, <sup>2</sup> T A Borodina. <sup>2</sup> <sup>1</sup>Telemedicine and eLearning Center, Donetsk National Medical University of Maxim Gorky, Donetsk, <sup>2</sup>MDR-TB and Administration, Regional Tuberculosis Hospital, Donetsk, Ukraine.  
e-mail: doctelemed@gmail.com

Multidrug-resistant tuberculosis (MDR-TB) is a major public health problem. In most countries, decisions are made by a special medical commission (SMC): a primary diagnosis of MDR-TB has to be confirmed by the commission and only after that can a patient receive medications (sometimes this process takes a few weeks). In the Ukraine, the SMC meetings require all medical documents to be transported to a regional hospital for a few days. This entails risk of physical damage, personal data leaks, besides the documents being unavailable for the local hospitals. During the SMC's meetings, a local medical practitioner presents all the patients. This presenter cannot be well informed about all details of the patients from every hospital. Thus, the present system incurs delays and risks. eHealth and telemedicine has the potential to improve MDR-TB care and management. An eHealth platform was created in the Donetsk region of the Ukraine. It connects four local centres for MDR-TB treatment, one regional anti-tuberculosis hospital and the Medical University (which provides certification and teaching for telemedicine, network monitoring and efficiency evaluation, general and technical support). The eHealth platform allows electronic document exchange, storage and tracking, direct communication with attending doctors and even patients, and epidemiological monitoring. The closed high-speed network (100 Mbit/s) was constructed especially for the purpose of anti-tuberculosis telemedical work. Desktop videoconferencing is used, and the software provides support for DICOM images. The web portal of the network (<http://www.itub.dn.ua>) allows access to the videoconferences. An electronic health records (EHR) system was specially created for the network, which is available via a separate link. During the 6 month of operation, there were 1540 telemedicine sessions via eHealth platform. The main reasons for a patient submission to the eHealth platform were: primary confirmation of diagnosis and approval of treatment (32%), monitoring of treatment at Stage 1 (53%) and at Stage 2 (3%), final control (6%), management of complications and treatment interruptions (6%). We found that the diagnosis was changed in 21% of the telemedicine cases, but there were no time delays. All patients receive medication very quickly. There are no major technical falls. The special-purpose anti-tuberculosis eHealth platform appears very successful in its first 6 months of operation.

### PD-959-31 Community-based MDR-TB treatment supervision is associated with improved treatment outcomes in rural Swaziland

B Kerschberger, <sup>1</sup> A Telnov, <sup>2</sup> A Mafukidze, <sup>1</sup> H Cox. <sup>3</sup>

<sup>1</sup>Medical, Medecins Sans Frontieres, Mbabane, Swaziland;

<sup>2</sup>Medical, Medecins Sans Frontieres, Geneva, Switzerland;

<sup>3</sup>Division of Medical Microbiology, University of Cape Town, Cape Town, South Africa.

e-mail: benadi11@yahoo.de

**Background:** Access to multi-drug resistant TB (MDR-TB) treatment is limited in resource constrained settings. Among barriers for scale-up are lack of decentralized care models and human resources in health. Although community treatment programs reported favourable outcomes, community engagement varies across settings. We assessed a programmatic approach where treatment provision - including intramuscular injections - was task shifted to lay people with minimal supervision by health professionals.

**Methods:** This is a retrospective cohort study assessing task shifting for MDR-TB treatment in adults ( $\geq 18$  years) in rural Shiselweni (Swaziland), 01/2009 to 10/2013. Treatment was provided i) ambulatory at primary/secondary care facilities by health professionals (Clinic group) or ii) by lay people for community based care (CT group). Patients with difficulties in daily access to health facilities (living in remote locations, adherence problems, elderly, disabled, stigmatized, socio-economic constraints) were eligible for CT follow-up. Kaplan-Meier and Cox proportional hazard analyses were used to compare the Clinic and CT groups for retention in care and time to ART initiation.

**Results:** Overall 304 patients were eligible for the main analysis, 170 (55.9%) were female, 252 (82.9%) were HIV co-infected and 116 (38.2%) were in the CT group. Baseline factors (demographics, TB baseline characteristics, disease severity) were similar in both groups. After adjustment for confounders, patients in the CT group were 78% ([aHR] 1.78, [95% CI] 1.02-3.11;  $p=0.04$ ) more likely to be retained in care. A similar but insignificant trend was seen when restricting the sample to HIV positive patients (1.69, 0.89-3.22;  $p=0.11$ ). The CT group had the same adjusted hazard of ART initiation (1.27, 0.73-2.24;  $p=0.43$ ). Final two year treatment outcomes were available for the 2009-11 treatment cohort ( $n=187$ ) and success rate was 60% (79/132) for the Clinic and 71% (39/55) for the CT group ( $p=0.16$ ).

**Conclusion:** MDR-TB patients with difficulties in daily access to health facilities received community based treatment by lay people. Bringing care closer to patients through task shifting was associated with improved treatment outcomes and provides for treatment scale-up. Our findings support the expansion of community-based MDR-TB programs, especially for settings where geographical access and lack of health professionals are main barriers to scale-up.

**PD-960-31 Psychological fallouts of MDR-TB**

A K Vasisht,<sup>1</sup> K Wason.<sup>2</sup> <sup>1</sup>health, Chest clinic, Moti nagar, New Delhi, <sup>2</sup>OB and HR, International Management Institute, New Delhi, India. e-mail: drakvasisht@gmail.com

**Introduction:** MDR-TB a major public health problem, exists in majority of the countries is a continuous threat to TB control programmes. Globally 3.6% of new cases and 20% of previously treated cases have MDR. As per WHO there were estd 450,000 new cases worldwide in 2012. Estd 9% of MDR cases have XDR. There were 0.5 mn new MDR cases in the world in 2011 and about 60% being in "BRICS" countries. As the tt is long, associated emotional trauma and isolation wrought by the disease is imperative. For sustained efficacy the tt has to be synced with better management of psychological fallouts of MDR which are unique from any other disease. The long tt and its side effects necessitate the role of mental health experts in treating TB.

**Objectives:** MDR and the dreaded XDR-TB present larger challenges, major being that of societal stigma and inpatient stabilization not just physically but also psychologically. TB not only affects patient's health, but has impact on their economic, emotional and social well-being. The study is envisaged as a psychological examination of patients undergoing treatment upon being identified with MDR. It involves in-depth psychological and demographic profiling of patient, care takers and families associated with MDR patients. The impact of the disease in different spheres of a patient's life be they social, familial or at the workplace are analyzed.

**Method:** The methodology of the study involves both quantitative aspect as well as in-depth interviews with patients to garner information on their aspirations and perceptions and struggles of stigma. Together with suitable psychometric scales, patient profiling has been carried out. Field surveys, as well as secondary research are used to corroborate and guide findings.

**Results:** The impact of the treatment on patient self image is studied and the self perceptions that emerge are recorded while undergoing treatment. The Study identifies these psychological correlates of behavior which may help predict future behavior and intent to complete the course of treatment. A predictive model of personality and psycho social support becomes the imperative which can facilitate successful completion.

**Conclusions:** The study becomes imperative to the success of the program. Any stand alone treatment of MDR at the medical basis cannot and should not be divorced from the massive psychological ordeal which the disease comes with. The study is aimed at better modifications and timely actions of sensitization and awareness.

**PD-961-31 Drivers and trajectories of resistance to new first-line drug regimens for tuberculosis**

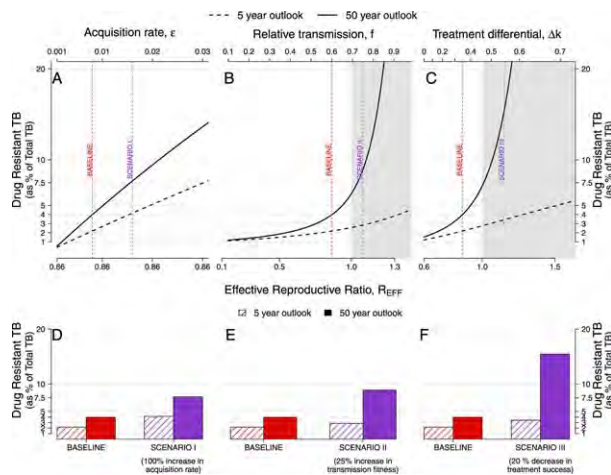
S Shrestha,<sup>1</sup> G Knight,<sup>2</sup> M Fofana,<sup>1</sup> T Cohen,<sup>3</sup> R White,<sup>2</sup> F Cobelens,<sup>4</sup> D Dowdy.<sup>1</sup> <sup>1</sup>Epidemiology, Johns Hopkins School of Public Health, Baltimore, MD, USA; <sup>2</sup>Infectious Disease Epidemiology, London School of Hygiene & Tropical Medicine, London, UK; <sup>3</sup>Division of Global Health Equity, Brigham and Women's Hospital, Boston, MA, USA; <sup>4</sup>Amsterdam Institute for Global Health and Development, Amsterdam, Netherlands. e-mail: sshres14@jhu.edu

**Background:** As we anticipate the launch of new first-line drug regimens for treatment of tuberculosis (TB), emergence of resistance is a key concern. Since population-level data on resistance to new drug regimens cannot be collected in advance, epidemiological models become important tools for understanding the likely dynamics of resistance as these novel drug regimens are launched.

**Methods:** Using data from the current epidemic of multi-drug resistant TB, we developed an epidemiological model of *M. tuberculosis* that includes two bacterial sub-populations, one that is susceptible (DS-TB) and one that is resistant to a hypothetical new first-line TB drug regimen (DR-TB). We characterized this system in terms of three key factors: (i) the probability of acquiring drug resistance during treatment; (ii) the transmission fitness of the drug resistant population relative to the drug-susceptible population; and (iii) the absolute reduction in the probability of treatment success as a result of drug resistance. We derive an expression for the effective reproductive ratio as a function of these three quantities, and study their effect on the future prevalence of drug resistance by simulating paradigmatic TB epidemics for 50 years following the launch of a hypothetical new first-line drug regimen.

**Results:** The effect of these factors varied over the year following the launch of a new regimen. For the first five years, the strongest predictor of DR-TB prevalence was the probability of acquired resistance during treatment. Over a longer term, however, the prevalence of DR-TB was driven by the resistant population's relative transmission fitness and the probability of treatment success – as also reflected in the composition of the effective reproductive ratio. Regardless of acquisition probability, transmission fitness, or recent infection ratio, high levels (> 10%) of drug resistance were unlikely to emerge within 50 years if, among all cases of DR-TB that were detected as having TB, 85% could be successfully treated.

**Conclusions:** These results suggest that (i) short-term surveillance cannot predict long-term emergence of drug resistance after launch of novel first-line TB drug regimens; and (ii) ensuring high treatment success of drug-resistant TB through early diagnosis and appropriate second-line therapy can mitigate many epidemiological uncertainties and make rapid emergence of drug-resistant TB very unlikely.



### PD-962-31 Drug resistant tuberculosis patient characteristics as reported in the South African electronic drug-resistant tuberculosis register

K Schnippel,<sup>1</sup> M Kamkuemah,<sup>1</sup> R Berhanu,<sup>1,2</sup> K Shearer,<sup>1</sup> m Naicker,<sup>3</sup> N Ndjeka.<sup>4</sup> <sup>1</sup>Health Economics and Epidemiology Research Office, Department of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, <sup>2</sup>TB Focal Point, Right to Care, Johannesburg, <sup>3</sup>National TB Programme, Wamtechnology, Pretoria, <sup>4</sup>National TB Programme, National Department of Health, Pretoria, South Africa. e-mail: kschnipp@gmail.com

**Background:** The South African Electronic Drug Resistant Tuberculosis (DR-TB) Register (EDRWeb) is the national reporting database in use since 2009.

**Method:** We performed a retrospective, de-identified descriptive analysis of patient-level data reported in the EDRweb in order to inform policy and management of DR-TB in South Africa.

**Results:** 37,963 patients were registered in EDRweb from 1 January 2009 – 30 September 2013. Transfers in from other DR-TB treatment sites (n=372) were excluded as they could not be matched to the initial registration. Entries missing registration number (n=45) and gender (n=140) were dropped for insufficient information. 5,769 registered entries (15.2%) were excluded for lack of treatment start date. The 31,730 DR-TB patients on treatment had a median age of 35.3 years (IQR: 27.8–43.7); 6.2% (n=1,958) were under 15 years old. 52.3% (n=16,609) were male. 1.3% had extrapulmonary (EP) TB. Multi-drug resistant (MDR) TB occurred in 75.5%; 9.0% had extensively drug-resistant (XDR) TB; others were diagnosed with mono- or poly- DR TB. There was no prior history of first or second line TB treatment in 29.5% (n=9,493) of patients. Smear microscopy and culture at DR-TB treatment initiation was missing or unknown for 58.1% and 57.8%, respectively; 24.1% (n=7,641) were smear positive and 41.3% (n=13,100) were culture positive. HIV status was missing or recorded as unknown for 28.6% (n=9,063); 15,848 (49.9% of all entries or 67.0% of those with HIV status) were reported as HIV-infected, of which 83.9% were

recorded as being on HIV anti-retroviral therapy. Registration was highest in 2012 (25.6% of entries, n=8,121). Only 3,719 (11.7%) were registered in the first 9 months of 2013. KwaZulu Natal (KZN) was the single largest province with 28.4% of entries. Between KZN, Western Cape and Eastern Cape, these three of the nine South African provinces accounted for 61.7% of all DR-TB patients reported since 2009.

**Conclusions:** The significant missingness of many key variables within the South African national DR-TB reporting system, including smear microscopy and culture results at treatment initiation, is a key limitation to using this dataset to inform policy and guidelines. The small number of EPTB and paediatric TB patients and the lower reporting numbers for 2013 may also be a result of missingness at a site level; with reporting lagging behind decentralization of treatment sites and improved diagnosis of DR-TB in South Africa.

### PD-963-31 The causing of MDR-TB patients not accepting treatment

Z Xu,<sup>1</sup> D Gong,<sup>1</sup> C Zhang.<sup>1</sup> <sup>1</sup>TB Control Department, Hunan TB Control Institution, China. e-mail: evan.xu21@gmail.com

**Background:** There were 1091 MDR-TB patients had been detected through drug sensitive test (DST) in designated MDR-TB hospital of Hunan province, China, from January 1, 2012 to December 31, 2013. According to the provincial MDR-TB control guideline, all patients have to accept a 24 months treatment regime including first 4–6 weeks hospitalization. However, only 419 cases started the treatment to the end of March 2014, the other 672(61.6%) patients did not receive any proper treatment although following up and tracing efforts were made by all level TB control personnel. This study intends to identify the reasons of patients who did not receive MDR-TB treatment

**Design/Methods:** The designated MDR-TB hospital would inform the county CDC staff about MDR-TB patients' information once the diagnosis was confirmed. CDC's personnel and/or the village doctors were due to trace patients to the designated hospital for treatment, and feedback the tracing results to hospital; then hospitals would record patients' treatment information and feedback to the county CDC every month. The patients not receiving treatment would be traced by county CDC as well as newly diagnosed MDR-TB patients, until all MDR-TB patients started treatment. The information feedback was done mainly through e-mail, QQ, MSN and telephone and the tracing procedure and results were recorded, collected and analyzed.

**Results:** Among the 672 cases who did not started MDR-TB treatment, the identified causes were the economic hardship (386, 57.4%), moving to other city for work (126, 18.8%), lacking of detail address and telephone number (47, 7%), refusing treatment (32, 4.8%), with other severe illness or too weak to be hospitalized (28, 4.2%), and death (14, 2.1%).



**Conclusion:** The leading causing of patients not accepting MDR-TB treatment was economic hardship in Hunan province. In addition, moving to other city for work, unknown contact information, refusing treatment, too weak or with other severe diseases and death were other important reasons. Therefore, reducing treatment expense and increasing the coverage of health insurance, improving the MDR-TB treatment affordability and availability need to be addressed to enhance the proportion of patients of accepting MDR-TB treatment.

#### PD-964-31 Household infection control: are we ready for community DR-TB care in Nigeria?

M Odo,<sup>1</sup> A Adamu,<sup>1</sup> B Olusola-faleye,<sup>1</sup> H Khamofu,<sup>1</sup> K Ochei,<sup>1</sup> K Torpey,<sup>1</sup> T Badru,<sup>2</sup> J O Obasanya.<sup>3</sup>

<sup>1</sup>Prevention, Care and Treatment, FHI360, Abuja,

<sup>2</sup>Monitoring and Evaluation, FHI360, Abuja, <sup>3</sup>National TB and Leprosy Control Program, Federal Ministry of Health, Abuja, Nigeria. Fax: (+234)94615511.

e-mail: mikeodo1@yahoo.com

**Background and challenges to implementation:** Globally, Nigeria is 10<sup>th</sup> among the 22 highest burdened TB countries, with an estimated prevalence of drug-resistant TB (DR-TB) of 2.9% among new cases and 14.3% among retreatment cases. Nigeria has limited treatment facility and has adapted the national guidelines to discharge DR TB patients into the community once they are clinically stable. This portends a huge need for Community-level infection control practices. We set out to assess the homes of the patients from the Lagos and Kano treatment facilities

**Intervention or response:** A descriptive study was conducted to assess the homes and household contacts of 61 DR-TB patients treated in Lagos and Kano treatment centers from inception. A trained tracking team made up of health workers assessed the homes and interviewer-administered questionnaires were used to assess the TB infection control knowledge of 236 close contacts of the patients. The household contacts were screened for TB and sputum was collected from symptomatic contacts for Gene Xpert assay. Verbal consent was obtained from each patient and GPS coordinates of each house were obtained and plotted on the maps of Lagos and Kano States

**Results and lessons learnt:** A total of 236 contacts were assessed; 52.1% had no knowledge of TB infection control, 9.3% had some knowledge, while 38.6% had good knowledge. Majority (73.7%) of the houses had no cross ventilation with 1 Window per Room (WPR) and were also overcrowded with mean Person per Room (PPR) of 3.4. 17.8% of the contacts were symptomatic while three contacts were diagnosed to have DR-TB.

**Conclusions and key recommendations:** The assessment revealed poor knowledge and practice of TB infection control among close contacts of the DR-TB patients thus necessitating a community level infection control guideline from government TB programs as well as strengthening infection control education by non-governmental organizations.

#### PD-965-31 e-TB manager implementation in Nigeria: progress and challenges

J O Obasanya,<sup>1</sup> LF Reciolino,<sup>2</sup> R Eneogu,<sup>1</sup> O Emmanuel,<sup>3</sup> A Adeyomoye,<sup>3</sup> O Oluwadare,<sup>3</sup> B Woldemariam,<sup>4</sup> P Suarez.<sup>2</sup>

<sup>1</sup>Ministry of Health, National Tuberculosis and Leprosy Control Program (NTBLCP), Abuja, Nigeria;

<sup>2</sup>Management Sciences for Health (MSH), Centre for Health Services (CHS), Arlington, VA, USA; <sup>3</sup>TB CARE I, (MSH), Abuja, Nigeria; <sup>4</sup>MSH, CHS, Addis Ababa, Ethiopia.

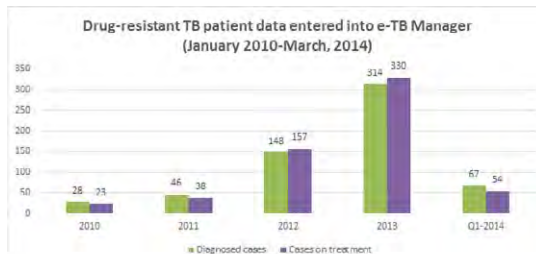
e-mail: reciolino@gmail.com

**Background** In 2011, Nigeria's National Tuberculosis and Leprosy Control Program (NTBLCP) expressed interest in establishing an electronic recording and reporting system to track data related to TB and drug-resistant TB (DR-TB) cases, drugs, and commodities. To achieve this goal, NTBLCP asked the USAID-funded TB CARE I project to implement e-TB Manager (e-TBM) in Nigeria. E-TBM is a web-based tool that integrates data across all aspects of TB and DR-TB control, including information on patients, medicines, laboratory testing, diagnosis, treatment, and outcomes.

**Methods** To implement e-TBM, TB CARE I and the NTBLCP provided 55 health facilities with computers and modems, trained 150 staff to use e-TBM, established a permanent monitoring system, and provided support to all implementing sites. These steps took place between 2010 and 2013 and involved the patient monitoring components of e-TBM. In January 2014, the partners implemented the medicine monitoring component and trained staff to enter drug supply data on monthly basis.

**Results** From January of 2010 to March of 2014, the trained staff entered data into e-TBM on 603 confirmed DR-TB cases. These 603 patients represented 90% of all DR-TB cases that were reported through the national, paper-based reporting system during this time period. Among these patients, 602 started DR-TB treatment and were monitored through e-TBM. Each year, staff tracked a larger quantity of DR-TB patients than the year before (see Graph). E-TBM implementation has allowed the NTBLCP to remotely monitor DR-TB data from health facilities all over the country. This data provides key information for decision making and is accessible at all times through a cloud server. Involving the NTBLCP in the implementation process encouraged staff uptake of the system and supported improvements in TB case and drug data management. Changing from a paper-based reporting system to an electronic, web-based system was challenging for field staff and some had to develop computer skills before they were able to use e-TBM.

**Conclusions** E-TBM implementation progress has been consistent over the past three years. Health facilities are gradually incorporating e-TBM data entry into their daily, routine tasks. The NTBLCP will continue to support e-TBM implementation to improve Nigeria's TB and DR-TB quantification processes, data management, and patient monitoring.



## 41. CASE-FINDING: SPECIAL INTERVENTIONS

### PD-966-31 Symptomatic screening and computer-aided radiography for active-case finding of tuberculosis: a prediction model for TB case detection

A Zaidi,<sup>1</sup> N Khalid,<sup>1</sup> R Philipsen,<sup>2</sup> B Van Ginneken,<sup>2</sup> S Khawaja,<sup>1</sup> A Khan.<sup>1</sup> <sup>1</sup>International Health, Interactive Research & Development, Karachi, Pakistan; <sup>2</sup>Department of Radiology, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands.  
e-mail: nashwa.khalid@irdresearch.org

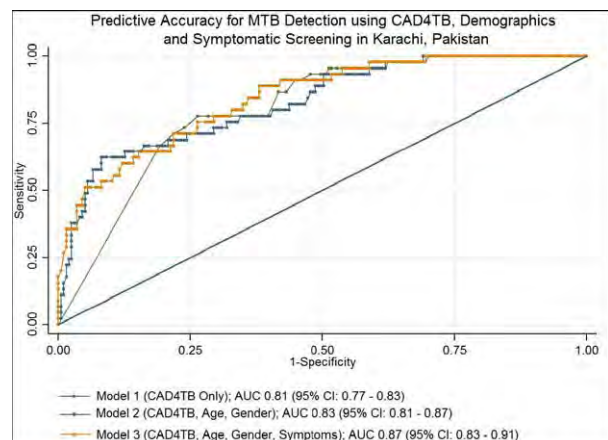
**Background:** Scale-up of rapid tuberculosis (TB) diagnostics through GeneXpert MTB/Rif has supported active-case finding for TB in high burden countries and is being utilized to increase case-notification as part of the TB Reach initiative. However, the high cost per test necessitates investigation of screening approaches that can better rationalize the use of GeneXpert. The aim of this study was to investigate predictive accuracy and validation of a prediction model based on symptomatic screening and computer-aided detection (CAD) radiography compared with GeneXpert MTB/Rif for TB case detection in a high TB burden setting.

**Methods:** Screening for TB was carried out at private Family Practitioner clinics in three low-income towns of Karachi, Pakistan. Suspects for TB were identified on the basis of the presence of cough, fever, hemoptysis, weight loss and night-sweats and were referred for chest X-ray (CXR). All CXRs were analyzed by CAD4TB v3.07 (Diagnostic Image Analysis Group, Nijmegen, The Netherlands), a CAD system developed for TB diagnosis. This system computes an abnormality score (0–100) by analyzing the shape, symmetry and texture of the lung fields. GeneXpert testing was carried out on all cases where good quality sputum samples could be obtained.

**Results:** 324 consecutive cases referred for CXR and with sputum samples were recruited into the study. Prediction models were constructed using logistic regressions with TB detection as a binary outcome variable and sequentially adding CAD4TB scores, demographics and symptomatic screening as explanatory variables. The final prediction model was constructed using backwards stepwise Akaike's Information Criteria multiple logistic regression and included CAD4TB scores (OR 1.08, 95% CI: 1.04 - 1.12), cough >2 weeks (OR 3.10, 95% CI:

1.09 - 5.51), age (OR 0.97, 95% CI: 0.95 - 0.98) and gender (OR 1.01, 95% CI: 0.73 - 1.38). The area under receiver operator curve (AUC) for the model was 0.87 (95% CI: 0.83 - 0.91). The AUC of a split-set cross validation model for assessing internal validation was 0.84 (95% CI: 0.78 - 0.89). The model was appropriately calibrated (Hosmer-Lemeshow  $\chi^2$  8.99, p-value 0.45).

**Conclusion:** Combining CAD4TB scores with patient demographics and symptomatic screening data offers high predictive accuracy for TB. Multi-center studies are required for external validation of the model in order to provide appropriate evidence for its use in screening in high TB burden settings.



### PD-967-31 Effectiveness evaluation of chest x-ray screening in specific populations

Y-T Liao,<sup>1</sup> J-H Cheng,<sup>1</sup> CB Hsu,<sup>1</sup> Y-F Huang,<sup>1</sup> C-H Chen.<sup>1</sup> <sup>1</sup>Ministry of Health and Welfare, Centers for Disease Control, Taipei, Taiwan. Fax: (+886) 2339 36149.  
e-mail: yuntsan@cdc.gov.tw

In Taiwan, the target population of chest X-ray (CXR) screening for pulmonary tuberculosis evolved over the past decades, from universal screening to targeted screening such as residents in mountainous area and economically disadvantaged population. Effectiveness evaluation of CXR screening was done by comparison of screening list from local health bureaus during 2011–2012 to list of nationwide tuberculosis (TB) cases detected in 2012 by active case finding in mountainous districts and economically disadvantaged people, respectively. TB case detection rates were similar in both years among mountainous people and not related to CXR examination in previous year, both exceeded 4-times than the national rate (previous examination status unknown, 289.4/100,000; previously unexamined, 230.8/100,000; and previously examined, 248.6/100,000). TB detection rate from CXR screening in disadvantaged people during 2010–2012 was 2X higher than national average (91.0/100,000 in 2010; 205.7/100,000 in 2011 and 113.2/100,000 in 2012). CXR screening strategy was proven to be very successful and effective in active case finding among either mountainous

or economically disadvantaged people, and should be continuously endorsed by Taiwan CDC to reduce the burden of TB in these high-risk populations.

#### PD-968-31 Contribution of NGO health facility in TB control: an experience from Rawthamkuppam of Villupuram District in Tamilnadu, India

S Kirani,<sup>1</sup> M Puthenchirayil,<sup>1</sup> P Varghese,<sup>1</sup> G Singh,<sup>1</sup> s.j. Jairaj,<sup>2</sup> Sr Anastasia,<sup>2</sup> R Sudhakar.<sup>3</sup> <sup>1</sup>Public Health, Catholic Bishop Conference of India Coalition for AIDS and Related Diseases, New Delhi, <sup>2</sup>NGO, Hemerijckx Rural Health Centre, Rawthamkuppam, <sup>3</sup>Public Health, District TB Centre, Villupuram, India.  
e-mail: drsumashivakumar@gmail.com

**Background and challenges to implementation:** India contributes 25% of the global TB burden\*. India being a second most populous country in the world, private health sector is the major partner in public health programme. Several studies indicated that almost 50% of the TB patients seek support from other than public health facility including general practitioners, private hospitals, NGO health facilities and rural medical practitioners. Revised National TB control Programme has taken steps to achieve "Universal access to TB care and treatment for all," to reach the unreached through synergising the efforts of all partners and stakeholders. The Govt of India developed special schemes as per the ITCs to involve private sector through financial assistance in year 2008, one of the important schemes is microscopy centre, responsible to provide AFB microscopy and treatment services.

**Intervention-** Hemerijckx Rural Health centre, a catholic health facility was established in Rawthamkuppam in Villupuram district in Tamilnadu. This centre was recognized by the District TB control and established a microscopy centre in 2012 in Mailam TB unit. CBCI CARD RCC project facilitated to sign MoU under NGO-PPM scheme with annual financial grant. The centre follows RNTCP standard algorithm for the managing cough symptomatic and TB cases.

**Results and lessons learnt:** Data was collected from the lab register of all 5 DMC of Tuberculosis unit for year 2012 and 2013. out 5 microscopy centre, 4 belong to public health system and 1 from NGO sector. Hemerijckx Rural Health centre contributed 26.5% and 29.3% of the TB cases in the TB unit in 2012 and 2013 respectively.

#### Results-

Year	Number of TB suspects examined in Mailam TB unit	Number of TB suspects examined in Hemerijckx Rural Health centre	Number of TB suspects found to be positive in Mailam TB unit	Number of TB suspects found to be positive in Hemerijckx Rural Health centre
2012 (Jan- Dec)	2380	696 (29.2%)	166	44 (26.5%)
2013 (Jan- Dec)	2182	950 (43.5%)	174	51 (29.3%)

**Conclusions** TB case notification can be improved with the involvement of other than public sector. There is need to involve private sector in TB control programme to achieve universal accessibility for TB care. References \*Annual status report 2014

#### PD-969-31 Active and semi-active case finding to increase tuberculosis case identification in rural Bangladesh: a cluster randomised trial

S A S Hossain,<sup>1</sup> N L Huq,<sup>1</sup> N Haque,<sup>1</sup> R Gazi,<sup>1</sup> MD Iqbal,<sup>1</sup> A Ahmed,<sup>1</sup> H Kabir,<sup>1</sup> K Zaman.<sup>1</sup> <sup>1</sup>TB and Leprosy, International Centre for Diarrhoeal Disease Research, Bangladesh (icddr), Dhaka, Bangladesh. Fax: (+880)2 8823963. e-mail: shahed@icddr.org

**Background:** TB burden is high in Bangladesh, particularly in rural areas. The case notification rate of the new smear positive pulmonary (NSP) TB under National Tuberculosis Control Programme (NTP) did not change much since 2006. We evaluated two strategies: active case finding (ACF) and semi active case finding (SACF) to find their impact on the identification of NSP TB among adults ( $\geq 15$  years). The study was carried out in Chakaria sub-district, a south-eastern rural area of Bangladesh where a sample based health and demographic surveillance system (HDSS) has been operating since 1999.

**Methods:** This was a community based cluster randomized control trial to compare the effectiveness of two new strategies with the standard NTP programme. Clusters of unions (one union having between 20000–24000 population) were randomized to receive either ACF or SACF for one year at quarterly cycles of 90 days in 2013. ACF included house to house symptom screening (cough  $\geq 2$  weeks) and referral, while SACF consisted of contact tracing of index cases at community and organizing "cough camp" in each union. At the cough camp sputum smears were prepared immediately after collection from the adult suspects who attended the camp. The primary outcome was to compare the area wise NSP TB notification rate per 100,000 population with that of the control unions implementing the passive case identification strategy under NTP.

**Results:** Under ACF 39252 adults were screened from 12505 households and 71 NSP TB cases were identified throughout year from the areas under this strategy. Under SACF 32 cough camps were organized where 692 suspects were examined and 26 NSP TB cases were identified at that point of care. At the same time contact tracing was conducted in 895 households and 6 cases were identified. In total 90 NSP TB cases were identified from the areas under SACF. The control unions identified 66 NSP cases in the same period. The case notification rates were 97/100,000, 134/100,000 and 102/100,000 population in the ACF, SACF and control unions respectively. A slight higher proportion of female cases was also identified under SACF.

**Conclusions:** The study findings indicate that 'cough camp' could be an effective supplementary strategy to the existing DOTS programme in finding undetected cases



and more female cases. Particularly in rural areas this approach could yield more case identification than house to house search or passive case detection.

#### **PD-970-31 High yield of contact investigation among household contacts of smear-positive pulmonary tuberculosis patients using GeneXpert MTB/RIF in Ethiopia**

B Tessema,<sup>1</sup> B Anagaw,<sup>1</sup> F Moges,<sup>1</sup> M Melese,<sup>2</sup> Y Kassie,<sup>2</sup> B Girma,<sup>2</sup> S Yifru,<sup>3</sup> YK Haile,<sup>4</sup> M Melese.<sup>1,2</sup>

<sup>1</sup>University of Gondar, Department of Medical Microbiology, Gondar, <sup>2</sup>HEAL TB project, Management Sciences for Health (MSH), Addis Ababa, <sup>3</sup>Pediatrics, University of Gondar, Gondar, <sup>4</sup>Health, USAID, Addis Ababa, Ethiopia. e-mail: bt1488@yahoo.com

**Background:** In Ethiopia, the National Tuberculosis Program (NTP) strategy of case notification is mainly on passive case finding whereby it only identifies patients coming to health facilities with sign and symptom complexes of tuberculosis (TB) by smear microscopy, X-ray, pathology or using the WHO clinical algorithms. Active case finding through contact screening is not a usual practice of the health care system in Ethiopia. Therefore, this study was aimed to determine the yield of TB contact investigation among household contacts of smear positive pulmonary tuberculosis patients using smear microscopy and GeneXpert MTB/RIF in North-west Ethiopia.

**Design/Methods:** Household contacts of patients with smear positive pulmonary tuberculosis were recruited at nine TB diagnostic health facilities in North Gondar zone of Amhara region between May 2013 and April 2014. Clinical screening of contacts was conducted in two weeks time after the index case diagnosed and started treatment. Sputum microscopy and GeneXpert tests were concurrently performed for presumptive tuberculosis cases.

**Results:** In this interim research period, 77 sputum smear positive TB patients were diagnosed in the nine health facilities. A total of 202 household contacts of 77 index cases were registered and screened for TB. Among 202 household contacts, 9 were diagnosed with tuberculosis (4,455 cases per 100,000 population). Of these, 2 were sputum smear microscopy positive, 2 were children who were unable to give sputum but diagnosed as per the national TB diagnostic algorithm and 5 were sputum smear microscopy negative but GeneXpert test positive.

**Conclusion:** Household contacts of patients with potentially infectious forms of tuberculosis have a high prevalence of TB disease. We recommend implementing contact investigation as part of the national TB case notification strategy, and a more simplified but sensitive point of care test development would be critical to reduce the cost and current implementation challenges of GeneXpert machines.

#### **PD-971-31 Feasibility study of the WHO recommendations for TB contact investigation in low- and middle- income countries: a pilot in a rural district, Zambia**

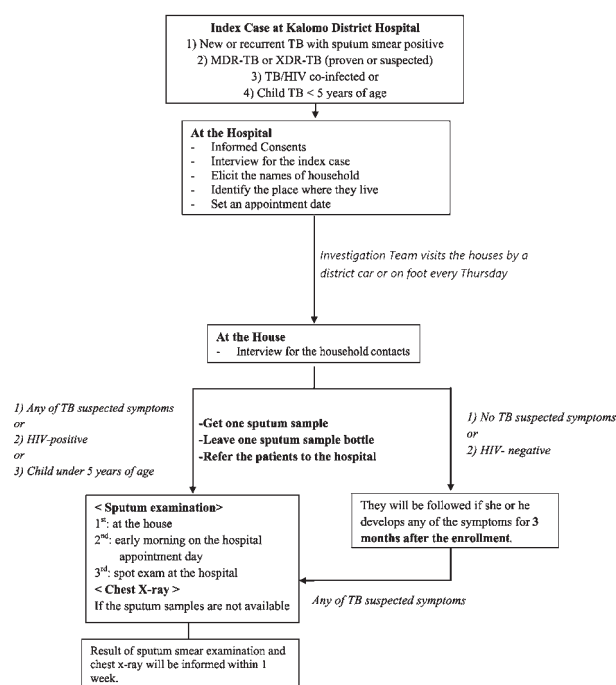
S Miyano,<sup>1</sup> V Chipeta,<sup>2</sup> K Komada,<sup>1,3</sup> K Chibwe.<sup>2</sup> <sup>1</sup>Bureau of International Cooperation, National Center for Global Health and Medicine (NCGM), Tokyo, Japan; <sup>2</sup>Kalomo District Community Health Office, The Ministry of Community Development, Mother and Child Health, Zambia, Kalomo, <sup>3</sup>SHIMA Project, The Ministry of Health, Zambia and Japan International Cooperation Agency (JICA), Lusaka, Zambia. Fax: (+260) 211 257 728. e-mail: s-miyano@it.ncgm.go.jp

**Background** There are few published studies for contact investigation of TB in Zambia as well as other low- and middle- income countries (LMICs). The "Recommendations for investigating contacts of persons with infectious tuberculosis in LMICs" were published by the WHO in December 2012. Our study aimed to assess the feasibility of the WHO policy in a rural district, Zambia.

**Intervention** Sputum smear positive pulmonary TB patients, who were registered at the Kalomo District Hospital between September and November 2013 and who lived under the hospital coverage area, were enrolled. The index cases were interviewed to elicit the household contacts. Investigation team composing of one nurse, one treatment supporter and one laboratory staff visited their house by a district vehicle and conducted interviews to them. The contacts with any of TB suspected symptoms, HIV-positive or under 5 years old were asked to go to the hospital for further examinations. The contacts without any symptoms were followed again 3 months after the first visit. The interviews were conducted with the standardized questionnaires attached in the recommendations.

**Results** Thirty-eight pulmonary TB cases were registered in the hospital. Of them, 12 cases were enrolled as index cases. The median age was 30.5 years and half were female. Eleven (91.7%) were categorized as new TB, 7 (58.3%) had cavity on chest x-ray and 6 (50%) were HIV-positive. Sixteen contacts in their households were evaluated by the team. Their median age was 13.0 years (half of them were less than 15 years old). Sixteen had any of TB suspected symptoms, 4 were HIV-positive (two of them also had at least one symptom) and 8 were under 5 years old. A total of 26 contacts needed further investigations in the hospital. Of them 22 were screened for sputum smear or chest x-ray. Finally one adult and child contacts were diagnosed as TB. It accounted for 3.3% of all contacts or 7.7% of further investigated.

**Conclusions** The WHO policy could play an important role in introducing clear vision and simple procedure of contact investigation that is not indicated in the Zambian guidelines. However, extra budget for fuel to visit households, shortage of human resources in investigation team, transportation for contacts who need further investigation in the hospital could be big barriers in practice. More cases need to be enrolled in the study to conclude the feasibility and yield of TB contact investigation in local settings.

**Algorithm of TB contact investigation**

### PD-972-31 Intensified community-based active tuberculosis case finding in Nepal: challenges and lessons learnt

S Gurung Pradhan,<sup>1</sup> M Caws,<sup>2</sup> R Dhital,<sup>1</sup> P Shrestha,<sup>3</sup> A Khatiwada,<sup>1</sup> R Sha.<sup>1</sup> <sup>1</sup>Health Programme Planning and Implementation, The Britain Nepal Medical Trust, Kathmandu, Nepal; <sup>2</sup>Clinical Sciences, Liverpool School of Tropical Medicine, Pembroke Place, Liverpool, UK; <sup>3</sup>Oxford University Clinical Research Unit, Patan Academy of Health Sciences, Patan, Nepal. Fax: (+977)014439108. e-mail: director@bnmt.org.np

The National TB Programme (NTP) of Nepal is on track to reach Millennium Development Goal targets for reduction in TB prevalence and mortality rates, but the TB incidence has not declined. The National TB case detection rate was 73% for two consecutive years-2011.2012 and increased to 78% in 2013. The Britain Nepal Medical Trust (BNMT) implemented intensified community based active TB case finding activities under TB REACH, Wave 2 funding in fifteen districts of Eastern and Central Nepal to support the NTP to meet the target of 82% case detection rate set by the National Strategic Plan, 2010- 2015. During the sixteen months of project implementation, January 2013 to April 2014, a programme of interventions to improve case detection were implemented to include contact tracing, mobile microscopy camps and initial defaulter tracing through training and mobilisation of Female/ Community Health Volunteers. Project data was regularly collected and analysed using the standard tools used by National Tuberculosis Programme in combination with the specific project information forms developed by the BNMT. Regular monitoring and supervision of project activities were done at various levels to ensure the quality of the activities and their improvement. From 7,499

index TB cases identified for contact tracing, 51,318 suspected contacts were prioritised for sputum smear microscopy, 48,318 of them provided three sputum samples and 1,938 new cases of active TB were diagnosed (4.0%). Two initial defaulters were traced and initiated on treatment. On an average, 6.4 symptomatic contacts per index case were screened for TB detection. Several challenges were encountered, including incorrect addresses in treatment records hampering tracing of index patients, reluctance of prioritised contacts in providing sputum samples (5.0%), access to microscopy services, and ensuring timely specimen transportation. Twenty- seven symptomatic contacts were screened to identify one new TB case in the community. This project demonstrates that active case finding approaches can be successfully implemented in Nepal and can significantly contribute to increasing National TB case detection rate and early diagnosis to reduce its severity and transmission. A major challenge remains the continuity of effective interventions like these through the national programme.



### PD-973-31 Could better access to CXR improve tuberculosis notifications in community-based active tuberculosis case finding in Cambodia?

N Lorent,<sup>1,2,3,4</sup> C Kong,<sup>2,4</sup> R Pe,<sup>2</sup> W De Rijk,<sup>5</sup> S Thai,<sup>2,4</sup> J Van Griensven,<sup>1,2</sup> T Kim,<sup>6</sup> L Lynen,<sup>1</sup> L Rigouts.<sup>5</sup> <sup>1</sup>Clinical Sciences, Institute of Tropical Medicine, Antwerp, Belgium; <sup>2</sup>Infectious Diseases, Sihanouk Hospital Center of HOPE, Phnom Penh, Cambodia; <sup>3</sup>Clinical Sciences, Institute of Tropical Medicine, Antwerp, Belgium; <sup>4</sup>Infectious Diseases, Sihanouk Hospital Center of HOPE, Phnom Penh, Cambodia; <sup>5</sup>Mycobacteriology Unit, Institute of Tropical Medicine, Antwerp, Belgium; <sup>6</sup>Mycobacteriology Laboratory, Sihanouk Hospital Center of HOPE, Phnom Penh, Cambodia. e-mail: natalielorent@yahoo.com

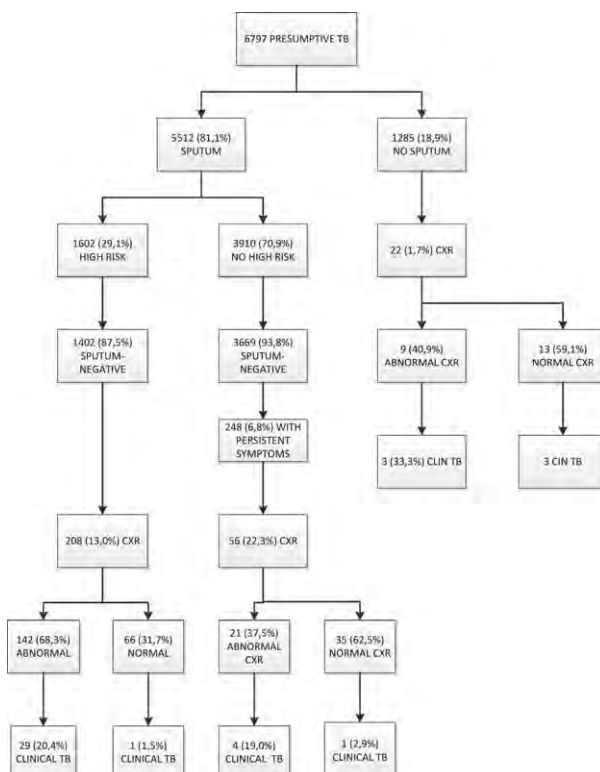
**Background:** Chest radiography (CXR) has a key role in detecting undiagnosed active tuberculosis (TB). However, the optimal use of CXR in active case-finding (ACF) remains to be determined as to its role as an (initial) screening or an add-on test. Moreover, access to and quality of CXR in high TB burden countries can be hazardous. We evaluated the uptake and yield of CXR as an add-on test for smear- and Xpert-negative presumptive TB patients in community-based ACF.

**Methods:** Prospective cohort study within community-based ACF in poor urban settlements of Phnom Penh,

Cambodia. All symptomatic individuals (any cough, fever, night sweats or weight loss) had sputum examined. Presumptive TB cases with negative sputum results (smear and Xpert) proceeded to CXR if (1) at increased risk of drug-susceptible/resistant TB (presumptive or confirmed HIV, previous TB history, TB contact) or (2) non-high risk but with persistent symptoms. We also recommended CXR for symptomatic subjects unable to expectorate. CXR required referral to hospital, where an experienced TB physician decided on patient management based on clinical and radiological findings ("clinical TB").

**Results:** Between 1/4/2013-1/2/2014 we enrolled 6797 presumptive TB cases. Of the 5512 (81,1%) who submitted sputum, 1402/1602 (87,5%) high-risk patients had negative sputum investigations; 208/1402 (13,0%) went on to have a CXR. Of the 3910 non-high risk patients, 248/3669 (6,8%) were smear and Xpert-negative and 56 (22,3%) proceeded to CXR. CXR was abnormal in 142/208 (68,3%) high-risk (98 with previous TB history) and 21/56 (37,5%) non-high risk patients. Clinical TB was diagnosed in around 20% for both groups (29/142 (20,4%) and 4/21 (19,0%), respectively). Of the 1285 symptomatic individuals who were unable to provide sputum, 22 (1,7%) were referred for CXR. CXR was abnormal in 9 (40,9%) and a decision to start TB treatment was made in 3 (33,3%).

**Conclusion:** In our community-based TB case-finding project referral for (non-mobile) CXR was challenging and uptake was limited. In those referred, abnormal CXR findings were common and contributed substantially to the diagnosis of smear-negative TB. Further research is warranted to explore how to overcome the barrier to access CXR.



### PD-974-31 Health counseling and testing and TB screening provide a vital link between clinics and communities for better health outcomes in Eden district, South Africa

M A Uys,<sup>1,2</sup> A Volschenk,<sup>1,2</sup> S Smit.<sup>3</sup> <sup>1</sup>Technical assistance, Foundation for Professional Development, Tshwane, <sup>2</sup>Technical assistance, The Aurum Institute, Johannesburg, , <sup>3</sup>Eden district, Department of Health, George, South Africa. Fax: (+27)11 326 3232. e-mail: margotu@foundation.co.za

**Background:** Health counseling and testing (HCT) provides a vital gateway to entering health care services. Lack of public transport, stigmatization of TB and HIV amongst communities are often barriers to accessing health care services. Providing basic screening for HIV and other chronic conditions and HIV testing in non-medical sites within communities in Eden district, Western Cape, is an alternative approach to preventative care supported by THAT'SIT (Tuberculosis, HIV, AIDS Treatment Support and Integrated Therapy), a PEPFAR funded technical support partner since 2007 in this area. Eden district (population approx 560 000) is characterized by many informal settlements (21% squatter communities) and 12% unemployment rate in rural and peri-urban settings. TB incidence is 844/100,000 one of the highest in the country with a <40% HIV co-infection rate.

**Intervention:** THAT'SIT introduced 4 mobile clinics to visit non-medical sites in 4 sub-districts in Eden. A nurse, data capturer and counselor accompany the mobile. Basic prevention services are provided, i.e. screening for TB, cervical cancer, hypertension, diabetes as well as HCT and family planning. The mobiles visit predetermined sites in consultation with the Department of Health. These sites may range from farms, industries, factories, off-road sites within the informal settlements, and serve amongst others high risk populations including commercial sex workers. All positive patients or those requiring more extensive care are referred to the nearest clinic for follow-up. HIV positive patients are linked to community health workers and other support groups within the communities after health consultation to address issues related to stigma.

**Results:** During the first quarter of 2014 a total of 6057 patients were attended to on the 4 mobiles, 5731 were screened for TB (94%), 210 were referred for further TB investigation, 5586 (92%) received HCT with results. Only 50 patients (.082%) tested HIV positive. Family planning was provided to 803 women and 39 had PAP smears for cervical cancer screening. In total 337 patients were referred to the nearest clinic and linked to a relevant support group for further medical and social management and care.

**Conclusions:** Health services can benefit by the provision of preventative services at non-medical service points to circumvent stigma and other issues that prevent clients from entering the primary health care services.



### PD-975-31 Cost-effectiveness analysis of household contact investigation and community active case finding for tuberculosis case detection in Urban Africa

J Sekandi,<sup>1,2</sup> K Dobbin,<sup>1</sup> J Oloya,<sup>1</sup> A Okwera,<sup>3</sup> CC Whalen,<sup>1</sup> P Corso.<sup>4</sup> <sup>1</sup>Epidemiology and Biostatistics, University of Georgia, Athens, GA, USA; <sup>2</sup>Epidemiology and Biostatistics, Makerere University School of Public Health, Kampala; <sup>3</sup>Medicine, Makerere University School of Medicine, Kampala, Uganda; <sup>4</sup>Health Policy and Management, University of Georgia, Athens, GA, USA. e-mail: jsekandi@musph.ac.ug

**Background:** Case detection by passive case finding (PCF) strategy alone is inadequate for detecting all tuberculosis (TB) cases in high burden settings such as Africa. Community Active Case Finding (ACF) and Household Contact Investigations (HCI) are effective case detection alternatives but empirical evidence of their cost-effectiveness is sparse. The objective of this study was to determine if ACF and HCI compared to PCF alone represent cost-effective alternative strategies in urban African.

**Design/Methods:** A static decision modeling framework was used to examine the costs and effectiveness of three TB case detection strategies; PCF alone, PCF+ACF, and PCF+HCI. Probability and cost estimates were obtained mainly from National TB program data, primary studies conducted in Uganda and published literature. The analysis was performed from the societal perspective over a 1.5 year timeframe. The main effectiveness measure was the number of true TB cases detected and the outcome was incremental cost-effectiveness ratios (ICERs) expressed as cost in 2013 US\$ per true TB case detected.

**Results:** Compared to PCF alone, the PCF+HCI strategy was cost-effective at a cost of US\$443.62 per additional true TB case detected but PCF+ACF was not cost-effective at US\$1492.95 per additional TB case detected. Sensitivity analyses showed that PCF+ACF would be cost-effective if the prevalence of chronic cough in ACF increased from 4% to 40% and the program costs for ACF reduced by 50%.

**Conclusion:** Under our baseline assumptions, the addition of HCI to an existing PCF program presented a more cost-effective strategy than the addition of ACF in the context of an African city. Therefore, implementation of household contact investigations as a part of the recommended TB control strategy should be prioritized.

### PD-976-31 Outcomes of tuberculosis contact tracing in a teaching hospital in Barcelona: an eight-years experience

L González,<sup>1</sup> MR Guerra,<sup>1</sup> L Muñoz,<sup>1</sup> J Dorca,<sup>2,3</sup> M Santin.<sup>1,3</sup> <sup>1</sup>Infectious Diseases, Bellvitge University Hospital-IDIBELL, Barcelona, <sup>2</sup>Pulmonary Medicine, Bellvitge University Hospital, Barcelona, <sup>3</sup>Clinical Sciences, University of Barcelona, Barcelona, Spain. e-mail: lauraml79@yahoo.es

**Background:** Investigation of contacts of patients with tuberculosis (TB) is a priority for TB control in high-

income countries. Although low rates of acceptance to treatment for latent TB infection (LTBI) have been reported, completion rates of preventive therapy (PT) may improve by a comprehensive programme in specialist TB Units (TBU).

**Methods:** Descriptive study of adherence to PT of TB contacts and reasons for its failure. The study included prospective-collected data of all referred contacts of pulmonary TB cases evaluated at the TBU of Bellvitge University Hospital in Barcelona (Spain) from 2005 to 2012. Evaluation consisted on baseline information gathering (demographics, relation with the index case and co-morbidities), clinical assessment, chest radiography and a test to detect LTBI. Patients with positive results were prescribed PT and then were thoroughly interviewed by a trained nurse in health education who would follow them up until the end of treatment. Regular reinforcement visits and active measures to promote and control adherence (questions regarding adverse events, abilities and understanding of treatment and checking isoniazid-metabolites in urine) were taken, as well as liver function tests at baseline and then in the first and third months.

**Results:** Of 2070 contacts screened, 666 (32.2%) were diagnosed with LTBI. 329 (49.4%) were men; mean age 41.9 (SD 16.4) years, and 243 (36.5%) had been born in high-TB endemic countries. 428 (64.3%) were close relatives of an index TB case, and 485 (72.8%) were prescribed six months of isoniazid therapy. Two patients refused PT and five finally did not need it, as the index case yielded non-tuberculous mycobacteria. Of 659 patients put on PT, 540 (81.9%) completed a whole-course. Reasons for not-finishing PT in 119 cases included: medical decisions (18), patient's decision for withdrawal (64), and irregular adherence to PT (24). Finally, thirteen patients were transferred to other health regions. Being foreign-born [OR 2.92 (95%CI 1.84-4.62)] and male [OR 1.64 (95%CI 1.03-2.62)] were found to be independently related with a lack of adherence. Age and type of PT regimen were not found significantly associated.

**Conclusion:** A comprehensive contact tracing evaluation by specialised staff can achieve satisfactory completion rates of PT. Reinforcement attitudes should be specifically strengthened in poor-adherent profiles, such as foreign-born individuals.

## 42. A POTPOURRI OF TB ISSUES

### PD-977-31 Patient and health system delays: health-care seeking behaviour among tuberculosis patients in Sana'a, Yemen, 2013

A Al-Shamiry,<sup>1</sup> N A A Thabit,<sup>2,3</sup> Abdu Al-Hamady.<sup>2,3</sup>

<sup>1</sup>Laboratory, National tuberculosis control program, Sana'a,

<sup>2</sup>Manger, National tuberculosis control program, Sana'a,

<sup>3</sup>Office, National tuberculosis control program, Sana'a, Yemen. Fax: (+96) 1-619213.

e-mail: al.shamiry1971@yahoo.com

**Background and challenges to implementation:** Early diagnosis and treatment is essential for effective tuberculosis (TB) control. Delay in TB diagnosis may increase infectivity and risk of death. This study was performed to assess delays in treatment of TB patients and its determinants in Sana'a city, Yemen.

**Intervention or response:** 439 newly registered TB patients attending TB treatment centers were enrolled. Data about health seeking behavior was collected by interview using a pre-structured questionnaire.

**Results and lessons learnt:** Of study group, 108 patients was smear positive pulmonary TB, 122 smear negative pulmonary TB, and 209 extra-pulmonary TB. The median patient delay for all types of TB was four weeks while the median of health service delay for pulmonary smear positive, pulmonary smear negative and extra-pulmonary was one, three and four weeks respectively. Patient delay (>3 weeks since onset of symptoms) was significantly higher among patient with lower standard living: Odds Ratio (OR)=1.9; 95% Confidence Interval (CI)=1.3-3.4; those who referred by private sectors: OR=1.6; 95% CI=1.1-2.4, and those who being self-employed: OR=2.5; 95% CI=1.0-6.0. Health service delay (>3 weeks since the first consultation) was significantly higher among those who; referred by government/co-operative sectors: OR=2.2; 95% CI=1.5-3.20; attended a general hospital: OR=4.5; 95% CI= 2.9-6.74, private physician: OR=1.9; 95% CI= 1.3-3.0; army hospital: OR=3.6; 95% CI= 1.49-8.64, and among patient with body exhaustion : OR=1.8 ; 95% CI= 1.19-2.6.

**Conclusions and key recommendations:** Patient and health service delay is high among Yemeni TB patients. Both patient and health services delay can be reduced with improvements of diagnostic facilities, trained staff, quality of services and by effective supervision.

### PD-978-31 Barriers in accessing TB control in Son La and Gia Lai provinces, Viet Nam: a qualitative and quantitative study

TH Truong Thi,<sup>1</sup> DC Nguyen.<sup>1</sup> <sup>1</sup>National TB program, National Lung Hospital, Hanoi, Viet Nam. Fax: (+84) 437 614 901. e-mail: thanhhuyenntp@gmail.com

**Background:** Detection of new smear positive TB case in the North West and Highland being lowest in the whole country. We conducted this study to determine the accessing barriers in TB control in those areas, along

with making recommendations in order to improve the patients' access to TB control, for increasing TB case detection rate.

**Design/Methods:** For the quantitative study, the structured questionnaire was applied to query 201 new smear positive TB patients who was enrolled consecutively to treatment from the first to the fourth quarter 2012. Chi square test was used to determine association between independent variables and group of patient that have delay at least 6 weeks in diagnosis and treatment at 95% confidence level. We also invited 14 officers from provincial, district and communal people committees, 2 staff from provincial health bureaus, 28 health care staff from provincial TB hospitals, district health centers, communal health posts, 40 TB and ex-TB patients and 32 TB suspects and healthy persons for in-depth interview. The content of interview then was analyzed to explore barriers of accessing to TB control.

**Results:** A total of 201 new smear positive TB patients participated in the study. The median total delay was 6 weeks (Inter-quartile range (IQR) 9 - 15). Factors associated with longer diagnosis and treatment included age ( $p=0.038$ ), education ( $p=0.002$ ), income ( $p<0.001$ ), payment scheme (0.001), the first healthcare facility that patient access ( $p<0.001$ ), place of sputum microscopy ( $p<0.001$ ), place of Xray ( $p<0.001$ ), place of treatment registration ( $p<0.001$ ), distance from patient house to healthcare facility ( $p<0.001$ ), knowledge ( $p<0.001$ ), perception( $p=0.014$ ). In-depth interview also indicated that complicated procedure of health insurance, poverty, language barrier, low education, poor knowledge and perception, limited awareness of community on TB control as well as low truth of the community on grass-roots level of healthcare system because of inadequate quantity and quality staff, poor and outdated infrastructure, equipments being barriers of TB control access.

**Conclusion:** Improving quality of grassroots healthcare system through training for staff, investment of equipments can make better truth of community. This could lead to reduce delay in TB diagnosis and treatment. Working with health insurance to get support of this system for TB diagnosis and treatment with simplified procedures could remove this barrier of community access to TB control.

Association between general characteristics of patients, TB control service, knowledge, TB perception and TB treatment delay

General characteristics	N	TB treatment delay (%)		P value
		<6 weeks	>= 6 weeks	
Average income				<0.001
<= 300,000 VND/month	38	28,9	71,1	
300,000-500,000 VND/month	26	23,1	76,9	
500,000-1,000,000 VND/month	54	50,0	50,0	
>1,000,000 VND/month	78	69,2	30,8	
Payment scheme				0.001
Out of pocket	29	41,4	58,6	
Health insurance	88	38,6	61,4	
Poverty card	83	66,3	33,7	
TB control service				< 0.001
Microscopy center patient accessed				
Provincial TB hospital	117	71,8	28,2	
District hospital	82	24,2	75,8	
Xray center that patient accessed				<0.001
Provincial TB hospital	112	72,3	27,7	
District hospital	46	26,1	73,9	
Private sector	16	25	75	

### PD-979-31 Increasing trend in non-tuberculous mycobacteria isolation in Shanghai, China: results from a population-based study

W Jie.<sup>1</sup> <sup>1</sup>Department of Tuberculosis Control, Shanghai Municipal Center for Disease Control and Prevention, Shanghai, China. e-mail: wu790429@sina.com

**Background:** Nontuberculous mycobacteria (NTM) are considered important opportunistic pathogen, which recently catches increasing attention due to its increased percentage of clinical isolation and/or infection worldwide. Few studies reported the isolation rate of NTM and related infection diseases in China. The objective of this study was to determine the trend and diversity of species of NTM isolated from pulmonary samples from patients with suspected TB, and to identify the characteristics associated with NTM infections in Shanghai, China.

**Design/Methods:** A retrospective study of all NTM isolates reported in Shanghai during 2008–2012 was conducted. We used conventional biochemical and 16S rRNA gene sequencing for species identification of mycobacteria. Drug susceptibility testing was routinely performed on isolates of NTM for isoniazid, rifampin, ethambutol and streptomycin by proportion method. We also determine the risk factors for patients infected with NTM compared to randomly selected patients infected with *M. tuberculosis* by multivariate logistic regression.

**Results:** The overall rate of NTM isolation among TB suspects with mycobacterial culture-positivity was 5.9%, with a significantly increasing trend from 3.0% in 2008 to 8.5% in 2012 (p for trend < 0.001). The most frequent organism was *M. kansasii* (45%), followed by *M. intracellulare* (20.8%) and *M. chelonae/abscessus* (14.9%). The overall proportion of drug resistance were 64.6%, 77.6%, 63.3% and 75.1% for isoniazid, streptomycin, rifampin and ethambutol, respectively. Patients who had increasing age (adjusted OR=1.64, 95% CI: 1.46-1.83), were local residents (adjusted OR=1.48, 95% CI: 1.10-2.00), were retreatment cases (adjusted OR=1.64, 95% CI: 1.18-2.29), had cavity on the chest X-ray radiography (adjusted OR=1.51, 95% CI: 1.16-1.96), and were sputum smear negative (adjusted OR=1.59, 95% CI: 1.16-2.18) were more likely to be infected with NTM isolation.

**Conclusion:** In conclusion, as prevalence of NTM isolation increased, clinicians in Shanghai should consider NTM as a possible cause of TB-like disease. Accurate species identification is imperative before proper treatment can be determined for diseases caused by the diversity of NTM species. Further study might need to investigate possible epidemiological links between some specific NTM species (e.g. *M. kansasii*) isolated from environment source with the clinical isolates.

### PD-980-31 Evaluation of Löwenstein-Jensen medium culture, MGIT 960 culture and different specimen types in diagnosis of bone and joint tuberculosis

H Huang,<sup>1</sup> GR Wang,<sup>1</sup> LP Zhao,<sup>1</sup> WJ Dong,<sup>2</sup> X Yu,<sup>1</sup> ST Chen,<sup>1</sup> YH Fu,<sup>1</sup> SB Qin.<sup>2</sup> <sup>1</sup>National Clinical Laboratory on Tuberculosis, Beijing Key laboratory on Drug-resistant Tuberculosis Research, Beijing Chest Hospital, Capital Medical University, Beijing Tuberculosis and Thoracic Tumor Institute, Beijing, <sup>2</sup>Department of orthopedics, Beijing Bone and Joint Tuberculosis Diagnosis and Treatment Center, Beijing Chest Hospital, Capital Medical University, Beijing Tuberculosis and Thoracic Tumor Institute, Beijing, China. e-mail: 276761010@qq.com

**Background:** Bacteriological evidence is of great importance in bone and joint tuberculosis (BJTB) diagnosis, while study on mycobacterial culture of BJTB patients is scarce. In this study, we compared Löwenstein-Jensen medium culture (L-J culture) with MGIT960 culture, evaluated specimen type influencing on culture yield, and validated PCR amplification of mycobacterium tuberculosis DNA using specimens collected from BJTB patients.

**Design/Methods:** Fifty-two cases who had been diagnosed as BJTB by pathological examinations were recruited between June 2011 and May 2012 from Beijing chest hospital, China. Samples of pus, cheese, granulation tissue and sequestrum were collected during surgical debridement. All the specimens were performed culture both by Bactec MGIT 960 system and by Lowenstein-Jensen medium. In addition, all of the pus samples were conducted real-time PCR amplification for *M. tuberculosis* DNA detection.

**Results:** A total of 191 specimens, including 52 pus specimens, 44 cheese specimens, 51 granulation tissue samples and 44 sequestrum specimens were collected from 52 BJTB patients. Granulation tissue was most likely to produce positive outcomes by L-J culture, and sequestrum was most likely to produce positive outcomes by MGIT 960 culture, but there was no significant difference with respect to recovery rate among different types of specimens either by L-J culture ( $\chi^2=0.638$ ,  $P=0.888$ ) or by MGIT960 culture ( $\chi^2=1.399$ ,  $P=0.706$ ). MGIT960 culture had significantly higher recovery rate than L-J culture both among single type of specimen groups and combined type of specimen groups. When culture and PCR test were combined, the recovery rate of pus reached 67.31% (35/52), which was significantly higher than that of either method alone ( $P<0.05$ ).

**Conclusion:** MGIT 960 culture is superior to L-J culture in BJTB diagnosis; pus, sequestrum, granulation tissue and cheese are usable specimen for mycobacterial culture, and it is important to collect different types of specimen from BJTB patient to pursue higher recovery rate; combination of culture and molecular techniques may have a better diagnostic significance.



### PD-981-31 Evaluation of TB follow-up sputum smears examinations in Brazil

A Wysocki,<sup>1</sup> BE Scatolin,<sup>1</sup> R Andrade,<sup>1</sup> T Arakawa,<sup>1</sup> A Beraldo,<sup>1</sup> ME Brunello,<sup>1</sup> SHF Vendramini,<sup>2</sup> TC Scatena Villa.<sup>1</sup> <sup>1</sup>Public Health, Ribeirão Preto School of Nursing - University of São Paulo, Ribeirão Preto, SP, <sup>2</sup>Professional Orientation and Public Health, São José do Rio Preto School of Medicine, São José do Rio Preto, SP, Brazil. e-mail: lilisew@yahoo.com.br

**Background:** Follow-up sputum smear examinations during tuberculosis (TB) treatment are the cornerstone to monitor therapeutic success. According to Brazilian TB Control Programme, all pulmonary TB patients (PTB) should perform three sputum smears during treatment. Considering national strategy priorities to control disease, to evaluate the incorporation of these actions is essential.

**Aim:** To analyze public health services' performance of sputum smear examination during follow-up in a TB priority setting of Brazil.

**Method:** Operational research conducted in São José do Rio Preto, São Paulo State, Brazil. Study population consisted of new cases and retreatment cases of PTB in treatment at public health services since the beginning of TB treatment decentralization to Primary Health Care services (PHC) in 2008, until 2011. PTB who undergone 6 months of treatment were included. Data was collected from the online TB reporting and recording system (TB-WEB) and medical records. To perform data analysis, health services were classified into two categories: PHC and Specialized Services (SS). Data were analyzed using descriptive statistics.

**Results:** Of the 455 TB patients diagnosed in the period, 351 (77.1%) was PTB. Of these, 268 (76.4%) had successful outcome, 204 (76.1%) were followed up by PHC and 64 (23.9%) by SS. Only 98 (36.6%) PTB in follow-up performed all sputum smear examinations at PHC (39.7%) and at SS (26.6%). The proportion of patients with all follow up examinations was higher among retreatment (40% vs. 36%) than in new cases. Nearly 27% of PTB was not tested during the intensive phase of follow-up, neither during continuation phase (35.8%). The follow-up examination at the end of treatment was the most commonly missed (41.8%). Among PTB followed-up at PHC and SS, 73% and 70.3% was tested on the intensive phase, 66.7% and 56.3% on the continuation phase; and 58.8% and 56.3% on end-of-treatment, respectively.

**Conclusion:** Nearly a third of PTB who complete 6 months of treatment did not all follow-up sputum smear examination and even in SS there were difficulties to perform this activity. These findings show implications for TB control in this setting, once the lack of follow-up examinations may result in ongoing TB transmission. More attempts need to be made to improve TB sputum smear examinations, especially among retreatment patients.

### PD-982-31 Feedback of TB test results using Skype® SMS messages for rapid treatment decisions in Abuja, Nigeria

S T Abdurrahman,<sup>1</sup> O Oladimeji,<sup>2,3</sup> L Lawson,<sup>2</sup> J O Obasanya,<sup>4</sup> G Ezugwu,<sup>2</sup> B Opoola,<sup>2</sup> R Dacombe,<sup>3</sup> L Cuevas.<sup>3</sup> <sup>1</sup>FCT Tuberculosis and Leprosy Control Programme (TBLCP), FCT Public Health and Human Services, FCT-Abuja, <sup>2</sup>Tuberculosis Research Unit, Zankli Medical Centre, FCT-Abuja, Nigeria; <sup>3</sup>Tropical Medicine, Liverpool School of Tropical Medicine, Pembroke place, Liverpool, UK; <sup>4</sup>National Tuberculosis and Leprosy Control Programme (NTBLCP), Federal Ministry of Health, Nigeria, FCT-Abuja, Nigeria. e-mail: droladfb@gmail.com

**Background:** Nigeria is a high TB burden country and sputum specimens are often processed at a location away from the clinic with significant delays between the time the sputum is tested and the clinic receiving the results. Patients return to collect results several days later. Laboratories with computers and internet could use low cost SMS messages to provide feedback.

**Design/Methods:** We compared the cost and time-to-release of laboratory results in four participating district hospitals in Abuja. We documented the time and cost of feedback before and after implementation of a system to send SMS text message using skype®. Staff were trained to use Skype with a dedicated account with credit to send SMS messages. SMS text was formatted to provide smear-microscopy and Xpert results.

**Results:** The median time to receive laboratory results was 72 (range 48–96) hours before the intervention. SMS-skype messages provided results within 24 hours. One SMS message included up to 4 patients at a cost of 4 Naira (\$0.024), which is lower than the cost of messages sent over a local phone network. DOT Staff asked patients to return the next day and found the approach easy to use, useful and more efficient than collecting physical results.

**Conclusion:** The method reduced the delay in the release of laboratory results and had low cost. Laboratories with access to internet could use similar information technologies to reduce delay to initiate treatment.

### PD-983-31 Benefits and barriers for tuberculosis patients to access and use social health insurance in Viet Nam

K Vu Duy,<sup>1</sup> HK Pham,<sup>2</sup> Minh Hoang Van,<sup>1</sup> Anh Tran Tuan,<sup>1</sup> My Tran Thi Tuyet.<sup>1</sup> <sup>1</sup>Center for Health System Research, Hanoi Medical University, Hanoi, <sup>2</sup>TB Unit, World Health Organization Office in Viet Nam, Hanoi, Viet Nam. e-mail: vuduykien@gmail.com

**Background:** Viet Nam is still facing a high burden of TB. The country ranks twelfth among the 22<sup>nd</sup> high-burden tuberculosis (TB) and the 14<sup>th</sup> among the 27 high-burden multi-drug resistant TB countries. Some TB diagnosis and treatment related services are covered by social health insurance (HI), but the financing for TB diagnosis and treatment still heavily relies on out-of-pocket health payment. Health insurance reimbursement mechanisms remain restricted and complicated, preventing the access

to health care benefits of TB patients. We implement this research to describe current health care benefits covered by HI, and to identify barriers to access HI services for TB patients at provincial and district levels.

**Design/Methods:** A cross-sectional study design was used to investigate HI services for TB patients in health facilities at provincial and district levels. In the study, 308 hospital records, together with discharge bills, were randomly collected from provincial and district levels Hai Phong and Dong Nai. 16 in-depth interviews were implemented with National Target Program (NTP) managers and TB patients at different levels.

**Results:** HI covered diagnosis and medicines based on the drug list stipulated by Ministry of Health. Insured TB patients only pay the amount of co-payment that depends on their type of health insurance card. In general, the average costs for sputum tests and x-rays were round 150,000 VND to 200,000 VND in both Hai Phong and Dong Nai. However, in Hai Phong, suspected TB patient was prescribed costly broad-spectrum antibiotics and antiviral, so the average cost of TB diagnosis at provincial level increased substantially to 4.6 mil VND. Antibiotics were used not only for suspect TB patient AFB (-) but also for TB AFB (+) that was not inline with the NTP guideline. If TB patients did not have HI cards, they had to pay on average cost 6 to 10 times higher than that of those who had health insurance cards. In one province where district TB units have not allowed to provide HI services, it was difficult for TB patients to get appropriate TB diagnosis as well as get HI reimbursement.

**Conclusion:** HI is very important for TB patients that allows them to access appropriate TB diagnosis and treatment services and provides them the financial protection. TB diagnosis package for TB diagnosis would be reviewed and standardized to reduce these costs for TB diagnosis. The health system should be reformed to better deal with TB in Viet Nam.

Table 1: Average costs for TB diagnosis given by mean (95% CI)

Unit: thousand VND

	Hai Phong			Dong Nai		
	Pulmonary TB (AFB +)	Pulmonary TB (AFB -)	p	Pulmonary TB (AFB +)	Pulmonary TB (AFB -)	p
<b>Provincial level</b>						
Sputum test	71.3±3.3	70.0±3.1	>0.05	87.6±5.7	110.1±5.8	<0.05
X-ray	88.7±8.2	105.8±9.0	>0.05	55.4±4.6	82.5±7.4	<0.05
Other relevance tests	505.2±105.4	586.6±50.3	>0.05	564.1±44.9	580.5±36.0	>0.05
Medicines and consumables	3498.1±353.6	3080.1±320.0	>0.05	198.9±33.9	170.1±28.3	>0.05
Hospital bed	391.0±42.8	438.1±33.5	>0.05	302.8±35.3	296.4±32.3	>0.05
<b>Total</b>	4692.6±372.9	4520.7±350.9	>0.05	1914.1±190.1	2056.1±152.0	>0.05
<b>District level</b>						
Sputum test	64.0±1.5	60.0±0.0	<0.05	60.8±0.5	NA	NA
X-ray	72.6±3.6	63.3±2.3	<0.05	32.0±0.0	NA	NA
Other relevance tests	213.0±16.6	80.9±13.3	<0.05	149.2±3.4	NA	NA
Medicines and consumables	194.3±38.1	23.6±7.5	<0.05	0.0±0.0	NA	NA
Hospital bed	92.0±20.8	30.6±3.7	<0.05	0.0±0.0	NA	NA
<b>Total</b>	744.3±79.0	294.2±25.8	>0.05	242.1±3.5	NA	NA

Note: The hospital records of pulmonary TB cases with AFB(-) were not kept at district DTUs in Dong Nai. Medicines were not included TB drugs because no TB drugs used during this period. NA: Not applicable

## PD-984-31 Factors associated with non-adherence to tuberculosis treatment among patients treated under DOTS in Akwa Ibom, South South, Nigeria

V Obot,<sup>1</sup> V Adams,<sup>2</sup> E Peters.<sup>3</sup> <sup>1</sup>Public Health, Ministry of Health, Uyo, <sup>2</sup>Community Health, University of Benin, Benin, <sup>3</sup>Internal Medicine, University of Uyo Teaching Hospital, Uyo, Nigeria. Fax: (+234) 424 52 311. e-mail: valerie\_\_obot@yahoo.com

**Background:** Tuberculosis remains a major public health problem in many countries of the world. Non-adherence to TB treatment can lead to prolonged infectiousness, drug resistance, relapse and death. This study assessed the factors associated with non-adherence to treatment by TB patients.

**Methodology:** A quantitative, cross sectional descriptive study of pulmonary TB patients diagnosed and treated for tuberculosis in Akwa Ibom State from January to December, 2010. Patients were assessed for knowledge and attitude to TB disease, association between socio demographic characteristics and adherence and other important factors related to patients and health care providers. Data collection instrument was a semi-structured questionnaire, which was interviewer administered and was analysed using stata 10.

**Results:** In this study, a total of 480 TB patients were interviewed. From the study it was observed that 110(31.1%) of the non-adherent had poor knowledge on key issues of TB disease while 18 (7.9%) of the adherent had poor knowledge. 111(33.25%) of non-adherent felt bad and ashamed of disease and 29(19.9%) of the adherent felt bad. A higher proportion of the non-adherent 156(46.7%) had to travel long distance to access care. The non-adherent 71(21.2%) had to pay over five hundred naira on every visit to treatment centre as transport cost while 13(9%) of the adherent spent up to five hundred naira. Friendly health care providers, lack of family support were other factors influencing adherence to TB treatment.

**Conclusion:** The result of this study shows the need for health care providers to continuously educate TB patients on treatment to improve their knowledge on the disease. Also more treatment centres should be established to improve access and reduce the financial burden of transport cost to patients. Finally health care providers should be trained on good patient and health care provider relationship.

## PD-985-31 Does type of tuberculosis treatment regimen, daily or intermittent, taken in the past affects recurrence of TB, a study in GTB Chest Clinic, Delhi?

R Nagar,<sup>1</sup> D Kundu,<sup>2</sup> S Chandra,<sup>2</sup> A Khanna.<sup>1</sup> <sup>1</sup>RNTCP, Directorate of Health Services, Delhi, <sup>2</sup>RNTCP, WHO Country Office for India, Delhi, India. e-mail: debashishkundu@yahoo.com

**Background:** In India, Tuberculosis (TB) patients are treated with short-course intermittent regimen (Thrice-weekly) following DOTS guideline under the Revised

National TB Control Programme (RNTCP) and using daily regimen following non-DOTS in the private sector. The patients once treated, are not followed-up unless they come to the health care provider, in public or private setting, again with symptoms mainly due to recurrence of TB disease. Recurrent TB is considered to be an important measure of the efficacy of TB treatment, has lower treatment success rate as compared to new TB patients and is associated with drug resistance. There is limited evidence under the programmatic setting on recurrence of TB after completion of treatment. This study was conducted to know the proportion of recurrence of TB disease after treatment completion from source of previous treatment - RNTCP and non-RNTCP in Guru Teg Bahadur (GTB) Chest Clinic of Delhi, India.

**Design/Methods:** A cross sectional study design was used. After the diagnosis of TB, every TB patient was asked by the treating medical officer about the history of TB treatment, duration since last TB treatment taken and occurrence of current symptoms in months, age, sex and source of previous treatment - RNTCP, following intermittent regimen, or non-RNTCP, following daily regimen. All registered recurrent TB patients from 1<sup>st</sup> January to 31<sup>st</sup> December 2012 were recruited for the study purpose. The data variables were collected by Senior TB Treatment Supervisors (STS) using a structured proforma and analyzed using Microsoft Excel.

**Results:** Of 214 recurrent TB patients registered in 2012, 148(69%) had source of previous treatment through intermittent regimen in RNTCP and 66 (31%) had taken daily regimen privately (Non-RNTCP). 119 (80%) TB patients recurred within 5 years of last completed TB treatment with intermittent regimen in comparison to 32 (48%) with daily regimen. Also, 11 (7%) TB cases recurred after 10 years in comparison to 31 (47%) with daily regimen.

**Conclusions:** The study observed high proportion (80%) of recurrence of disease among TB patients within 5 years after being successfully treated in RNTCP. A patient who has taken daily regimen for TB Treatment was less likely to be a recurrent TB and if TB recurs, it occurs after a longer period of time. RNTCP in line with the Standards of TB Care in India (STCI) could consider offering daily regimen to TB patients.

#### **PD-986-31 True outcomes of notified lost to follow-up patients in a TB reference hospital in Douala, Cameroon**

J Noeske,<sup>1</sup> A Wandji,<sup>2</sup> C Kamgue,<sup>2</sup> C Kuaban.<sup>3</sup>

<sup>1</sup>Tuberculosis, Consultant, Yaounde, <sup>2</sup>CPP, Laquintinie Hospital, Douala, <sup>3</sup>Internal Medicine, University of Yaounde I, Yaounde, Cameroon. Fax: (+237)33 43 33 60. e-mail: juergennoeske@yahoo.fr

**Background:** In Cameroon, TB is treated within a national programme in a network of public and private basic management units (BMU) according to international recommendations. The treatment success rate reported for the 2012 patient cohort was 80.2% with

about 8% of patients declared lost to follow-up (LF). Treatment success rates in bigger urban BMU's and especially in reference hospitals are far lower than in rural units due to LF. We determined the true outcomes of patients notified as LF in the TB reference hospital of Douala, the economic capital of Cameroon.

**Materials and methods:** The study was conducted in the Centre de Pneumo-Phtisiologie (CPP) in Douala and included all patients with smear positive pulmonary TB (PTB) who were consecutively diagnosed and put on treatment between April 1, 2012 and March 31, 2013. All LF patient and/or his/her contacts, identified via a register review, were contacted by telephone to get the real outcome of their TB-disease. Interviews were conducted at patients' homes or in a health facility of convenience with a semi-structured questionnaire. For all LF patients identified and visited a new sputum examination was carried out using smear microscopy and GenXpert. Administrative and ethical clearance for the study was obtained from the Littoral Regional Health Authorities.

**Results:** During the period of study, 131 (9.9%) patients were registered as LF. After eliminating apparent errors in registration (double entries etc.), a total of 121 (92%) patients were retained for evaluation but only 93 (77%) of the latter could be retrieved. Of the 93 patients finally analyzed, 45 (48%) were erroneously registered as LF: 13 (14%) died during treatment and 32 (34%) finished their treatment in another health facility without getting the status of a 'patient transferred out'. The number of true LF was 48 (52%). Two patients among the true LF were identified with active TB disease.

**Conclusion:** Large urban health facilities in charge of TB care, habitually with different care providers in charge of the same patient and an isolated registration unit, are at risk of registration errors which might impact program performance indicators and subsequent interventions based on erroneous data.

#### **PD-987-31 Analysis of PM2.5 and air nicotine concentration in selected indoor public places**

W Li,<sup>1</sup> W Zheng,<sup>1</sup> GH Jiang,<sup>1,2</sup> Y Yang,<sup>1</sup> Yi Pan.<sup>1</sup>

<sup>1</sup>Non-communicable Disease Control and Prevention, Tianjin Centers for Disease Control and Prevention, Tianjin, <sup>2</sup>Public Health, Tianjin Medical University, Tianjin, China. e-mail: liweicdc@126.com

**Background and challenges to implementation:** Acknowledge the situation of secondhand smoking exposure in main public places in Tianjin. Provide data to improve the implementation of Tianjin Smokefree Law. **Intervention or response:** PM2.5 was measured for 30 min in 44 public places by Sidepak AM510. Air nicotine concentrations were measured for 5-7 days in 10 of them. Additionally, on-site observation and questionnaire survey were carried on.

**Results and lessons learnt:** PM2.5 concentration in the 5 kinds of places: 50µg/m<sup>3</sup> in the lobbies of the hospitals, 119 µg/m<sup>3</sup> in the male washing rooms of the hospitals; 73µg/m<sup>3</sup> in the lobbies of the governments, 123µg/m<sup>3</sup> in the male washing rooms of the governments; 69µg/m<sup>3</sup> in



the lobbies of the traffic waiting rooms, 117 $\mu$ g/m<sup>3</sup> in the male washing rooms of the traffic waiting rooms; 153 $\mu$ g/m<sup>3</sup> in the restaurants; 144 $\mu$ g/m<sup>3</sup> in the bars. PM<sub>2.5</sub> concentration in Restaurants was the highest among the 5 kinds of public places. The second was bars. The male washrooms in other places had high PM<sub>2.5</sub> than lobbies of them. Average PM<sub>2.5</sub> concentrations were positively correlated (Spearman's correlation coefficient 0.281,  $p < 0.05$ ) with active smoking density. Air nicotine concentrations were strongly and positively correlated with PM<sub>2.5</sub> concentrations,  $r = 0.553$ ,  $p < 0.001$ .

**Conclusions and key recommendations:** Secondhand smoke exposure in Tianjin was still serious. PM<sub>2.5</sub> monitoring results of this study showed that the highest place, the restaurant, beyond the WHO recommended outdoor 24 hours average PM<sub>2.5</sub> concentration standard 20 times, its value 539.0 $\mu$ g/m<sup>3</sup>, as the places there are people who eat a variety of age composition, exposure to such high concentrations of among PM<sub>2.5</sub>, especially be chronically ill, the elderly and children, causing serious injury. Air nicotine concentration test results consistent with the PM<sub>2.5</sub> monitoring results, government offices, governments in tobacco control and traffic waiting places have done relatively well, the individual values are higher in the men's washing room. Restaurants, bars generally high value detection, detection of certain monitoring point values beyond the standard curve method nearly 10 times the maximum limit of quantification. Tianjin Tobacco Control Regulation was formally implemented on May 31, 2012. Sum up the results of its implementation, find the problems during the implementation will give help and guidance to other cities in China. Survey result showed that public support for smoking ban in public places has increased to 95% in Tianjin. All aspects have improved, residents smoking rate is also showing a downward trend, but the key venues indoor exposure to secondhand smoke is still at a high level. The results of this study will also assess the implementation of the Regulations provides data to support, so as to promote the participation of various departments to intensify tobacco control efforts, and jointly create a smoke-free environment.

### 43. BIDIS, BLOOMBERG, BALI AND BEHAVIOUR: FRONTIERS IN TOBACCO CONTROL

#### PD-988-31 Assessment on smokefree venues establishment in national chronic disease demonstration areas and tobacco control status

LH Wang,<sup>1</sup> JX Ma,<sup>1</sup> YM Bai,<sup>1</sup> J Yang,<sup>1</sup> N Ji.<sup>1</sup> <sup>1</sup>National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing, China. e-mail: jiningbeijing@126.com

**Background:** In order to further strengthen NCD prevention and control work in China, the construction of national demonstration areas (hereinafter referred as

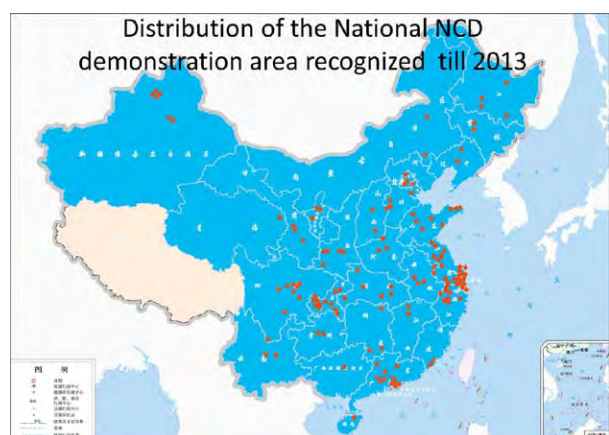
"NDAs") of NCD comprehensive prevention and control was launched in 2010 by the National Health and Family Planning Commission. By the end of 2013, 140 districts or counties have been named NDAs (39 in 2011 and 101 in 2012, Fig. 1). In order to control tobacco use in China, a program "Integrating tobacco control into the implementation strategy of the National Plan on NCD Control and Prevention in China" was carried out under the support from The Union, aiming to improve tobacco control capacity building and tobacco control policy intervention in the contexts of NDAs.

**Objective:** To collect baseline data and understand the present tobacco control work in NDAs.

**Methods:** The data between 2010 to Jun 2011 were collected from the work reports and the community diagnosis reports of the 39 NDAs.

**Results:** The coverage rate of tobacco-free health institutions: Among the 39 NDAs, 32 (82.1%) achieved that all health institutions went smoke free. Geographically, 20 out of 24 NDAs (83.3%) in the eastern region, 6 out of 8 (75.0%) in the central region, and 6 out of 7 (85.7%) in the western region achieved that all health institutions go smoke-free. Tobacco-free environments outside health system: Thirty (76.9%) out of 39 NDAs provided the information on the creating of tobacco-free environments outside health system. The median of the number of tobacco-free environments outside health system is 12.5 and the interquartile range is 30.75. Smoking prevalence of male adults: Among the 39 NDAs, 89.7% (35/39) provided the smoking prevalence of male adults. 27 out of 35 (77.1%) NSAs had lower male adult smoking prevalence than the national average 52.9% that is reported in the WHO Global Tobacco Epidemic, 2013. Geographically, The number of NDAs with the smoking prevalence among male adults higher than 52.9% were 4 out of 21 (19.0%) in the eastern region, 3 out of 7 (42.9%) in the central region and 1 out of 7 (14.3%) in the western region; 4 out of 29 (13.8%) in the urban areas and 4 out of 6 (66.7%) in the rural areas.

**Conclusion:** The outcomes showed that, indicators on tobacco control in the evaluation system applied in national demonstration area were not specific enough. Further amendments were needed to complete the evaluation system in order to achieve the goal of decreasing the adult smoking prevalence to 25% by 2015.



**PD-989-31 Opinion of the people in Bali regarding the presence and the implementation of the Bali provincial smokefree law**

K Suarjana,<sup>1</sup> IMK Duana,<sup>1</sup> IWG Artawan Eka Putra,<sup>1</sup> KH Mulyawan,<sup>1</sup> A Swandewi,<sup>1</sup> T S Bam.<sup>2</sup> <sup>1</sup>Health Policy and Administration, School of Public Health, Denpasar, <sup>2</sup>Tobacco Control, The Union Against Tuberculosis and Lung Diseases, Jakarta, Indonesia.  
e-mail: ketut\_suarjana@rocketmail.com

**Background:** Indonesia is the third highest burden of smokers in the world. The number of smokers reached 62.8 million and the prevalence among age  $\geq 10$  years increased from 29.2% to 34.7% in 2010. The high prevalence also seen in Bali Province, 31.0% in 2010. Smoking causes diseases not only among smokers but also the people around them and the environment. Hence, since 2012 Bali provincial government has implemented provincial smoke-free law at seven areas. The law is important to protect the environment and provide healthy air to the community. However, its implementation remain need support and participation from the community. Therefore we conducted opinion poll among the people in Bali regarding the smoke-free environment.

**Design/Methods:** The study is a cross-sectional survey and involving 1099 samples. The samples were the people in all over Bali which selected proportionately based on smoke free area and regencies. The respondents were either the smoker or non-smoker who ever visited or met at the smoke-free areas. Data was collected by interview using structured questionnaire then analyzed descriptively.

**Results:** Around 94% of the respondent (on average 33.7 years olds) aware the harm of smoking (non-smokers aware around 96,5%, while the smokers aware around 90,9%). In addition, 88% of the respondents stated their support to the implementation of the smoke-free law (The non-smokers supported around 93%, the smokers supported 80,5%). The most supported areas for smoking ban is at the health service areas (95%). However, the study also found that there were remain violation (people smoking). The highest violation, around 65% were found at religious places (most is temples), while the lowest one found at health service areas (26%)

**Conclusion:** The awareness of the community regarding the harmful of smoking is high. So that the support in the implementation of the smoke-free law is high as well, despite there are remain violation. Hence, it is needed more assertive enforcement particularly to those areas of violation and appropriate strategy to make the community participation more effective in terms of supporting the implementation of the smoke-free law.

**PD-990-31 Photographic evidence can strengthen tobacco control interventions**

B Pandya,<sup>1</sup> P Lal,<sup>2</sup> R Parmar.<sup>1</sup> <sup>1</sup>Operations, Population Services International (PSI), Jaipur, <sup>2</sup>Technical Advisor, International Union Against Tuberculosis and Lung Disease (The Union), New Delhi, India. e-mail: bhaskar@psi.org.in

**Background** – In India, the tobacco law states that direct or indirect advertisements of tobacco products are prohibited under section 5 of the 2003 COTPA Act. Nonetheless, tobacco companies continue to market their products outside points of sale using backlit billboards, stickers, and posters. According to the Global Adult Tobacco Survey in 2010, in Rajasthan, 28.4% of adults were aware of advertisements for cigarettes, 47% for bidis and 54.7% for smokeless tobacco. Until recently, the COTPA Act had not been enforced because District Tobacco Control Committees (DTCC) didn't exist.

**Intervention-** Population Services International conducted a series of meetings with health officials and the District Collector in order to raise awareness of non-compliance with the COPTA Act. PSI officials took photographs of 177 point of sale advertisements from 33 different market places in Udaipur City, which were submitted to the District Collector who is also Chairman of the new DTCC. Upon receipt of the photographic evidence, the District Magistrate and Collector of Udaipur conducted a meeting with tobacco distributors to issue directives for compliance with the law. Under Section 5 of the Act, distributors were directed to remove all tobacco advertising from points of sale in Udaipur. Despite this effort, PSI officials observed that very few tobacco shop advertisements had been removed. PSI again took and shared photographs of the points of sale with the District Collector to alert him to the Section 5 violations. The District Collector again conducted a meeting with the tobacco industry officials with their legal advisor. The District Collector strictly ordered them to remove all advertisement boards from all points of sale in Udaipur. The District Collector also formed an anti-tobacco squad and directed the team to monitor and enforce points of sale in the Udaipur city.

**Results:** After a fifteen day period, more than 750 point of sale advertisements had been removed from the city. Most large retailers have removed their advertisements.

**Conclusion:** Photographic evidence can be a useful tool in advocating for the enforcement of policies that help prevent tobacco use.

**PD-991-31 Role of Bloomberg Philanthropist funding support in advancing tobacco control programmes in India**

B Gopalan,<sup>1</sup> R J Singh,<sup>1</sup> R Kumar.<sup>1</sup> <sup>1</sup>Tobacco Control, International Union Against Tuberculosis and Lung Disease, New Delhi, India. Fax: (+91) 11 4605 4430.  
e-mail: bgopalan@theunion.org

**Background and challenges to implementation:** The Bloomberg Initiative (BI) Grants Program was started in 2006 providing technical and funding support to

government ministries and agencies, non-governmental organizations, civil society organizations, and universities in more than 40 countries including India. India is a home of 275 million tobacco users (both Smoking and Smokeless). In India BI Grants Program partnering with Governments / NGOs supports National / Sub National level projects to develop and deliver high-impact evidence-based tobacco control interventions.

**Intervention or response:** All 68 grants with total obligation of US\$15.510millions since 2007 both completed and currently active were reviewed for their population outreach; measures achieved towards capacity building; Legislation enforcement including smoke-free; support to National Program; documented successes from advocacy; MPOWER policy development and implementation; coalition and networks built; inter-sectoral involvement; policy focussed strategic research & monitoring and prioritising tobacco control in the country.

**Results and lessons learnt:** The major outcomes are - 17 cities, 50 districts and 4 States have achieved high smokefree compliance and gone smokefree thus protecting more than 110 Million people. - Six protocols to assess enforcement and compliance to ban on TAPS, mandatory pack warnings, and protection of youth provisions of COTPA. - Enforcement of Section 5(prohibition of TAPS) scaled up in 10+ states - Effective enforcement of Section 6 of COTPA (Protection of Youth) lead to large number of tobacco free educational institutes and districts. - 7 States developed technical guidelines to enforce COTPA - Nationwide Gutka Ban

**Conclusions and key recommendations:** The Bloomberg Grants programme has contributed significantly to prioritising tobacco control in India. BI support has provided deliverable in terms of Capacity Building and Strengthening of National Tobacco Control Programs. National & Sub National Governments have benefited from the Initiative resulting in overall implementation of the MPOWER policy package in the country. BI continued support to India is the need of the hour till National/Sub National Governments take complete lead in TC Activities.

#### **PD-992-31 Muslim communities learning about second-hand smoking: a pilot clustered randomised controlled trial**

S Karam Shah,<sup>1</sup> H Tilbrook,<sup>1</sup> C Fairhurst,<sup>1</sup> A Sheikh,<sup>2</sup> D Torgerson,<sup>1</sup> A Amos,<sup>2</sup> H Thomson,<sup>3</sup> K Siddiqi.<sup>1</sup> <sup>1</sup>Health Sciences, University of York, York, <sup>2</sup>General Internal Medicine and Primary Care, University of Edinburgh, Edinburgh, <sup>3</sup>Office of the Director of Public Health, Leeds City Council, Leeds, UK. e-mail: sarwatdopasi@hotmail.com

**Background:** In the UK, 40% Bangladeshi and 29% Pakistani men smoke cigarettes regularly as compared to the national average of 24%. This in turn, renders non-smokers in their households more vulnerable to second-hand smoke (SHS) exposure than general population – leading to poor health outcomes. This can be prevented by implementing smoking restrictions in homes and cars. We conducted a pilot trial of ‘Smoke-free Homes’ - an

intervention adapted to enable Muslim religious leaders to persuade Bangladeshi and Pakistani communities to implement smoking restrictions in their homes. To our knowledge, this is the first public health intervention trial in Islamic religious settings

**Design/Methods:** We designed a pilot cluster randomised controlled trial involving mosques (clusters) across West Yorkshire and Birmingham. Each cluster was randomised and allocated to one of the trial arms (intervention vs. control).

**Intervention** clusters received Smoke-free Homes, delivered by the religious leaders, trained in its use. We recruited households with at least one smoker and a non-smoker, attending the participating mosques. Our primary outcome was saliva cotinine levels obtained from non-smokers both before and after the intervention in both arms.

**Results:** Out of the 24 mosques approached, 19 agreed to participate and 14 were recruited due to logistical and budgetary implications. Of these, seven were allocated to each trial arm and six out of seven delivered the intervention. About 544 households attending these mosques expressed an interest to participate and 209 met the eligibility criteria and were recruited. Out of those recruited, 187 (89%) households provided saliva sample at the baseline, of which 61% samples (113/187; 95%CI 54–68) indicated exposed to SHS among non-smokers. Response rate to household survey and saliva sample, at five months follow-up were 80% and 69%, respectively.

**Conclusion:** Mosques are a feasible setting for public health interventions that can be utilised to encourage positive change among Muslim communities; however research involving human tissue sampling among these communities can prove very challenging.

#### **PD-993-31 e-cigarettes: The Union responds to an evolving challenge to public health**

M Wisotzky,<sup>1</sup> G Quan.<sup>2</sup> <sup>1</sup>Tobacco Control, International Union Against Tuberculosis and Lung Disease, Edinburgh, UK; <sup>2</sup>China Office, International Union Against Tuberculosis and Lung Disease, Beijing, China. e-mail: mwisotzky@theunion.org

**Background and challenges to implementation:** Electronic cigarettes (ECs) or electronic nicotine delivery systems (ENDS) are devices which vaporise and deliver to the user's lungs a chemical mixture typically composed of nicotine, propylene glycol and other chemicals. Many ENDS are offered in flavours attractive to adolescents. The safety of ECs or ENDS has not been scientifically demonstrated; nor is there conclusive evidence of their effectiveness for harm reduction or cessation. Marketing, awareness and use of ENDS continue to grow rapidly. ENDS could undermine the de-normalisation of tobacco use [Article 12 World Health Organization Framework Convention on Tobacco Control (WHO FCTC)] and hamper the implementation smoke free policies (Article 8 WHO FCTC).

**Intervention or response:** In 2013 The Union conducted a review of existing scientific literature and released a position statement at the 44<sup>th</sup> World Lung Conference.



The position statement was released in a media conference, published in 2014 issue of The International Journal of Tuberculosis and Lung Disease. It has been disseminated and utilized as a technical assistance tool to governmental and professional entities at the global, national, and sub-national level for policy and programmatic guidance. An internal Union action plan has been developed which includes updating the Union policy with emerging literature, research, country policies, and industry activities relative to manufacture and marketing and integrating the policy into existing Union technical assistance, grants and communications activities.

**Results and lessons learnt:** The Union position statement strongly supports the regulation of the manufacture, marketing and sale of ECs and ENDS. The statement has been used by governments and international organizations to shape their own policies. The evolving science and rapidly expanding marketing of ECs means that the policy statement must be continually updated to reflect emerging policies at the country and organizational level, additions to the science base, trends in EC use by children, trends in EC manufacturing and tobacco industry activities.

**Conclusions and key recommendations:** Issues surrounding ECs/ENDS are rapidly evolving. The Union must maintain a strong and timely response in collaboration with a wide variety of partners, with a goal of protecting public health based on the current science.

### PD-994-31 Community level determinants of tobacco use in Ballabgarh Block, north India

A Krishnan,<sup>1</sup> RS Rath,<sup>1</sup> P Misra,<sup>1</sup> B Nongkynrih.<sup>1</sup> <sup>1</sup>Centre for Community Medicine, All India Institute of Medical Sciences, New Delhi, India. e-mail: kanandiyer@yahoo.com

**Background:** In India Non-Communicable Diseases are among the major causes of death and for whom tobacco use is perhaps the most important risk factor. Community level variables are among the least studied determinants of these diseases. This study objective was to profile the tobacco related environment in two selected North Indian communities and study the association tobacco store density with tobacco use among its residents.

**Methods:** We conducted community audit of 20 randomly selected rural and urban communities (10 villages and 10 urban colonies) of Ballabgarh block, from May-Sept 2013. All tobacco stores were mapped and number of publicly displayed advertisements promoting or discouraging tobacco use and number of persons smoking in streets were noted during the community walk. Tobacco stores were assessed using a checklist for adherence to national tobacco laws. Fifteen consenting men and women aged 18–65 years from each community were randomly selected and their tobacco consuming practices assessed by household face-to-face interviews using WHO STEPs questionnaire. Association between tobacco store density and tobacco use was assessed using logistic regression after adjusting for other variables grouped at community (urban/rural, attitude towards tobacco use); family (socio-economic status indicators,

smoker in the family)) and individual level (age, sex, knowledge of tobacco use, employment, marital status, media exposure).

**Results:** The median tobacco store density was 34.7 per square Km (IQR:9.01–91.05 ) in urban areas and 82.9 (IQR:75.5–110.8) in rural areas. No tobacco related signage were publicly displayed in the communities. Of the 220 tobacco stores assessed, tobacco related national laws were violated by displaying tobacco advertisements on the façade (8%), by openly displaying tobacco products (24%), by being located within 100m of educational establishments (10%) and by employing children below legal age for employment (5%). After adjustment for other variables, it was found that adults living in areas with tobacco store density greater than the median were 2.6 times (95% CI: 1.3–5.4) as likely to consume tobacco as compared to those living in lower density areas. **Conclusion –** High tobacco-selling density in this study population and legal violations by the stores highlight the need for a stricter approach to addressing environmental determinants of tobacco use in the country.

Table 1. Key tobacco use indicators in the study communities

Indicators	Rural (n=296)	Urban (n = 256)
Current Tobacco Use	24.0%	12.2%
Presence of tobacco user in the house	43.2%	28.1%
Aware of banning of smoking in public places	33.1%	59.0%
Aware of compulsory health warning on tobacco products	18.6 %	43.0%

### PD-995-31 Developing a behaviour change intervention for smoking cessation within primary care in Nepal

S Baral,<sup>1</sup> BB Sharma,<sup>2</sup> B Khadka,<sup>2</sup> S Khanal,<sup>1</sup> R Pant,<sup>3</sup> S Manandhar,<sup>1</sup> H Elsey,<sup>4</sup> J Newell.<sup>4</sup> <sup>1</sup>Research, COMDIS-HSD, Health Research and Social Development Forum (HERD), Kathmandu, <sup>2</sup>National Health Education Information and Communication Centre, Ministry of Health and Population, Kathmandu, <sup>3</sup>Programme Director, Ministry of Health and Population, National Tuberculosis Centre, Bhaktapur, Nepal; <sup>4</sup>LIHS, COMDIS-HSD, Nuffield Centre for International Health and Development Centre, Leeds, UK. Fax: (+977)1 4 10 20 16. e-mail: sushilbaral@hotmail.com

A high proportion of patients visiting primary Health Care Centres (PHCCs) present with respiratory symptoms, 17% men and 11% women. Evidence suggests effectiveness of psychological support for tobacco dependence (WHO 2004), particularly where trained health workers (HWs) provide advice. Thus, we aim to test the feasibility to include a behavioural support for smoking cessation within primary health care systems in Nepal. The study was conducted in government PHCCs in 3 phases:

- 1) Exploratory study using evidence review, semi-structured interview and focus group discussion;
- 2) **Action research:** discussion with government stakeholders and PHCC staff to identify the intervention package: counseling was one of the key interventions, in which, we used the Stages of Change Model (Prochaska et al, 2002) and the processes described by Michie et al 2008 to behavior change intervention; and

**3) Implementation and follow up:** the intervention was implemented and follow-up of the patients at 3 months. **Findings:** the action research and the ongoing implementation provided a number findings at different levels: denial of smoking habits by patients; poor acceptance of lung health patients who were identified as smokers to attain counseling sessions; weak motivation of health workers to identify smoking habits of OPD attendants and refer them for counseling; and difficulty to identify smokers in OPD which could be linked to the sociocultural norms of the society where cigarette is often frowned. Health systems barrier for the effective implementation were: weak implementation of smoking cessation intervention within the Practical Approach to Lunghealth (PAL); weak motivation of HWs as consequence of increased workload; high rates of HWs absenteeism and unfulfilled sanctioned posts in PHCCs; difficult to spare time for counseling by HWs in PHCCs. **Conclusion:** there is potential of identifying smokers among patients visiting OPD and sign-up them to smoking quit mechanism provided that HWs are motivated and allocate adequate time for counseling. The findings are indicative to some issues that act as barriers to the effective implementation of smoking cessation in PHCCs - health systems, patients and community- which need attention. Findings from follow-up study among patients who were enrolled into the intervention, which is yet to be completed, will provide better insights into whether or not the intervention is effective and scalable in the context of PHC settings in Nepal.

**Developing a Behaviour Change Intervention for Smoking Cessation within primary care in Nepal.**

Number of patients in the 3 PHCC who have received the intervention

Table 1: Number of patients receiving the smoking cessation intervention (22<sup>nd</sup> april 2014)

	Lumbini PHCC	Dhakhai PHCC	Gokarna PHCC	Total
No. of patients receiving a part of the intervention (ie brief advice in opd and a leaflet)	29	16	55	100
No. of patients receiving counselling (counselling using a flip book)	17	12	13	42
No. of patients setting a quit date	17	12	13	42
No. of patients who showed up on their quit date	10	1	3	14

**PD-996-31 A cross country comparison of social determinants of health and tobacco use: findings from the Global Adult Tobacco Survey (GATS)**

GH Tee,<sup>1</sup> J Morton,<sup>2</sup> T Aris,<sup>3</sup> L Zhao,<sup>1</sup> J Rarick.<sup>4</sup> <sup>1</sup>Center for Communicable Diseases Research, Institute for Public Health, Kuala Lumpur, Malaysia; <sup>2</sup>Office on Smoking and Health, Center for Disease Control, Atlanta, GA, USA; <sup>3</sup>Director's Office, Institute for Public Health, Kuala Lumpur, Malaysia; <sup>4</sup>Office for Tobacco Free Initiative, WHO Western Pacific Regional Office, Manila, Philippines. Fax: (+60) 0322823114. e-mail: helentee.gh@moh.gov.my

**Background:** Tobacco consumption continues to be the leading cause of preventable deaths globally. This paper

aims to examine the influence of selected socio-demographic variables on tobacco use in five countries participated in the Global Adult Tobacco Survey (GATS) in 2011 - 2012.

**Methods:** We analysed internationally comparable representative household survey data collected via face-to-face interview from 33,482 respondents aged  $\geq 15$  years in Malaysia, Indonesia, Argentina, Romania and Nigeria for determinants of tobacco used within each country. Socio-demographic variables analysed included gender, age, residency, education, wealth index and awareness of smoking health consequences. Current tobacco use was defined as smoking or use of smokeless tobacco daily or occasionally. Former smokers were excluded from the analysis.

**Results:** The overall prevalence of tobacco use varied from 5.5% in Nigeria to 35.7% in Indonesia and was significantly higher among males in all five countries. Odds ratios for current tobacco use were significantly higher among males for all countries [with the greatest odds among Indonesian men (OR=67.4, 95% CI: 51.2–88.7)] and urban areas in Romania. The decreasing trends of tobacco used with increasing age were seen in Malaysia and Indonesia, whereas the reverse was true for Argentina and Nigeria. For educational level and wealth index, significant trends of decreasing tobacco used with increasing educational levels and wealth index were seen in Malaysia, Indonesia and Romania. Significant negative association between current tobacco use and awareness of adverse health consequences of smoking were found in all five countries except Argentina.

**Conclusions:** The findings from this study had shown that males and the socially and economically disadvantaged population were at the greatest risk of tobacco use. Tobacco control intervention should target this segment of population and to incorporate educational interventions to increase knowledge of adverse health consequences of smoking.

**PD-997-31 Smoking behaviour and motivation to quit among patients with chronic obstructive pulmonary disease**

M Smirnova,<sup>1</sup> E Yastrebinskaya,<sup>1</sup> O Sukhovskaya.<sup>1</sup>

<sup>1</sup>Russian Advisory Telephone Line of Help for Smoking Cessation (Russian Quitline), Research Institute of Phthisiopulmonology, Sankt-Petersburg, Russian Federation. Fax: (+7) 812 244 96 26. e-mail: sukhovskaia@mail.ru

**Background:** Smoking is the most important risk factor of development and progression Chronic Obstructive Pulmonary Disease (COPD) and smoking cessation is a necessary component of treatment. The effectiveness of treating the syndrome of nicotine addiction mostly depends on the motivation to quit smoking and smoking behavior. The aim of the study was to analyze the motivation to quit smoking and psychological characteristics of patients with COPD.

**Design/Methods:** Smokers with COPD (45–70 year, 98 male and 19 female) were interviewed about smoking, Fagerstrom's nicotine dependence test (ND), motivation

to quit smoking and smoking behavior ( questionnaire of Horn).

**Results:** Patients with COPD smoked from 10 to 45 cigarettes per day (23,64 +1,8 during 20–50 years (38,60+4,22 years), ND=6,12+0,51 (5 –10 units). The main reason the smoking was: it helps cope with stress. The most smokers tried to quit smoking more 3 times. 47,5% had the strong degree of withdrawal. The main reasons to stop smoking were: current health condition - 30,4%; 5,7% - physician's recommendation; 17,4% -the request of relatives; 8,3% - for the economic cost; 6,6% - example for children or for the sake of children's health. Only 10,8% of respondents said that enjoyment of smoking has changed since developed their disease. The recommendation about smoking cessation were given only 4,3% of patients. The leading factors of smoking were: relaxing effects of smoking. In 12% of cases stimulating effect of smoking was the leading factor. The effectiveness of smoking cessation in cases of stimulating effect of smoking was lower than in relaxing effect of smoking. Effectiveness of smoking cessation were higher in men in comparison with women and in married men (compared to unmarried).

**Conclusion:** Physicians should be to assist smokers with COPD to quit smoking and often give advice to stop smoking. It is also advisable to involve in this process patients' relatives; teach patients relaxation and stimulation techniques

#### 44. DAVID VS. GOLIATH: FIGHTING THE MEDIA WAR AGAINST THE TOBACCO INDUSTRY

##### PD-1000-31 Behaviour change among tobacco retailers after enforcement of COTPA Act 2003: a rapid survey in Nagaur, Rajasthan

B Pandya,<sup>1</sup> P Lal,<sup>2</sup> R Parmar,<sup>1</sup> R Kumar.<sup>1</sup> <sup>1</sup>operation, Population Services International (PSI), Jaipur, <sup>2</sup>Technical Advisor (Tobacco Control), International Union Against Tuberculosis and Lung Disease (The Union), New Delhi, India. e-mail: bhaskar@psi.org.in

**Background:** Tobacco use is a leading cause of death and disability in India, killing 8–10 lakh people a year. As a result, the Cigarettes and Other Tobacco Products Act 2003 (COTPA) was enacted for tobacco control in India. Two of the key provisions are: (1) direct and indirect advertisement and promotion of tobacco products is prohibited and (2) selling tobacco products to individuals under the age of 18 is prohibited. In April 2013, PSI/India started providing technical support to district government departments to implement COTPA in Nagaur district. PSI also runs one month smoke free campaign for creating awareness on tobacco control Law and harmfulness of tobacco. PSI/India sensitized local newspapers to highlight the harmful effects of tobacco and the provisions under COTPA.

**Materials and methods:** The survey was conducted in March 2014, one year after the start of PSI/India's

intervention. Semi-structured interviews were conducted to assess knowledge, perceptions and behavior of 37 randomly selected tobacco vendors on COTPA in Nagaur. The sample size represents 5% of the total tobacco vendors in Nagaur.

**Results:** Three quarters (75.7%) of the respondents reported that they are aware of COTPA. Among those, 45.2% reported that they learned of COTPA from government officials, while 43.2% reported that they heard about it from a NGO. Most of tobacco vendors (97%) responded that three months ago they had never heard of COTPA, but their awareness increased after government officials started fining up to Rs 200 for violating COTPA provisions. Over half (56.7%) of respondents reported that they were unaware that advertisement of tobacco products is an offense and 37.8% reported that Tobacco companies provide the advertisement materials. only 13.5% reported that sales have dropped after installing a warning sign that selling tobacco products to individuals under the age of 18 is an offense.

**Conclusion:** As part of a smoke free campaign, awareness through media and subsequent enforcement by key government departments increases tobacco vendors' awareness and knowledge of COTPA. This increased awareness resulted in compliance of COTPA at points-of-sale in Nagaur. PSI/India is planning to scale up this intervention in other program intervention districts.

##### PD-1001-31 Tobacco advertisement, promotion and sponsorship in Naogaon district: a baseline survey

MAU Ahsan,<sup>1</sup> SM Mahbubus Sobhan,<sup>1</sup> huq Syed Mahfuzul Huq,<sup>2</sup> Sobu Md. Abdus Sobur.<sup>3</sup> <sup>1</sup>Ministry of Health & Family Welfare, National Tobacco Control Cell, Dhaka, <sup>2</sup>Tobacco Control, World Health Organization, Dhaka, <sup>3</sup>Ministry of Health & Family Welfare, Civil Surgeon Office, Naogaon, Bangladesh. Fax: (+880)29580255. e-mail: ahsan5965@gmail.com

**Background:** It is well documented that tobacco advertisement, promotion and sponsorship (TAPS) increases tobacco use. According to clause-4 of Tobacco Control Act, 2005 of Bangladesh "No one is allowed to provide any gift incentive, scholarship or hold any tournament with the aim to encourage the use of tobacco products". However in the recent past it is noted that tobacco industries are continuing tobacco advertisement specially at the point of sale. Several reports have been published in the local and national newspapers about the TAPS by Tobacco Industry. Sometimes it is challenging to convince the policymakers and also the law enforcing agencies regarding the violation of the law by the industries. However in grass root level the tobacco industries are very much vigilant and active.

**Objectives:** The objective of the study is to conduct a baseline survey regarding the tobacco advertisement, promotion and sponsorship at Naogaon, a northern district of Bangladesh. It is a part of the program to establish Naogaon district as a model district on TAPS ban in Bangladesh.



**Methods:** A cross sectional study has been conducted in October 2012 with a structured questionnaire. It has done in two steps: 1) Data collected by observation by a check list from district headquarter and from all sub-districts town of the district to see the visible advertisement of tobacco products. 2) In-depth interview was done with 65 retailers of tobacco products randomly chosen from all over the districts.

**Results:** The study shows that 31% retailers of tobacco products received gift from the tobacco company during the last 3 months, whereas 20% retailers report that the company has distributed free sample or gifts to the customer during the same time. Among the observed 599 shops 24% are dedicated tobacco shops, however 38% dedicated shops are made according to some tobacco products brand color. Posters has been found in 48% tobacco shops however 32% point of sale is decorated with colored flyer of different tobacco company. There are no billboards for tobacco advertisement found in the district and no sponsorship for any tournament or event noticed during the last 3 months.

**Conclusion:** Although in the tobacco control act all kinds of advertisement are completely prohibited however the tobacco industries continue advertisement in a very cunning way. Lack of experience and capacity to handle the issue according to law are giving pace to the industries.

#### **PD-1002-31 China experience: developing evidence-based integrated mass media campaigns to support national and sub-national smokefree initiative and policy**

W Chen.<sup>1</sup> <sup>1</sup>Public Health Communication, World Lung Foundation, New York, NY, USA .  
e-mail: wchen@worldlungfoundation.org

**Background and challenges to implementation:** With a smoker population of over 300 million and 1 million tobacco-related deaths every year, nowhere else is the issue of tobacco and its control more critical than in China, specifically, where more than 60% of adult men are smokers and 7 out of 10 adults are regularly exposed to SHS. Mass media tobacco control campaigns can contribute to increasing knowledge about tobacco-related harms and counter the social acceptability of smoking and motivating behaviour change among smokers. Most importantly, mass media campaigns can also play a significant role in building support for tobacco control policies.

**Intervention or response:** Since ratifying the FCTC in 2005, the tobacco control movement in China has grown, slowly but surely. On December 29, 2013, the General Office of the CPC Central Committee and General Office of the State Council jointly released Notice on Officials Shall Take the Lead in Making Public Places Smoke Free, which has been regarded as a milestone of tobacco control in China.

**Results and lessons learnt:** Since 2008, the World Lung Foundation has worked with central government and over 20 key cities to conduct more than 70 strong public

education campaigns by adopting international best practice, in an effort to increase public awareness of the health harms associated with tobacco use and second-hand smoke exposure.

**Conclusions and key recommendations:** In 2014, the World Lung Foundation partnered with the health promotion arm of National Health and Family Planning Commission, the Chinese Center for Health Education, as well as smoke free model cities- Shenzhen and Harbin, which have passed city-level 100% smoke free legislation, to design and execute China's evidence-based tobacco control mass media campaign. This presentation will look at the well-developed evidence-based national and subnational campaigns to support the smoke free effort effectively, and will also introduce some of the key findings from the campaigns, and explore strategies in China.

#### **PD-1003-31 Assessing compliance to Indian tobacco control legislation on print media in India**

M Sharma.<sup>1</sup> <sup>1</sup>Tobacco Control, International Union Against TB and Lung Disease, New Delhi, India. Fax: (+91) 11 46 054 430. e-mail: msharma@theunion.org

**Background and challenges to implementation:** Section-5 of Indian tobacco control legislation (COTPA) prohibits COTPA-2003) prohibits direct and indirect advertisements of tobacco products in print media, electronic media, television and cinema, outdoors. Ever since the rules are put in place, although the direct advertisement are seldom seen but tobacco companies are often circumventing the law through trademark diversification and surrogate advertising. Tobacco companies have been violating the law by changing its marketing tactics and indirect/surrogate advertisement have been infiltrated in virtually all media. The present study was conducted to measure the compliance of prohibition of advertisement in 'print media' as defined under Section-5 of COTPA 2003 and subsequent rules.

**Intervention or response:** Survey was done for the period of one year starting April, 2012 to March, 2013 across three different Jurisdictions in India (Shimla city in Himachal Pradesh, Vadodara city in Gujarat and Chennai city in Tamil Nadu). More than 5000 newspapers and magazines were randomly selected in the three cities and assessed according to the pretested observational checklist on Section 5 compliance.

**Results and lessons learnt:** Overall, in none of the newspaper and magazines, any direct advertisement of tobacco products was found. However, in newspapers (0.1%) and magazines (1%), there were advertisements of no-tobacco products which had similar brand names/trademarks at that of tobacco products. Similarly, surrogate advertisements were also present in more than 2% of total newspapers and magazines across the three cities.

**Conclusions and key recommendations:** Tobacco industry is still continuing to carry TAPS in the name of brand stretching and surrogate advertisements to market its

brands. Print media is powerful media for them. Media houses must be sensitized about the legal provisions under Section 5. Government must initiate actions against the tobacco industry for promoting the TAPS in the print media.

### **PD-1004-31 Rural penetration through media involvement for effective implementation of COTPA in Himachal Pradesh, India**

N Sharma,<sup>1</sup> R J Singh.<sup>2</sup> <sup>1</sup>Civil Society, Himachal Pradesh Voluntary Health Association, Shimla, <sup>2</sup>Tobacco, The Union, South East Asia, Delhi, India. Fax: (+91)01772670346. e-mail: nar.sharma@gmail.com

**Background and challenges to implementation:** Himachal Pradesh has a higher incidence of smoking for men (33.6%) as compared to the national average (32.7%). As per GATS 2010, 21.2% of adults consume tobacco in some form or other. About 40% of the adult male consumes tobacco of which 33% smoke and 3.8% adult women consume tobacco with majority smoking. The exposure to second hand smoke at home is 83% in Himachal Pradesh (HP) and is among the highest in India. Involvement of media for proactive advocacy, information dissemination has a strong and forceful impact on community with minimal expenses.

**Intervention or response:** Involving media in tobacco control activities was a daunting task as the media had no experience on highlighting an issue which had social relevance such as tobacco issues and moreover the use of tobacco is socially accepted norm. Secondly, tobacco industry's contribution in forms of advertisement is too lucrative a proposition to earn money for the media houses. Thus sensitizing the media by HPVHA to highlight an issue of tobacco control took many sensitization workshops and one to one interaction in last 3 yrs.

**Results and lessons learnt:** In a span of three years, more than 7000 media items were published in about 25 local and national newspapers by the print media and exclusive bites highlighted in electronic media too even at lower levels such as villages etc. With media raising the issue, a pressure was created on stakeholders to effectively implement an enforcement mechanism. The news of effective implementation of tobacco control laws encouraged local governing bodies such as panchayats etc to debate on tobacco control in its general houses and motivated them to pass resolutions for declaring smoke free jurisdiction. 90% of local governing bodies forced officials/ policy makers to declare the state as Smoke Free. HPVHA's news on smoke free which was highlighted in media totally free of cost, when calculated at the prevailing market rates amounted to Rs 77,948,089.

**Conclusions and key recommendations:** Involving stakeholders and community members is essential in implementation of social laws. The media acts as a via media to highlight violations and success stories. The involvement of media creates awareness and acceptability among the community to obey rules and encourage policy makers and other stakeholders to implement the

provisions of laws. Thus the media advocacy had really contributed to achieve the status of Smoke Free in the state.

### **PD-1005-31 TAPS Ban: the Bangladesh experience**

A-E- Sadat.<sup>1</sup> <sup>1</sup>WHO & Tobacco Control Program, Ministry of Health and Family Welfare, Dhaka, Bangladesh. e-mail: asadatnabr@yahoo.com

**Background:** As per the tobacco control law 'Tobacco Advertisement, Promotion and Sponsorship (TAPS)' is banned in Bangladesh. However the tobacco industry is continuing TAPS either violating the law, or by using a few loopholes of the law itself. So far the enforcement of TAPS ban at field level is weak. The National Tobacco Control Cell (NTCC) of Ministry of Health & Family Welfare (MOH&FW) took the initiative of turning a North-Western district of Bangladesh to a TAPS free model district with the objective of developing a model on subject. WHO provided technical support.

**Method:** The project continued from July 2012 to June 2013. During this time one inception meeting and an advocacy workshop was organized at district headquarters involving stakeholders including government officials, local elites, members of civil society, business community and NGOs, media and others. One such advocacy meeting was arranged in each sub-district as well. Eleven dedicated tobacco control task force committee meetings were arranged at eleven sub-districts (including district headquarters sub-district) to coordinate this project. Twelve dedicated mobile court operations were organized during implementation period to enforce TAPS ban in the district. Public awareness on harms of tobacco and tobacco control law was created through showing anti-tobacco clips in cinema halls and through local cable TV. Senior Government officials paid supervisory visits to the field to ensure effective implementation of the project. The model was evaluated through pre and post assessment. Members of Rover Scout collected data on TAPS from the field using structured check list and questionnaire independently.

**Results:** The results show that, there was 81% reduction in number of posters with tobacco product advertisement within shops selling tobacco products and 86% reduction of the same outside shops in project area. No billboards or banners were found with tobacco advertisement during baseline or end-line survey. Ninety six percent coloured flyers with advertisement decorating the shops disappeared by the end of the project. Seventy eight percent shopkeepers stopped displaying cigarette packets in front of their box kiosk through glass window. Gifts given to shopkeepers and buyers by tobacco companies reduced by 85% and 69% respectively. Tournament supported and lottery arranged by tobacco companies stopped completely.

**Conclusion:** Public awareness & monitoring by tobacco control task force would reduce TAPS.

**Table-1:** Advertisement found in the point of sale (n= Number of shops observed)

Advertisement at point of sale	Pre-assessment (n=599) n (%)	Post-assessment (n=591) n (%)	Decrease (%)
Posters found in the shop	290 (48)	54 (9)	81
Colored flyer found hanging in the shop	189 (32)	7 (1)	98
Tobacco packs used for advertisement at the shop	208 (35)	45 (8)	78
<b>Promotion(n=65)*</b>			
Retail shopkeepers received gifts from the company in last 3 months	20 (31)	3 (5)	85
Consumers received gifts from company through retail shopkeepers	13 (20)	4 (6)	69
Arrangement of lottery in last 3 months	1 (1.5)	0 (0)	100
<b>Sponsorship</b>			
Sponsored any competition in last 3 months	2 (3)	0 (0)	100

\* Sub sample of shops taken

### PD-1006-31 Effect of mass media campaign in Jinan city on public attitudes and perceptions involving implementation of the law

R Cao,<sup>1</sup> SM Ruan,<sup>2</sup> J Zhang,<sup>3</sup> C Chang,<sup>4</sup> XH Zhang,<sup>5</sup> X Zhang.<sup>3</sup> <sup>1</sup>Business Office, Jinan municipal Center for Disease Control and Prevention, Jinan, <sup>2</sup>Office, Jinan municipal Center for Disease Control and Prevention, Jinan, <sup>3</sup>Institute for chronic NCD prevention and control, Jinan municipal Center for Disease Control and Prevention, Jinan, <sup>4</sup>Institute for communicable and endemic disease prevention and control, Jinan municipal Center for Disease Control and Prevention, Jinan, <sup>5</sup>Immunization services division, Jinan municipal Center for Disease Control and Prevention, Jinan, China. e-mail: amoeba1982@sina.com

**Objective:** To evaluate in an all-round way the publicity effect of the tobacco control advertisement “Secondhand Smoking: Invisible Killer” (In hospitals and in offices), which was put in the city television platform of Jinan Municipal Bureau of Radio and Television Mobile TV Co., Ltd. so as to provide reference for improving the propaganda strategy of Jinan City’s tobacco control. **Methods:** In the five districts with city TV platform coverage, to choose 10 public places with intensive population flow and conduct a survey of 900 residents aged 18–45 years old, who have been in Jinan for 6 months and over. The sex ratio is 1:1.

**Results:** The response rate of the survey was 87.9% and 30.6% of the respondents were smokers. In the last year, 89.9% of the respondents have seen relevant advertisements on the hazards of smoking and 36.9% of them have read the “Invisible Killer Advertisement”. Smokers (46.3%) outnumbered the non-smokers (32.8%) ( $P=0.035$ ) in remembering the afore-said advertisement. Age and sex have no effect on whether to remember the advertisement. The vast majority of the respondents who have read the “Invisible Killer Advertisement” admitted its impact on them. They were exposed to the advertisement through buses (41.4%), television and the Internet (31.3%), hospitals and clinics (28.3%), and outdoor display screens (26.3%). There were significant differences among the groups of diverse ages in obtaining the

advertisement ( $P=0.011$ ). The respondents aged 18–25 years old made it mainly through television and the Internet. The respondents had a positive awareness of the hazards of smoking, but 19.0% of them still believed that the hazards of smoking are exaggerated and 4.5% of them regard smoking as a noble act. There were 10.8% of the respondents quitting smoking. Those who attempted to quit smoking in the last year accounted for 56.1% and those planning to quit smoking in the future, 36.6%. Whether they have read the advertisement or not made no significant differences concerning their quitting smoking.

**Conclusions:** The “Invisible Killer Advertisement” has a good coverage but limited impact on the smoking-related behavior of smokers. Based on the current carriers, we should continue to increase the broadcasting frequency on bus TVs and expand the propaganda carriers such as mobile phones and networks. In the mean time, we should increasingly enrich the content of tobacco control advertisement, providing more guidance and help to smokers.

### PD-1007-31 Direct advertisements of tobacco products still exist in Indian outdoor media? Results of a compliance survey across three jurisdictions in India

R Kumar,<sup>1</sup> A Chauhan,<sup>2</sup> P Lal,<sup>1</sup> R J Singh.<sup>1</sup> <sup>1</sup>Tobacco control, International Union Against Tuberculosis and Lung Disease, New Delhi, <sup>2</sup>Public health, SIHFV, Shimla, India. e-mail: rkumar@theunion.org

**Background:** India being signatory to FCTC, has an obligation to impose comprehensive ban on tobacco advertising, promotion and sponsorship (TAPS). Section 5 of Indian tobacco control legislation (COTPA) prohibits all forms tobacco products advertisements in all media including outdoors. However, one can find several violations in the outdoor media especially on billboards, public transport vehicles and transit stations. Present study was conducted to map the ongoing violations and status of compliance to Section 5 of COTPA and subsequent rules related to ban on TAPS in India.

**Design/Methods:** A cross-sectional survey using a tool developed by The Union South East Asia, New Delhi was conducted in 1<sup>st</sup> quarter of 2013 across three jurisdictions (Chennai, Vadodara and Shimla) in India. Advertisements on billboards, transit media and street furnitures were looked at city centre, bus stations, railway stations, taxi stands, national highways, road intersections, local fair sites, stadium, areas around larger educational institutions, market places, event sites and auto rickshaw stands in each jurisdiction.

**Results:** There were total 27 direct advertisements of smokeless tobacco products (of eight tobacco companies) in Chennai city displayed as wall writing on private premises companies distribution’s vehicles and traffic sign boards. Besides this, there were, total 44 violations surrogate advertisements and brand stretching/trademark diversification in these jurisdictions [Chennai city (29),



Vadodara city (12) and Shimla (3)]. Billboards, public transport vehicle and transit media are most common mode of outdoor advertisements.

**Conclusions:** Despite complete ban, direct advertisements are still carried out in India. Outdoor media is also being exploited by tobacco industry for TAPS as a medium for surrogate advertisements, brand stretching and trademark diversification. The current level of violations in outdoor media by tobacco companies warrants an immediate stronger action from the law enforcer.

#### **PD-1008-31 Health warnings on cigarette packages and interest in quitting: findings from the Global Adult Tobacco Survey (GATS)**

T Aris,<sup>1</sup> J Morton,<sup>2</sup> GH Tee,<sup>3</sup> L Zhao,<sup>2</sup> J Rarick.<sup>4</sup> <sup>1</sup>Director's Office, Institute for Public Health, Kuala Lumpur, Malaysia; <sup>2</sup>Office on Smoking and Health, Center for Disease Control, Atlanta, GA, USA; <sup>3</sup>Center for Communicable Diseases Research, Institute for Public Health, Kuala Lumpur, Malaysia; <sup>4</sup>Office for Tobacco Free Initiative, WHO Western Pacific Regional Office, Manila, Philippines. Fax: (+60)0322823114. e-mail: helentee.gh@moh.gov.my

**Background:** Health warnings (HW) on cigarette packages have been shown to increase awareness on smoking health risk, instill fear intensity to the effects of smoking, stimulating thoughts in quitting, preventing smoking initiation and promote cessation among smokers. This study examines findings from the Global Adult Tobacco Survey (GATS) in five countries in assessing the effects of HW on cigarette packages and interest in quitting.

**Methods:** GATS is a national household survey using multi-stage cluster sample design to produce internationally comparable data on tobacco use and indicators of tobacco control. We analysed the data from 33,482 respondents aged 15 years and older who participated in the GATS during 2011–2012 in Malaysia, Indonesia, Argentina, Romania and Nigeria. Current smokers were asked "In the last 30 days, did you notice any health warnings on cigarette packages?", "In the last 30 days, have warning labels on cigarette packages led you to think about quitting?" and "During the past 12 months, have you tried to stop smoking?". These indicators were analysed by selected socio-demographic characteristics.

**Results:** Romanian (98.0%) and Malaysian (94.1%) men had the highest proportion of noticing health warnings on cigarette packages. Whereas for women, it was in Romania (97.6%) and Argentina (89.3%). However, only about 70% of men in Argentina (75.3%), Malaysia (70.9%) and Nigeria (70.0%) thought about quitting smoking because of the HW on cigarette packages. In women, the proportion ranged from 50.6% (Nigeria) to 100% (Indonesia). In addition, less than 50% of men and women [except for Malaysian females (63.5%) and Nigerian females (54.8%)] tried to quit smoking in the past 12 months.

**Conclusions:** These cross country data provided analyses on the awareness of HW on cigarette packages and their effectiveness in prompting smokers to think and tried to quit smoking within a country and cross-country comparison. These analyses provide great opportunity

for countries to assess the effectiveness of their HW labels in communicating the risk of smoking to all current smokers. Countries can use these evidence-based findings to target tobacco control interventions to increase quit rates among current smokers and prevent smoking initiation among non-smokers.

#### **PD-1009-31 Pictorial health warning: a breakthrough in tobacco control in Indonesia**

L.S. Sulistyowati,<sup>1</sup> A.S. Bunga Untung,<sup>2</sup> T S Bam.<sup>3</sup>

<sup>1</sup>Ministry of Health, Health Promotion Centre, Jakarta,

<sup>2</sup>Ministry of Health, Health Promotion Centre, Jakarta,

<sup>3</sup>International Union Against Tuberculosis and Lung Disease, Tobacco Control Department, Jakarta, Indonesia.

e-mail: tsbam@theunion.org

**Background:** In Indonesia, two out three males (67%) and 2.7% females smoked tobacco. Among current smokers, 72.2% noticed health warnings on cigarette packages of whom only 27.1% thought quitting smoking. Indonesia has not signed WHO Framework Convention on Tobacco Control yet but some policy works on progress.

**Objectives:** To explain the pictorial health warning (PHW) policy initiative for effective public education and information on danger of tobacco use. **Approaches:** Approaches included amendment of Health Law 2009 with subsequent regulation and decrees passed. The texts of the law in regard to health warning were strengthened through litigation and made the PHW mandatory.

**Results:** Current health warning in cigarette packs is only on text "Smoking can cause maternity problems and birth defect, cancer, heart attack and impotency" that covers about 15% either side of the pack. With a strong civil society advocacy along with the Ministry of Health, government regulation with PHW was passed in 2012 and subsequently a ministerial decree number 28 was issued in April 2013. The new warnings, which are scheduled to enforce in June 2014, will include five pictures that will appear on 40% of both the front and back of cigarette packages. A new regulation of Ministry of Finance No. 62, 2014 would further strengthen the implementation.

**Conclusion:** PHW builds upon the evidence base indicating that prominent health warnings that combine pictures and text are more effective than text only messages in engaging smokers, increasing knowledge about risks, promoting thoughts about quitting, and decreasing demand for cigarettes.

#### **PD-1010-31 Media advocacy for implementation of stronger pictorial health warnings on all tobacco packs in India**

B Mathew.<sup>1</sup> <sup>1</sup>Tobacco Control, Voluntary Health Association of India, Delhi, India. e-mail: binoymathew84@gmail.com

**Background and challenges to implementation:** Pictorial health warnings are an effective measure to warn tobacco users of the harm of tobacco use. Pictorial warnings on packaging of tobacco products is legally mandated as per

India's national tobacco control legislation Cigarettes & Other Tobacco Products Act (COTPA 2003)

**Intervention or response:** Using earned media to create pressure on policymakers and to put indirect pressure on the Government to maintain compliance of Pictorial Health Warnings. The strategy was to ensure that news items or stories come out to attract the attention of the government and the public. To do so, VHAI decided to increase consumer awareness about the issue of pictorial warnings in the news through a sustained strategy of media engagement. We increased our interactions with the media, both on a one-to-one basis and through Press Meets and Media Sensitization Workshops from January – December 2012. Brief yet accurate press releases were also issued to the print media as templates for stories.

**Results and lessons learnt:** A total of 20 press meets were held on pack warnings in Delhi and 15 states of India. To sustain the media's engagement with the issue, over the course of a year, about 25 to 30 press releases were shared with journalists on the pack warning in Delhi and 15 states. This strategy of media advocacy resulted in nearly 150 stories in National and Vernacular Media.

**Conclusions and key recommendations:** The Government notified a completely new set of visuals to serve as pack warnings from April 1, 2013. The media was sensitized and in the process, a personal rapport began was developed with journalists. VHAI's state level network, tobacco control partners and linkages with vernacular media helped to make the PW issue an All-India campaign.

#### **PD-1011-31 Media advocacy for the implementation of regulating smoking in films**

**M Bhavna.**<sup>1</sup> <sup>1</sup>Tobacco Control, Voluntary Health Association of India, Delhi, India. e-mail: binoymathew84@gmail.com

**Background and challenges to implementation:** India, the world's largest producer of movies produces more than 1000 movies a year in several languages. Bollywood represents the Indian Hindi movie industry and the worldwide viewership for their movies is estimated to be about 3 million. Bollywood movie stars in India are public figures, have large fan followings and exercise tremendous influence on the behavioural attitudes of adolescents. One of the major influences on the uptake of teen tobacco use is the glamorization of tobacco use in movies and on television. Movies are seen as very influential for kids and teens.

**Intervention or response:** Using earned media to create pressure on policymakers and to put indirect pressure on the Government to ensure implementation of the rules notified by the Government of India which firmly intended to regulate the depiction of tobacco use in Films and Television w.e.f the prescribed date of implementation. The strategy was to ensure that news items or stories come out to attract the attention of the government and the public. To do so, VHAI decided to increase consumer awareness about the issue of smoking scenes in films through a sustained strategy of media

engagement. We increased our interactions with the media, both on a one-to-one basis.

**Results and lessons learnt:** In order to sustain the media's engagement with the issue, over the period of time, about 8 to 10 press releases were shared with the journalists and this strategy of media advocacy resulted in nearly 40 – 45 stories in National and Vernacular Media during May to December 2012.

**Conclusions and key recommendations:** From November 2012 onwards, the new films screened at movie halls started showing the disclaimers of 30 seconds each on the ill-effects of tobacco use with strong graphic pictures of cancer affected mouth, pictures on how smoking causes heart attacks, effects of second hand smoke etc both in English & Hindi that appeared in the beginning and during the interval of the movie.

#### **PD-1012-31 Field-based study in seven states of India to evaluate and recommend an effective strong pictorial health warning on tobacco product packages**

**S Gupta.**<sup>1</sup> <sup>1</sup>Tobacco Control, Voluntary Health Association of India, Delhi, India. e-mail: binoymathew84@gmail.com

**Background and challenges to implementation:** Tobacco product packages are effective mediums for informing current and potential users about the harmful impact of tobacco use. Research evidences exist to prove that effective warning labels increase knowledge about risks associated with smoking and can influence future decisions about smoking. Large and graphic warnings can motivate tobacco users to quit, discourage non-smokers/non-users from initiating and keep ex-users from starting again.

**Intervention or response:** A qualitative study was carried out by Voluntary Health Association of India (VHAI) with the support of its state chapters, through focus group discussions and individual interviews. The main objective of this study was to explore and gather public opinion regarding the new shortlisted set of pictorial health warnings presented by the Ministry of health and family welfare, and assess feedback on the range of messages conveyed through these warnings. Focused group discussions (FGDs) were carried out with different sets of respondents in the rural and urban areas of 7 states representing all four regions in India (viz- Arunachal Pradesh, Bihar, Orissa, Uttar Pradesh, Madhya Pradesh, Andhra Pradesh & Kerala). The sample size of the study in each of the states was 100. The participants were segregated into 3 different groups of women, men and youth. Possible suggestions for improving / modifying the warnings also formed a part of this discussion. Structured individual interviews were also conducted with tobacco users, non users & retailers of all tobacco products to assess their opinion towards the pictorial health warnings and its impact. A total of 11 pictures, including 8 provided by Ministry of Health and Family Welfare, were field-tested.

**Results and lessons learnt:** As a result of the study, out of the 11 pictures, one warning showing a cancer-affected

mouth, which was recommended by maximum respondents during the field testing, was notified by the Ministry of Health and Family Welfare, Government of India.

**Conclusions and key recommendations:** The Indian Tobacco Control Act, (COTPA) 2003 provides for placement of pictorial health warnings on all tobacco products covering 40% of the principal display area in the front panel of the pack. It also provides for rotation of the warnings every 12 months or earlier as prescribed by the Parliament.

### PD-1013-31 Tobacco industry interference in India: games the industry plays

B Mathew.<sup>1</sup> <sup>1</sup>Tobacco Control, Voluntary Health Association of India, Delhi, India. e-mail: binoymathew84@gmail.com

**Background and challenges to implementation:** Tobacco industry one of the most profitable industries in the world. Tobacco companies use their enormous wealth and influence both locally and globally to market their deadly products. Even as advocacy groups and policy makers work to combat the tobacco industry's influence, new and manipulative tactics are used by tobacco companies and their allies to circumvent tobacco control efforts.

**Intervention or response:** We keep a close track and monitor tobacco industry tactics and also overview the Tobacco Advertising Promotion Sponsorship

**Results and lessons learnt:** Monitored Different Types of Tobacco Industry Tactics in India: Package Advertising: During festival seasons, colourful packagings of tobacco products with special designs have become a common sight. Product Placement in Movies: Industry has been successful in product placement in movies and promoting tobacco through film stars. Corporate Social Responsibility Activities (CSR): As part of the image building exercise, most of the tobacco companies engage in social, culture activities and promote their corporate logo, company and brand names under the guise of philanthropic activities. Trademark Diversification: Tobacco industry directly promotes their company trademarks by using the same to sponsor other activities and events. Internet Promotions: The industry effectively and discreetly uses social networking sites like "Facebook" to promote its products. One can find many groups in the name of cigarette brands on social networking sites. The products are aggressively promoted on these sites through & among the youth. Free Sampling: Promotion of their new tobacco products & distribution of free samples among the youth.

**Conclusions and key recommendations:** Even as advocacy groups and policy makers work to combat the tobacco industry's influence, new and manipulative tactics are used by tobacco companies and their allies to circumvent tobacco control efforts. It is important for tobacco control advocates to know which companies are present in their country, how and where they operate, the types and quantity of products sold, and marketing tactics used to sell tobacco products. By being informed

about all aspects of the tobacco industry within a country, advocates are better equipped to fight for effective tobacco control policies.

## ORAL ABSTRACT PRESENTATION SESSIONS

### 11. DRUG MONITORING AND ADVERSE EVENTS

#### OAP-280-31 Therapeutic drug monitoring for first-line tuberculosis agents in adults

K Wilby,<sup>1</sup> M Ensom,<sup>2</sup> F Marra.<sup>2</sup> <sup>1</sup>College of Pharmacy, Qatar University, Doha, Qatar; <sup>2</sup>Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC, Canada. e-mail: fawziah@mail.ubc.ca

**Background:** Therapeutic drug monitoring (TDM) is widely used to optimize efficacy and safety of many commonly used drugs today. Although TDM of first-line antitubercular drugs is used during treatment of tuberculosis (TB), it is currently unknown if this enhances therapeutic efficacy or safety. The primary objective of this review was to summarize and evaluate the available literature describing clinical and pharmacokinetic outcomes associated with TDM of first-line treatment agents in TB patients. Secondary objectives were to summarize and evaluate the available literature describing pharmacokinetic outcomes.

**Methods:** A systematic literature review using MEDLINE, EMBASE, International Pharmaceutical Abstracts, Google, and Google Scholar was conducted for articles describing TDM outcomes for first-line tuberculosis agents in adults. A total of 38 studies were included in the review; 32 assessed rifampin, 24 isoniazid, 16 pyrazinamide, and 15 ethambutol.

**Results:** Of the included studies, 25 reported on clinical outcomes pertaining to TDM, 34 on percentage of patients achieving concentrations in the therapeutic range, 10 on impact of dosage adjustment on achieving target concentrations, 16 on HIV or diabetes patients on anti-TB medications. Studies did not show any meaningful effect of TDM on clinical outcomes. Majority of the studies showed standard dosing does not achieve target concentrations for the first-line anti-TB drugs. Presence of HIV and diabetes appeared to indicate achievement of lower than target concentrations.

**Conclusions:** No clear indication for TDM in the general TB population was found but evidence for TDM in special populations (HIV, diabetes) needs to be assessed in further clinical trials.



### OAP-281-31 Comparative characterisation of mycobacteria isolates using conventional and molecular methods

P Nwadike,<sup>1</sup> A.O. Koker,<sup>2</sup> C C Onubogu, Phd,<sup>1</sup> N. Nwokoye,<sup>1</sup> N Onyejebu,<sup>1</sup> M Gidado,<sup>3</sup> O Idigbe.<sup>1</sup>

<sup>1</sup>National TB REFERENCE LAB, National Tuberculosis Reference Laboratory, Nigeria Institute for Medical Research Yaba, Lagos State, Lagos, <sup>2</sup>Department of Medical Microbiology, University of Lagos, Nigeria, College of Medicine, University of Lagos, Lagos, <sup>3</sup>TB CARE 1 Project, Abuja Nigeria, KNCV/TB CARE 1, Abuja, Nigeria. e-mail: petrousbone@yahoo.com

**Introduction:** Globally the burden of Tuberculosis (TB) has been on the increase, especially in developing countries and Nigeria inclusive. Although there are several species of mycobacterium, however not all cause diseases in human. The species that cause TB in immune-competent individuals belong to the *Mycobacterium tuberculosis* complex (MTBC). Successful treatment of TB disease depends largely on identifying the bacilli and treating with the correct combination of drugs, as Non-Tuberculous Mycobacterium (NTM) does not respond to MTBC regimen.

**Objective:** To identify different species of Mycobacterium using the Geno Type Mycobacterium CM.

**Methodology:** Sputum samples from 1867 TB suspects were processed between February and August, 2011 using Ziehl Nelson (ZN) smear microscopy at the National TB Reference Laboratory, of the Nigerian Institute of Medical Research Lagos, Nigeria. Smear positive samples were cultured on Lowenstein-Jensen (LJ) medium. Mycobacterial isolates obtained were characterized and identified by molecular (Geno Type Mycobacterium CM) method, using the conventional biochemical method as gold standard.

**Result:** Out of 95 smear positive samples cultured, 57 (60%) were Mycobacterial isolates with contamination rate of 3.2%. Specie identification with Geno Type Mycobacterium CM was possible for 45 (78.9%) isolates while conventional methods were able to identify 41 (71.9%) to specie level, with 10 (17.5%) inconclusive identification. Among the identified Mycobacterial Species were *M. tuberculosis* complex, *M. fortuitum*, *M. abscessus*, *M. immunogenum*, *M. intracellulare*, *M. gardinae* and *M. scrofulaceum*. Turn-around time for molecular and biochemical methods were 8 hours and 10 days respectively.

**Conclusion:** The data above suggest that Geno Type Mycobacterium CM is a veritable tool with high specificity for identifying Mycobacterium isolates to specie level. The low turn-around time will facilitate early detection and better management of patient with correct drug regime.

### OAP-282-31 A randomised controlled trial of protein calorie supplementation in HIV-infected patients with tuberculosis

A Magohe,<sup>1</sup> M Bakari,<sup>1</sup> T Mackenzie,<sup>2</sup> I Maro,<sup>1</sup> A Urasa,<sup>1</sup> K Hendricks,<sup>2</sup> R Waddell,<sup>2</sup> F C Von Reyn.<sup>2</sup> <sup>1</sup>Research, Muhimbili University of Health and Allied Sciences, Dar Es Salaam, United Republic of Tanzania; <sup>2</sup>Research, The Geisel School of Medicine at Dartmouth, Hanover, NH, USA. e-mail: katanaalbertmagohe@gmail.com

**Background:** We have shown that women in Tanzania with tuberculosis and newly diagnosed HIV infection have dietary deficiencies in energy and protein intake. We conducted a randomized controlled trial to determine if energy and protein supplementation would improve health outcomes in this setting.

**Design/Methods:** We enrolled 151 women in their first two weeks of anti-Tb therapy with newly diagnosed HIV and before being initiated on ART and randomized them to receive either a Protein Calorie Supplement (PCS, 1062 kCal, 42 gm protein) plus Micronutrients (MNS) or MNS control alone for 6 months. Assessments included dietary intake, food insecurity, anthropometrics and CD4 count.

**Results:** Median CD4 at baseline was 203 among 76 women randomized to PCS-MNS and 189 among 75 women randomized to MNS only. Median BMI at baseline was 20 in both groups. Median CD4 change at 2 months (just before initiation of ART) was 65 and 57 among those randomized to the PCS (N=47) and MNS (N=52) groups respectively. Median BMI change at 2 mos was 1.19 and 0.78 for those randomized to the PCS (N=47) and MNS (N=52) only groups respectively. Median CD4 change at 8 mos was 490 vs 399 for the PCS (N=22) and MNS (N=25) groups respectively, and median BMI change was 1.11 vs and 2.87.

**Conclusion:** A controlled trial of protein-calorie supplementation in women with active tuberculosis and newly diagnosed HIV infection has shown an initial trend toward improved CD4 response in those receiving the intervention. Full data on outcomes in all 151 women will be presented. Funding: National Institutes of Health, 1R01HD057614 and Fogarty International Center, D43-TW006807 Clinicaltrials.gov NCT01635153

### OAP-283-31 Genetic polymorphism NAT2 gene and incidence of hepatotoxic adverse reactions in patients with pulmonary tuberculosis

A Kazakov.<sup>1</sup> <sup>1</sup>Research Institute of Phthisiopulmonology, I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation. e-mail: axelex@yandex.ru

**Setting:** One of the reasons for the imperfect high efficiency of treatment of socially important diseases such as tuberculosis are frequent hepatotoxic adverse reactions to anti-TB drugs. Evaluation of patients predisposing to such reactions may be provided in recognition of the polymorphism of N-acetyltransferase-2 genes (NAT2) which are responsible for the metabolism of isoniazid.

**Objectives:** to identify mutations in NAT2 genes which are associated with increased frequency of hepatotoxic adverse reactions to isoniazid in patients with pulmonary tuberculosis.

**Material and methods:** The study is single-center, case-control, is included 62 patients in age from 18 up to 55 years old with respiratory tuberculosis and signs of drug-induced hepatitis, received isoniazid in standard dosages. These patients were studied NAT2 genotype by polymerase chain reaction method with restriction analysis.

**Results:** In this group of patients homozygous for the NAT2\*4 gene consistent with genotype of fast acetylators is 3,1%\* (n=2), heterozygous consistent with genotype of average acetylators is 18% (n=12), and 78,1%\* (n=50) of patients have not got mutations corresponding NAT2\*4 what is typical for genotype of slow acetylators (\*-  $\chi^2 = 37.31$ ).

**Conclusions:** In case the patient has a genotype corresponding to genotype of slow acetylators, the risk of hepatotoxic reactions is higher than in patients with homozygous for NAT2\*4 gene. Thus, rapid molecular genetic diagnostics of NAT2 gene mutations allows timely correct the dose of isoniazid and prevent the development of hepatotoxic adverse reactions.

#### OAP-284-31 Paradoxical reactions in HIV-negative patients with spinal TB: our experience

L Ramani,<sup>1</sup> M Mehta,<sup>1</sup> K Tiwari,<sup>1</sup> M Darmalingam.<sup>1</sup>

<sup>1</sup>Respiratory Medicine, Whipps Cross University Hospital, London, UK. e-mail: lucilleramani@gmail.com

**Background:** The aim of this case series is to describe our experience of spinal tuberculosis (TB) paradoxical reactions (PRs) over a 5 year period, highlighting the importance of the spine as a site of PRs, which can result in serious morbidity and calling attention to how no clear guidance exists in its management.

**Methods:** All cases of spinal TB between January 2009 and March 2014 were identified at Whipps Cross University Hospital, East London using the London TB Register. The case notes, blood profiles, microbiology and radiology for each patient were reviewed. A patient was labelled as a case of spinal TB if they had: (1) clinical symptoms suggestive of TB; (2) radiology consistent with spinal TB; (3) microbiologically confirmed TB or histology suggestive of TB; and (4) worsened after a period of initial improvement with new spinal lesions, despite being on appropriate anti-TB treatment. All patients had non-compliance, drug resistance and further pathology excluded.

**Results:** There were 379 cases of TB over the 63 month period, with 29 of these being spinal. We identified 3 cases of PR within the spine. Time-to-onset of PR was 2 months, 3 months and 6 months. 2 patients had attempted CT guided drainage of paraspinal abscesses, 1 of which failed. All 3 patients had high dose oral steroids, 2 of which made full recoveries, with no residual functional deficit. 1 patient failed to respond, resulting in substantial neurological deficit and morbid-

ity. This patient is currently undergoing a period of rehabilitation.

**Conclusion:** Spinal PRs have a notable paucity in the literature. Due to the risk of irreversible neurological deficit, PRs at this site can be particularly concerning and require prompt diagnosis using a high index of suspicion. In addition, PRs can present atypically late. Median reported time to onset of PR is 60 days. 1 patient from our case series presented significantly later than this. Further studies are essential to better characterise PRs in HIV negative patients and its most appropriate management (both medical and surgical), particularly in cases of spinal involvement.

#### OAP-285-31 No evidence of QT prolongation with a four-month TB regimen with gatifloxacin at 400mg/day substituting for ethambutol

P Oliaro,<sup>1</sup> C Merle,<sup>2</sup> B Bah,<sup>3</sup> F Kassa,<sup>4</sup> T Mthiyane,<sup>5</sup>

A Ndiaye,<sup>6</sup> E Amukoye,<sup>7</sup> K Fielding.<sup>2</sup> <sup>1</sup>WHO/TDR, UNICEF/ UNDP/World Bank/ WHO Special Programme for research and Training in Tropical Diseases, Geneva, Switzerland; <sup>2</sup>IDE, London School of Hygiene & Tropical Medicine, London, UK; <sup>3</sup>Service de Pneumo-Phtisiologie, Hôpital Ignace Deen, Conakry, Guinea; <sup>4</sup>CNHPP, Programme National de lutte contre la tuberculose, Cotonou, Benin; <sup>5</sup>Tuberculosis, MRC, Durban, South Africa; <sup>6</sup>PNLT, Programme National de Lutte contre la Tuberculose, Dakar, Senegal; <sup>7</sup>Pneumology, KEMRI Institute, Nairobi, Kenya. e-mail: oliarop@who.int

**Background:** Fluoroquinolone (FQ) antibiotics variably affect ventricular repolarisation, measured as prolonged QT interval on the ECG. Gatifloxacin is a fourth-generation FQ. The potential for QT prolongation was compared in a randomised Phase 3 trial (OFLOTUB) between standard 6-month (Control) and a short regimen with gatifloxacin given at 400mg/d for 4 months replacing ethambutol (Test). We also compared the appropriateness of commonly used and new QT corrections in this population.

**Methods:** The study was conducted in 5 African countries (Senegal, Benin, Guinea, Kenya, South Africa). ECG measurements were recorded at baseline and at week 4, 8 and end of treatment (week 16: Test; week 24: Control arm) 1–5 hours after drug intake (coinciding with drug peak plasma levels). Analyses were conducted as per International Conference on Harmonisation guidelines.

**Results:** At baseline (n=1686 ECGs), uncorrected QT increased markedly with heart rate ([HR] median 96/min, interquartile range 83–106). The Bazett formula ( $QTcB = QT/RR^{0.5}$ ) overcorrected; Fridericia ( $QTcF = QT/RR^{0.33}$ ) undercorrected for HR; a non-linear model estimated the best correction to be  $QT/RR^{0.4081}$  in this adult African TB population. At follow-up, as patient conditions improved with treatment and HR slowed down, Fridericia gave the best correction and was used for between-treatment comparisons. The peak QTcF value in follow-up was >480ms for 21 patients, 0.9% (7/807) and 1.8% (14/801) in the Test and Control arms (risk difference 0.9%, 95%CI -2.0% to 2.3%, p=0.12);

5 and 4 patients, respectively had a QTcF>500ms which dropped to <450msec except in all but one patient in the Control arm. Overall 106 (6.6%) patients had a peak measurement change from baseline of >60ms, which was similar by treatment arm (adjusted difference 0.8%, 95%CI -1.4% to 3.1%, p=0.47). A clinically non-significant difference was found in mean peak QTc: adjusted mean difference 2.5ms (95%CI 0.2 to 4.8, p=0.032). No clinical signs/symptoms attributable to prolonged QT were detected.

**Conclusions:** A 4-month regimen with gatifloxacin at 400mg/d did not carry an increased risk of QT prolongation over standard TB treatment. Possible use in combination with second-line drugs with QT prolongation potential should be further studied. The Fridericia correction is appropriate for follow-up measurements for this population but might underestimate QT prolongation at baseline TB.

### OAP-286-31 Pharmacokinetic and safety/tolerability study of higher oral and intravenous doses of rifampicin in adult tuberculous meningitis patients

vyck Yunivita,<sup>1</sup> S Dian,<sup>2</sup> A.R Ganiem,<sup>2</sup> E Hayati,<sup>2</sup> T.H Achmad,<sup>3</sup> R Van Crevel,<sup>4</sup> R Aarnoutse,<sup>5</sup> R Ruslami.<sup>1</sup>  
<sup>1</sup>Pharmacology and Therapy, Universitas Padjadjaran, Bandung, <sup>2</sup>Neurology, Universitas Padjadjaran, Bandung, <sup>3</sup>Biochemistry, Universitas Padjadjaran, Bandung, Indonesia; <sup>4</sup>Internal Medicine, Radboud University Nijmegen Medical Centre, Nijmegen, <sup>5</sup>Pharmacy, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands.  
 e-mail: sofiatidian@gmail.com

**Background:** Intensified treatment using high dose intravenous (IV) rifampicin (=RIF) reduced mortality of tuberculous (TB) meningitis (Ruslami, LID 2013). We now explored if higher doses of oral RIF has a similar pharmacokinetic (PK) profile compared to high dose IV and safe.

**Design/Methods:** A phase 2 randomized, 3-arm, 2-period PK study was conducted on adult TB meningitis (aged > 17 years) patients hospitalized at Hasan Sadikin Hospital, Bandung, Indonesia. Eligible subjects were randomized to oral RIF 750 mg (~15mg/kg), 900 mg (~20mg/kg), or IV 600 mg (~13 mg/kg) for 14 days in combination with other standard TB drugs. After 14 days of treatment all patients continued with standard treatment. PK of RIF was assessed twice, at first 3 day and at day 14 (steady state) of treatment. Total plasma concentrations of RIF were measured by a validated UPLC method. RIF AUC<sub>0-24</sub> was determined using noncompartmental approach using Winonlin.

**Results:** Thirty patients were randomly assigned to receive 750 mg oral (n=11), 900 mg oral (n=9), and IV 600 mg (n=10) of RIF. After 3 days, geometric mean (range) AUC<sub>0-24</sub> of 750 mg oral, 900 mg oral and IV RIF 600 mg were 131.4 mg.h/L (38.1-275.1), 164.8 mg.h/L (66.9-291.2), and 145.7 mg.h/L (77.7-430.2), respectively. AUC<sub>0-24</sub> of 750 mg oral RIF was 10% lower, while AUC<sub>0-24</sub> of 900 mg oral RIF was 13% higher than that of 600 mg IV RIF. As for maximum

concentration (C<sub>max</sub>), IV administration led to a higher C<sub>max</sub>. Geometric mean (range) of RIF C<sub>max</sub> among 3 groups were 14.3 mg/L (6.1-22.2), 16.2 mg/L (5.7-28.3), and 24.7 (13.9-37.8) mg/L respectively. There was no difference of C<sub>max</sub> data after 3 and 14 days (p > 0.05). Hepatotoxicity was the most common adverse event (15/30 patients) and equally distributed among groups. Nine patients experienced grade 3 or 4 hepatotoxicity (one had a reversible grade 4 hepatotoxicity). No hypersensitivity occurred and no patient died because of hepatotoxicity or other RIF serious side effect. No significant difference in AUC<sub>0-24</sub> of RIF was found between those who experienced with and without severe hepatotoxicity.

**Conclusion:** The study showed that oral RIF 900 mg (~20mg/kg) had a similar PK profile compared to IV RIF 600 mg (~13 mg/kg) and that it was safe. The previous findings with high-dose IV RIF should be replicated with a high oral dose, and even higher dose of RIF should be explored. Finding the right dose of RIF could alter the standard of care and reduce mortality and morbidity of TB meningitis.

Table. Pharmacokinetics of rifampicin at the first three day of treatment

	Dose of rifampicin		
	750 mg p.o. (n=10)	900 mg p.o. (n=9)	600 mg IV (n=9)
AUC <sub>0-24</sub> (mg.h/L)	131.4 (38.1-275.1)	164.8 (66.9-291.2)	145.7 (77.7-430.2)
C <sub>max</sub> (mg/L)	14.3 (6.1-22.2)	16.2 (5.7-28.3)	24.7 (13.9-37.8)
T <sub>max</sub> (h; median, range)	2.1 (1.1-8.1)	2.3 (1.9-8.1)	1.5 (1.5-1.8)
t <sub>1/2</sub> (h)	5.4 (3.2-15.7)	6.1 (3.8-14.7)	4.9 (3-15.6)
CL/F (L/h)	5.7 (2.7-19.7)	5.5 (3.1-13.4)	4.1 (1.4-7.7)
V/F (L)	44.7 (26.6-129.7)	47.9 (35.0-104.6)	28.2 (19.9-38.5)

Data were in geometric mean (min-max), unless otherwise indicated. p.o: per oral, IV: intravenous, AUC<sub>0-24</sub>: area under the time-concentration curve up to 24 h after dose, C<sub>max</sub>: maximum plasma concentration, T<sub>max</sub>: time to C<sub>max</sub>, t<sub>1/2</sub>: half-life, CL/F: apparent clearance, V/F: apparent volume of distribution, F: bioavailability.

### OAP-287-31 Rapid oral desensitisation: alternative therapeutic very useful in major anti-tuberculosis drugs allergy

H Daghfous,<sup>1</sup> Z Haifa,<sup>1</sup> S Ben Saad,<sup>1</sup> moun Ben Khelifa,<sup>1</sup> F Tritar.<sup>1</sup> <sup>1</sup>Respiratory Department, Abderahman Mami Hospital, Ariana, Tunisia. Fax: (+216) 7182 1184.  
 e-mail: hafaoua.daghfous@yahoo.fr

**Background:** Desensitization with drugs may be indicated in some clinical situations. Experience with anti-tuberculous (anti-TB) drugs is limited. **Objective:** Evaluate the effectiveness of rapid oral desensitization for cases with side-effects to both isoniazid (INH) and rifampicin (RFP).

**Patients and Methods:** Rapid oral desensitization protocols for INH and RFP were performed in 4 departments of Pneumology between 2002 and 2012. These protocols included increasing doses of drug, administered with resuscitation equipment at bedside, over a short period of



time, until the therapeutic dose. Diluted oral pills were be used for desensitization.

**Results:** Eighteen rapid oral desensitization were done in 15 cases (7 men and 8 women, mean age: 33 years). Urticarial reactions were noted in all cases, anaphylaxis and angioedema were occurred in 3 and 4 cases. Desensitization for RFP was undertaken in 13 patients. The 1st administration was 0,1 mg and the final dose was 600 mg in all cases. Desensitization for Isoniazid (INH) was tried in 5 patients with a mean 1st dose of 0,25 mg and a final dose respectively 200 mg (n=2), 250 mg (n=1) and 300 mg (n=2). Cumulative dose of INH and RFP was reached after 150 minutes in all cases. Successful desensitization therapy was achieved in 13 cases (4 INH, 9 RFP). But failure of desensitization was concluded in 4 cases.

**Conclusion:** This multicentric study illustrate the benefits of rapid oral desensitization to major anti-TB drug, allowing to reintroduce the drug and guaranteeing the success of the patients therapy.

## 12. FINDING CASES: HOW GOOD ARE OUR NOTIFICATION SYSTEMS?

### OAP-288-31 Active case finding: a much needed strategy to increase TB case detection in unreachable areas

R K Fatima,<sup>1</sup> E Qadeer,<sup>1</sup> D A Enarson,<sup>2</sup> S G Hinderaker.<sup>3</sup>  
<sup>1</sup>Research, National Tuberculosis Control Program Pakistan, Islamabad, Pakistan; <sup>2</sup>Research, International Union Against Tuberculosis and Lung Disease and University of Stellenbosch, Western Cape, South Africa; <sup>3</sup>Research, HSLP UK, London, UK. Fax: (+92)51 8438 081.  
 e-mail: drrazia\_fatima@yahoo.com

**Background:** In Pakistan, patients with symptoms suggestive of tuberculosis (TB) seek care from a wide array of health-care providers. Therefore, many people with TB are expected to be missed from notifications in the national TB program. To evaluate the increase in case notification of smear positive TB by active case finding at community based chest camps by engaging the private providers.

**Design/Methods:** A cross sectional study of tuberculosis case detection associated with a project using an integrated intervention and chest camps. We evaluated an active case detection intervention retrospectively in 5 randomly selected districts with urban slums of Sindh Province Pakistan.

**Results:** From April 2011 to September 2012, the total number of clients seen in the camps was 165,280. Of all attendees, 13,481 (12.7%) were examined by sputum smear microscopy. The proportion smear positive was significantly higher among those from engaged private providers than among those referred from camps (OR 1.54, 95% CI 1.42-1.66). During the project, the total number of smear positive TB notifications increased over the intervention period from 5,158 to 8,275.

**Conclusion:** Active case detection by engaging private providers and chest camps can significantly increase the number of smear positive TB case notifications.

### OAP-289-31 How much is TB screening worth? Estimating the value of active case finding for tuberculosis in South Africa, China and India

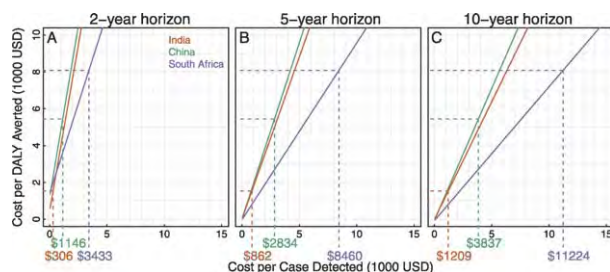
A Azman,<sup>1</sup> J Golub,<sup>2</sup> D Dowdy.<sup>1</sup> <sup>1</sup>Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, <sup>2</sup>Center for Tuberculosis Research, Dept. of Medicine, Div. of Infectious Diseases, Johns Hopkins School of Medicine, Baltimore, MD, USA. e-mail: azman@jhu.edu

**Background:** Current approaches are unlikely to achieve the aggressive global tuberculosis (TB) control targets set for 2035 and beyond. Active case finding (ACF) may be an important tool for augmenting existing strategies, but evidence of its impact and cost-effectiveness is scant. In the absence of data, models can offer "best available evidence" estimates of impact and cost-effectiveness of ACF to guide decision-making.

**Design/Methods:** We constructed dynamic models of TB in India, China, and South Africa to explore the medium-term impact and cost-effectiveness of ACF activities, conceptualized separately as discrete (two-year) campaigns and as continuous activities integrated into ongoing TB control programs. Our primary outcome was the cost per disability adjusted life year averted; we sought to identify the cost per case detected under which ACF would meet recommended cost-effectiveness thresholds.

**Results:** Discrete campaigns costing up to \$1,200 (95% Uncertainty Range [UR] 856- 2,108) per case actively detected and started on treatment in India, \$3,800 (95% UR 2,692-6,356) in China, and \$11,200 (95% UR 10,086-21,197) in South Africa were all highly cost-effective. Prolonged integration was even more effective and cost-effective. Short-term assessments of active case finding dramatically underestimated potential longer-term gains; for example, an assessment of an ACF program at two years might find a non-significant 11% reduction in prevalence, but a 10-year evaluation of that same intervention would show a 33% reduction.

**Conclusion:** Active case finding can be a powerful and highly cost-effective tool in the fight against tuberculosis. Given that short-term assessments may dramatically underestimate medium-term effectiveness, current willingness to pay may be too low. Active case finding should receive strong consideration as a basic tool for TB control in most high-burden settings, even when it may cost over \$1,000 to detect and initiate treatment for each extra case of active TB. Figure. Incremental cost-effectiveness versus cost per case detected and treated within discrete ACF campaigns. Dashed lines and corresponding numbers show the cost per case detected to meet the "highly cost-effective" threshold in India (red), China (green), and South Africa (purple). Panel A considers only effects that occur in the first two years, whereas B and C consider costs and effects over five and ten years, respectively.



### OAP-290-31 Tuberculosis incidence among person born in the 22 high-burden countries now living in the United States

P K Moonan,<sup>1</sup> J Oeltmann.<sup>1</sup> <sup>1</sup>Division of Tuberculosis Elimination, U.S. Centers for Disease Control and Prevention, Atlanta, GA, USA. Fax: (+1)404-639-8959. e-mail: pmoonan@cdc.gov

**Background:** There are 22 countries that account for >80% of the world's burden of tuberculosis (TB). Persons born in these countries who subsequently move to low burden areas account for additional TB cases and often influence the local epidemiology. Since 2004, the majority of reported tuberculosis cases in the United States occurred among foreign-born persons. Thus, the index of suspicion for TB among foreign-born persons remains high. Previous studies have suggested that persons recently migrating to low burden countries often have a TB incidence similar to their home countries.

**Objective:** To describe the TB incidence among persons who migrated from the 22 high burden countries now living in the United States.

**Methods:** We used data from publicly available reports from the U.S. Centers for Disease Control and Prevention, the American Community Survey and the World Health Organization. We calculated annual TB case rates among persons born in the 22 high burden countries now living in the United States during 2005–2012. We compared calculated country-specific TB incidence rates among persons living in the United States and those reported for each country by the World Health Organization.

**Results:** Among the 57,379 foreign-born TB cases reported in the United States, 20,147 (35%) occurred among persons born in the 22 high burden countries. In 2012, the cumulative TB incidence of persons from the 22 high burden countries living in the United States was 22.7 per 100,000 population, substantially lower than the cumulative global estimate of 159.3 per 100,000 population of their home-country counterparts. The difference in TB incidence among persons living in the United States as compared to their home-country counterparts varied from country to country, but the largest differences occurred among persons from South Africa (–8517%) and the Russian Federation (–3781%).

**Conclusion:** Clinicians in low burden countries, like in Europe and North America, should remain vigilant for diagnosing TB among foreign-born persons. However, the risk of TB, even among persons from the highest

burden countries, is considerably less than rates reported among the counterparts in their countries of birth. These data underscore the importance of pre-immigration TB screening and treatment policies and further investment in TB prevention and care activities abroad.

### OAP-291-31 Case notification rate and risk factors for tuberculosis among HIV-infected patients after ART initiation in Myanmar

YN Aung,<sup>1</sup> STT Tun,<sup>2</sup> S K K Zaw,<sup>3</sup> S Hla Myint,<sup>3</sup> A Thida,<sup>3</sup> T Lwin,<sup>4</sup> M Shwe,<sup>5</sup> P Clevenbergh.<sup>2</sup> <sup>1</sup>Monitoring and Evaluation, International Union Against Tuberculosis and Lung Disease (The Union), Mandalay, <sup>2</sup>Integrated HIV Care, The Union, Mandalay, <sup>3</sup>TB Unit, The Union, Mandalay, <sup>4</sup>Health, Disease Control, Ministry of Health, Nay Pyi Taw, <sup>5</sup>Health, National AIDS Program, Ministry of Health, Nay Pyi Taw, Myanmar. Fax: (+95) 271082. e-mail: dr.yunandaraung@gmail.com

**Background:** In 2012, tuberculosis (TB) incidence was 377(322–435)/100,000 persons/year in general population in Myanmar. In HIV infected patients, TB is the most common opportunistic infections. Anti-retroviral treatment (ART) has been shown to reduce the incidence of TB. Isoniazid Prophylaxis Therapy (IPT) and infection control are additional methods implemented by the National TB Program. This study aims to assess the case notification rate (CNR) of TB, the effect of ART on TB CNR and risk factors associated with occurrence of TB among HIV patients enrolled into Mandalay General Hospital.

**Design/Methods:** Retrospective cohort study of patients enrolled between May 2005 and January 2014, followed up for at least 1 month, ART naive, no TB at the time of enrollment, no prior history of TB and TB free during first month after enrollment. Patients' information was extracted from electronic database. TB CNR was calculated. Multivariate logistic regression was done to identify risk factors for TB.

**Results:** Total 3,561 patients were enrolled in the study. Median length of follow up was 1.22 years (IQR: 0.5–2.2). Findings were: male 52%, median age: 35 years (IQR: 30–41), median baseline BMI: 19 kg/m<sup>2</sup> (IQR: 17–22), median baseline CD4: 142 cells/mm<sup>3</sup> (IQR: 71–241), median baseline haemoglobin (Hb): 12gm% (IQR: 10–13). 35% (1222/3561) received IPT. 117 new TB cases occurred during 5464 Person-Years (PY) of follow up. The overall TB CNR was 2141 per 100,000 PY (95%CI: 1774–2561). TB CNR was 7500/100,000 PY (95%CI: 5772–9549) within 3 months of ART start, 1753/100,000 PY (95%CI: 1202–2466) within 3 months to 1 year of ART start, 724/100,000 PY (95%CI: 415–1174) within 1 year to 3 years of ART start and 1406/100,000 PY (95%CI: 645–2653) over 3 years of ART start. Risk factors for TB were: male sex (OR:3.12,  $p < 0.01$ , 95%CI: 1.9–5.14), baseline CD4 less than 100 cells/mm<sup>3</sup> (OR: 4.7,  $p < 0.01$ , 95%CI: 1.67 – 13.25), baseline Hb below 10 g% (OR: 1.79,  $p < 0.01$ , 95%CI: 1.18–2.73) and WHO stage 3 or 4 (OR: 3.83,  $p < 0.01$ , 95%CI: 1.97 – 7.45). IPT was protective (OR: 0.11,  $p < 0.01$ , 95%CI: 0.04–0.31).

**Conclusion:** TB CNR among HIV infected patients is reduced after 3 months on ART to rebound after 3 years possibly due to ART failure. Male sex, low baseline CD4, anaemia at enrollment, advanced WHO stage were found to be the independent risk factors for TB. IPT has protective effect. Early health seeking, early initiation of ART, diagnosis of first line ART failure and IPT are required to reduce the risk of TB among HIV patients.

### OAP-292-31 Strengthening tuberculosis notification by private health sector: a way forward for improving tuberculosis care, Jharkhand, India

R Pathak,<sup>1</sup> R Dayal,<sup>2</sup> V Ghule,<sup>1</sup> B Gupta,<sup>3</sup> A Sreenivas,<sup>1</sup> K Rade,<sup>1</sup> S Balakrishnan,<sup>1</sup> A Soren.<sup>4</sup> <sup>1</sup>TB Control in India, WHO country office for India, New Delhi, , <sup>2</sup>Department of Health and Family Welfare, Govt. of Jharkhand, State Tuberculosis Centre, Ranchi, <sup>3</sup>Department of Health and Family Welfare, Govt. of Jharkhand, District Tuberculosis Centre, Bokaro, Jharkhand, Bokaro, <sup>4</sup>Department of Health and family Welfare, Govt. of Jharkhand, District Tuberculosis Centre, Dumka, Jharkhand, Dumka, India.  
e-mail: pathakr@rntcp.org

**Background:** India accounts for the highest tuberculosis (TB) burden in the world. An estimated 2.86 million TB cases have been reported in 2012. However, the Revised National TB Control Programme of India (RNTCP) notified 1.48 million TB cases and almost half of the estimated were missed in programme notification. India has a robust private health sector with almost half of all patients with TB seek care in the private sector as the first point of care even for patients who are eventually treated in the public sector. It has been reported that delay in diagnosis and non-adherence to treatment are comparatively more in the private health sector. This highlights the need to engage the private sector and improve the TB notification and overall the qualities of TB care in the country. **Methodology:** Based upon the population structure and people profile, districts Bokaro and Dumka were selected for evaluating the TB notification from the private sector in Jharkhand during April-September 2013 using a standard formats for health establishment registration and TB notification reporting by registered health facilities. The data was digitalized in newly adapted RNTCP notification software 'NIKSHAY', a case based web based information and communication technology for TB Notification. To evaluate TB notification by private sector data was extracted from the NIKSHAY portal and de-duplicated by cross matching with TB register.

**Results:** Of 91 private health facilities registered for TB notification, 19 (21%) notified TB cases during the study period. Among TB notifying health facilities 10% were laboratories, 25% were multispecialty hospitals and 53% were single private practitioners. In the same period the districts notified 2716 TB cases of which 331 were by the private health facilities contributing to ~12.2% of overall TB notification of which 246 (74%) were male and 77 (26%) were female. Among notified cases, ~7%

were of age below 15 years in private sector compared to ~3% in public sector.

**Conclusions and key recommendations:** While the collaborative efforts between RNTCP and private sector in the district has improved TB notification, 79% of registered private health facilities missed the opportunity to notify TB cases. Private health facilities are important sources of TB notification to bring down the missing cases. However, more efforts are needed to identify the constraints and gaps in involving the private sector health facilities in TB notification.

Table 1: Characteristics of Private health facilities registered and notifying TB patients in districts between April to September 2013 of Bokaro & Dumka, Jharkhand

Type of Health facilities	Health facilities registered in Nikshay	Number (%) of TB cases notified
State	Bokaro & Dumka	Bokaro & Dumka
Private Hospital/Clinic/Nursing Home etc.(multi)	32	19
Private Laboratory	11	2
Private Practitioner/Clinic etc.(single)	48	310
<b>Total (Private Health Facilities)</b>	<b>91</b>	<b>331</b>
Notified health facilities & TB notification in Public sector	68	2385
<b>Overall health facilities registered in Nikshay</b>	<b>106</b>	<b>2716</b>
Percentage contribution from health facilities other than Public		12.2%

### OAP-293-31 Aetiology of "TB symptoms" amongst people attending for HIV care in South Africa

Y Hanifa,<sup>1</sup> S Toro Silva,<sup>1</sup> F Sahid,<sup>2,3</sup> A Von Gottberg,<sup>4,5</sup> N Ndlovu,<sup>6</sup> V Chihota,<sup>6,7</sup> S Charalambous,<sup>6,7</sup> A Grant.<sup>1</sup> <sup>1</sup>Clinical Research, London School of Hygiene & Tropical Medicine, London, UK; <sup>2</sup>Medicine, Chris Hani Baragwanath Hospital, Johannesburg, <sup>3</sup>Clinical Medicine, University of the Witwatersrand, Johannesburg, <sup>4</sup>The Centre for Respiratory Diseases and Meningitis, National Institute for Communicable Diseases, Johannesburg, <sup>5</sup>University of the Witwatersrand, Johannesburg, <sup>6</sup>Research - Epidemiology, The Aurum Institute, Johannesburg, <sup>7</sup>School of Public Health, University of the Witwatersrand, Johannesburg, South Africa. e-mail: yhanifa@hotmail.com

**Background:** WHO recommends screening people living with HIV (PLHIV) for TB at each clinical encounter, with further evaluation of those screening positive. TB symptoms are common amongst PLHIV and despite negative TB investigations a proportion remain symptomatic. As part of the XPHACTOR study, which evaluates a novel algorithm to prioritise TB investigation in the context of Xpert MTB/RIF roll-out, we undertook a substudy to evaluate causes for persistent "TB symptoms" amongst ambulatory adults attending for HIV care.

**Methods:** In the XPHACTOR study a systematic sample of clinic attendees were screened for TB and Xpert requested if high priority for TB according to XPHACTOR algorithm (any of: cough, BMI<18.5, CD4<100, weight loss ≥10%). All were reviewed monthly, with reinvestigation if indicated, to 3 months when sputum and blood were taken for TB culture. We systemically evaluated a consecutive sample of participants with persistent TB symptoms (any of: cough, fever, night sweats) at both enrolment and 3 months, or ≥5% measured weight loss at 3 months, and without TB



diagnosis. All were assessed by a clinician and investigated using standard protocols appropriate to symptoms. **Results:** 114/1074 (11%) participants were eligible at 3 months. Among 83 evaluable participants, 37 were pre-ART at enrolment (76% female, median age 34 years, median CD4 261 cells/mm<sup>3</sup>); and 50 on-ART (78% female, median age 44 years, median CD4 492 cells/mm<sup>3</sup>, median duration on ART 65 months). Among on-ART group compared with pre-ART group, 33/50 (66%) vs. 33/37 (89%), 14/50 (28%) vs. 5/37 (14%), and 6/50 (12%) vs. 1/37 (3%), had  $\geq 5\%$  weight loss, persistent cough or persistent night sweats respectively ( $>1$  symptom per participant). Final diagnoses (Table) were available for 40 participants. The most common diagnoses were TB 12/40 (30%); likely asthma or COPD 7/40 (18%); underlying malignancy 4/40 (10%), Hodgkin's lymphoma (n=2), renal cell carcinoma (n=1), metastatic carcinoma primary-unknown (n=1); and weight loss resolving after ART initiation 3/40 (8%). Among those with microbiologically confirmed TB 5/7 (71%) had previously had  $\geq 1$  negative Xpert.

**Conclusions:** Undiagnosed TB is the main cause of persistent symptoms in this population who have previously undergone systematic screening and investigation for TB, particularly amongst those who are ART-naïve. PLHIV with persistent "TB symptoms" require ongoing evaluation for TB which should include TB culture and imaging studies.

Table: Final diagnoses for persistent "TB symptoms" in adult clinic attendees with HIV in South Africa

Diagnosis	On ART (N=24) n (%)	Pre-ART (N=16) n (%)	Total (N=40) n/N (%)
Microbiologically confirmed TB <sup>1</sup>	5/24 (20.8)	2/16 (12.5)	7/40 (17.5)
Probable TB <sup>2</sup>	1/24 (4.2)	4/16 (25)	5/40 (12.5)
Likely asthma / COPD	2/24 (8.3)	5/16 (31.3)	7/40 (17.5)
Underlying malignancy <sup>3</sup>	4/24 (16.7)	0	4/40 (10)
Weight loss resolved after ART initiation	0	3/16 (18.8)	3/40 (7.5)
Post TB bronchiectasis / chronic effusion	3/24 (12.5)	0	3/40 (7.5)
Type 2 diabetes	2/24 (8.3)	1/16 (6.3)	3/40 (7.5)
Lower respiratory tract infection	2/24 (8.3)	0	2/40 (5)
Chronic rhinosinusitis related cough	2/24 (8.3)	0	2/40 (5)
<i>Bordetella pertussis</i> infection	1/24 (4.2)	0	1/40 (2.5)
ACE inhibitor induced cough	1/24 (4.2)	0	1/40 (2.5)
GORD related cough	1/24 (4.2)	0	1/40 (2.5)
Chronic diarrhoea due to Giardiasis	0	1/16 (6.3)	1/40 (2.5)

<sup>1</sup>Xpert® (n=1), culture+ for *M. tuberculosis* (n=6)

<sup>2</sup>Abdominal ultrasound suggestive of extrapulmonary TB (n=3), pleural effusion (n=1), pericardial effusion (n=1)

<sup>3</sup>Confirmed Hodgkin's lymphoma (n=2), metastatic renal cell carcinoma (n=1), metastatic carcinoma primary unknown (n=1)

COPD = chronic obstructive pulmonary disease; GORD = gastroesophageal reflux disease

sumptive TB (those with cough for 2 weeks or more) by health care providers working in high work load outpatient settings of tertiary-level health care facilities. TB cases thus missed continue to suffer and spread the infection to others. One of the administrative measures recommended for infection control is fast tracking of cough patients. To improve TB case finding and infection control in health care settings, a 'cough corner' (a dedicated counter in the outpatient setting manned by an existing health care provider who was trained to counsel patients and fast-track them to TB diagnosis and treatment) was established at Dr Zakir Hussain Municipal Hospital in Nashik, Maharashtra, India in December 2013. In addition, all the health care providers of the hospital were sensitized to route presumptive TB patients through the 'cough corner'. In this study, we aimed to assess the impact of this intervention on TB case finding and treatment initiation.

**Methods** We reviewed the programme records (TB laboratory and treatment register) and extracted aggregate data on number of presumptive TB patients examined, number of TB patients diagnosed and time to treatment initiation during the period January-March 2014 and compared them with that of the period January-March 2013.

**Results** During January-March 2014, there was an increase in number of presumptive TB patients examined and pulmonary TB cases diagnosed by 24% and 36% respectively as compared to January-March 2013 with approximately same new adult outpatient visits (~9000 patients) during both periods. The median time (Inter Quartile Range) to treatment initiation from date of diagnosis among smear-positive TB cases decreased from 4 (1–5) days in January-March 2013 to 1 (1–3) day in January-March 2014.

**Conclusion** Sensitization of health care providers and enhanced visibility and support via 'cough corner' helped to improve detection of TB cases and reduced the time to treatment initiation. As an existing health care provider was used for manning the 'cough corner', this intervention appears feasible and scalable to other similar high-workload settings. Future research should focus on the impact of this intervention on infection control.

## OAP-294-31 Finding "missing" TB patients: impact of a dedicated "cough corner" in a busy out-patient public health setting of Maharashtra, India

S Dapkekar,<sup>1</sup> B Pawar,<sup>2</sup> A Kumar,<sup>3</sup> P Malik,<sup>1</sup> A Sreenivas,<sup>1</sup> N Wilson,<sup>4</sup> A Nikam.<sup>2</sup> <sup>1</sup>Tuberculosis, WHO Country Office for India, New Delhi, <sup>2</sup>Tuberculosis and Leprosy Control, Directorate of Health Services, Maharashtra, Pune, <sup>3</sup>Research, The Union, South-East Asia Regional Office, New Delhi, <sup>4</sup>Public Health, Independent Public Health Consultant, New Delhi, India. e-mail: drshankardapkekar@gmail.com

**Background** Finding the source of 'missed' cases and innovative measures to detect them are required to achieve universal access to TB care. Previous programme reviews and research studies have showed that there were missed opportunities in identifying patients with pre-

## OAP-295-31 Using epidemiologic data and community engagement to address the burden of tuberculosis among foreign-born populations in New York City

S Ahuja,<sup>1</sup> J Sullivan Meissner,<sup>1</sup> L Trieu,<sup>1</sup> M Macaraig,<sup>1</sup> M Alexander,<sup>1</sup> J Burzynski.<sup>1</sup> <sup>1</sup>Bureau of Tuberculosis Control, New York City Department of Health and Mental Hygiene, New York, NY, USA. e-mail: sahuja@health.nyc.gov

**Background:** NYC is a global city with 37% of the population born outside the United States. While TB rates declined from 51.1/100,000 in 1992 to 8.0/100,000 in 2013, the proportion of foreign-born TB cases increased from 18% to 84%. This disparity in TB burden suggests core TB control activities are not sufficient in the foreign-born. Well-documented barriers

to healthcare among the foreign-born hamper TB case detection, contact identification, and treatment initiation/adherence, while the diversity of NYC's population challenges a one-size-fits-all approach. From 2001–2010, 143 countries were represented among 9630 TB cases; TB incidence and patient characteristics varied by country of birth (Table). To focus resources, we used numerous data sources to identify foreign-born groups at higher risk and inform the development of targeted interventions to reduce TB.

**Intervention:** NYC surveillance reports, census data, and TB patient data were reviewed. Priority populations were selected by a multidisciplinary team based on several factors; supplemental data analyses were initiated for the 3 groups selected. Health needs assessments—including qualitative data collection among TB patients, community representatives and healthcare providers—were conducted to engage stakeholders and identify community-specific resources and needs. Internal and external partners helped refine data collection and analysis methods.

**Results:** Mexican, Tibetan, and Chinese communities were selected as priority populations based on high TB burden, incidence, clustering, population size and potential for extending interventions to other foreign-born groups. We engaged 30+ local and international government, community and healthcare organizations and conducted 54 semi-structured key informant interviews about healthcare-seeking practices and TB knowledge/experience. Partnerships with healthcare providers and community organizations facilitated needs assessment implementation and the development and dissemination of tailored TB educational materials.

**Intervention** development, implementation and evaluation are ongoing.

**Conclusions:** Shifting TB burden to a diverse foreign-born population led to a strategic, data-driven approach to enhancing TB control in NYC. Detailed analysis of local epidemiology was critical for identifying groups at higher risk and prioritizing resource allocation, while needs assessment facilitated stakeholder engagement and identified community-specific resources and needs.

Table. Select characteristics of New York City tuberculosis patients by top 20 countries of birth

Country of Origin	N	Median age in years (range)	Median years in US (range) <sup>1</sup>	HIV+ (%)	TB Incidence in NYC (per 100,000)
United States	2786	46 (0–101)	N/A	28	5.5
Foreign-born	6844				
Bangladesh	211	34 (3–75)	3 (0–27)	1	43.7
China	1214	49 (9–96)	9 (0–71)	1	41.7
Colombia	84	46 (2–89)	15 (0–50)	12	11.8
Dominican Republic	478	41 (1–88)	10 (0–59)	8	13.7
Ecuador	576	30 (1–89)	4 (0–47)	3	47.7
Guinea	79	33 (1–59)	2 (0–20)	28	NA
Guyana	166	43 (1–84)	9 (0–57)	10	11.5
Haiti	394	44 (2–90)	11 (0–70)	26	43.5
Honduras	111	37 (2–71)	6 (0–43)	21	36.7
India	371	37 (4–89)	5 (0–43)	2	46.9
Jamaica	88	49 (1–81)	19 (0–55)	14	5.1
Korea	237	47 (16–93)	11 (0–40)	1	NA
Mexico	471	30 (3–84)	6 (0–83)	7	32.8
Nepal	155	28 (9–70)	2 (0–20)	1	NA
Pakistan	179	43 (4–88)	5 (0–40)	1	52.4
Peru	145	38 (16–89)	6 (0–53)	6	48.0
Philippines	288	49 (7–96)	7 (0–64)	2	51.6
Trinidad & Tobago	78	45 (13–77)	15 (0–41)	24	8.3
Vietnam	80	48 (18–87)	13 (0–30)	1	58.9

### 13. EPIDEMIOLOGY: WHERE IS TB? HOTSPOTS, HOSPITALS AND THE HIGHLANDS OF MEXICO

#### OAP-296-31 Spatial and temporal distribution of tuberculosis in the highlands region of Chiapas, Mexico: preliminary results

A Gómez-Velasco,<sup>1</sup> H Sánchez-Pérez,<sup>1,2</sup> E Valencia,<sup>1</sup> R Batista-Martínez,<sup>3</sup> A Bencomo-Alem,<sup>4</sup> W Bonifaz,<sup>1</sup> JA Muños-Hernández.<sup>5</sup> <sup>1</sup>Sociedad, Cultura y Salud, El Colegio de la Frontera Sur, San Cristobal de las Casas, <sup>2</sup>ECOSUR, Grupos de Investigación en Salud para América y África Latinas, San Cristobal de las Casas, Mexico; <sup>3</sup>The Department of Anthropology, Colorado State University, Fort Collins, CO, USA; <sup>4</sup>Salud Publica, Programa de Tuberculosis, Instituto de Salud del Estado de Chiapas, San Cristobal de las Casas, Chiapas, <sup>5</sup>Sistemas de Salud, Instituto Nacional de Salud Publica, Cuernavaca, Morelos, Mexico. Fax: (+52) 967 674 9021. e-mail: agv23@yahoo.com

**Background:** Despite having adopted the DOTS program in 1996, the Highlands region of Chiapas, Mexico, still has one of the highest tuberculosis (TB) rates in Mexico. It is well known that social and environment factors contribute to TB dynamic transmission, but TB control efforts are traditionally focused on the individual patient. However, TB transmission moves beyond individual cases to include public spaces such as communities and cities. The identification of larger geographical areas with on-going TB transmission, using geographic information systems (GIS) technology, can provide strategies to improve TB control efforts. In this study, we used GIS to identify, grade and map across municipalities that conform the studied region.

**Design/Methods:** Based on four data sources: the National Surveillance System platform (SINAVE), household surveys, hospital-users surveys and visits to institutionalized and autonomous health centers, we gathered TB cases from 1997 to 2012 comprising the nineteen municipalities of that the Highlands region of Chiapas. The annual population per municipality was obtained from National Council Population (CONAPO), we then calculated the annual incidence rate per 100,000 inhabitants and mapped using ArcGis 9.3 GIS Software having universal transverse Mercator co-ordinate system.

**Results:** A total of 1326 TB cases were detected from 1997–2012; however, this number does not reflect the real magnitude of the disease due to under-diagnosis in the region. By analyzing the incidence rate per municipality per year, instead of number of cases only, and using GIS, we determined marked variation on the incidence rate within the region. For example, in 1998 there were eight municipalities (44%) with twice the incidence rate in comparison with the state and national levels, but in 2012 there was only one municipality. Furthermore, we identified two municipalities clusters of high incidence of TB: one grouped from the 1998 to 2000 period, and the second from the 2006 to 2007. This discrepancy may partially be explained due to the uneven population growth and internal migration within the region.

**Conclusion:** Using GIS, we identified clusters with high incidence rate of TB which health services were unable to detect with conventional methods. Therefore, a suitable strategy can be implemented accordingly to the socioeconomic and cultural characteristics in those areas with containing TB clusters.

### OAP-297-31 Spatial relationship between territories with socioeconomic vulnerability and deaths for pulmonary tuberculosis, in Sao Luis, Maranhão, Brazil

M Yamamura,<sup>1</sup> M Santos Neto,<sup>1</sup> F Chiaravalloti Neto,<sup>2</sup> M Popolin,<sup>1</sup> MCC Garcia,<sup>1</sup> L B B Rodrigues,<sup>3</sup> I Fronteira,<sup>4</sup> R Arcencio.<sup>1</sup> <sup>1</sup>Department of Maternal-Infantile Nursing and Public Health, Ribeirão Preto School of Nursing, University of São Paulo, Ribeirão Preto, SP, <sup>2</sup>Public Health, College of Public Health, University of São Paulo, São Paulo, SP, <sup>3</sup>Institute for Health Sciences, Federal University of Mato Grosso, Sinop, MT, Brazil; <sup>4</sup>International Public Health and Biostatistics, Institute of Hygiene and Tropical Medicine of the University Nova of Lisboa, Lisbon, Portugal.  
e-mail: mellinayamamura@yahoo.com.br

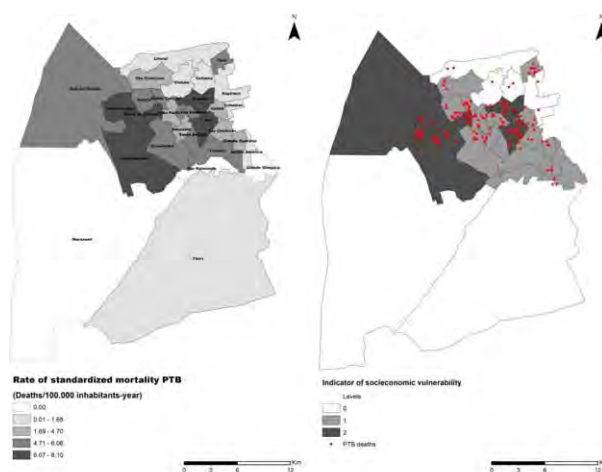
**Background:** Among the various prerogatives considered to achieve the elimination of Tuberculosis (TB) by 2050, it possible to mention the social determinants of the disease. The aim was to verify the spatial relationship between socioeconomic indicators and deaths from Pulmonary Tuberculosis (TB).

**Design/Methods:** Ecological study performed in São Luís, Maranhão, Brazil. It was considered the TB deaths between 2008 and 2012 according to the International Classification of Diseases, version 10. It was possible to construct social indicators through the analysis of principal components (APC), in the Statistica 10.1 software, and considering the variables of education, employment, income, sanitation conditions and households agglomeration that were obtained by the Demographic Census of the Brazilian Institute of Geography and Statistics, in 2010. The ecological aggregate considered for the study was the area of consideration. The geocoding of deaths was carried out in Terraview 4.2.2. It was performed the calculation of mortality rates for TB and standardized by age. It was used the multiple linear regression through the method of least squares and spatial regression to test the spatial dependence between social indicators and mortality rates for TB. In order to do that, it was utilized the R software.

**Results:** It was identified 193 deaths for TB that reverberated in rates from 0.00 to 8.10 deaths per 100,000 residents/year. In the PCA, two components showed total variance of 73.07%. The first component (56.75%) was defined as a socioeconomic development indicator and the second one (16.32%) determined a socioeconomic vulnerability indicator, with the levels: 0) low vulnerability, 2) intermediate vulnerability and 3) high vulnerability (Figure 1). In a multiple linear regression, the indicator of socioeconomic vulnerability was significant ( $p=0.0042$ ), with an adjusted  $R^2$  of 23.86%, and with the existence of spatial dependence (Moran  $I=0.2855$ ,  $p=0.0001$ ). The best model to address

the existing spatial dependence was the Model of Spatial Error that enabled to verify which areas with high vulnerability presented the highest mortality rates.

**Conclusion:** Deaths for TB are related to the territories with higher socioeconomic vulnerability. Therefore, they must be prioritized as areas of social and public investment, so that the technologies achieve those socially vulnerable groups and favor the achievement of the established goals.



**Figure 1:** The thematic maps of mortality rates distribution for TB, from 2008 to 2012, and the classification of consideration areas into three levels, according to the socioeconomic vulnerability indicator in São Luís, Maranhão, Brazil, 2014.

### OAP-298-31 Spatial scan statistic in the detection of risk areas to the hospitalisations for tuberculosis in Ribeirão Preto, SP, Brazil

MP Popolin,<sup>1</sup> M Yamamura,<sup>1</sup> I Freitas,<sup>1</sup> MCC Garcia,<sup>1</sup> M Santos Neto,<sup>1</sup> M Touse,<sup>1</sup> LH Arroyo,<sup>1</sup> RA Arcêncio.<sup>1</sup> <sup>1</sup>Maternal-Infant Nursing and Public Health, Ribeirão Preto School of Nursing, University of São Paulo, Ribeirão Preto, SP, Brazil. e-mail: marcelapopolin@yahoo.com.br

**Background:** Despite the important advances in the control of tuberculosis (TB), in the XXI century, the technological resources for diagnosis and treatment of the disease do not always reach out the populations in an equitable and fair manner, which ultimately trigger hospitalizations for TB that could be avoided. Thus, the aim was to analyze the spatiotemporal and spatial distribution of hospitalizations for TB in order to detect areas of risks about the occurrence of such event.

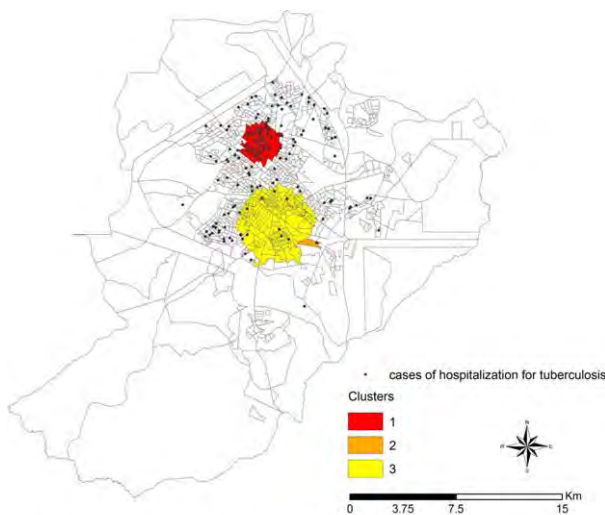
**Design/Methods:** Ecological study conducted in Ribeirão Preto, whose data was obtained from the Hospital Admissions System of the Unified Health System, from 2006 to 2012. It was possible to consider the clinical forms of TB whose hospitalizations are classified as avoidable. It was adopted the census tract as the geographical unit of the study. The population data was standardized for gender and age. The Terraview 4.2.2 software performed data geocoding. It was possible to carry out the statistical analysis of scanning to detect spatiotemporal and spatial areas of low and high relative risks through the use of the discrete model by Poisson. In relation to the spatiotemporal analysis, it was considered



the time accuracy in years. It was adopted the statistical significance when  $P < 0.05$ .

**Results:** It was recorded 169 admissions for TB, most males (79.29%) with a mean and median age of 48 years old. In the spatial analysis, three significant clusters were identified (Figure 1). Cluster 1 ( $p=0.001$ ), which consisted of 70 census tracts, presented an average rate of 10.9 cases per 100,000 inhabitants and relative risk of 3.47 (low RR). Cluster 2 ( $p=0.001$ ), which consisted of a census tract, showed an average hospitalization rate of 104.8 cases per 100,000 residents and relative risk of 28.59 (high RR). In the studied area, there is located a male prison. Cluster 3 ( $p=0.015$ ), which consisted of 214 sectors, showed an average rate of 1.1 per 100,000 residents and relative risk of 0.25 (low RR). In the spatiotemporal analysis, it was not identified areas or clusters with statistical significance.

**Conclusion:** The clusters visualization allowed the identification of areas with higher and lower risks of hospitalization for TB, and from the study, it was possible to establish priority areas of investment for health services.



**Figure 1:** Spatial clusters of hospitalizations for tuberculosis controlled by sex and age, in Ribeirão Preto, SP, Brazil (2006-2012).

### OAP-299-31 Mortality and associated factors of Chinese patients with extensively drug-resistant tuberculosis and pre-extensively drug-resistant tuberculosis

N Chu,<sup>1</sup> XL Zeng,<sup>1</sup> Y Zhang,<sup>2</sup> Wei Jing,<sup>1</sup> H Duan,<sup>1</sup> J Wang,<sup>1</sup> QF Wang,<sup>1</sup> LH Nie.<sup>1</sup> <sup>1</sup>Tuberculosis, Beijing Chest Hospital, Beijing, China; <sup>2</sup>Global Research and Services, Family Health International 360, Durham, NC, USA. e-mail: yzhang@fhi360.org

**Background:** The growing epidemic of extensively drug-resistant tuberculosis (XDR TB) and pre-extensively drug-resistant tuberculosis (pre-XDR TB) poses a serious public health challenge in China. Evaluating the survival outcomes of Chinese patients with XDR TB and pre-XDR TB is important for understanding the social impact of this epidemic. However, relevant data in the

literature is limited and likely underestimated the real situation, since the rate of loss to follow-up was particularly high in this patient population.

**Design/Methods:** Medical records of all patients diagnosed with XDR TB or pre-XDR TB from May 2011 to April 2012 at a regional tuberculosis referral center were reviewed. Active tracking was conducted to contact patients or family members by phone or home visit to obtain patients' vital status by April 2014. Logistic regression models were used to evaluate the factors associated with death.

**Results:** Among 149 patients evaluated, 55 were diagnosed with XDR TB and 94 were diagnosed as pre-XDR TB. 47 (32%) patients were women, and the median age at diagnosis was 43 years. Vital status was ascertained for 140 (94%) patients, including 52 XDR TB and 88 pre-XDR TB cases. Among 36 cases of death, the vital status of 31 (86%) was obtained through active tracking rather than medical record review. During 3 years from the latest diagnosis, 37% (19/52) patients with XDR TB and 19% (17/88) patients with pre-XDR TB were dead. 17 (11%) cases were cured, including 2 of XDR TB cases. In uni-variable models, XDR TB, older age, lower body mass index (BMI) and lower hemoglobin level at diagnosis were associated with increased risk of death. In multi-variable models, BMI < 18.5 (OR=3.3,  $p$  value=0.01), hemoglobin concentration at diagnosis < 110 gram/liter (OR=2.3,  $p$  value=0.06), and XDR TB (OR=2.2,  $p$  value=0.07) remained significant.

**Conclusion:** With active tracking, this study found a significantly higher mortality among Chinese patients with XDR TB and pre-XDR TB than previous reports. Patients with XDR TB, lower BMI or baseline anemia are at higher risk of death and should be given particular attentions. Disease burden related to XDR TB and pre-XDR TB in China needs to be re-evaluated, and the linkage of care, from diagnosis to palliative care, for this patient population should be strengthened.

### OAP-300-31 Tuberculosis in New York City: insights from a dynamic transmission model

N Stennis,<sup>1</sup> S Ahuja,<sup>1</sup> A Azman,<sup>2</sup> D Dowdy.<sup>2</sup> <sup>1</sup>Bureau of Tuberculosis Control, New York City Department of Health and Mental Hygiene, New York City, NY, <sup>2</sup>Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA. e-mail: nlevy@health.nyc.gov

**Background:** Since 1992, rates of tuberculosis (TB) have declined dramatically in New York City (NYC) despite ongoing in-migration. These gains have primarily been driven by a decrease in the number of cases and rates among the United States (US)-born population. Foreign-born cases now constitute over 80% of the total TB burden in NYC, and sustained declines in TB incidence among the foreign-born may be harder to achieve, making the national goal of elimination increasingly difficult.

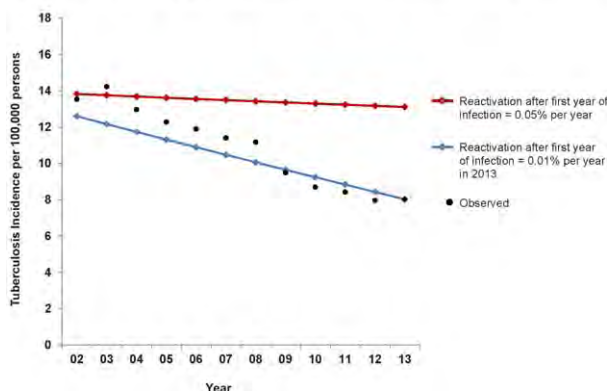
**Methods:** We constructed a dynamic transmission model of TB in the adult population of NYC, stratified by US- and foreign-birth. The model was calibrated to replicate observed trends in TB epidemiology (incidence and mortality, stratified by birth origin) from 1995–2013,

assuming ongoing importation of new TB cases based on reported immigration rates and global TB incidence. We evaluated rates of local transmission and reactivation that would be consistent with these observed trends, given continued TB importation. We then compared the projected population-level impact of screening and preventive therapy (e.g., in newly arrived immigrants) to that of active case finding in key populations.

**Results:** Assuming continued importation of TB in this simplified model framework, commonly cited estimates for the rates of TB transmission and reactivation led to unreasonably high estimates of TB incidence, suggesting that one or both of these values has likely declined in NYC over the last 20 years. A model where local TB transmission was extinguished and the annual risk of reactivation after the first year of infection remained constant at 0.05% resulted in stable TB incidence (Figure, red line), whereas one in which reactivation fell to 0.01% per year by 2013 fit the data well (blue line). In most model iterations, sustained declines in TB incidence were unattainable without further intervention, consistent with recent observations in NYC. Both preventive therapy and active case finding led to >20% reductions in projected TB incidence by 2025, but neither intervention on its own resulted in TB elimination.

**Conclusion:** Rates of TB transmission and/or reactivation have likely declined in NYC since the 1990's. Preventive therapy and active case finding will both be necessary to further reduce TB incidence in NYC, but achieving elimination will require additional interventions. This novel model of TB transmission in NYC demonstrates the utility of modeling for public health practice.

Figure: Tuberculosis incidence rates in New York City under zero transmissions per active tuberculosis case and varying assumptions for the rate of reactivation, 2002-2013



### OAP-301-31 Reduced tuberculosis notification and trends in gender disparities during large scale-up of TB-HIV care in rural Swaziland (2009–2013)

B Kerschberger,<sup>1</sup> A Antierens,<sup>2</sup> A Telnov.<sup>2</sup> <sup>1</sup>Medical, Medecins Sans Frontieres, Mbabane, Swaziland; <sup>2</sup>Medical, Medecins Sans Frontieres, Geneva, Switzerland.  
e-mail: benadi11@yahoo.de

**Background:** Gender disparity in tuberculosis (TB) has been reported with higher proportion of male cases

globally. We describe changes in gender distribution and TB case notification in a high TB/HIV prevalence setting during the large scale-up of TB/HIV care in rural Swaziland (2009–2013). Health services were decentralized from 3 secondary to 22 primary care facilities and anti-retroviral therapy (ART) coverage increased from 40% in 2009/10 to >80% in 2012/13.

**Design/Methods:** This is a retrospective cohort study using patient level data on first line TB treatment case notification (aged  $\geq 16$  years) and outpatient (OPD) consultation data from rural Shiselweni (Swaziland) (01/2009 to 12/2013). Gender differences were described using frequency statistics and chi-square test. Poisson regression was used to calculate population, gender and age adjusted incidence trends of TB notification.

**Results:** Overall access to OPD care was higher in women (1,040,681 (60%) vs 683,779 (40%) consultations). During the same time period, a total of 7,522 TB cases were reported, the median age was 35 (IQR 28–47) years and 73.3% (n=5,594) were HIV co-infected. The male/female ratio increased steadily from 0.8 to 1.1 for HIV co-infected and 1.1 to 1.8 for HIV negative TB cases. Overall annual TB notification declined from 2,369 in 2009 to 833 in 2013 and was higher for HIV co-infected TB cases (–64.6% vs HIV neg.: –45.5%;  $p < 0.01$ ). In multivariate analysis, the overall incidence risk decreased by 66% ([adjusted incidence risk ratio] aIRR 0.34; 95%CI 0.32–0.37). By gender, the decline was most pronounced in HIV co-infected females (–70.3%, [967 to 287] vs HIV pos. males: –57.6%, [771 to 327];  $p < 0.01$ ) and HIV negative females (–58.6% [181 to 75] vs HIV neg. males: –33.8% [201 to 133];  $p = 0.05$ ). Overall, adjusted TB notification incidence was increased by 32% for males (aIRR 1.32, 1.26–1.37). At diagnosis, females were less immunocompromised ([median CD4 count] 187, IQR 80–326) when compared to males (130.5, IQR 59–259;  $p < 0.01$ ) and were more likely on ART (32.4% vs 26.5%;  $p < 0.01$ ).

**Conclusion:** During ART scale-up, decline in TB case notification was most pronounced in HIV co-infected females leading to changes in gender disparity. Higher HIV burden among women intertwined with better access to TB/HIV care increased case detection and treatment for both diseases. Females appear to more benefit from TB/HIV service decentralization and attention needs to be paid to males to improve timely access.

### OAP-302-31 Detection of tuberculosis infection hotspots according to activity spaces in an inner urban setting in Shinjuku, Tokyo, 2003–2011

K Izumi,<sup>1,2</sup> A Ohkado,<sup>1</sup> K. Uchimura,<sup>1</sup> Y Murase,<sup>3</sup> Y Tatsumi,<sup>4</sup> K Fukuuchi,<sup>5</sup> H Watanabe,<sup>6</sup> N Ishikawa.<sup>4</sup>

<sup>1</sup>Epidemiology and Clinical Research, Japan Anti-Tuberculosis Association, Research Institute of Tuberculosis, Kiyose, <sup>2</sup>Graduate School of Biomedical Sciences, Nagasaki University, Nagasaki, <sup>3</sup>Mycobacterium Reference and Research, Japan Anti-Tuberculosis Association, Research Institute of Tuberculosis, Kiyose, <sup>4</sup>Director's Office, Japan Anti-Tuberculosis Association, Research Institute of Tuberculosis, Kiyose, <sup>5</sup>Director's Office, Koto Public Health Center, Koto, <sup>6</sup>Health, Shinjuku Public Health Center, Shinjuku, Japan. e-mail: kizumi95@gmail.com

**Aim:** Most previous tuberculosis (TB) hotspot studies have been limited by spatial analysis restrictions regarding residential addresses at diagnosis. In this study, we aimed to determine the spatial features of patient density based on the activity spaces where diagnosed patients had mainly resided during waking hours to estimate the possible TB transmission hotspots in an inner-urban setting in Japan.

**Methods:** Notified bacillus-positive TB patients in Shinjuku, Tokyo, between 2003 and 2011 were included in the present study. All TB bacilli isolated from each enrolled TB patient were subjected to restriction fragment length polymorphism (RFLP) analysis. A genotype cluster was defined as a group of patients with identical RFLP-band patterns. The calculated annual numbers of TB patients per km<sup>2</sup> (TB patient density) were based on activity space census tracts (CTs). Inverse distance-weighted (IDW) maps were created, and hotspots and coldspots were detected by Getis-Ords Gi\* (a spatial statistical method) and stratified according to the residential and genotype clustering statuses. Urban environmental variables within hotspots and coldspots were compared with the Mann-Whitney U test.

**Results:** Using an IDW map, we identified a patient density peak (41.7/km<sup>2</sup>/year) near the Shinjuku railway station, which is among the busiest transport hubs in Japan. Thirteen CTs (2.5 km<sup>2</sup>, 13.7% of the study area) and 36 CTs (1.1 km<sup>2</sup>, 6.3%) were detected as hotspots and coldspots, respectively. Of these, 61.6% of hotspots and 37.7% of coldspots comprised commercial zones. The densities of “amusement and recreation service” and “laundry, beauty, and bath service” facilities were significantly higher in hotspots than in coldspots ( $p < 0.0001$ ). The genotype-clustered and non-clustered homeless TB patient densities were notably concentrated near the station in the IDW map and formed strong hotspots with 99% confidence. However, the density of non-homeless genotype-clustered general inhabitants peaked slightly (8.2/km<sup>2</sup>/year) near the station, thus forming a weak hotspot (90% confidence), whereas the non-clustered TB patients were spread homogeneously, indicating no hotspot.

**Conclusion:** The activity space-based TB patient density analysis highlighted local transmission areas and hotspots with distinct urban environmental features.

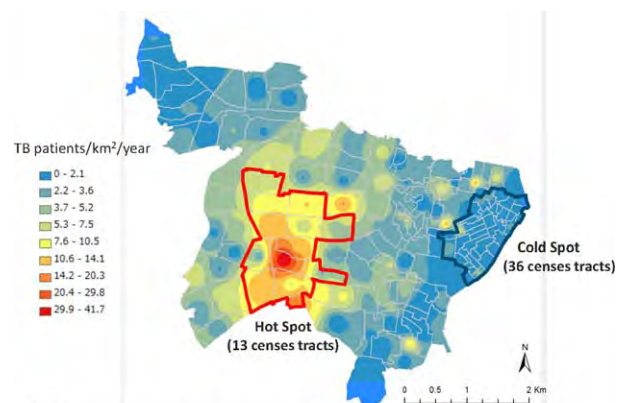


Figure. Inverse Distance Weighted (IDW) map (background) and Hot Spot Analysis (Getis-Ord Gi\*) (overlay) with annual number of TB patients per km<sup>2</sup>, using notified bacillus-positive TB patients of general inhabitants, foreigners, and the homeless in Shinjuku, Tokyo, 2003-2011

### OAP-303-31 Incorporating tuberculosis strain typing data into routine contact tracing investigations: experience from the field

M Munang,<sup>1</sup> C Browne,<sup>1</sup> S Khanom,<sup>2</sup> J Evans,<sup>2</sup> G Smith,<sup>2</sup> P Hawkey,<sup>2</sup> S Welch,<sup>1</sup> M Dedicoat.<sup>1</sup> <sup>1</sup>Infection and Tropical Medicine, Birmingham Heartlands Hospital, Birmingham, <sup>2</sup>Midlands Regional Centre for Mycobacteriology, Public Health England, Birmingham, UK. e-mail: melinda.munang@heartofengland.nhs.uk

**Background:** Strain typing of tuberculosis (TB) isolates by 24 loci mycobacterial interspersed repetitive unit-variable number tandem repeats (MIRU-VNTR) is now a routine laboratory tool for TB control in low-burden countries but its effectiveness has not been well established. We identified risk factors for clustering, characterised the main clusters and quantified the number of additional TB cases found after routine cluster investigation in Birmingham, UK (population 1.28 million, TB incidence 58 per 100,000 in 2012).

**Design/Methods:** Clustered ( $n=437$ ) and non-clustered ( $n=548$ ) cases notified between January 2010 and December 2013 were compared to identify risk factors for clustering. A dedicated TB nurse conducted all cluster investigations. Routinely available epidemiological information was reviewed and semi-structured interviews were undertaken with relevant cases. Network density (ratio of confirmed epidemiological links to total number of possible links, assuming an undirected network) for each cluster was calculated. Decisions on public health intervention were made at a monthly multi-disciplinary meeting.

**Results:** In multivariate analysis, UK birth (odds ratio [OR], 3.4; 95% confidence interval [CI], 2.6-4.6,  $P < 0.001$ ) Black Caribbean ethnicity (OR, 4; CI, 1.8-10,  $P < 0.001$ ), history of cannabis use (OR, 6.8; CI 3.3-15.8;  $P < 0.001$ ) and alcohol abuse (OR, 9.6; CI 4.8-22;  $P < 0.001$ ) were significantly associated with clustering. Sixty percent (81/136) of clusters were investigated and 119 patients were interviewed. Of 6 large clusters (median number of patients in each cluster 35, range 21-50), the cluster network density was low (range 0.38-1.98%). Three of the large clusters were endemic in



the UK-born population and the other 3 had a high proportion (71–87%) of foreign-born cases. Micro-epidemics within each large cluster could be identified but no additional public health intervention occurred. Strain-typing and cluster investigation were able to stem 2 outbreaks in casual transmission settings involving a religious venue and a workplace where expanded contact tracing was undertaken. The involved clusters were small (13 and 3 patients each). Overall 145 additional contacts were identified following cluster investigation, of which 27 had latent TB and 1 had active TB.

**Conclusion:** Incorporating strain-typing data in the TB service improves diagnosis of latent and active infection but requires investment in data management systems and human resource. Current capacity for enhanced epidemiological investigation on the frontline in the UK is limited and should be developed to maximize the utility of typing tools. In similar intermediate-burden settings, it may be more efficient to separate contact tracing (incorporating typing information) from routine medical and nursing case management.

## 14. TB CONTROL STRATEGIES: WHAT IS EFFECTIVE?

### OAP-305-31 Improving the quality and usage of TB surveillance data in Uganda

D Tollefson,<sup>1</sup> A Naguudi,<sup>2</sup> D Mumphe Mwanja,<sup>2</sup> D Muwonge,<sup>2</sup> J Imoko,<sup>3</sup> F Mugabe,<sup>2</sup> E Bloss.<sup>1</sup> <sup>1</sup>Division of Tuberculosis Elimination, US Centers for Disease Control and Prevention, Atlanta, GA, USA; <sup>2</sup>Central Unit, Uganda National Tuberculosis and Leprosy Programme, Kampala, <sup>3</sup>TB Unit, World Health Organization - Uganda, Kampala, Uganda. e-mail: vtu3@cdc.gov

**Background:** Robust national-level tuberculosis (TB) surveillance is needed to monitor progress towards TB targets, yet many countries struggle to collect and report accurate surveillance data. In Uganda, an evaluation using the World Health Organization's Checklist of Surveillance Standards and Benchmarks identified gaps in national TB surveillance, namely high underreporting and lack of data use. To close these gaps and strengthen the national TB surveillance system, the Uganda National TB and Leprosy Programme (NTLP) partnered with the U.S. Centers for Disease Control and Prevention and African Field Epidemiology Network to develop and implement an intervention for all NTLP TB staff called TB Data – Improving Quality and Usage (TB-IQu).

**Intervention:** TB-IQu was designed using the Performance of Routine Information System Management framework and lessons learnt in other health sectors. Standard operating procedures (SOPs) for all data-related processes were created and published; tools and processes for conducting data quality audits were developed and piloted; and quarterly subnational TB meetings were reformed to include graphical analysis of TB variables over time using a simple data analysis

template. An interactive curriculum was designed to train staff to use these tools. Staff participating in these processes contributed feedback regularly in meetings to improve TB-IQu.

**Results and lessons learnt:** TB-IQu rollout is ongoing. National and high-level subnational TB staff were trained to apply new procedures and tools. Data audit and analysis exercises conducted by staff identified gaps in the surveillance system and reporting errors. For example, time series analyses revealed previously unknown data quality problems in reporting zones. Group evaluations amongst TB staff revealed positive feedback on a template that enabled those with limited computer literacy to analyze data, but additional training and simplification of the tool was necessary to ensure acceptance and use by all subnational staff.

**Conclusions and key recommendations:** TB-IQu is helping Uganda strengthen the quality of TB surveillance data by enabling staff at all levels to actively use and evaluate TB data. The Uganda NTLP should continue to roll out TB-IQu and monitor its acceptance and viability over time. TB-IQu can be easily adapted in other countries to improve accuracy of case notification and strengthen TB surveillance.

### OAP-306-31 High relapse among successfully treated new smear positive TB patients under National TB Programme: retrospective cohort study from Gujarat, India

P Dave,<sup>1</sup> A Shah,<sup>2</sup> Sand Bharaswadkar,<sup>2</sup> K Rade,<sup>2</sup> A Sreenivas,<sup>2</sup> P Malik,<sup>2</sup> B Modi,<sup>3</sup> N Kulshreshtha.<sup>4</sup> <sup>1</sup>Health and Family Welfare, Government of Gujarat, Gandhinagar, <sup>2</sup>Tuberculosis, World Health Organization country office in India, Delhi, <sup>3</sup>Preventive & Social Medicine, Government Medical College Jamnagar, Jamnagar, <sup>4</sup>Central TB Division, Ministry of Health & Family Welfare, Government of India, Delhi, India. e-mail: shaha@tbcindia.nic.in

**Background** India contributes 27% of New Smear Positive (NSP) and 47% of relapse TB cases among global notification by High Burden Countries. Under Revised National Tuberculosis Control Programme (RNTCP), India follows WHO recommended DOTS strategy over nearly two decades; uses intermittent regimen to treat drug sensitive tuberculosis throughout the course; reports 88% treatment success among NSP TB cases without any policy of long term follow-up of patients for relapses (<5% considered acceptable for efficacy of treatment regimens). Dang District in Gujarat, West India has a relatively confined tribal population with almost no private healthcare sector treating TB. We followed up the cohorts of NSP TB cases treated successfully predominantly under RNTCP in the Dang district with an objective to ascertain the relapse rate among them.

**Methods** All TB cases registered under RNTCP for treatment, since inception from 2003 to 2013 were line-listed and digitalized from Dang district records using EpiData Entry software. Source of previous TB treatment was ascertained from the respective treatment card of each relapse TB case. In case no written information

on previous source of treatment available, search by name was performed in the database of NSP cases in previous cohorts and was correlated with age and sex for confirmation. Proportion of relapse among successfully treated NSP cases over the years, time interval from successful treatment to relapse and correlation of relapse with age, sex, duration of initial TB treatment was calculated.

**Results** In district Dang, between 2003–2013, of the 991 NSP patients whose treatment outcomes were available, 894 (90%) were successfully treated and 112 (13%) of them relapsed from TB. Among those who relapsed, the median (IQR) time interval from successful treatment to relapse was 192 (IQR: 181–209) days. The age, sex and duration of treatment were not associated with proportion of relapse ( $p=0.55$ ).

**Conclusions** There is constant high relapse (13%) of TB among NSP cases successfully treated with intermittent treatment under direct observation under RNTCP over 10 years' time. Most of these recurrences occurred within six months of successful treatment. We believe that in view of ample evidences including this study, programme may consider policy updates to daily regimen to reduce relapses and device mechanism to long term follow up of successfully treated drug sensitive TB cases.

Table: Percentage of relapse among successfully treated New Smear Positive TB cases in year-wise cumulative cohort, Dang, Gujarat.

Year	NSP successfully treated for TB Cumulative cohort (a)	Relapses, out of a	% relapse
2003	91	10	11%
2004	195	25	13%
2005	266	37	14%
2006	347	49	14%
2007	465	68	15%
2008	548	77	14%
2009	664	90	14%
2010	771	102	13%
2011	894	112	13%
Total	894	112	13%

### OAP-307-31 Non-smear conversion at two months follow-up and treatment outcomes in new smear positive cases of pulmonary tuberculosis in Cotonou, Benin

A Wachinou,<sup>1</sup> W Bekou,<sup>1</sup> D Affolabi,<sup>1</sup> G Agodokpessi,<sup>1</sup> SS Ade,<sup>1</sup> S Azon,<sup>1</sup> E Vitohode,<sup>1</sup> S Anagonou.<sup>1</sup> <sup>1</sup>National Hospital for Tuberculosis and Pulmonary Diseases, National Tuberculosis Programme, Cotonou, Benin.  
e-mail: wachinouprudence@yahoo.fr

**Background** In resource limited settings, sputum smear status at two months is routinely used to predict tuberculosis (TB) treatment outcomes in newly diagnosed pulmonary TB cases. We conducted this study to identify factors associated with the non-conversion of sputum smears at the end of the intensive phase and to evaluate the influence of non-smear conversion on treatment outcomes.

**Patients and Method** This was a retrospective study based on data from new smear positive cases of

pulmonary tuberculosis registered at the National Hospital for Tuberculosis and Pulmonary Diseases of Cotonou in 2011 and 2012. Data were analysed with Epidata analysis and Statistical Package for the Social Sciences (SPSS 21).

**Results** A total of 1243 patients were studied. There were 820 (64%) males and 423 (34%) females with a mean age of 33.6 years (95%CI: 32.9–34.3). HIV status was positive in 240 (19.3%) patients. Sputum smears did not convert in 236 (19%) patients at the end of the intensive phase. The bacillary load was low (+/- or 1+) in most of the non-conversion cases (90%). In logistic regression, HIV positive status (adjusted OR=1.795, 95%CI: 1.252–2.574) and a 3+ bacillary load at the diagnosis point (adjusted OR=5.14, 95%CI: 3.001–8.808) were significantly associated with non-conversion of sputum smears at the end of the intensive phase. Positive smears at two months of treatment were significantly associated with failure ( $p<0.001$ ) and death ( $p<0.01$ ).

**Discussion and Conclusion** Positive smear sputum at two months could be a good marker to predict poor treatment outcome in resource constrained settings. Surprisingly, HIV positive status was associated with positive sputum smear at the end of the intensive phase. This needs to be further investigated.

### OAP-308-31 Public health solutions for combatting TB in a low income country: experience from Afghanistan

GQ Qader,<sup>1</sup> M Rashidi,<sup>1</sup> M Seddiq,<sup>2</sup> SD Mahmoodi,<sup>2</sup> M Persuad,<sup>3</sup> SM Sayedi,<sup>1</sup> M Akhgar,<sup>2</sup> P Suarez.<sup>3</sup> <sup>1</sup>TB CARE I, Management Sciences for Health (MSH), Kabul, <sup>2</sup>National TB Program, Ministry of Public Health of Afghanistan, Kabul, Afghanistan; <sup>3</sup>TB CARE I, Management Sciences for Health (MSH), Arlington, VA, USA. e-mail: gqader@gmail.com

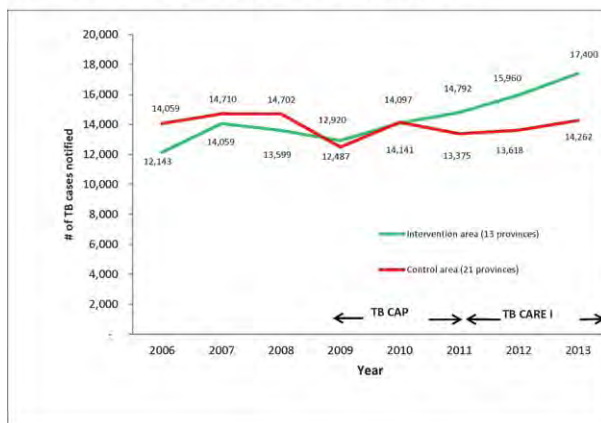
**Background:** Afghanistan is among the world's 20 countries with the highest TB burden. The nation's annual TB incidence rate is 189 per 100,000 population and its TB prevalence rate is 358 per 100,000 population. One of the main reasons for such high TB incidence and prevalence rates is that Afghanistan has a TB case notification rate of just 52 percent.

**Methodology:** Since 2009, the national TB program (NTP) has been working to improve TB control with support from the USAID-funded TB Control Assistance Program (TB CAP), and its follow on, TB CARE I. These partners have developed standard operation procedures (SOPs) for TB case detection, treatment, infection control and have trained frontline health care staff in 13 provinces to use these SOPs. They have also disseminated clinical guidelines and the SOPs, patient information, education and communication materials, health worker educational materials, and patient treatment packs to 2,000 health facilities country wide. To ensure staff are making proper use these materials and applying the skills they learned during the trainings, the NTP and TB CARE I staff conducted on-site supervision, monitoring, and refresher trainings for the participating health workers.

**Results:** In 2014, a technical team from the NTP and TB CARE I reviewed TB surveillance data from 2006 to 2013 to assess the impact of these interventions on the TB case notification rate in Afghanistan. In the intervention provinces, between 2009 and 2013, presumptive TB case identification increased by 118% (t-statistic 2.64, 95% CI,  $p=0.009$ ), case notification for all forms of TB rose by 35% (t-test 5.13, 95% CI,  $p<0.00001$ ), sputum smear positive (SS+) TB case detection increased by 22% (t-statistic 4, 95% CI,  $p=0.0001$ ), and the treatment success rate (TSR) improved by 7%. However, in the 21 control provinces, during same period, presumptive TB case identification improved by just 84%, case notification for all forms of TB increased by 14%, SS+TB case detection increased just 2%, and TSR increased by 3%.

**Conclusion:** The development and dissemination of SOPs for TB case detection, educational materials, and treatment packages, coupled with health worker trainings, supervision, and monitoring, contributed to a significant increase in TB case notification in the 13 intervention provinces. The NTP should expand this approach throughout Afghanistan to reduce the nation's high TB incidence and prevalence.

Figure: Trend of TB case notification in intervention and control areas, 2006-2013



### OAP-309-31 The relevance of cost-effectiveness analysis in the implementation of tuberculosis-related interventions in the community

Y Agbassi,<sup>1</sup> S Touré.<sup>1</sup> <sup>1</sup>Project management, ACONDA-VS-CI, Abidjan, Côte D'Ivoire.  
e-mail: ayjpatrick@gmail.com

**Background:** Of the 24222 tuberculosis (TB) cases detected in 2012 in Cote d'Ivoire (CI), 14660 new cases were smear-positive pulmonary TB cases. It is therefore very important to roll back this form of TB in CI. This triggered the implementation of a TB Reach project whose objective is to increase the number of TB cases detected within the general population and HIV patients on 17 intervention sites in Abidjan and in the western part of CI. After 3 months of project implementation, only 28% of suspect patients were getting tested. Suspects were not going to health-facility for the TB test. Against this drawback, 2 community strategies have

been designed to improve the percentage of tested among the suspect patients. We implement a cost-effectiveness analysis (CEA) to determine which strategy is the most cost-effective.

**Intervention:** The strategy 1 consisted in retrieving patients smear samples in community. The strategy 2 consisted in incentivizing patients to come within health facilities to getting tested. We selected 4 sites in Abidjan by strategy for the CEA. The selected sites were as similar as possible. The study has been conducted from June to August 2013. The data collection has been done by reviewing the monitoring and evaluation tools of community counselors on intervention sites. The analysis has been conducted in three steps: determining the cost of the strategies, determining the effectiveness of the strategies (effectiveness measured in terms of number of detected cases and the percentage of tested cases among suspects) and comparing the cost-effectiveness ratio. The most cost-effective strategy will be implemented on all the intervention sites

**Results:** Costs = 484.67 Euros for strategy 1 / 36.59 Euros for strategy 2 Effectiveness = 197 tested persons among 295 suspects (67%) for strategy 1 / 2 tested persons among 29 suspects (7%) for strategy 2 Cost-effectiveness ratio = 2.46 Euros for strategy 1 / 18.29 Euros for strategy 2. The strategy 1 is the most cost-effective. It is better retrieving smear samples within communities than incentivizing people to go to the health facilities.

**Conclusion:** The strategy 1 will be implemented on all intervention sites to improve the TB detection among suspect cases. CEA should be conducted by all programmes for implementing the right interventions in order to get better health results. The retrieving strategy will improve the results of the TB reach project as well as those of the national tuberculosis program.

### OAP-310-31 The Management and Organizational Sustainability Tool (MOST) contributes to improved management and technical capacity at Uganda's National TB Programme

E Kizito,<sup>1</sup> M Ruhweza,<sup>1</sup> D Birabwa,<sup>2</sup> C Aguti Ongom,<sup>1</sup> E Birabwa,<sup>3</sup> F Mugabe,<sup>4</sup> S Balcha,<sup>3</sup> D Mwanja,<sup>2</sup> <sup>1</sup>Track Tuberculosis Activity Project (TRACK TB), Management Sciences for Health (MSH), Kampala, <sup>2</sup>Mulago National Referral Hospital, Department of Clinical Services, Kampala, <sup>3</sup>United States Agency for International Development (USAID), Uganda Office, Kampala, <sup>4</sup>Ministry of Health, National Tuberculosis and Leprosy Programme (NTLP), Kampala, Uganda, e-mail: marygmudiope@gmail.com

**Background:** Until recently, Uganda's National Tuberculosis and Leprosy Program (NTLP) had limited management and technical capacity to plan, implement, and monitor TB control activities. Furthermore, the Program did not have annual operational plans or annual reports. From May of 2013 to January of 2014, the PEPFAR- and USAID-funded TRACK TB project helped the NTLP improve its operations by training the central unit's staff to use the Management and Organizational Sustainability



ity Tool (MOST) for TB. MOST for TB is a structured, participatory process that allowed the NTLP to assess its own management performance and develop an action plan to improve operations by establishing and monitoring a concrete set of prioritized indicators.

**Intervention:** In May of 2013, TRACK TB held a workshop to support participants from the NTLP and partner organizations in using the MOST for TB. During this workshop, participants worked together to evaluate the NTLP using the MOST for TB assessment tool. Based on the assessment results, participants developed an action plan to improve the NTLP's performance in five priority areas: human resource management, supportive supervision, annual operational planning, community participation in TB control, and monitoring and evaluation (M&E). Participants also selected a team of change agents to oversee implementation and monitoring of the action plan. To track the NTLP's progress, TRACK TB established five indicators for each of the priority areas and assigned each indicator a maximum performance score of one point. For nine months, TRACK TB then tracked the NTLP's performance using these indicators.

**Results and lessons learnt:** Between May of 2013 to January of 2014, the NTLP's performance improved in four of the five priority areas (see Table). The NTLP now has an annual plan, submits annual reports to the Ministry of Health, conducts regular performance reviews and zonal supervision visits, and has a database for collecting district-level TB control data.

**Conclusion and key recommendations:** The MOST for TB strengthened the NTLP's management and technical capacity and enabled the Program to improve its annual operational planning, supervision systems, and M&E activities. MOST for TB should also be used to improve TB control programs at the zonal and district levels.

### **OAP-311-31 The effectiveness of BCG vaccination in preventing *Mycobacterium tuberculosis* infection and disease in Greenland**

S Michelsen,<sup>1</sup> B Soborg,<sup>1</sup> A Koch,<sup>1</sup> L Carstensen,<sup>1</sup> S Hoff,<sup>2</sup> E Agger,<sup>2</sup> J Wohlfahrt,<sup>1</sup> M Melbye.<sup>1</sup> <sup>1</sup>Department of Epidemiology Research, Statens Serum Institut, Copenhagen, <sup>2</sup>Department of Infectious Disease Immunology, Statens Serum Institut, Copenhagen, Denmark. e-mail: swm@ssi.dk

**Background:** The Bacillus Calmette-Guerin vaccine (BCG) remains the only licensed vaccine against tuberculosis (TB). The vaccine's protective effect in preventing disseminated TB among children is well documented, whereas the protective effect against pulmonary TB is less clear. New data suggests the vaccine might also protect against *Mycobacterium tuberculosis* infection (MTI). Greenland has experienced a continuously high TB incidence reaching 157 per 100,000 inhabitants in 2012. BCG vaccination was first introduced nationwide to all neonates in 1955. From 1991 through 1996 the vaccine program was temporarily discontinued due to nationwide policy changes, but re-introduced in 1997. The study aim was to use the transient stop in BCG

vaccination in Greenland in order to evaluate the effect of the BCG vaccine on MTI and TB.

**Design/Methods:** The MTI study: A cross-sectional study conducted in 2012 evaluated the BCG effect on MTI prevalence. The study population comprised of East Greenlanders born 1982–2006. MTI outcome was defined by a positive Quantiferon TB Gold in-tube test. Associations between vaccination and MTI were estimated using logistic regression. The TB study: A registry-based cohort study with follow up until the end of 2012 was used to evaluate the BCG effect on TB incidence. The study population included the same East Greenlandic birth cohorts (born 1982–2006). A unique personal identifier given to all Greenlanders at birth allowed for individual follow-up of all participants in the national TB notification system. TB is mandatory notifiable in Greenland and case definitions follow WHO criteria. Associations between vaccination and TB were estimated using Cox regression.

**Results:** The MTI study included 953 participants (participation rate 80%) hereof 81% BCG vaccinated. 29% had MTI; 23% among vaccinated and 57% among non-vaccinated. BCG vaccination reduced the odds of MTI; odds ratio 0.52 (95% confidence Interval [CI] 0.32-0.85)  $p=0.01$ . Vaccine effectiveness against MTI was 20%. The TB study included 1,697 participants who were followed for 21,148 person years. 6% of participants were notified with TB; 4% among vaccinated and 11% among non-vaccinated. The majority of TB cases were pulmonary. BCG vaccination reduced the risk of TB; hazard ratio 0.50 (95% CI 0.26-0.95),  $p=0.03$ , yielding a vaccine effectiveness of 50%.

**Conclusions:** BCG vaccination was effective in reducing both MTI and TB in a TB high-endemic setting in Greenland.

## **15. LESSONS LEARNT FROM IMPLEMENTATING XPERT MTB/RIF**

### **OAP-312-31 Determinants of Xpert MTB/RIF performance, including bacterial load and PCR inhibition, using specimens from different body compartments**

G Theron,<sup>1</sup> J Peter,<sup>1</sup> G Calligaro,<sup>1</sup> R Meldau,<sup>1</sup> C Hanrahan,<sup>2</sup> H Khalfey,<sup>1</sup> B Mayosi,<sup>1</sup> K Dheda.<sup>1</sup>

<sup>1</sup>Medicine, University of Cape Town, Cape Town, South Africa; <sup>2</sup>Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MA, USA. e-mail: grant.theron@gmail.com

**Background:** The determinants of Xpert MTB/RIF sensitivity for pulmonary and extrapulmonary tuberculosis (TB) and the role of PCR inhibition are poorly understood.

**Methods:** We compared culture time-to-positivity (TTP; a surrogate of bacterial load), MTB/RIF TB-specific and internal positive control (IPC)-specific CT values, and clinical characteristics in patients with suspected TB (HIV-infected and -uninfected) who provided expecto-

rated (n=438) or induced sputum (n=128), tracheal aspirates (n=71), bronchoalveolar lavage fluid (n=152), pleural (n=76), cerebral spinal fluid (CSF; n=152), pericardial fluid (n=131), or urine (n=173) specimens.

**Results:** Median bacterial load (TTP in days) was the strongest associate of MTB/RIF positivity in each fluid. TTP correlated with CT values in pulmonary specimens but not extrapulmonary specimens (Spearman's coefficient 0.5043 versus 0.1437;  $p=0.030$ ). Inhibition affected a greater proportion of pulmonary than extrapulmonary specimens (IPC CT >34: 6% (47/731) versus 1% (4/381;  $p<0.0001$ ), however, "false-negative" CSF specimens (MTB/RIF-negative, culture-positive) displayed marginally greater PCR inhibition than "true-positive" specimens [internal positive control CT of 27.80 (27.10–28.70) versus 27.10 (26.5–27.15;  $p=0.0236$ )]. Pulmonary specimens had greater load compared to extrapulmonary specimens [TTPs of 11 (7–16) versus 22 (18–33.5) days;  $p<0.0001$ ]. HIV-infection was associated with a decreased likelihood of MTB/RIF-positivity in pulmonary specimens but an increased likelihood in extrapulmonary specimens.

**Conclusions:** Mycobacterial load, which displays significant biological variation across different body compartments, is the main determinant of MTB/RIF-positivity rather than PCR inhibition. MTB/RIF CT is a poor surrogate of load in extrapulmonary specimens.

### OAP-313-31 Use of Xpert MTB/RIF in decentralised public health settings and its effect on pulmonary TB and DR-TB case finding in India

KS Sachdeva,<sup>1</sup> N Raizada,<sup>2</sup> A Sreenivas,<sup>3</sup> R Thakur,<sup>2</sup> S Kulsange,<sup>2</sup> C N Paramasivan.<sup>2</sup> <sup>1</sup>Central TB Division, Ministry of Health and Family Welfare, Government of India, New Delhi, <sup>2</sup>India, Foundation for Innovative New Diagnostics, New Delhi, <sup>3</sup>India, World Health Organization, New Delhi, India. e-mail: drneerajraizada@gmail.com

**Background:** WHO endorsed Xpert MTB/RIF; a cartridge based nucleic acid amplification test with high sensitivity and specificity; detects TB and rifampicin resistance simultaneously within 2 hours. This study assessed the impact of upfront Xpert MTB/RIF testing on detection of TB and rifampicin resistant TB (DR-TB) cases.

**Methods:** The study was conducted from March 2012 till December 2013, using a phased implementation approach, in 18 selected sub-district level TB programme units (TUs) in India in diverse geographic and demographic settings, with a population coverage of 8.8 million. A baseline phase in 14 TUs captured programmatic data without active intervention, and an intervention phase in 18 TUs had Xpert MTB/RIF offered to all presumptive TB and presumptive DR-TB cases. Negative binomial regression models were used to estimate changes in detection of TB and DR-TB cases, adjusting for clustering and other covariates.

**Results:** The 14 study TUs which participated in both phases, adjusted total pulmonary TB (PTB) case notification increased from 94.8 (95% CI 79.7–113) per

100,000 person-years (PY) in baseline phase, to 114 (95% CI 92.2–141) per 100,000 PY in intervention phase. Similarly, adjusted DR-TB case notification increased from 1.79 (95% CI 1.19–2.68) to 11.2 (95% CI 7.30–17.1) per 100,000 PY. In the baseline phase, among 10819 presumptive TB cases, 1,571 (14.8%) PTB cases were bacteriologically-confirmed, and additional 465 (4.3%) were clinically-diagnosed. In intervention phase, presumptive TB cases with upfront testing on Xpert MTB/RIF were 1.3 times more likely (95% confidence interval (CI) 1.2–1.5) to be diagnosed with PTB. Among 2,764 PTB cases with positive rifampicin resistance results by Xpert MTB/RIF, the positive predictive value (PPV) was 96.6% (95% CI 95.3–97.7) among previously treated TB cases and 91.8% (95% CI 88.7 – 94.2) among new TB cases.

**Conclusion:** Routine implementation of Xpert MTB/RIF as the initial diagnostic test in public health facilities in India increased substantially total PTB and DR-TB case notification, and provides robust data demonstrating potential impact of this strategy to augment TB case finding

TB and DR-TB case notification rates (per 100,000 person years) (CNR) during baseline and intervention phase (95% confidence limits)

Estimate	Total Pulmonary TB cases	Bacteriologically confirmed Pulmonary TB case	DR-TB
Overall CNR in baseline phase	94.5 (79.5 – 113)	64.0 (51.3 – 79.7)	1.36 (0.89 – 2.07)
Overall CNR in intervention phase	113 (95.8 – 134)	91.9 (74.1 – 114)	6.28 (4.77 – 8.28)
% Increase in CNR owing to intervention	20.0 (9.4 – 31.4)	43.6 (28.0 – 61.2)	363 (214 – 584)
P	<10 <sup>-3</sup>	<10 <sup>-3</sup>	<10 <sup>-3</sup>

\*Controlling for clustering, past history of anti-TB treatment

### OAP-314-31 Understanding the diagnostic cascade of tuberculosis: insights from a transmission model

A Sun,<sup>1</sup> C Denking,<sup>2</sup> D W Dowdy.<sup>3</sup> <sup>1</sup>School of Medicine, Johns Hopkins University, Baltimore, MD, USA; <sup>2</sup>TB Program, Foundation for Innovative New Diagnostics, Geneva, Switzerland; <sup>3</sup>Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA. Fax: (+1) 410 614 0902. e-mail: david.w.dowdy@gmail.com

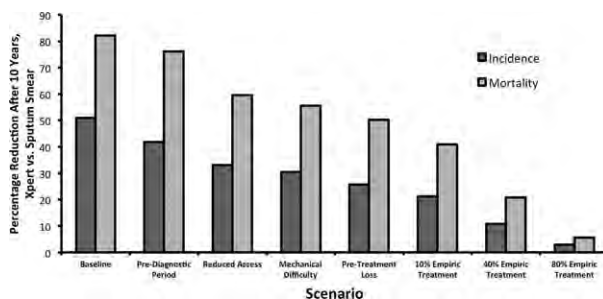
**Background:** Diagnostic tests for tuberculosis (TB) do not function in isolation but rather form part of a larger "diagnostic cascade." The effect of this cascade on the population-level impact of novel TB diagnostics has not been quantified.

**Methods:** We used ordinary differential equations to construct a transmission model of the TB epidemic in a representative population in India. With this model, we projected the impact of scaling up Xpert MTB/RIF (Cepheid, Inc.) on TB incidence and mortality. We first constructed a "baseline" model that assumed immediate care-seeking and complete linkage between diagnostic test result and treatment. We then compared results from this model against sequential models that incorporated seven different "steps" in the TB diagnostic cascade: pre-diagnostic delay, reduced access to testing facilities, mechanical difficulties in diagnostic testing, pre-treat-

ment loss to follow-up, and empiric treatment (at levels of 10%, 40%, and 80%).

**Results:** Without Xpert, TB incidence was projected to fall from 176 to 144 per 100,000/year over ten years. In the baseline scenario, Xpert reduced TB incidence to 69.5 per 100,000/year (52% reduction relative to diagnosis with smear) and mortality to 5 per 100,000/year (82% reduction). Sequential incorporation of steps in the diagnostic cascade reduced the impact of Xpert (Figure), with projected ten-year reductions in incidence of 39% after including a 4.5-month pre-diagnostic period, 30% after also accounting for people without access to care, 28% after incorporating mechanical difficulty, and 27% after including pre-treatment loss to follow-up (Figure, dark bars). Corresponding reductions in mortality were 75%, 58%, 54%, and 51% (Figure, light bars). Empiric diagnosis dramatically affected projected impact of Xpert. Assuming 40% empiric treatment in the idealized baseline scenario blunted the projected Xpert-associated reduction in incidence from 52% to 36%. When added to the other elements of the “diagnostic cascade” above, empiric treatment for 10%, 40%, and 80% of smear-negative TB cases attenuated the projected impact of Xpert from a 27% reduction in incidence to 22%, 11%, and 3%, with impact on mortality following a similar trajectory (6% reduction at 80% empiric treatment).

**Conclusions:** Depending on the gaps in the TB diagnostic cascade, the population-level impact of implementing the same diagnostic test, in the same population, could vary from profound to almost imperceptible.



### OAP-315-31 rpoB mutations not detected by phenotypic and genotypic DST methods in a population with high MDR-TB burden

A O Ojo,<sup>1</sup> E Ardizzoni,<sup>1</sup> B De Jong,<sup>1</sup> A Van Deun,<sup>1</sup> L Rigouts,<sup>1</sup> T Kotrikadze,<sup>2</sup> G Torrea.<sup>1</sup> <sup>1</sup>Mycobacteriology, Prince Leopold Institute of Tropical Medicine, Antwerp, Belgium; <sup>2</sup>Médecine, Médecin Sans Frontière, Paris, France. Fax: (+32) 3 247 63 33. e-mail: gtorrea@itg.be

**Background:** The diagnosis of rifampicin (RMP) resistance relies on phenotypic and genotypic DST methods. The rapid phenotypic method Bactec MGIT960 is used as the reference standard. Mutations in the rpoB gene are responsible for over 95% of RMP resistance, but strains with certain ‘disputed’ rpoB mutations are not detected as RMP resistant by MGIT960. However, they also lead to bacteriologically poor outcome of rifampicin-based

first-line treatment. The objectives are to estimate the prevalence of such ‘disputed’ mutations among strains identified as RMP-susceptible yet poly-resistant by MGIT960 and isolated in Abkhazia and Zugdidi, Georgia, high MDR-burden settings and to correlate with the type of patient (new case or retreatment).

**Design/Methods:** In this retrospective study, 216 stored isolates previously found susceptible to RMP yet resistant to a combination of two or three other first-line drugs by MGIT960 from new and retreatment cases were submitted for sequencing of the rpoB gene. In addition, Xpert MTB/RIF, GenoType MTBDRplus (version 2, LOT OV00046) and minimal inhibitory concentration (MIC) on Löwenstein-Jensen medium were tested for isolates harboring mutations.

**Results:** 16 (7%) of 216 isolates showed mutations in the rpoB gene: 8 L533P, 2 H526N, 2 L511P, 1S531L, 1I572L, 1 V664A, and 1 double point mutation D516Y and N518D. Of these, V664A and I572L are outside the rpoB hot-spot region, and were not previously reported in literature. Xpert MTB/RIF showed rifampicin resistance in all isolates harboring mutations in the rpoB hot-spot region, whereas the Genotype MTBDRplus missed all 8 strains with L533P. MIC values revealed high level resistance for 10 strains, borderline for 3 strains and susceptibility for 2 strains harboring L511P, with high evidence of RMP resistance and V664A that seems not to be related to RMP rifampicin. Eleven of 16 patients were new cases and 3 retreatment cases.

**Conclusion:** MGIT960 missed RMP-resistance in 7% of poly-resistant TB cases in these settings. The significance of the previously undescribed I572L and V664A mutations is uncertain, although the 572 mutation caused an increased MIC. Xpert picked up all resistance based on mutations in the hot-spot region, but MTBDRplus (version 2, LOT OV00046) gave false susceptible results for strains with mutation at codon 533. The majority of the mutated strains were from new cases, highlighting their potential to spread.

### OAP-316-31 Implementing GXP in a Pediatric HIV-TB Clinic in Swaziland

R Golin,<sup>1,2</sup> P Ustero,<sup>1,2,3</sup> G Mtetwa,<sup>2</sup> K Ngo,<sup>3</sup> M Muyaya,<sup>2</sup> M Matshaba,<sup>1,2</sup> A Mandalakas.<sup>3</sup> <sup>1</sup>Pediatrics, Baylor College of Medicine, Houston, TX, USA; <sup>2</sup>Tuberculosis, Baylor College of Medicine Children's Foundation - Swaziland, Mbabane, Swaziland; <sup>3</sup>Global Tuberculosis Program, Baylor College of Medicine, Houston, TX, USA. Fax: (+268) 2404 0214. e-mail: golin@bcm.edu

**Background:** Swaziland is the epicenter of the HIV and TB pandemics; yet the estimated TB case detection rate is 43%. Many of the missed cases presumably are children. To enhance diagnosis and improve access to MDR-TB treatment, Baylor College of Medicine Children's Foundation – Swaziland (BCMCF-SD) leveraged WHO TB Reach funding to incorporate GeneXpert TB/Rif (GXP) testing within our integrated TB-HIV clinical program and systematically assessed operational measures.

**Intervention/Response:** BCMCF-SD scaled up efforts to collect specimens on children with presumptive TB, to



assure baseline GXP and culture for those starting TB treatment. Specimens were collected via gastric (GA) or nasopharyngeal (NPA) aspiration, or expectoration. Systems were developed to 1) ensure the prompt return of patients in whom MTB was detected and 2) 100% referral of those with rifampicin resistance.

**Results and Lessons Learnt:** Over 800 samples have been processed on BCMCF-SD's GXP machine; 52.4% from pediatric patients. In children < 5 years, MTB was detected in 1%. In children 5 - 14 years old, MTB was detected in 1.6%; detection increases to 4.3% when analysis was restricted to samples collected via GA or NPA. Of note, rifampicin resistance was detected in all of these samples. BCMCF-SD obtained an average of 58 GXP samples per month prior to procuring its GXP machine. The average number of GXP samples per month has increased to 104 since having an in-house machine. Prior to having its own GXP machine, BCMCF-SD sent samples to a referral hospital and received GXP results on average after 3.5 days. On-site integration of GXP has decreased time to GXP results to 1.18 days. Since the 2013 implementation of GXP at BCMCF-SD, 29 pediatric patients have been started on TB treatment including 4 (14%) with TB confirmed by GXP and 25 (86%) with clinically diagnosed TB.

**Conclusions and Key Recommendations:** BCMCF-SD's experience provides further insight into operationalizing GXP in pediatric TB diagnosis. GXP does not diminish the importance of clinical diagnosis for pediatric TB, especially considering the challenges with obtaining adequate samples. Nonetheless, GXP's role in diagnosing pediatric TB should not be overlooked given its ability to decrease time to diagnosis and treatment, especially for patients requiring MDR-TB treatment. In addition, having a GXP machine on site has led to a behavior change as demonstrated by the increase in samples obtained after procuring a GXP machine.

#### **OAP-317-31 Factors associated with adherence to the South African algorithm for the diagnosis of TB amongst persons living with HIV**

K McCarthy,<sup>1,2</sup> V Chihota,<sup>1</sup> A Grant,<sup>3</sup> S Ginindza,<sup>1</sup> S Charalambous,<sup>1,2</sup> G Churchyard,<sup>1,2</sup> K Fielding.<sup>4</sup>

<sup>1</sup>Epidemiology, The Aurum Institute, Johannesburg, <sup>2</sup>School of Public Health, University of the Witwatersrand, Johannesburg, South Africa; <sup>3</sup>Clinical Research, London School of Hygiene & Tropical Medicine, London, <sup>4</sup>Infectious Disease Epidemiology, London School of Hygiene & Tropical Medicine, London, UK.

e-mail: kmccarthy@auruminstitute.org

**Background:** The South African Department of Health algorithm for the diagnosis of TB among HIV-positive persons advises additional investigations (chest-x-ray (CXR), sputum culture, trial of antibiotics) for persons with negative smear or Xpert MTB/RIF (Xpert) sputum tests. We reviewed health care worker (HCW) investigation practices in a cluster randomised trial comparing Xpert to microscopy (XTEND study), in order to (i) assess the effect of Xpert implementation on adherence

to the algorithm and (ii) establish patient factors associated with adherence to the algorithm by HCWs.

**Design/Methods:** XTEND participants ( $\geq 18$  years), who were tested for TB by HCWs from 10 intervention (using Xpert) and 10 control (using microscopy) clusters (2 primary health clinics [PHCs]/cluster), were interviewed to obtain complete medical history. Six months from enrolment, clinical records were reviewed and laboratory results were obtained. Partial or complete adherence to the algorithm was defined as any of CXR, sputum culture or referral to hospital documented in the PHC clinical record. HIV status at enrolment was determined through self-report and clinical record review.

**Results:** Among 4665 XTEND participants 4035 (86%) had a negative index test for TB, of whom 2153 (53%) were known to be or tested HIV positive at enrolment. Among these participants, only 37% (791/2153) had evidence of partial/complete adherence to the algorithm. The proportion with further investigations in the Xpert and control arms respectively were similar (33% [341/1031] vs 40% [450/1122]), unadjusted risk ratio (RR) 0.66 [95% CI: 0.34-1.30]; adjusted RR 0.70 [95% CI: 0.36-1.37]). Factors associated with having further investigations included age  $\geq 40$  years (OR=1.42; 95%CI 1.08-1.86), having 2 or more TB symptoms (OR=1.53; 95% CI=1.14-2.03) and Karnofsky score  $< 90$  (OR=2.09; 95% CI 1.33-3.26). Body mass index  $> 25$  mitigated against further investigations (OR 0.71; 95% CI 0.56-0.89). In the Xpert arm, a Karnofsky score  $< 90$  was associated with having further investigations (OR 2.99; 95%CI=1.52-5.85).

**Conclusion:** The majority of participants did not have further investigations. The implementation of Xpert did not improve HCW adherence to the TB investigation algorithm among HIV-positive persons with negative sputum tests. HCWs were more likely to conduct further investigations when HIV-positive persons with negative smear or Xpert sputum tests are older, have more TB symptoms, or are more ill.

#### **OAP-318-31 High rates of early initiation of weakened MDR-TB regimens based on South Africa's Xpert MTB/RIF diagnostic algorithm**

K Jacobson,<sup>1,2</sup> M Barnard,<sup>2,3</sup> O Shapira,<sup>4</sup> M Bosman,<sup>3</sup> P Van Helden,<sup>2</sup> R M Warren.<sup>2</sup> <sup>1</sup>Infectious Diseases, Boston University School of Medicine, Boston, MA, USA; <sup>2</sup>Faculty of Medicine and Health Sciences, Stellenbosch University, Tygerberg, <sup>3</sup>Tuberculosis Reference Laboratory, National Health Laboratory Services, Cape Town, South Africa; <sup>4</sup>Nano-Spect, Inc, Boston, MA, USA. Fax: (+1) 617 638 8070. e-mail: kjacobso@bu.edu

**Background:** Xpert MTB/RIF rapidly detects *Mycobacterium tuberculosis* (MTB) and rifampicin (RIF) resistance, enabling physicians to initiate patients on multi-drug resistant (MDR) TB treatment within days of specimen collection. In South Africa, the current algorithm indicates that RIF resistant TB patients start standardized MDR therapy without knowledge of resistance to 2<sup>nd</sup> line drugs (amikacin (AMI), ethion-

amide (ETH), ofloxacin (OFX)). Resistance to these drugs is only known once the MTBDRplus line probe assay (LPA) and culture-based drug susceptibility tests (DSTs) are reported. We aimed to quantify the additional time delay until 2<sup>nd</sup> line DSTs were reported and the percentage of patients requiring regimen adjustment based on those results.

**Design/Methods:** We retrospectively identified all patients diagnosed with RIF resistant MTB by the Xpert at the National Health Laboratory Services TB Reference Laboratory, Cape Town, between 1/9/11 and 17/1/12. We calculated time from specimen collection to reporting of 2<sup>nd</sup> line DST results and final susceptibility patterns.

**Results:** 384 patients had RIF resistant MTB diagnosed by Xpert, of whom 250 (65.1%) had 2<sup>nd</sup> line DST results (47 had no additional testing done, 46 samples did not grow or lost viability, 30 samples were contaminated, 10 had LPA only, 1 sample lost). Mean patient age was 33.2 years (10.7 SD), 40% female, 70% HIV positive of those tested; 40% smear positive, 51% smear negative, 9% no smear done. Median time from sputum taken to 2<sup>nd</sup> line DST result reported was 54 days (IQ range 48–66) overall; smear positive cases took a median 49 days (IQ range 43–55) while smear negative cases took a median 62 days (IQ range 52–72). 19.6% of patients were infected with MDR MTB resistant to at least one 2<sup>nd</sup> line drug, of which 5.6% were extensively drug resistant (XDR) TB and 12.0% pre-XDR TB.

**Conclusion:** Under current program conditions, nearly a fifth of patients diagnosed with RIF resistant MTB by Xpert are started on a weakened standardized 5-drug MDR regimen with the indication to adjust therapy not apparent for almost 8 weeks. Such delays risk worsened outcomes for individual patients and potentially fuel amplification of 2<sup>nd</sup> line drug resistance on a community level.

### **OAP-319-31 GeneXpert module failures: South Africa's Xpert MTB/RIF national programme experience and impact on costs**

S Molapo,<sup>1</sup> L Berrie,<sup>1</sup> P Marokane,<sup>1</sup> V Magida,<sup>1</sup> L Scott,<sup>2</sup> W Stevens.<sup>1,2</sup> <sup>1</sup>National Priority Programs, National Health Laboratory Service, Johannesburg, <sup>2</sup>Molecular Medicine and Haematology, University of the Witwatersrand, Johannesburg, South Africa. e-mail: leigh.berrie@nhls.ac.za

**Background:** This study investigated the rate of Xpert analyzer module failures during the period of national programme implementation in South Africa (March 2011 and November 2013) and assessed the cost implications thereof for overall maintenance.

**Method:** The analysis was conducted across all 207 National Health Laboratory Service smear microscopy centres providing diagnostic services across all 9 provinces. Xpert had been installed to replace smear microscopy as the frontline diagnostic assay. The performance of 3,564 Xpert modules was reviewed from first initial installation to time of Xpert module first failure. Factors contributing to elevated error rates were analysed from the Xpert software run files linked to error

codes. The overall module failure rate was calculated and presented as the mean, median, minimum and maximum time to failure. The difference in costs between repair and replacement as needed and the supplier quoted extended warranty option was calculated in order to determine whether it was cost-effective to extend the warranty at current pricing. All data was entered and analysed in MS Excel. Descriptive statistics were applied and graphically presented.

**Results:** A total of 515 modules were replaced since program inception. 79% (n=405) were attributed to module failure which reflected an overall rate of 11.36% of all modules. The most common reasons for module replacements were attributed to temperature fluctuations and instrument malfunction (62.95%). Other reasons were characterised as cartridge integrity (13.84%), sample processing errors (16.96%), power failures (3.13%) and software issues (2.23%). The median time to failure was 452 days (0–1008). Significant variation was observed in failure rates across modules. The estimated incremental maintenance costs ranged from 53 thousand to 1.7 million USD in the years 2011–2019 due to the number of modules. The option for the extended warranty has been shown to be more expensive with the total cost saving of 15.72% or 967 thousand USD if the option of repair and replacement as needed was chosen.

**Conclusion:** The implementation of the Xpert has allowed laboratories to increase automation, streamline workflow and reduce human resources. Maintenance of analyzers remains a significant problem in resource limited settings and needs to be quantitated and costed to ensure sustainability of programs. History of the refurbished modules that are reused is unknown and remains a concern.

## **16. THE DEPTHS OF DRINKING, DRUGS AND DEPRESSION IN TB**

### **OAP-320-31 Tuberculosis and alcoholism in Brazil: a cross-sectional study (2007–2011)**

O Rodrigues,<sup>1</sup> A De Paula Lobo,<sup>1</sup> J Toledo,<sup>1</sup> H Barroso Bernal,<sup>1</sup> F Moherdau,<sup>1</sup> J N Lima,<sup>1</sup> D Barreira.<sup>1</sup> <sup>1</sup>National Tuberculosis Program, Ministry of Health, Brasília, DF, Brazil. e-mail: olga.rodrigues@saude.gov.br

**Background:** Alcohol use is an important risk factor for the development of active tuberculosis (TB). The aim of this study was to describe the clinical profile and treatment outcomes of new TB cases notified as alcohol users in Brazil.

**Design/Methods:** By using the Brazilian National Information System for Notification of Diseases (Sinan), it was conducted a cross sectional study. The new TB cases reported from 2007 to 2011 that had information (“yes” or “no”) for the variable “alcohol use” were selected and evaluated by socio-demographic data (sex/age), HIV test performance, TB-HIV co-infection and TB treatment outcomes (“cure”, “dropout” or “TB-related death”).

**Results:** In the study period, 359,677 new TB cases were notified, of which 86.2% (310,014) had information about "alcohol use" and were selected. In the study group, alcohol use was referred in 14.8% (45,863) of the total cases. Among the alcohol users, 89.1% (40,878) were male, 75% (34,401) were aged 30–59 years old, 59.3% (27,214) performed the HIV test and the co-infection rate was of 10% (4,593). Regarding the treatment outcomes, 63.7% (29,215) were cured, 15.0% (6,877) dropped out and 5.8% (2,669) were TB-related deaths.

**Conclusion:** Alcohol use, tuberculosis and worse treatment outcomes appear to be linked in Brazil. In the study period, the co-infection rate was higher amongst the alcohol users (10%) than in the general population (7.4%) and the treatment outcomes were also worst: lower cure rate (63.7% versus 73.1%), higher drop out rates (15% versus 9.7%) and TB-related deaths (5.8% versus 3.3%). It is worth mentioning that in Brazil, there is another databank used to measure deaths-related causes, which is more precise and detailed. In spite of this, the results point out the must of a better understanding of TB-related deaths on alcohol users and also the need to develop strategies to reduce harmful consequences related to alcohol use.

### OAP-321-31 Emotional distress in Angolan patients with several types of tuberculosis

B Xavier,<sup>1</sup> B Peixoto.<sup>2</sup> <sup>1</sup>Infetocontagiosas, Hospital Sanatório do Huambo, Huambo, Angola; <sup>2</sup>Sciences, CESPU-Instituto Superior de Ciências da Saúde- Norte, Gandra, Portugal. e-mail: bruno.peixoto@iscsn.cespu.pt

**Background:** Common mental disorders (CMD) make a significant contribution to disability and burden of disease in low-income countries. The prevalence of CMD in Tuberculosis (TB) patients in low-income countries, and its association with clinical and sociodemographic variables it is subject of debate. The aim of this study is to determine the prevalence of emotional distress and associated factors in Angolan patients with several types of TB.

**Design/Methods:** The study was conducted at the Sanatorium Hospital of Huambo. 81 inpatients with several types of TB (pulmonary, disseminated, Pott's disease) were assessed through the Hospital Anxiety and Depression Scale (HADS). The scale total score it is related to emotional distress and it encompasses two dimensions: Anxiety and Depression. Several clinical and sociodemographic variables were studied in relation to distress, anxiety and depression. Finally, a multiple linear regression was performed in order to determine the most influencing variables on emotional distress.

**Results:** 73% of the sample presented significant levels of emotional distress. Patients with disseminated TB, from female gender, widows and treated with central medication and other antibiotics, presented significant higher levels of distress. A diagnosis of disseminated TB and the use of central medication and others antibiotics were related to higher levels of anxiety and depression. Female

gender and subjects without any monthly income obtained higher levels of depression. Married subjects obtained higher levels of anxiety. The multiple linear regression ( $\beta=7,403$ ;  $p \leq .001$ ) showed that diagnosis, gender, marital status and treatment are the main determinants of emotional distress

**Conclusion:** This study found high rates of emotional distress in TB patients. The severity of the diagnosis, gender, marital status and treatment, are the main determinants of distress. Oddly, socioeconomic factors like level of instruction, housing and sanitary conditions, and daily access to food and level of income shoed no relation with distress. HIV co-infection it is not related to emotional distress level. This study strengthens the need to screen for emotional distress in order to improve TB patients health outcomes.

### OAP-322-31 TB and excess alcohol use among the foreign born, USA, 1997–2012

T Volkmann,<sup>1</sup> P Moonan,<sup>1</sup> R Miramontes,<sup>1</sup> E Pevzner,<sup>1</sup> J Oeltmann.<sup>1</sup> <sup>1</sup>Division of TB Elimination, Centers for Disease Control and Prevention, Atlanta, GA, USA. e-mail: xdh4@cdc.gov

**Background:** Foreign-born (FB) persons continue to account for an increasing proportion of all tuberculosis (TB) disease in the United States (US). Excess alcohol use is associated with poor treatment outcomes and complicates management of TB. A review paper by Rehm, et al. indicated that about 10% of global TB cases could be eliminated in the absence of alcohol use. We described the epidemiology of excess alcohol use among FB persons with TB aged >15 years in the US.

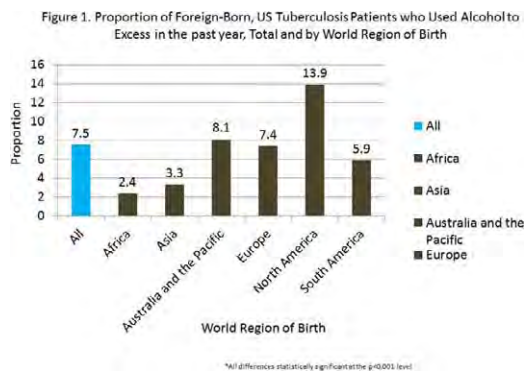
**Design/Methods:** We used data reported to the U.S. National Tuberculosis Surveillance System for 1997–2012. We determined the proportions of excess alcohol use reported within the past 12 months at the regional, sub-regional, and country levels and examined geographical differences using  $\chi^2$  tests.

**Results:** Overall, 211,537 of 215,400 patients had excess alcohol use status documented. Of these, 117,851 (55.7%) were FB. Among the FB, the prevalence of excess alcohol use was 7.5%. Patients born in two regions exceeded the overall prevalence of excess alcohol use; North America (13.9%), and Australia and the Pacific (8.1%). Patients from Africa (2.4%) and Asia (3.3%) had the lowest prevalence (Figure 1). All differences in regional prevalence were statistically significant. Among United Nations' designated sub-regions, patients from Central America (14.9%), North America (14.8%), Northern Europe (11.0%), and Micronesia (10.0%) had the highest prevalence of excess alcohol use. At the country level, patients from Puerto Rico (21.0%), Cuba (19.4%), Poland (18.9%), Costa Rica (18.3%), and Antigua & Barbuda (18.2%) had the highest prevalence. Patients from Mexico constituted 22.6% of all FB cases, and prevalence of excess alcohol use among those patients was 15.5%.

**Conclusion:** Excess alcohol use varies significantly based on FB patients' geographic origins. Excess alcohol use



was almost six times more common among FB North American patients than among FB African patients. Given these disparities and limited TB control resources, TB control programs in the US should continue to screen all patients for excess alcohol use, with particular attention paid to assessing and addressing alcohol abuse among patients from countries with high levels of excess alcohol use. Globally, further research is needed to determine whether the patterns observed in US data are consistent and would require additional resources to scale-up alcohol treatment programs commensurate with the local epidemiology of the problem.



### OAP-323-31 Harm, liberty and tuberculosis in persons with severe and persistent mental illnesses

D Silva.<sup>1</sup> <sup>1</sup>Centre for Research on Inner City Health, St. Michael's Hospital, Toronto, ON, Canada.  
e-mail: diego.silva@utoronto.ca

**Background:** The harm principle, which generally states that individuals are free to act so long as they do not harm other non-consenting persons, is commonly invoked to help isolation and DOT in TB care. TB in persons with severe and persistent mental illnesses (SPMI) provides the opportunity to evaluate the application of the harm principle in a real-world context. TB in persons with SPMI is an ideal case study because (a) the treatment of TB and mental illness are two examples where liberty restrictions are often justified by appealing to the harm principle and (b) the goal of arresting the spread of TB (e.g. through isolation) may conflict with the goals of mental health (e.g. reducing social isolation). It is currently unknown how healthcare workers in public health and mental health conceptualize the harm principle, and moreover, whether their views resonate with policy.

**Design/Methods:** This paper presents the results of a mixed methods study that includes interviews and an online survey with healthcare workers and administrators in public health units and mental health centres in Toronto, Canada. Twenty interviews were conducted and analyzed via thematic analysis. An online survey, where items were generated by reference to philosophical interpretations of the harm principle (including JS Mill, Joel Feinberg, Joseph Raz, and Immanuel Kant), was

distributed and analyzed via logistic regression. The response rate was 49.7% (n=109).

**Results:** The three themes that emerged from the interviews included the importance of establishing the goal of care, accounting for the context surrounding liberty restrictions, and balancing the goals of mental health and public health. The survey findings suggest significant disagreement about whether someone with TB should be forced to receive treatment (49%=Agree/Strongly Agree; 45%=Disagree/Strongly Disagree). A majority of respondents also felt that individuals should obey public health isolation orders even if it causes psychological distress (80%=Agree/Strongly Agree) or makes an individual psychiatrically ill (63%=Agree/Strongly Agree).

**Conclusion:** The findings provide an understanding of how harm and liberty is conceptualized by public health and mental health workers. The participants demonstrated nuanced moral reasoning that can enrich and provide real-world context to the existing ethics literature on the topic of the harm principle and liberty restrictions.

### OAP-324-31 Alcohol use is a strong independent risk factor for tuberculosis in urban Tanzania

N Boillat Blanco,<sup>1,2,3</sup> C Daubenberger,<sup>1</sup> S Gagneux,<sup>1</sup> LT Minja,<sup>2</sup> A Kelemani,<sup>2</sup> M Mganga,<sup>4</sup> K Reither,<sup>1</sup> N Probst-Hensch.<sup>5</sup> <sup>1</sup>Parasitology and Infection Biology, Swiss Tropical and Public Health Institute, Basel, Switzerland; <sup>2</sup>Biomedical Sciences, Ifakara Health Institute, Dar es Salaam, Tanzania; <sup>3</sup>Infectious Diseases, Lausanne University Hospital, Lausanne, Switzerland; <sup>4</sup>National Tuberculosis Program, Kinondoni Municipal Council, Dar es Salaam, Tanzania; <sup>5</sup>Epidemiology, Swiss Tropical and Public Health Institute, Basel, Switzerland. e-mail: noemie.boillat@chuv.ch

**Background** Alcohol use increases the incidence of tuberculosis (TB) reactivation and the risk of bad TB treatment outcome. In Sub-Saharan Africa, outside of South Africa, few data are available on the pattern of alcohol use in TB patients. We analyzed the prevalence of alcohol use among TB patients in Dar es Salaam, Tanzania.

**Methods** We conducted a case-control study between July 2012 and March 2014. Adults with TB diagnosed in 2 hospitals in Dar es Salaam were included in the study. Healthy volunteers without past history of TB were recruited among people accompanying patients at the outpatient department of these hospitals. Data on socio-demographic variables and alcohol use were collected. Screening for HIV was performed. Weekly alcohol consumption was defined as regular alcohol use. Independent predictors of regular alcohol use among TB cases were identified by multivariable logistic regression analysis using Stata software (StataCorp, College Station, TX, version 11.2).

**Results** Overall, 387 TB patients and 509 healthy controls were included. Among TB cases, 76% had pulmonary smear+ TB, 20% pulmonary smear- TB and 4% extrapulmonary TB. Compared to controls, patients

with TB were more often male (63 versus 53%;  $p=0.002$ ), had a higher prevalence of HIV infection (31 versus 12%;  $p<0.001$ ) and a lower socio-economical status (46% vs 26%). The prevalence of regular alcohol use was higher among TB patients compared to controls (15% vs 6%;  $p<0.001$ ). Surprisingly, tobacco use was not independently associated with TB (Table). Among TB cases, factors associated with regular alcohol use were male sex (adjusted odds ratio aOR[95%CI] 3.3[1.2–9.4]), tobacco use (aOR[95%CI] 6.9[3.4–14.1]) and extrapulmonary TB (aOR[95%CI] 6.9[1.8–26.2]).

**Conclusions** TB patients have high rate of regular alcohol use irrespective of their socio-economical and HIV status as well as their level of tobacco smoking. These results point to alcohol consumption as an important preventive target in the fight against TB.

	TB cases N=387	Non-TB controls N=509	Factors associated with TB Bivariate / Multivariable analysis	
	N (%)	N (%)	OR (95% CI)	P value
Age, years; mean (sd)	35 (12)	37 (14)	1 (1-1) / 1 (1-1.1)	0.005 / 0.005
Male sex	243 (63)	268 (53)	1.5 (1.2-2) / 1.7 (1.2-2.4)	0.002 / 0.002
HIV infection	116 (31)	62 (12)	3.2 (2.3-4.5) / 3.4 (2.7-5.6)	<0.001 / <0.001
Low socio-economic status	179 (46)	130 (26)	2.5 (1.9-3.3) / 2.7 (1.9-3.7)	<0.001 / <0.001
Tobacco use	96 (25)	104 (20)	1.3 (0.9-1.8) / 0.5 (0.3-0.8)	0.1 / 0.002
Regular alcohol use	58 (15)	29 (6)	2.9 (1.8-4.7) / 3.4 (2–5.8)	<0.001 / <0.001

### OAP-325-31 The “Sputnik” programme as effective approach for treatment of tuberculosis in people with drug dependence

A Solovyeva,<sup>1</sup> D Taran,<sup>2</sup> I Gelmanova.<sup>3</sup> <sup>1</sup>TB Programs in Russia, Partners in Health, Tomsk, <sup>2</sup>TB programs in Russia, Partners in Health, Moscow, Russian Federation; <sup>3</sup>TB Programs in Russia, Partners in Health, Boston, MA, USA. e-mail: solovyova@pih.ru

**Introduction** Epidemiological studies show that in some regions of Russia, injecting drug users (IDUs) account for 2–3% of the population and are at a high risk for developing TB (WHO, 2005). At present, the organization of inpatient TB treatment in Russia does not meet the needs of patients with addiction. The aim of the Sputnik intervention is to achieve an 80% adherence rate (calculated as the proportion of doses taken over the total number of doses prescribed) among TB patients defaulting from the standard ambulatory program. **Method** The following drug-susceptible and drug resistant TB patients were eligible for referral to the program: patients who refused to start treatment or stopped taking medications; those missing more than 25% of prescribed doses; those

with a history of default in the previous 6 months; and those considered to be at high risk for default for other medical, social or economic reasons. Due to limited program capacity, patients are only referred to the Sputnik program after all standard options are exhausted and can be enrolled in the program at any point during their treatment if they are deemed to be at a high risk for default.

**Results** In 2006, at the beginning of the program, all staff was trained on the basis of the “Harm Reduction - Tomsk” initiative with a focus on making contact with IDUs, motivational counseling, prevention of opiate overdoses, etc. During the four years of the project (18.11.06–31.12.12), 138 patients were included in the Sputnik program, 96.4% of which were smear and/or culture positive. Among the patients referred to Sputnik, drug addiction was 4.5 times more likely as compared to the rest of the patient population. During this period, the program treated 49 IDUs (all of them with drug resistant tuberculosis). To date, the outcomes are as follows: cured 32 (65.3%), defaulted 8 (16%), failed treatment 6 (12%), died due to reasons unrelated to tuberculosis 2 (4%).

**Discussion** Patient adherence to treatment, calculated as the proportion of doses taken over the total number of doses prescribed, increased from 55% prior to enrolment to 70%.

**Results** from this Tomsk-based program shows that a comprehensive approach focused on the patient’s ability to overcome the correlation between substance abuse, psychological and social problems, and rejection of treatment. This mechanism can be scaled-up and implemented in the country as a whole and worldwide.

### OAP-326-31 Facteurs associés à la dépression chez les patients tuberculeux à Yaoundé, Cameroun

EW Pefura-Yone,<sup>1</sup> L Simo.<sup>2</sup> <sup>1</sup>Internal Medicine and Specialities, Faculty of Medicine and Biomedical Sciences, University of Yaounde 1, Yaounde, <sup>2</sup>DLM, Ministry of Public Health, Yaounde, Cameroon. e-mail: pefura2002@yahoo.fr

**Introduction:** Très peu d’études ont été réalisées en Afrique sub-saharienne sur la relation entre la dépression et la tuberculose. Les objectifs de cette étude étaient de déterminer la prévalence de la dépression et investiguer les facteurs associés à la dépression chez les patients tuberculeux à Yaoundé, Cameroun.

**Méthodes :** Cette étude de cohorte prospective incluant tous les adultes traités pour tuberculose a été réalisée de janvier 2012 à décembre 2013 dans le service de pneumologie de l’Hôpital Jamot de Yaoundé. La dépression mentale et l’anxiété généralisée ont été respectivement évaluées par les auto-questionnaires PHQ-9 (Patient Health questionnaire-9) et GAD-7 (General Anxiety Disorder-7). La régression logistique a été utilisée pour rechercher les facteurs associés à la dépression chez les patients tuberculeux. Le seuil de signification retenu était de  $p<0,05$ .

**Résultats :** Des 314 patients définitivement inclus, 200(63,7%) patients étaient de sexe masculin et leur âge médian était de 34(25–43,8) ans. La consommation d'alcool était retrouvée chez 64,6% des patients et 20,4% des patients étaient des fumeurs actifs. La tuberculose pulmonaire et extra-pulmonaire étaient respectivement retrouvées chez 239(76,1%) et 75(23,9%) patients. La prévalence de la dépression (intervalle de confiance à 95%) était de 32,5%(27,3%–37,7%) et 32,4% des patients déprimés avaient aussi une anxiété généralisée. L'infection à VIH était retrouvée chez 39,2% des patients. La dépression majeure était retrouvée chez 45 (14,3%) patients. Les facteurs indépendants associés à la dépression étaient le sexe féminin [odds ratio (intervalle de confiance à 95%) : 3,38(1,98–5,76)], la tuberculose pulmonaire [2,17(1,11–4,25)] et les patients qui avaient déjà été traités par le passé pour une tuberculose [2,62(1,33–5,18)]. La présence de la dépression n'avait pas d'impact négatif sur l'issue du traitement antituberculeux.

**Conclusion :** La dépression est fréquente chez les patients tuberculeux à Yaoundé. La recherche des déterminants de la dépression chez les malades tuberculeux et l'évaluation attentive de la dépression devraient permettre une prise en charge optimale de cette co-morbidité chez ces malades.

#### **OAP-327-31 Prevalence of substance dependence among susceptible TB patients in a private sector hospital in Karachi, Pakistan**

Z. Barry,<sup>1</sup> M. Jaswal,<sup>1</sup> S. Khowaja,<sup>2</sup> A. Bhurgri,<sup>1</sup> H. Hussain.<sup>1</sup>  
<sup>1</sup>TB-MDR, The Indus Hospital, Karachi, <sup>2</sup>International Health, Interactive Research and Development, Karachi, Pakistan.  
 e-mail: maria.jaswal@industbcontrol.org

**Background:** Pakistan ranks sixth amongst the twenty-two TB high-burden countries in the world, accounting for one of the major health problems in Pakistan. Substance abuse is the most commonly reported behavioral risk factor among TB patients. The objective of this study was to find out substances our TB patients frequently use.

**Method:** A retrospective review was performed to analyze substance dependence in TB patients at Indus Hospital. Data were collected from 1,234 newly enrolled adult patients counseled at baseline from February 2012 to February 2014. The patients were categorized as substance dependent if they were positive on three of the seven criteria within the same year as defined by Diagnostic Statistical Manual of Mental Disorder Text Revision (DSM IV-TR). Tolerance, increase amount of substance and persistent desire or unsuccessful efforts to cut down or control substance use were observed in our patients.

**Results:** Of the 1,234 TB patients 590 (48%) were males and 644 (52%) were females. Overall 20% (252/1,234) of patients reported taking different substances were categorized as substance dependent out of which 82% (206/252) were males while 18% (46/252) were females. Cigarette smoking (up to a pack/day) was the most

common addiction among patients, higher in males 51% (105/206) compared to 4% (2/46) females. 10% (21/206) of males used Niswar (smokeless tobacco) compared to 4% (2/46) females. Ghutka was comparatively more common in females 24% (11/46) than males 9% (18/206). Chewable tobacco was used by 7% (14/206) males compared to 35% (16/46) females. 5% (11/206) males used pan compared to 2% (1/46) females. Alcohol and charas (hashish) were respectively used by 0.5% (1/206) males only. 21% (44/206) males were addicted to multiple substances compared to 11% (5/46) females. The Indus Hospital provided special counseling to these patients about adverse reactions of substance on TB treatment and general health to ensure treatment compliance.

**Conclusion:** TB and substance abuse programs need to work hand in hand since substance abuse is associated with negative treatment outcomes. Effective interventions need to be developed by TB programs to address the need of patients who abuse substances.

## **17. PROPHYLACTIC THERAPIES**

#### **OAP-328-31 Improving the uptake of INH preventive therapy through sensitisation and individualised mentoring**

V. Ibeziako,<sup>1</sup> S. Dutt,<sup>1</sup> O. Olupitan,<sup>1</sup> P. Dakum,<sup>1</sup> O. Ogbanufe.<sup>2</sup> <sup>1</sup>Clinical, Institute of Human Virology Nigeria, Abuja, <sup>2</sup>Center for Disease Control and Prevention, Abuja, Nigeria. e-mail: vizeziako@gmail.com

**Background:** The increasing prevalence of HIV has resulted in an increase in prevalence of Tuberculosis worldwide especially in resource limited settings. The uptake of infection control strategies especially INH preventive therapy (IPT) among PLWHAs in Nigeria has been poor as a result of poor knowledge of the effectiveness of INH among health care providers. This intervention is aimed at improving the utilization of IPT among healthcare providers working in HIV settings through group sensitization and individualized mentoring. 24 healthcare facilities (7 tertiary level and 17 secondary level facilities) in 4 geopolitical zones in Nigeria (South west, South South, North West, and North central) were selected for the exercise.

**Intervention:** Individual interviews and focus group discussions involving consultants and medical officers in each of the facilities were carried out to determine the reasons for poor uptake of IPT. Site based interactive group sensitization exercise was then carried out at each facility by trained health professionals, using the National infection control guideline and the WHO guideline for intensified tuberculosis case finding and IPT for PLWHAs in resource constrained settings. This was followed by individualized mentoring sessions at facilities that had not enrolled any patient following 2 months of the sensitization.

**Results:** Utilization data was collected from the facility IPT registers, at baseline and monthly for a period of 4 months following the intervention through site based



monitoring and evaluation officers. Within 4 months, 21 (87.5%) of the 24 facilities had commenced IPT utilization. Only 3(12.5%) of the facilities still had 0% uptake. 6(25%) of the 24 targeted healthcare facilities required additional individualized mentoring sessions within the first 2 months. Overall, patient enrollment for IPT improved from 0% to 43% of the targeted 2162 patients in all 24 facilities.

**Conclusion:** IPT utilization can be improved by delivering group sensitization and individualized mentoring sessions to healthcare providers working in high burden TB settings.

### OAP-329-31 High completion rate of isoniazid preventive therapy among HIV-infected patients receiving care in two clinics in Kinshasa, DR Congo

M Yotebieng,<sup>1,2</sup> P Lelo,<sup>3</sup> P Ndjibu,<sup>3</sup> J Lusiana,<sup>3</sup> L Wenzel,<sup>3</sup> E Edmonds,<sup>2</sup> J-P Kabuayi Nyengele,<sup>4</sup> W Behets.<sup>2,5</sup>

<sup>1</sup>College of Public Health, Division of Epidemiology, Ohio State University, Columbus, OH, <sup>2</sup>Epidemiology, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; <sup>3</sup>Kinshasa School of Public Health, University of Kinshasa, Kinshasa, <sup>4</sup>Direction of Diseases (4th direction), Ministry of Health, Kinshasa, Democratic Republic of Congo; <sup>5</sup>School of Medicine, University of North Carolina at Chapel Hill, chapel Hill, NC, USA. Fax: (+1) 614 688 3533. e-mail: yotebieng.2@osu.edu

**Background:** Isoniazid preventive therapy (IPT) is recommended for HIV-infected persons. However, implementation has been slow, impeded by barriers and challenges including the fear of non-adherence.

**Objective:** To describe the outcomes of routine IPT implementation in two HIV clinics in Kinshasa, Democratic Republic of Congo.

**Methods:** After working with national authorities to adapt the algorithms for IPT, the first isoniazid order was received in October 2012. All HIV-infected patients  $\geq$  one year of age receiving care in the Bomoi and Kalembe Lembe clinics in Kinshasa, in whom active tuberculosis (TB) had been excluded using the World Health Organization screening algorithm, were initiated on IPT for a minimum of six months according to the national algorithm.

**Results:** As of June 2013, 2078 HIV-infected patients had initiated IPT. The median time in care prior to IPT initiation was 2.8 [interquartile range (IQR): 1.4, 4.5] years. By this date, 1723 of those patients had terminated IPT for various reasons including toxicity (32, 1.9%), diagnosis of active TB (9, 0.5%), treatment completed (1574, 91.4%), death (3, 0.2%), interruption (19, 1.1%) and other reasons [mainly poor adherence including loss to follow-up (96, 5.6%)]. Of the patients who terminated IPT, the median duration of IPT was 6.0 (IQR: 6.0, 6.3) months, 473 (27.4%) were male, 457 (26.5%) were  $\leq$ 15 years of age, 446 (25.9%) had been treated previously for TB, and 297 (17.2%) were not on antiretroviral treatment (ART) at IPT initiation. Multivariable logistic regression suggested that younger patients and those not on ART were less likely to complete IPT: adjusted odds ratio 0.77 (95% confidence interval (CI): 0.49, 1.20) for 1–15 year-

olds and 0.86 (95% CI: 0.58, 1.29) for 16–35 year-olds compared to older patients, and 0.72 (95% CI: 0.47, 1.12) for non-ART patients compared to those on ART.

**Conclusion:** IPT can be provided safely in routine care even in very resource-constrained settings.

### OAP-330-31 Tuberculin skin test response in HIV-infected patients in Benin, West Africa

A Wachinou,<sup>1</sup> D Affolabi,<sup>1</sup> SS Ade,<sup>1</sup> G Agodokpessi,<sup>1</sup> W Bekou,<sup>1</sup> G Ade,<sup>1</sup> S Anagonou,<sup>1</sup> M Gninafon.<sup>1</sup>

<sup>1</sup>National Hospital for Tuberculosis and Pulmonary Diseases, National Tuberculosis Programme, Cotonou, Benin. e-mail: wachinouprudence@yahoo.fr

**Background:** HIV increases the risk of re-activation of latent tuberculosis infection (LTBI). Isoniazid (INH) chemoprophylaxis, which is recommended in HIV infected individuals, has shown to be effective only in patients with tuberculin skin test (TST) positive. No data are available on TST response in HIV infected patients in Benin.

**Patients and Method:** A cross-sectional study was conducted from June 2012 to march 2013 at three HIV clinics and the reference laboratory of the National Programme of HIV/AIDS in Cotonou, Benin. Consecutive adults with positive HIV test, naive for HAART and without any tuberculosis disease history were enrolled. For all the participants, tuberculin skin test (TST) and CD4 counts test were performed. The TST cut-off chosen for the analysis was 5 mm.

**Results:** Out of the 830 HIV positive patients included, 53% were female. BCG scars were identified in 622 patients (75%). 68.2% (n=644) had a CD4 count less than 350 cell/mm<sup>3</sup>. 500 (60%) did not react (TST=0 mm). The non-reactors represented 70% and 54,5 % (n=644) of the patients with CD4 < 200 cells/mm<sup>3</sup> and CD4  $\geq$  200 cells/mm<sup>3</sup> respectively (p=0,002). 330 patients (39,8%) had TST  $\geq$  5mm. The proportion of TST+ was 25.9% for patients with CD4<200cells/mm<sup>3</sup> and 41.1% for patients with CD4  $\geq$  200 cells/mm<sup>3</sup> (p=0,001).

**Conclusion:** The proportion of TST positive was higher in patients with CD4 $\geq$ 200 cells/mm<sup>3</sup> than patients with CD4<200 cells/mm<sup>3</sup>. The overall proportion of TST positive was 39,8%. Therefore, care must be taken by the National Tuberculosis Programme before implementing INH prophylaxis, because giving INH prophylaxis without performing TST, may lead to some overtreatment since only few of the targeted people could really benefit from it.

### OAP-331-31 Clinician barriers, enablers, and incentives associated with use of isoniazid preventative therapy among people living with HIV in Ethiopia

J Lai,<sup>1</sup> DJ Dare,<sup>2</sup> Z Gashu,<sup>2</sup> R Fantu,<sup>3</sup> A Meressa,<sup>2</sup> B Feleke,<sup>3</sup> A Abashaw.<sup>1,2</sup> <sup>1</sup>International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA; <sup>2</sup>HIV/AIDS, TB, The John Hopkins Technical Support for Ethiopia HIV/AIDS Initiative (JHU-TSEHAI), Addis Ababa, Ethiopia; <sup>3</sup>Ethiopia, Center for Disease Control, Ethiopia, Addis Ababa, Ethiopia. e-mail: jlai11@jhu.edu

**Background:** Efforts to roll out Isoniazid Preventative Therapy (IPT) as part of the national TB-HIV control strategy and essential care package for people living with HIV (PLHIV) across Ethiopia has had limited success. Despite evidence underscoring the importance of IPT in reducing HIV associated morbidity, there is little empirical research examining why this policy has failed to become practice. The objective of this study is to examine the barriers, enablers, and incentives that clinicians face in using IPT among PLHIV.

**Design/Methods:** Primary data was collected through questionnaires and focus group discussions (FGDs) among 133 clinicians providing TB-HIV services across 67 health facilities supported by The Johns Hopkins University Technical Support for the Ethiopian HIV/AIDS, ART Initiative (JHU-TSEHAI). Bivariate and multivariate analysis in STATA 11.2 was used to determine predictors for high IPT coverage and provide descriptive data on clinician barriers, enablers and incentives to prescribing IPT. FGDs were coded using Atlas.ti.

**Results:** In the bivariate analysis, high IPT rate was associated with clinician training and perception that IPT had no negative side effects on patients. Data also indicated that health centers were more likely to have high IPT rates than hospitals, as were facilities where TB/HIV guidelines could be confirmed onsite. Table 1 summarizes results of bivariate analysis. In the multivariate model, two predictors were found to have an association with high IPT rate: facility type being a health center (OR 5.71; CI 1.44-22.67) and clinician perception that that IPT had no negative side effects on patients (OR 5.62; CI 0.63-6.06). Concerns about INH resistance and ruling out of active TB were noted, but did not have statistically significant correlation with IPT uptake. FGDs largely reflected data found in questionnaires, although inconsistent INH supply was more prominently highlighted as a barrier.

**Conclusion:** Clinicians perceive IPT as an important intervention but findings indicate that inconsistent supply of INH, gaps in training, and limited availability of national guidelines are some of the key barriers among clinicians in prescribing IPT.

**Interventions** that target clinicians from hospitals, work towards improving clinician capacity in management of IPT side effects, and address the inconsistent INH supply are essential to achieve improved IPT uptake rates as indicated by national policy.

Table 1: Factors associated with high IPT rates among clinicians providing IPT services at TSEHAI sites, bivariate analysis results

Predictor	IPT Rate <60%	IPT Rate >60%	Odds Ratio	SE	95% CI	Z	P
Clinician feels MDR-TB rate increases with IPT	71%	29%	0.66	0.15	0.41-1.05	-1.74	0.08
Clinician agrees that IPT had negative side effects on patients	67%	33%	5.64	4.38	1.23-25.82	2.23	0.02
Clinician completed TB/HIV Training	66%	34%	3.08	1.52	1.17-8.10	2.28	0.02
Clinician completed Palliative Care Training	59%	41%	3.24	1.49	1.31-8.00	2.55	0.01
TB/HIV Guidelines Confirmed onsite at clinician's facility	67%	33%	2.93	1.51	1.08-8.04	2.09	0.03

### OAP-332-31 Implementation of isoniazid preventive therapy in an HIV clinic in Cambodia: high rates of toxicity when combined with antiretroviral therapy

K Choun,<sup>1</sup> S Thai,<sup>1</sup> N Lorent,<sup>2</sup> B Chim,<sup>1</sup> J Vangriensvan.<sup>2</sup> <sup>1</sup>Infectious Disease Department, Sihanouk Hospital Centre of HOPE, Phnom Penh, Cambodia; <sup>2</sup>Clinical Sciences, Institute of Tropical Medicine, Antwerp, Belgium. Fax: (+855) 23 882 614. e-mail: kimchengchoun@sihosp.org

**Background:** Data on the feasibility and completion rates of isoniazid preventive therapy (IPT) in HIV infected-patient within Asia are limited. Within a hospital-based HIV-program in Phnom Penh, Cambodia, we determined the proportion completing IPT (300 mg/day self-administered for 6 months) and reasons for non-completion.

**Design/Methods:** We conducted a retrospective cohort study using HIV/IPT program data from February 2011 to August 2013. All patients underwent symptom screening and further investigations (including sputum microscopy/culture) if symptom screening was positive. Those with tuberculosis (TB) ruled-out were started on IPT, with monthly follow-up visits. As per national guideline, IPT was only prescribed to those not (yet) on antiretroviral treatment (ART). IPT completion was defined as taking IPT for at least 22 of the planned 24 weeks. ART was started according to WHO eligibility criteria; stavudine/lamivudine/nevirapine was the preferential first line regimen.

Table. Reasons for non-completion of IPT

Reason	Total, N (%)	ART during IPT, N (%) N=207	No ART during IPT, N (%) N=234
Total	96 (100%)	54 (26.1%)	42 (17.9%)
Toxicity	56 (58.3%)	45 (21.7%)	11 (4.7%)
Livertoxicity	24 (25.0%)	19 (9.2%)	5 (2.1%)
Livertoxicity & skin rash	15 (15.6%)	13 (6.3%)	2 (0.9%)
Skin rash	13 (13.6%)	11 (5.3%)	2 (0.9%)
Neuropathy	4 (4.2%)	2 (1.0%)	2 (0.9%)
Lost to follow-up	19 (19.8%)	3 (1.5%)	16 (6.8%)
Tuberculosis during IPT	12 (12.5%)	5 (2.4%)	7 (3.0%)
Patient decision (refusal)	4 (4.2%)	0 (0.0%)	4 (1.7%)
Drug interaction	1 (1.1%)	0 (0.0%)	1 (0.4%)
Transfer to other hospital	4 (4.2%)	1 (0.5%)	3 (1.3%)

**Results:** Among 441 ART-naïve patients starting IPT (median age: 34.9 years (IQR: 31.3–42.8); median CD4 count 360 cells/μL (IQR: 225–585); 286 (65%) female), 207 (47%) started ART during IPT at a median of 4

weeks (IQR, 2–6) after commencing IPT (“concurrent ART”). The remaining 234 received IPT without subsequent ART initiation. In total, 345 (78%) completed IPT. Among those with concurrent IPT/ART, completion rate was 74% (153/207). Those without concurrent ART had a higher completion rate (82%; 192/234;  $P=0.039$ ). The main reason for non-completion with concurrent ART was drug toxicity (mainly rash and liver toxicity), occurring in 21.7% (45/207). Without concurrent ART, the main reason for non-completion was lost to follow-up (Table). Fourteen (3.2%) patients were diagnosed with TB while on IPT, including three with a positive TB culture at baseline. An additional 14 TB cases were diagnosed after IPT, only three were bacteriologically confirmed.

**Conclusion:** Although overall completion rates were acceptable, IPT discontinuation was common in those subsequently initiating ART. Assessing ART-eligibility prior to IPT initiation is warranted. For ART-eligible patients, ART should be initiated first and IPT postponed.

### OAP-333-31 Initial results of isoniazid preventive therapy in Lesotho

J Sanders,<sup>1,2</sup> M Mokhali,<sup>1</sup> E Mohapi.<sup>1,2</sup> <sup>1</sup>Pediatrics, Baylor College of Medicine Children's Foundation - Lesotho, Maseru, Lesotho; <sup>2</sup>Pediatrics, Baylor College of Medicine, Houston, TX, USA. e-mail: jsanders@bcm.edu

**Background:** In an effort to combat the devastating HIV and tuberculosis (TB) epidemics in Lesotho, the Ministry of Health launched National Guidelines for the three I's: Intensified Case Finding (ICF), Isoniazid Preventive Therapy (IPT) and Infection Control (IC) in September 2011. All HIV-infected persons over one year of age are eligible for IPT as part of a comprehensive package of HIV care and treatment services. Routine use of IPT in HIV-infected persons is new in Lesotho, and the Baylor College of Medicine - Bristol-Myers Squibb - Children's Clinical Center of Excellence - Lesotho (COE) - a pediatric and family HIV clinic - served as a pilot site for national implementation.

**Design/Methods:** IPT was implemented at the COE beginning in April 2012 in conjunction with ongoing clinical services that include antiretroviral therapy. The National Tuberculosis Programme provided a dedicated IPT register for clinical and programmatic monitoring. This is a retrospective review of the IPT register. HIV-infected patients enrolled between April 2012 and June 2013 are included in the analysis. Children under 5 years of age, regardless of HIV status, who received IPT as post-exposure prophylaxis for known TB exposure are excluded.

**Results:** 89% of patients who began IPT successfully completed the six-month course of therapy. Records for 2337 patients are included in this analysis. 2089 (89.3%) completed IPT. 71 patients (3.0%) transferred out of the clinic, and 87 (3.7%) defaulted treatment. Diagnosis of active tuberculosis while receiving IPT was low, and only 42 patients (1.8%) were begun on TB treatment. Only 37

patients (1.6%) stopped IPT due to side effects or toxicity. Outcomes are reported below based on age.

	1–4 years	5–14 years	15+ years	Totals
Completed IPT	250	1229	610	2089
Transferred out	11	23	37	71
Defaulted IPT	9	32	46	87
Developed TB	1	29	12	42
Died	3	6	2	11
IPT stopped due to side effects/toxicity	3	25	9	37
Totals	277	1344	716	2337

**Conclusion:** IPT can be successfully implemented in ART clinics in Sub-Saharan Africa. Adverse effects and development of TB disease are uncommon. Longitudinal follow-up of this cohort will provide information regarding the benefits of IPT in HIV-infected persons in Lesotho.

### OAP-334-31 Coverage of antiretroviral and cotrimoxazole prophylactic therapies among HIV-positive tuberculosis patients in Africa region

O Adetokunboh,<sup>1</sup> T Balogun,<sup>1</sup> M Oluwasanu.<sup>2</sup>

<sup>1</sup>Interdisciplinary Health Sciences, Stellenbosch University, Cape Town, South Africa; <sup>2</sup>Health Promotion, University of Ibadan, Ibadan, Nigeria. e-mail: adetok\_sic@yahoo.com

**Background:** World Health Organization (WHO) recommended antiretroviral therapy (ART) for all people living with HIV who are co-infected with Tuberculosis (TB). Cotrimoxazole prophylaxis therapy (CPT) was also recommended for the same set of people. CPT in people living with advanced HIV disease prevents opportunistic infections such as *Pneumocystis jirovecii* pneumonia (PCP) and toxoplasmosis. Studies have shown that ART and cotrimoxazole prophylaxis will help prevent infections and prolongs life in these patients. African region has the highest HIV positive incidence TB cases among the WHO global regions with 30 African countries classified as the high TB/HIV burden countries. This study evaluates the trend of ART and CPT coverage among the individuals with TB/HIV co-infections in the high TB/HIV burden countries in Africa.

**Design / Methods:** We analysed the secondary data from the WHO global TB database (October 2013 data). Paired data mean-comparison test was conducted to determine the mean difference (MD) of percentage of HIV positive TB patients on ART and CPT between 2010 and 2012 among 27 of the 30 countries. Analyses were conducted with the use of Stata/IC version 12.1.

**Results:** 90% (27 out of 30) of the sub-Saharan African countries had complete data for the period under review. The average percentage of HIV positive TB patients on ART in the African HIV/TB high burden countries in 2012 was 59.1%, mean difference 21.3%, 95% CI 13.1–29.5,  $p=0.0000$ . In 2012, 9 of the countries were  $>95\%$  in their ART coverage while 6 were  $<50\%$ . The average percentage of patients on CPT in 2012 was 76%, mean difference 3.7%, 95% CI  $-5.1-12.6$ ,  $p=0.3935$ . 11



countries were above >90% mark for CPT coverage in 2012. Angola recorded maximal coverage and progressed from 43% to 100% for both ART and CPT (2010 – 2012).

**Conclusion:** ART coverage for TB/HIV patients in the African high burden countries increased significantly between 2010 and 2012, while CPT coverage was more or less stagnated in many countries. However, there is much to be done to achieve the goal of provision of good quality of life and reduction in mortality in these patients with HIV/TB co-infections. There is also need to look very closely to know why some countries are still lagging behind or even retrogressing while some are progressing significantly.

### OAP-335-31 Implementation of isoniazid preventive therapy (IPT) among HIV-positive female sex workers in Mombasa, Kenya

S Lacourse,<sup>1,2</sup> R Deya,<sup>3</sup> S Graham,<sup>1,2,4</sup> L Masese,<sup>1</sup> W Jaoko,<sup>4</sup> K Mandaliya,<sup>5</sup> R.S. McClelland.<sup>1,2,3,4</sup>

<sup>1</sup>Department of Epidemiology, University of Washington, Seattle, WA, <sup>2</sup>Department of Medicine, Division of Allergy and Infectious Diseases, University of Washington, Seattle, WA, USA; <sup>3</sup>Institute of Tropical and Infectious Diseases, University of Nairobi, Nairobi, Kenya; <sup>4</sup>Department of Global Health, University of Washington, Seattle, WA, USA;

<sup>5</sup>Department of Medical Microbiology, University of Nairobi, Nairobi, Kenya. e-mail: smlacourse@gmail.com

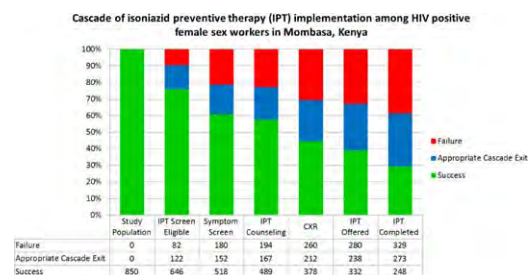
**Background:** Tuberculosis (TB) is the leading cause of death in HIV infected individuals. Female sex workers (FSW) in Kenya have a high HIV prevalence, and therefore are at increased risk for TB. Isoniazid preventive therapy (IPT) decreases risk of progression from TB infection to disease. Despite WHO recommendations that HIV infected persons without evidence of active TB be offered IPT, there has been limited global uptake of this intervention. Our objective was to characterize the cascade of IPT delivery and identify correlates of cascade success in a cohort of FSWs.

**Design/Methods:** This is a retrospective study in a FSW cohort offered IPT as part of routine HIV care from March 2000–January 2010. In this program, women were not eligible for IPT if they had a history of active TB or irregular clinic attendance. Eligible women were evaluated with a symptom screen. Those without symptoms were referred for IPT counseling and CXR. Women with a negative CXR were offered IPT. Success through the IPT cascade included accomplishing each step through completion of 6 months of IPT. Women were considered to have appropriately exited the cascade if they developed medication intolerance, pregnancy, or active TB. Failure included defaulting or not being referred to the next step. We compared characteristics of FSWs who had success versus those who defaulted from the IPT program.

**Results:** Among 850 HIV positive FSWs, median age was 31 years (IQR 26–35) with median CD4 of 402 (IQR 291–604) cells/μL at enrollment. There were 204 (24%) women who were not initially eligible for IPT, including 117 (13.8%) with a history of TB. The largest proportion

of failures occurred at initial symptom screen (29.8%, 98/329), followed by CXR evaluation (20%, 66/329) and IPT completion (14.9%, 49/329), and were primarily due to default (85.7%, 282/329) (Figure). Twenty nine women were diagnosed with TB during IPT evaluation, including 1 after IPT initiation. The majority of women offered IPT completed the course (74.7%, 248/332); less than 5% had medication intolerance. Women who completed IPT were older (median age 32 vs. 29 years,  $p=0.0001$ ), had worked longer as sex workers (median years 2 vs. 1,  $p=0.005$ ), and had lower CD4 (median 387 vs. 461  $p=0.003$ ) compared to those who defaulted.

**Conclusion:** IPT was successfully provided to HIV positive FSWs in this setting in coastal Kenya. New strategies to decrease default and target bottlenecks in the IPT care cascade are needed.



## 18. MDR-TB MANAGEMENT: NEW APPROACHES

### OAP-336-31 Resistance to ethambutol, pyrazinamide, streptomycin and second-line drugs amongst MTB strains susceptible to isoniazid and rifampicin by the MODS assay

A Mendoza,<sup>1</sup> A Alarcon,<sup>1</sup> E Castillo,<sup>2</sup> A San Miguel,<sup>3</sup> E Leo,<sup>4</sup> L Asencios,<sup>4</sup> N Quispe,<sup>4</sup> D Moore.<sup>5</sup> <sup>1</sup>Lima, Estrategia Sanitaria Nacional de Prevencion y Control de la Tuberculosis, Lima, <sup>2</sup>Lima, Direccion Regional de Salud Callao, Callao, <sup>3</sup>Lima, Direccion de Salud Lima Sur, Lima, <sup>4</sup>Lima, Instituto Nacional de Salud, Lima, Peru; <sup>5</sup>Clinical Research, London School of Hygiene & Tropical Medicine, London, UK. e-mail: mendozalberto@hotmail.com

**Background:** Peru has established universal access to detection of resistance to isoniazid (H) and rifampicin (R) through pretreatment rapid direct DST. If a strain is found to be susceptible to H and R by rapid DST the patient receives conventional first-line treatment with HRZE (Z, pyrazinamide; E, ethambutol) and no further DST is performed.

**Objective:** to determine the prevalence of resistance to E, Z, streptomycin (S) and second line drugs in strains determined to be H and R - susceptible by MODS.

**Methods:** As part of external quality assurance, samples determined to be susceptible to isoniazid and rifampin by MODS from three regional government laboratories were processed by the indirect agar proportion method

and pyrazinamidase assay at the National TB Reference Laboratory in Lima.

**Results:** Between 2009 and 2010 complete first and second line drug susceptibility test results were obtained for 315 of 324 strains deemed susceptible to H and R by MODS. The MODS-proportion method concordance for H and R was 90.5% (285/315) and 97.5% (307/315) respectively. The prevalence of resistance to extended first line and second line agents for these 315 strains is presented in the table.

Drugs	Resistance	Resistance (CI 95%)
Ethambutol	5/315	1.6% (0.6 – 3.5)
Pyrazinamide	6/315	1.9% (0.7 – 3.9)
E & Z	2/315	0.6% (0.1 – 2.1)
Streptomycin	30/315	9.5% (6.6 – 13.2)
Ciprofloxacin	1/315	0.3% (0.02 – 1.6)
Kanamycin	2/315	0.6% (0.1 – 2.1)
Capreomycin	2/315	0.6% (0.1 – 2.1)
Ethionamide	16/315	5.1% (3.0 – 7.9)
PAS	1/315	0.3% (0.02 – 13.2)
Cycloserine	0/315	0.0% (0.0 – 0.9)

**Conclusion:** Resistance to E, Z and second line drugs is very low among strains determined to be H and R susceptible by MODS. These results support the policy to universal access to rapid detection of H and R resistance and the decision to treat those HR susceptible strains with a HRZE regimen.

#### OAP-337-31 Association between regimen composition and sputum culture conversion in patients with multidrug-resistant tuberculosis

C Yuen,<sup>1</sup> E Kurbatova,<sup>1</sup> J Ershova,<sup>1</sup> T Dalton,<sup>1</sup> P Cegielski,<sup>1</sup> and Global Petts Investigators. <sup>1</sup>Division of TB Elimination, CDC, Atlanta, GA, USA. Fax: (+1) 404-639-1566. e-mail: ies3@cdc.gov

**Background:** World Health Organization (WHO) guidelines for the treatment of multidrug-resistant tuberculosis (MDR TB) recommend a regimen consisting of four second-line drugs that are likely to be effective and pyrazinamide. To gain insight into how regimen design affects treatment response, we analyzed treatment and microbiological data from the Preserving Effective Tuberculosis Treatment Study.

**Methods:** Using Cox proportional hazards analysis, we analyzed associations between initial sputum culture conversion and both the number of drugs in a regimen and the presumed effectiveness of these drugs based on baseline drug susceptibility testing (DST). For each individual drug received by a patient, we calculated the number of days during which the drug was included in a patient's regimen between initiation of MDR TB treatment and sputum culture conversion or censoring.

**Result:** In multivariable analysis, receiving an average of  $\geq 6$  potentially effective drugs per day was associated with a 38% higher likelihood of sputum culture conversion than receiving 5 to  $< 6$  potentially effective drugs (hazard ratio 1.38, 95% confidence interval 1.12–1.70). Addition of pyrazinamide or a drug to which baseline DST indicated susceptibility to regimens were

associated with greater increases in the likelihood of sputum culture conversion than addition of a drug to which baseline DST indicated resistance. Adding a drug for which DST was not performed to the regimen was beneficial only if a minimum number of effective drugs was present in the regimen.

**Conclusions:** MDR TB regimens including more potentially effective drugs than the five currently recommended by WHO may encourage improved response to treatment in patients with MDR TB.

#### OAP-338-31 *Mycobacterium tuberculosis* resistance to bedaquiline

K Andries,<sup>1</sup> C Villellas,<sup>1</sup> N Coeck,<sup>2</sup> N Lounis,<sup>1</sup> B De Jong,<sup>2</sup> A Koul.<sup>1</sup> <sup>1</sup>Antimicrobial Research, Janssen Research & Development, Beerse, <sup>2</sup>Mycobacteriology, Institute Tropical Medicine, Antwerp, Belgium. e-mail: kandries@its.jnj.com

**Background:** New drugs are finally reaching patients suffering from drug-resistant TB. History of TB treatment has shown the importance of understanding mechanism(s) that lead to resistance, so that recommendations for appropriate use can be made and drug susceptibility testing methods can be developed. The mechanism of action of bedaquiline (BDQ, TMC207), an ATP synthase inhibitor, was discovered through whole genome sequencing of 3 BDQ-resistant mutants. When a larger set of BDQ resistant isolates was generated, target-based mutations were identified in only 30% (15/53) of the isolates, suggesting the existence of additional mechanism(s) of resistance.

**Design/Methods:** TB isolates with increased MICs for BDQ were selected and sequenced in search of non-target based mechanisms of resistance. Selected isolates were studied in vitro and in mice to understand the translational effect of non-target based resistance.

**Results:** 12 paired isolates were investigated: 3 were isolated in vitro, 3 from mice and 6 from patients in a BDQ clinical trial. In all 12 isolates, non-target based resistance to BDQ was due to changes (point mutations, insertions or deletions) in Rv0678, a transcriptional repressor gene of the operon encoding the MmpS5-MmpL5 efflux pump system. These changes resulted in 3 to 10-fold increases in the MICs of both BDQ and clofazimine (CFZ). BDQ had decreased bactericidal activity in mice infected with Rv0678 mutants. The efflux pump inhibitor verapamil decreased the MICs of BDQ and CFZ in both drug-sensitive and drug-resistant isolates. However, the combination of verapamil with BDQ did not improve the bactericidal effect of BDQ monotherapy in mice infected with a non-resistant strain. The reduced bactericidal effect in mice infected with Rv0678 mutants could not be overcome by higher doses of BDQ, nor by combining verapamil with BDQ.

**Conclusion:** Efflux-based resistance to BDQ leads to reduced bactericidal efficacy of BDQ and cannot be reversed by combining BDQ with the efflux pump inhibitor verapamil. Efflux-based cross-resistance between BDQ and CFZ may have clinical implications.

**OAP-339-31 A single-tube single-color assay for all allelic variants of the first line gene targets inhA, katG and rpoB that cause MDR-TB**

W Wangh,<sup>1</sup> J Rice,<sup>1</sup> K. Pierce,<sup>1</sup> V Allerheiligen,<sup>2</sup> M Eckart,<sup>2</sup> D Hain.<sup>2</sup> <sup>1</sup>Department of Biology, Brandeis University, Waltham, MA, USA; <sup>2</sup>Hain Lifescience, Nehren, Germany. e-mail: wangh@brandeis.edu

**Background:** MDR TB is due to resistance to either or both isoniazid and rifampicin. An allele specific assay for both of these drugs is urgently needed to enhance treatment and conserve antibiotic capacities.

**Methods:** A multiplex LATE-PCR reaction has been constructed that generates single-stranded DNA amplicons for the rpoB, katG, and inhA promotor gene targets, as well as an internal control. These four amplicons are detected with four sets of Lights-On/Lights-Off probes label with Quasar 670 and/or a Black Hole Quencher. Probe-target hybridization takes place at end-point over a wide range of temperatures below the annealing temperature. The temperature ranges for the four sets of probes overlap, making it possible to maximize the amount of information generated in a single color. The amplifiable internal control generates a specific low temperature signal to confirmation polymerase activity. An additional non-amplifiable internal control generates a second specific high temperature signal. Together these controls can be used to calibrate each reaction, as well as to quantify the amount of each gene target. Another proprietary reagent is added to the reaction mixture to ensure primer specificity throughout amplification.

**Results:** A large number of strains that harbor various combinations of inhA, katG, and rpoB alleles have been tested. Each strain displays its own "fluorescent signature" reflecting its underlying allele sequence. But, not every fluorescent signature agrees with its archival sequence information. Additional sequencing proves that the fluorescent signatures invariably correctly identify the alleles present in the strain. Some strains are also revealed to contain mixtures of allelic variants. A reference library for immediate recognition of fluorescent signatures of known alleles will be used to rapidly establish whether a clinical sample is sensitive or resistant to isoniazid and/or rifampicin at particular dose.

**Conclusions:** This highly informative, very sensitive and accurate single color multiplex assay has both clinical and research applications. It will soon be available for use as a kit on a dedicated device. Support by Hain Lifescience.

**OAP-340-31 Treatment outcomes in a large cohort of patients with drug-resistant tuberculosis co-infected with the HIV**

M Bastard,<sup>1</sup> M Bonnet,<sup>1</sup> T Dlamini,<sup>2</sup> K Kimenye,<sup>3</sup> A Hayrapetyan,<sup>4</sup> MSF TB Advisory Group,<sup>5</sup> F Varaine,<sup>6</sup> E Sanchez-padilla.<sup>7</sup> <sup>1</sup>Clinical Research Department, Epicentre, Geneva, Switzerland; <sup>2</sup>National Tuberculosis Program, National Tuberculosis Program, Mbabane, Swaziland; <sup>3</sup>Programmatic Management of Drug resistant Tuberculosis, Programmatic Management of Drug Resistant Tuberculosis, Nairobi, Kenya; <sup>4</sup>National Tuberculosis Program, National Tuberculosis Program, Yerevan, Armenia; <sup>5</sup>TB Working Group, Medecins Sans Frontieres, Geneva, Switzerland; <sup>6</sup>Medical Department, Medecins Sans Frontieres, Paris; <sup>7</sup>Clinical Research Department, Epicentre, Paris, France. e-mail: esanchez@epicentre.msf.org

**Background:** The emergence of resistance to anti-tuberculosis (DR-TB) drugs and the HIV epidemic represent a serious threat for reducing the global burden of TB. Few studies describe treatment outcomes in patients co-infected with DR-TB and HIV.

**Design/Methods:** We analyzed retrospectively the DR-TB treatment outcomes of HIV-TB co-infected patients from a large cohort of 7597 patients in 5 different countries, treated with an individualized regimen based on WHO guidelines. Predictors of unsuccessful outcome (death + defaulter + failure) and of death were identified.

**Results:** Of the 406 HIV-TB co-infected patients, 85.0% came lived in Kenya or Swaziland. The median (IQR) age was 33 years old (28–40), 51.8% were males and 51.2% were MDR. Almost all patients were receiving cotrimoxazole preventive therapy (97.0%) and 76.4% were on antiretroviral therapy (ART), of which 82.3% had started it before initiating DR-TB treatment. The median time between the initiation of ART and DR-TB treatment was 7.8 months for patients already on ART and 1.4 months for patients that started after DR-TB treatment. Treatment outcomes were assessed in 178 patients that started treatment before 2011. Of these, 68% succeeded treatment. Of the 56 mono or poly-resistant TB, 73.2% succeeded, 3.6% failed, 7.1% defaulted and 16.1% died. Of the 118 MDR, 64.4% succeeded, 5.9% failed, 12.7% defaulted and 17.0% died. The absence of ART was the only independent factor associated with an unsuccessful outcome (HR 3.85; 95%CI 1.92-7.69) and with death (HR 5.00; 95%CI 2.27-11.11).

**Conclusions:** Treatment success of MDR-TB HIV co-infected patients are comparable to the success reported in recent systematic reviews. Unsuccessful outcome was mainly due to death, which was significantly increased in patients who did not receive ART. Systematic and rapid introduction of ART is also crucial to reduce mortality of DRTB and HIV co-infected patients. Shorter DRTB regimen using new drugs should be also evaluated in HIV-DRTB co-infected patients.



### OAP-341-31 Dose-ranging activity of clofazimine in the mouse model of tuberculosis chemotherapy

D Almeida,<sup>1,2</sup> N Ammerman,<sup>1,2</sup> C Moodley,<sup>1</sup> B Ncgobo,<sup>1</sup> R Swanson,<sup>1</sup> A Dorasamy,<sup>1</sup> J Adamson,<sup>1</sup> J Grosset.<sup>1,2</sup>

<sup>1</sup>(K-RITH), KwaZulu-Natal Research Institute for Tuberculosis and HIV, Durban, <sup>2</sup>Center for Tuberculosis Research, Johns Hopkins University, Baltimore, MD, USA.  
e-mail: nicole.ammerman@k-rith.org

**Background:** Recently, the anti-leprosy drug clofazimine (CFZ) has been shown to be highly effective against drug-resistant tuberculosis (TB). However, the optimal dosing strategy for incorporating CFZ into TB treatment has not been defined. In order to maximize the therapeutic potential of this drug, a dose-ranging study was conducted in the mouse model of TB.

**Design/Methods:** Mice were infected by low-dose aerosol with *M. tuberculosis*, and six weeks after infection treatment was initiated for groups of mice randomized to receive one of the following dosing regimens: daily administration of CFZ at 25 mg/kg (equivalent to 100 mg/day in humans), 12.5 or 6.25 mg/kg; or loading doses of 50, 100 or 200 mg/kg followed by thrice weekly administration at 25 mg/kg. CFZ was administered by oral gavage. Groups of mice were sacrificed on the day of treatment initiation and on days 1 and 2 and weeks 1, 2, 4, 8 and 12 of treatment to determine CFU counts in lungs and spleens and CFZ concentration in the serum and tissues.

**Results:** The trough CFZ levels in the serum and tissues (lungs, liver and spleen) were dose-dependent: They reached 0.50, 1.20 and 1.50 µg/ml in the serum, and about 20, 50 and 100 µg/g in the tissues of mice treated with 6.25, 12.5 and 25mg/kg, respectively. After a week of no bactericidal activity, the lung and spleen CFU counts declined by approximately 1.5, 2.0 and 3.5 log<sub>10</sub> at weeks 4, 8 and 12 of treatment, respectively, regardless of the CFZ dose.

**Conclusion:** Decreasing doses of CFZ did translate into decreased serum and tissue concentrations, but did not translate into decreased activity, suggesting that lower doses of CFZ may be safely used without compromising efficacy.

### OAP-342-31 The individual-tailored treatment regimens for multidrug-resistant tuberculosis

T Ivanushkina,<sup>1</sup> S Borisov,<sup>1</sup> N Litvinova.<sup>1</sup> <sup>1</sup>Clinical Department, Moscow Research and Clinical Center for TB Control, Moscow, Russian Federation. Fax: (+7)499 7852082. e-mail: sebarsik@gmail.com

**Background.** The adequate chemotherapy regimen (included min 3–4 drugs) in TB patients is often impossible due to the drug-resistance and/or drugs intolerance. In such cases the individual-tailored regimens (ITR) are essential, but the efficacy and safety of ITR, included second-line TB drugs and drugs of the WHO's "fifth group": linezolid (Lz), macrolides (azithromycin, clarithromycin), carbapenems (meropenem, imipenem+cilastatin) isn't yet clear.

**Methods.** The prospective unblinded non-randomized one-centered study includes 100 pulmonary TB pts (18–71 y.o., 60 male and 40 female) with MDR (63 pts, 23 new and 40 re-treatment) or XDR (37 pts, 7 and 30, accordingly). The ITR's formation was performed by WHO's recommendations and based on total both express and liquid and solid media DST and concomitant diseases and symptoms of the drug intolerance consideration. In MDR TB Lz (600 mg daily) was included in 100%: as 3rd drug in 9 patients (14,3%), 4th – in 26 (41,3%), 5th – in 23 (36,5%), 6th – in 5 (7,9%). Moxifloxacin (Mox) was included in 41 patients (65,1%), macrolides – in 7 (11,1%), carbapenems – in 9 (14,3%) and Isoniazid (H) in high doses – in 21 (33,3%). In XDR TB Lz was included in ITR totally in 100%: as 3rd drug – in 13 (35,1%), 4th – in 14 (37,8%), 5th – in 9 (24,3%), 6th – in 1 (2,7%). Mox was included in 29 pts (78,4%), macrolides – in 11 (29,7%), carbapenems – in 7 (18,9%) and H in high doses – in 18 (48,6%).

**Results.** The sputum smear negativation totally score 95,0% (95 pts) was obtained: in MDR TB – 74,6% after 8 wks, 93,7% after 12 wks, 96,8% after 16 wks, 98,4% after 24 wks and in XDR TB – 51,4% after 8 wks, 62,1% after 12 wks, 78,4% after 16 wks, 86,5% after 24 wks, 89,2% after 32 wks. The severe adverse events were observed totally in 56,0% pts: attributed to Lz – in 10,0% (in 9,0% – peroneal neuropathy, in 4,0% – anemia and in 1,0% – obstinate vomiting, thrombocytopenia were not registered), attributed to azithromycin – in 2,0% (tachycardia, the drug was stopped), attributed to carbapenems were not registered.

**Conclusion.** The regimens included drugs of the WHO's "fifth group" are comparatively safe and high-effective in intensive phase of ITR in MDR (at least 6 months) and XDR (at least 8 months) TB pulmonary patients, in spite of long-term ineffective previously treatment. The problem of the optimal length of the continuous phase of such ITR must be resolved in the further investigation.

### OAP-343-31 Association of previous treatment history with treatment outcome among patients with multidrug-resistant tuberculosis

P Cegielski,<sup>1</sup> J Ershova,<sup>1</sup> C Kvasnovsky,<sup>1</sup> E Kurbatova,<sup>1</sup> T Dalton,<sup>1</sup> C C Contreras,<sup>2</sup> J Campos Caoili,<sup>3</sup> and Global Petts Investigators. <sup>1</sup>Division of TB Elimination, CDC, Atlanta, GA, USA, <sup>2</sup>TB, Socios en Salud Sucursal, Lima, Peru, <sup>3</sup>TB, Tropical Disease Foundation, Manila, Philippines. Fax: (+1) 404-639-1566. e-mail: ies3@cdc.gov

**Introduction:** Rapid molecular methods for the detection of drug-resistant TB are being rolled out worldwide at an unprecedented pace, primarily targeting previously treated patients, but only 48% of multidrug-resistant (MDR) tuberculosis (TB) patients have successful treatment outcomes. The objective of this analysis was to compare the treatment success rate of new versus previously treated MDR TB patients.

**Methods:** From January 2005 to December 2008, we enrolled consecutive consenting adults who were starting treatment with second-line drugs for locally confirmed pulmonary MDR TB in 9 countries. Countries were

stratified as Green Light Committee (GLC)-approved or as non-GLC programs. Treatment outcomes were defined according to WHO guidelines. We compared the proportion of patients with each outcome among three groups of patients classified by treatment history as: no previous treatment, previous treatment with first line drugs (only), and previous treatment with second line drugs.

**Results:** In total, 1761 patients were enrolled and complete data were available for 1725. Among patients with no previous treatment, previous treatment with first line drugs, and previous treatment with second line drugs, the proportions with successful treatment outcomes, respectively, were 68.1%, 63.5%, and 55.4% ( $P=0.002$ ) in the GLC-approved programs ( $n=983$ ). In the non-GLC programs ( $n=742$ ), the proportions were 65.7%, 51.2%, and 32.4% ( $P<0.0001$ ).

**Conclusions:** Among MDR TB patients undergoing treatment, a prior TB treatment history was associated with poor outcomes in both GLC and non-GLC programs. Globally, MDR TB treatment success rates are unacceptably low, but the proportion of cases reported to have good and poor treatment outcomes should be interpreted in light of the mix of new and previously treated patients who start treatment.

## 19. TB DRUG TREATMENT REGIMENS/ TRIALS

### OAP-344-31 A novel five-month regimen for category II pulmonary tuberculosis patients in China: a multi-center, randomised and controlled cohort study

W Sha,<sup>1</sup> H Xiao,<sup>1</sup> Q Zhang.<sup>1</sup> <sup>1</sup>Tuberculosis, Shanghai Pulmonary Hospital, Tongji University, Shanghai, China. e-mail: shfksw@126.com

**Background:** Category II pulmonary tuberculosis patients are treated with a standardized 8-month regimen in China. The cure rate of this regimen was decreasing gradually because of the prevalence of drug-resistant TB. It is urgent to develop a new regimen for Category II patients that could improve the cure rate and decrease the possibility of drug-resistant occurrence.

**Design/Methods:** In this national wild, randomized, controlled, multi-center clinical trial, we assigned 570 patients (all of whom were negative for the human immunodeficiency virus) with Category II pulmonary tuberculosis into 4 different regimen groups. Group A received WHO standardized regime. Group B and C received a regimen which started with 2 months of pasiniazide(Pa), ofloxacin(Ofx)/levofloxacin(Lfx), rifampin(R), ethambutol(E) and pyrazinamide(Z), following 6 months of Ofx/LfxPaR. Group D received a regimen of 5 months of Moxifloxacin(Mfx) Pa Rifabutin(Rfb)EZ. Sputum smear and cultures were assessed monthly with the use of solid medium. The primary efficacy end point was the proportion of patients with

sputum-culture conversion in solid medium at the end of therapy.

**Results:** Among the 542 patients who were assessed for efficacy, 123 patients received standard regimen (group A), 142 received group B regimen, 137 received group C and 140 group D. The treatment success of 4 groups were 68.3%, 72.5%, 71.5% and 81.4% respectively (B vs A:  $p=0.450$ ; C vs A:  $p=0.569$ ; D vs A:  $p=0.014$ ). Drop off rate was also lower of group D compared to group A (11.4% vs 20.3%  $p=0.047$ ). Further Univariate analyses showed that those who are 30–59 years old (treatment success A vs D: 68.7% vs 83.0%  $p=0.037$ ), default from category I treatment (treatment success A vs D: 63.6% vs 92.6%  $p=0.029$ ) and have never used fluoroquinolone during first treatment (treatment success A vs D: 68.2% vs 81.7%  $p=0.031$ ) had better outcomes treated with regimen D than A. The incidence of AE were 30.2%. There was no difference of adverse event incidence among four groups.

**Conclusion:** The novel regimen of PaRbtMfxEZ had better efficacy than standardized regimen and could shorten the treatment course to 5 months. The efficacy of regimen containing Ofloxacin or Levofloxacin was not higher than standardized regimen. In the area where DST could not be carried out, this new regimen could be used replacing standardized WHO category II regimen.

### OAP-345-31 A randomised, 2-stage design trial of rifapentine 450mg or 600mg in place of rifampicin for intensive phase treatment of smear-positive pulmonary TB

R Dawson,<sup>1</sup> K Narunsky,<sup>1</sup> J Hoffman,<sup>2</sup> H McIlleron,<sup>3</sup> A Whitelaw,<sup>4</sup> K Dooley,<sup>2</sup> N Gupte,<sup>5</sup> S Dorman.<sup>2</sup> <sup>1</sup>Lung Institute, University of Cape Town, Cape Town, <sup>2</sup>School of Medicine, Johns Hopkins University, Baltimore, MD, USA; <sup>3</sup>Department of Medicine, University of Cape Town, Cape Town, <sup>4</sup>Division of Medical Microbiology, University of Cape Town, Cape Town, South Africa; <sup>5</sup>Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, USA. e-mail: susandorman2@gmail.com

**Background:** Potent chemotherapy may allow reduction in TB treatment duration. Daily rifapentine (RPT) has potent activity in mouse models of TB, but its optimal dose in humans is unknown. We assessed the antimicrobial activity, tolerability, and safety of RPT 450 mg vs RPT 600 mg substituted for rifampicin (RIF) during daily intensive phase treatment of drug-susceptible pulmonary TB.

**Design/Methods:** A randomized, open-label, phase 2, adaptive 2-stage trial was conducted in Cape Town, South Africa. Adults with sputum smear positive suspected pulmonary TB were enrolled. HIV-positive participants with  $CD4<200$  were excluded. Participants were randomized 1:1:1 to receive RPT 450 mg, RPT 600 mg, or RIF 600 mg in addition to isoniazid, pyrazinamide, and ethambutol for 8 weeks (intensive phase). Directly-observed therapy was administered 7 days/week for 8 weeks, without food guidance. Sputum cultures were performed weekly. The primary efficacy endpoint

was sputum culture status on solid LJ medium at completion of intensive phase among enrolled participants whose baseline sputum culture was positive for drug-sensitive *Mycobacterium tuberculosis* and who in addition completed intensive phase per the protocol. Sample sizes for stages 1 and 2 were set at 11 and 38 per arm, respectively, given preset parameters of  $p_0=0.60$ ,  $p_1=0.80$ ,  $\alpha=0.10$ ,  $\beta=0.10$ . A RPT regimen would be rejected at the end of stage 1 if  $\leq 6$  of 11 participants assigned to the regimen had culture conversion on solid medium. Stage 1 and 2 results were combined for safety and efficacy analyses.

**Results:** 153 participants were enrolled (median age 29 years, 76% male, 76% with cavitary disease). Both RPT regimens met pre-specified criteria to advance into stage 2. At completion of intensive phase, LJ culture conversion to negative was observed in 85% (35/41), 96% (43/45), and 94% (34/36) of participants in the RPT 450 mg, RPT 600 mg, and RIF groups (p-value not significant for any pair-wise comparison). In an intention-to-treat analysis of all enrolled participants, the rates of discontinuation (for reasons other than microbiological late exclusion) were similar (2.0% [1/54], 2.0% [1/51], and 8.3% [4/48] in the RPT 450 mg, RPT 600 mg, and RIF groups), as were grade  $>3$  adverse events (2.0% [1/54], 2.0% [1/51], and 8.3% [4/48] in the RPT 450 mg, RPT 600 mg, and RIF groups).

**Conclusion:** In this adaptive, 2-stage clinical trial, there was a trend towards poorer efficacy with RPT 450 compared with RPT 600 mg. RPT was safe and well-tolerated. Studies of daily RPT at doses higher than 600 mg daily are warranted to identify the optimal dose.

#### **OAP-346-31 Evaluating the efficacy and safety of latent tuberculosis treatment regimens through Bayesian network analysis: a systematic review and meta-analysis**

D Zenner,<sup>1,2</sup> H Stagg,<sup>2</sup> R Harris,<sup>1</sup> L Muñoz,<sup>3</sup> I Abubakar,<sup>1,2</sup> M Lipman.<sup>4</sup> <sup>1</sup>Centre for Infectious Disease Surveillance and Control, Public Health England, London, <sup>2</sup>Research Department of Infection and Population Health, University College London, London, UK; <sup>3</sup>Tuberculosis Unit, Infectious Diseases Department, Bellvitge University Hospital, Barcelona, Spain; <sup>4</sup>Centre for Respiratory Medicine, Royal Free London NHS Foundation Trust, London, UK.  
e-mail: dominik.zenner@phe.gov.uk

**Background:** Effective treatment of latent tuberculosis infection (LTBI) is an important component of TB elimination programmes. Newer regimens with reduced pill burden and treatment duration are being introduced. This study aims to compare all LTBI treatment regimens by utilising a Bayesian network approach, which for the first time allows head-to-head comparisons to evaluate efficacy and toxicity.

**Methods** Two independent researchers mined PubMed, EMBASE, Web of Science, the Cochrane library and reference lists of previous papers without language restriction, published until January 2014. We included human randomised controlled trials with recorded endpoints on efficacy or toxicity. For the Bayesian

network approach, data were analysed using a full random effects mixed treatment comparison model. Odds ratios were obtained for all treatments vs. placebo and the median of the posterior distribution and 95% credibility intervals (CrI) calculated. Regimens were then ranked for efficacy and hepatotoxicity. We also compared our results with a conventional meta-analysis.

**Results** The search strategy yielded 1,214 publications of which 53 fitted our inclusion criteria, examining 15 treatments for TB and 10 for adverse events. In Bayesian network analysis, the RFB-INH regimen ranked highest at preventing active TB (rank 2, 95% CrI 1–14; OR=0.28, 95% CrI 0.05–1.49) followed by RMP-INH-PZA regimens (rank 3, CrI 1–8; OR=0.34 95% CrI 0.18–0.62). The use of 6 months or more of INH also appeared effective (rank 8, CrI 5–11; OR=0.64 95% CrI 0.48–0.83). Three to four months of RMP appeared to have least toxicity (rank 1, CrI 1–3) and regimens containing PZA generally had poor adverse effect rankings. These results were consistent with a conventional meta-analysis of the same studies but effect estimates were more modest in the Bayesian approach.

**Discussion** Our findings show that recommended regimens using six months of INH, 3–4 months of RMP, INH-RMP or Rifampentine-INH combination therapies are all effective and safe. Rifamycin-containing regimens appear to be promising alternatives to INH monotherapy, though more trial data are needed to determine the optimal drug (combination), dosage and duration of treatment.

#### **OAP-347-31 The addition of clofazimine to the first-line drug regimen leads to relapse-free cure in three months in the mouse model of tuberculosis**

N Ammerman,<sup>1</sup> D Almeida,<sup>1</sup> S Tyagi,<sup>1</sup> S-Y Li,<sup>1</sup> P Converse,<sup>1</sup> J Grosset.<sup>1</sup> <sup>1</sup>Center for Tuberculosis Research, Johns Hopkins University, Baltimore, MD, USA.  
e-mail: nicole.ammerman@k-rith.org

**Background:** A key drug for the treatment of leprosy, the phenazine-based dye clofazimine (C) has recently been associated with highly effective and significantly shortened regimens for the treatment of multidrug-resistant tuberculosis (TB). Consequently we hypothesized that C may also shorten the duration of treatment for drug-susceptible TB and conducted a controlled trial in the mouse model of TB chemotherapy comparing the activity of the 6-month standard regimen for TB, i.e., 2 months of rifampin (R), isoniazid (H), pyrazinamide (Z) and ethambutol (E) followed by 4 months of RH, with that of the same regimen in which C has been substituted for E.

**Design/Methods:** BALB/c mice were aerosol-infected with *M. tuberculosis*. Four weeks after infection, treatment was initiated with either the 6-month standard regimen (2RHZE/4RH) or a 4-month C-containing regimen (2RHZC/2RHC). Daily drug doses were: R 10 mg/kg; H 10 mg/kg; Z, 150 mg/kg; E, 100 mg/kg; C, 25 mg/kg. Decline of CFU counts in lungs and spleens



during treatment was assessed at weeks 1, 2, 4, 8, 12 and 16 for both groups of mice, and 20 and 26 for mice receiving the standard regimen. Culture-positive relapses were assessed six months after stopping treatment for 8, 12 and 18 weeks in mice treated with C-containing regimen and for 16, 20 and 26 weeks in mice treated with the standard regimen.

**Results:** All untreated control mice were dead by 5 weeks post-infection. In treated mice, no additive effect of C was observed at week 1. CFU decline was then faster in C-treated mice, and culture conversion was obtained at weeks 12 and 20 in mice treated with C-containing regimen and in mice treated the standard regimens, respectively. Relapse-free cure was obtained after 3 and 6 months of treatment for the mice that received the C-containing and standard regimens, respectively.

**Conclusion:** The old leprosy drug C appears a promising anti-TB drug with the potential to shorten the duration of TB chemotherapy by at least half (3 months vs 6 months) in the experimental murine model of TB.

#### **OAP-348-31 Understanding the RIFAQUIN trial: risk factors for unfavourable outcome for patients on a four-month intermittent rifapentine and moxifloxacin regimen**

P Phillips,<sup>1</sup> M Hatherill,<sup>2</sup> S Charalambous,<sup>3</sup> S Mungofa,<sup>4</sup> S Zizhou,<sup>5</sup> J Van Dijk,<sup>6</sup> J Shepherd,<sup>7</sup> A Jindani.<sup>8</sup>

<sup>1</sup>Tuberculosis, MRC Clinical Trials Unit at UCL, London, UK; <sup>2</sup>SATVI, University of Cape Town, Cape Town, <sup>3</sup>Tuberculosis, Aurum Institute, Johannesburg, South Africa; <sup>4</sup>Tuberculosis, Harare City Health Department, Harare, <sup>5</sup>Tuberculosis, Medical Directorate of Mashonaland East, Marondera, Zimbabwe; <sup>6</sup>Tuberculosis, Macha Medical Mission, Macha, Zambia; <sup>7</sup>Tuberculosis, CDC/ BOTUSA, Gaborone, Botswana; <sup>8</sup>Infection and immunity, St George's, University of London, London, UK. Fax: (+44) 2 076 704 829. e-mail: patrick.phillips@ucl.ac.uk

**Background:** RIFAQUIN was a multi-centre randomised phase III trial conducted in Southern Africa, enrolling patients with newly-diagnosed smear-positive drug-sensitive TB. The 6-month regimen with a continuation phase of once-weekly moxifloxacin and 1200mg rifapentine was non-inferior to the standard 6-month control, but the 4-month regimen with a continuation phase of twice-weekly moxifloxacin and 900mg rifapentine was inferior with a greater proportion of unfavourable outcomes (failure and relapse). Using data from the trial, the objective of this study was to identify significant risk factors for unfavourable outcome, and identify patient subgroups where there were differences between arms.

**Methods:** The analyses were conducted on a per-protocol population, excluding patients with treatment changes for reasons other than failure. Logistic regression, adjusted for treatment arm, was used to identify baseline factors and markers during treatment that predicted an unfavourable outcome in all patients. Important subgroup analyses were evaluated by studying the interaction between the variable and the treatment allocation

using a generalized linear model with an identity link function.

**Results:** A total of 513 patients were included in the analysis. Although smoking status, sex, weight and baseline bacillary load were associated with an unfavourable outcome, only culture results at 2 and 3 months were independent risk factors (adjusted OR 4.13 95% CI 1.66-10.28 and 13.36 95% CI 4.01-44.52 respectively). In sub-group analyses, the difference in the proportion unfavourable between the 4-month and control regimen was greater in patients with a positive smear or culture at 2 or 3 months. There was a suggestion that patients of lower weight or who did not smoke or had a positive culture at 2 months, did slightly better on the 6-month arm than the control.

**Conclusions:** There were no clear patient subgroups where the 4-month regimen was adequate. The culture result at 2 months was a strong predictor of unfavourable outcome, but was a poor surrogate marker, likely due to the very different regimen continuation phases. It is striking that neither HIV status nor presence of cavitation at baseline were found to be important independent risk factors, but this may be due to the low numbers of unfavourable outcomes in the 6-month and control regimens. Funded by the European and Developing Countries Clinical Trials Partnership (EDCTP).

#### **OAP-349-31 High dose rifampicin: a phase II trial comparing 10, 15 and 20 mg/kg rifampicin for two months**

M Boeree,<sup>1</sup> G Kibiki,<sup>2</sup> P Phillips,<sup>3</sup> K Reither,<sup>4</sup> S Gillespie,<sup>5</sup> M Hoelscher,<sup>6,7</sup> G Plemper Van Balen,<sup>1</sup> R Aarnoutse.<sup>8</sup>

<sup>1</sup>Pulmonary Diseases, Radboud University Medical Center, Nijmegen, Netherlands; <sup>2</sup>Kilimanjaro Clinical Research Institute, Kilimanjaro Christian Medical Centre, Moshi, United Republic of Tanzania; <sup>3</sup>MRC Clinical Trials Unit, University College of London, London, UK; <sup>4</sup>Department of Medical Parasitology and Infection Biology, Swiss Tropical and Public Health Institute, Basel, Switzerland; <sup>5</sup>School of Medicine, University of St. Andrews, St. Andrews, UK; <sup>6</sup>Division of Infectious Diseases and Tropical Medicine, Medical Centre of the University of Munich (LMU), Munich, <sup>7</sup>Partner site Munich, German Centre for Infection Research (DZIF), Munich, Germany; <sup>8</sup>Clinical Pharmacy, Radboud University Medical Center, Nijmegen, Netherlands. e-mail: georgette.plempervanbalen@radboudumc.nl

**Aim:** In 1971, the dose of 10 mg/kg rifampicin (RIF) was arbitrarily chosen. Current murine and human data show that an increase in dose of RIF may significantly shorten treatment duration. The primary aim of this study (ClinicalTrials.gov NCT00760149) was to compare three doses of RIF for safety, tolerability, pharmacokinetics (PK) and efficacy.

**Methods:** 150 Adult Tanzanian smear-positive pulmonary tuberculosis (TB) patients were randomized to receive either 600 (10 mg/kg), 900 (15 mg/kg) or 1200 mg (20 mg/kg) RIF with standard doses of isoniazid, pyrazinamide and ethambutol daily for two months. Safety and tolerability were assessed. Blood samples

from 75 patients were collected before and at 1, 1.5, 2, 2.5, 3, 4, 6, 8, 10 and 24 hours after treatment intake after at least 28 days of intensive phase treatment. Colony forming units (CFU) of *Mycobacterium tuberculosis* on solid media and time to culture positivity (TTP) in liquid media were assessed at baseline and days 2, 4, 7 then weekly to 56 days.

**Results:** For the three arms, 381 out of 1005 reported adverse events (AEs) were related to RIF: 335/821 grade 1, 35/160 grade 2, 11/20 grade 3, 0/0 grade 4 and 0/3 grade 5. All AEs including the three deaths were equally distributed over the arms. Geometric mean areas under the plasma concentration versus time curve 0-24h (total exposure, AUC<sub>0-24h</sub>) were 23.9, 48.4 and 75.6 h\*mg/l in the 600 mg, 900 mg and 1200 mg group respectively ( $P < 0.01$ ). Geometric mean maximum observed plasma concentrations (C<sub>max</sub>) also increased with higher doses (5.3, 9.3 and 13.6 mg/l for 600, 900 and 1200 mg RIF, ( $P < 0.01$ ). There was no difference between arms in decline in logCFU over 56 days, although the increase in logTTP was moderately steeper with increasing dose. The proportion of sputum culture conversion after 56 days was highest on both LJ and MGIT in the 1200mg arm as compared to the 900 mg and 600 mg arms: 83% compared to 77% and 81% respectively on LJ and 60%, 52% and 50% respectively on MGIT.

**Conclusions:** Treatment with 1200 mg RIF for 2 months was safe and well tolerated. Administration of 1200 mg instead of 600 mg RIF increased the geometric mean AUC<sub>0-24h</sub> and C<sub>max</sub> values more than twofold. A dose related trend in efficacy was observed in the MGIT results. Based on the results of this trial and a dose escalating study, 12 week treatment with 20 or 35 mg RIF/kg are currently investigated in a multiple arm, multiple stage design within the PanACEA consortium.

### OAP-350-31 Randomised trial of bactericidal activity of eight-weeks treatment with moxifloxacin, Pa-824 and pyrazinamide in drug sensitive & Multidrug-resistant TB

D Everitt,<sup>1</sup> R Dawson,<sup>2</sup> A Diacon,<sup>3,4</sup> D Burger,<sup>5</sup> A Conradie,<sup>6</sup> R Schall,<sup>7</sup> C Van Niekerk,<sup>6</sup> C Mendel.<sup>1</sup> <sup>1</sup>R&D, TB Alliance, New York, NY, USA; <sup>2</sup>Centre for Tuberculosis Research Innovation, University of Cape Town, Cape Town, <sup>3</sup>R&D, Task Applied Sciences, Cape Town, <sup>4</sup>DST/NRF Centre of Excellence for Biomedical TB Research, Stellenbosch University, Cape Town, <sup>5</sup>University of Free State, Quintiles, Pretoria, <sup>6</sup>R&D, TB Alliance, Pretoria, <sup>7</sup>Department of Biostatistics, University of Free State, Bloemfontein, South Africa. Fax: (+1) 212.227.7541. e-mail: joanna.breinstein@tballiance.org

**Background:** New regimens that are shorter, less costly, better tolerated, and oral are urgently needed to treat TB, especially multi-drug resistant (MDR) TB. The combination of moxifloxacin (M), the nitroimidazole Pa-824 (PA), and pyrazinamide (Z) had excellent bactericidal activity in patients with Drug Sensitive (DS) TB over 14 days in a previous study.

**Methods:** This was an 8 center open-label clinical trial conducted in Tanzania and S. Africa. We randomized

smear positive patients with DS-TB in equal proportions to daily M 400 mg plus PA 100 mg plus Z 1500 mg (M-PA100-Z), or to M 400 mg plus PA 200 mg plus Z 1500 mg (M-PA200-Z) or to weight-adjusted isoniazid (H), rifampicin (R), pyrazinamide (Z), and ethambutol (E) for 8 weeks of treatment. Patients with MDR-TB received M-PA200-Z. The primary endpoint was the rate of change in colony forming units (CFU) from sputum on solid culture over 8 weeks.

**Results:** We included 181 DS-TB and 26 MDR-TB subjects with median age of 28 years, and 19.5% were HIV-infected. In the 8-week analysis only 9 MDR-TB subjects were included, as 17 others were late exclusions, mostly for Z resistance. The 2 DS experimental treatment arms had greater average reductions in CFU counts than HRZE over 8 weeks, and the reduction was significantly larger for the M-PA200-Z arm compared to HRZE ( $p < 0.05$ ): Average daily decreases in LogCFU over the 8 week treatment period were: M-PA200-Z = 0.155 CI [0.133; 0.178], M-PA100-Z = 0.133 CI [0.109; 0.155], M-PA200-Z MDR = 0.117 CI [0.070; 0.174], and H-R-Z-E = 0.112 CI [0.093; 0.131]. The rate of decline in CFU over days 7–14 correlated highly with that over days 7–56, with correlation coefficients ranging from 0.90–0.98. For the analysis of the first 14 days, data were available on most Subjects with MDR-TB, although some withdrew because of Z resistance. During this period of treatment, the estimate of mean daily EBA LogCFU(0–14) was 0.136 and 0.111, respectively, for MDR-TB patients with Z susceptible and Z resistant isolates at baseline, compared to the EBA LogCFU(0–14) of the DS subjects taking HRZE of 0.137.

**Conclusions:** The M-PA-Z regimen has activity against both DS-TB and MDR-TB that extends from 2 weeks through 2 months and is greater than that of HRZE in patients with DS-TB. Z susceptibility appears to enhance the activity of the regimen for MDR infection. In late 2014, this regimen will be evaluated in a Phase 3 trial, the first registration trial to treat subjects with both DS- and MDR-TB with the same regimen.

### OAP-351-31 Pharmacokinetic-pharmacodynamic analysis of an intensified regimen containing high dose rifampicin and moxifloxacin for tuberculous meningitis

L Te Brake,<sup>1</sup> S Dian,<sup>2</sup> A.R Ganiem,<sup>2</sup> C Ruesen,<sup>3</sup> T.H Achmad,<sup>4</sup> R Ruslami,<sup>5</sup> R Van Crevel,<sup>3</sup> R Aarnoutse.<sup>1</sup> <sup>1</sup>Pharmacy, Radboud University Medical Center, Nijmegen, Netherlands; <sup>2</sup>Neurology, Faculty of Medicine, Universitas Padjadjaran, Bandung, Indonesia; <sup>3</sup>Internal Medicine, Radboud University Medical Center, Nijmegen, Netherlands; <sup>4</sup>Biochemistry, Faculty of Medicine, Universitas Padjadjaran, Bandung, <sup>5</sup>Pharmacology and Therapy, Faculty of Medicine, Universitas Padjadjaran, Bandung, Netherlands. e-mail: lhm.tebrake@gmail.com

**Background.** Previously we described that a higher dose of rifampicin i.v. resulted in lower mortality at 6 months (35% versus 65%) in patients with TB meningitis (TBM) [1]. Large inter-individual variability in concentrations of TB drugs was observed. Considering that concentrations

of TB drugs are the intermediary link between doses administered and their eventual effects, the current study examined drug concentrations-response relationships in TBM patients.

**Methods.** In an open-label, randomised, phase 2 clinical trial performed in Bandung, Indonesia, 60 TBM patients were randomized to receive standard dose (450 mg oral) or high dose rifampicin (600 mg i.v), and moxifloxacin (400 mg or 800 mg) or oral ethambutol (750 mg) combined with pyrazinamid, isoniazid and corticosteroids. After 14 days all patients continued with standard TB treatment. PK sampling was performed once in every patient during the first 3 days of treatment. Differences in measures of exposure (total exposure, AUC; peak concentration, Cmax) between patients who had died and survived were tested with independent samples t tests. Relationships between drug exposure and mortality were examined using Cox regression. A Receiver Operating Characteristic-curve and exposure-response curve were constructed to determine a rifampicin cut-off value.

**Results.** Compared to patients who died during the 2 weeks of intensified regimen, surviving patients had significantly higher geometric mean rifampicin plasma AUC<sub>0-6h</sub>, plasma Cmax and CSF Cmax (Table 1). For moxifloxacin such a trend could not be observed. Patients exposed to one interquartile range (IQR) higher rifampicin exposure had a 43-32% lower relative likelihood (HR=0.57-0.68) of dying at any given point. The rifampicin threshold Cmax plasma below which mortality is predicted with an optimal degree of sensitivity and specificity was 9.6 mg/L. From an exposure-response curve, it appeared that not much survival benefit can be expected by increasing the plasma rifampicin Cmax above approximately 22.5 mg/L.

**Conclusions.** We found a clear concentration-effect relationship, with higher rifampicin exposure leading to better survival of TBM. The current dose of rifampicin used for treating TBM is probably suboptimal; higher doses of rifampicin should be evaluated, including oral (rather than intravenous) preparations with sufficient exposure. The use of fluoroquinolone as part of intensified regimen needs further study. 1. Lancet Infect Dis 2013;13:27-35.

**Table 1.** Geometric mean rifampicin plasma AUC<sub>0-6h</sub>, plasma Cmax and CSF Cmax during the first 3 days of the intensified regimen per outcome measure.

	Dead at 2 weeks	Alive at 2 weeks	P-value*
AUC <sub>0-6h</sub> (mg/L/h)	26.6 (n=10)	51.3 (n=45)	0.018
Cmax plasma (mg/L)	7.7 (n=10)	13.3 (n=45)	0.036
Cmax CSF (mg/L)	0.21 (n=10)	0.40 (n=45)	0.031
	Dead at 6 months	Alive at 6 months	
AUC <sub>0-6h</sub> (mg/L/h)	36.6 (n=21)	52.2 (n=31)	0.118
Cmax plasma (mg/L)	9.3 (n=21)	13.9 (n=31)	0.088
Cmax CSF (mg/L)	0.30 (n=19)	0.39 (n=31)	0.298

\* Differences in measures of exposure between patients who had died and survived were tested with independent samples t tests.

## 20. BEST PRACTICES IN PATIENT ADHERENCE AND SUPPORT

### OAP-352-31 Preferential adherence to antiretroviral therapy over TB treatment: a qualitative study of drug-resistant TB-HIV co-infected patients in South Africa

A Daftary,<sup>1,2</sup> N Padayatchi,<sup>2</sup> M O'Donnell,<sup>2,3</sup> <sup>1</sup>ICAP, Columbia University, New York, NY, USA; <sup>2</sup>Centre for the AIDS Programme of Research in South Africa (CAPRISA), University of KwaZulu Natal, Durban, South Africa; <sup>3</sup>Division of Pulmonary, Allergy and Critical Care Medicine, & Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY, USA .  
e-mail: ad2254@columbia.edu

**Background:** Adherence to antiretroviral therapy (ART) and second-line antituberculosis medications is essential to achieve successful outcomes among individuals co-infected with HIV and multi or extensively drug-resistant tuberculosis (M/XDR-TB). Preliminary work with XDR-TB/HIV co-infected patients in KwaZulu-Natal, South Africa, found poorer rates of self-reported adherence to XDR-TB treatment compared to ART. In this study, we delineated patient-related barriers and facilitators to dual adherence using qualitative methods.

**Methods:** In 2012-13, 6 gender-stratified focus groups were conducted with 23 consenting adult inpatients receiving treatment for either MDR-TB (n= 2) or XDR-TB (n= 21) at a specialist TB hospital; 17 patients were on concurrent ART. Focus group discussions were thematically analyzed via discursive open, axial, and selective coding. The qualitative approach allowed for a more contextualized understanding of patients' adherence related decision-making.

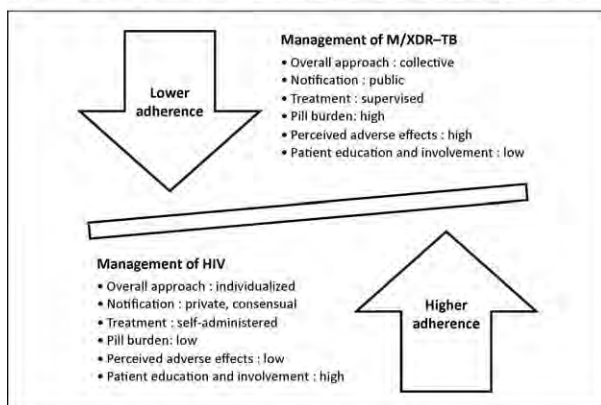
**Results:** In all focus groups, participants shared personal stories about their TB diagnosis, HIV serostatus, and experiences with TB treatment and/or ART. This enabled in-depth analyses of three intersecting themes that characterized multidimensional issues shaping adherence to treatment: (i) Preferential adherence to ART – participants expressed a preference for ART over M/XDR-TB treatment as a result of its greater tolerability, lower pill burden, and a commitment toward ART; (ii) Greater social morbidity of M/XDR-TB – participants perceived treatment outcomes and the social morbidity associated with M/XDR-TB, characterized by public notification, stigma, and clinical and social isolation to be worse when compared with HIV; (iii) Lack of education and support for M/XDR-TB – poor communication, low patient involvement, and provider supervision of treatment exacerbated participants' negative experiences with TB-related care.

**Conclusion:** Barriers and facilitators to treatment adherence for drug-resistant TB and HIV appear to be unique, warranting distinct examination and targeted intervention. To improve adherence, it is critical that new regimens for drug-resistant TB be developed with better efficacy, lower pill burden, and fewer adverse effects; for the first time, such improved regimens are on the



horizon. Equally important is the need for a more cohesive approach to treatment support that promotes patient involvement, empowerment, and treatment literacy for HIV and for TB.

Figure 1: Delineating barriers and facilitators to treatment adherence for M/XDR-TB and HIV



### OAP-353-31 Strengthening community-based TB care improves TB case notification rates in Amhara and Oromia regions, Ethiopia

M Ensermu,<sup>1</sup> M Melese,<sup>4</sup> Z Habtamu,<sup>2</sup> K Gessese,<sup>3</sup> D Jerene,<sup>4</sup> B Girma,<sup>4</sup> P Suarez,<sup>6</sup> <sup>1</sup>Help Ethiopia Address Low TB Performance (HEAL TB) project, Programme for Appropriate Technology for Health (PATH), Addis Ababa, <sup>2</sup>Oromia Regional Health Bureau, Department of Disease Prevention and Control, Addis Ababa, <sup>3</sup>Amhara Regional Health Bureau, Department of Disease Prevention and Control, Bahir Dar, <sup>4</sup>HEAL TB, Management Sciences for Health (MSH), Addis Ababa, Ethiopia; <sup>5</sup>MSH Centre for Health Services, Arlington, VA, USA. e-mail: mensermu@msh.org

**Background:** In Ethiopia, a strong presence of community health workers at the village level provides ample opportunities for organizing community-based TB care. However, the national TB program (NTP) has identified a lack of simplified operational tools and inadequate supports as key barriers. In 2012, the NTP began addressing these constraints with support from the USAID-funded Help Ethiopia Address Low TB Performance (HEAL TB) project.

**Intervention:** In October of 2012, we carried out a baseline survey of community TB care among 1,793 households. Based on the survey results and as per the NTP recommendations, we began implementing the following interventions (1) supported the NTP in finalizing national training materials; (2) Supported train-the-trainer course on TB care for national and regional level TB focal persons to cascade the training (3) Provided job aides and recording and reporting tools to the community health posts; (4) Supported health facility staff in conducting regular supportive supervision to community-based health workers; and (5) monitored progress and addressed challenges during monthly catchment area meetings.

Table1. Performance Indicators for Community-based TB Care in Amahara & Oromia regions, Ethiopia, 2014

Indicator	October, 2012 Baseline	October, 2013
Health posts providing DOTs	516 (12%)	1,112 (25%)
Presumptive TB cases identified by community health workers	Not available	22,867
TB cases diagnosed among presumptive TB cases referred by community health workers	Not available	747 (3.3% of all presumptive TB cases identified)

**Results:** In the first year of implementation, the number of health posts providing DOTs increased from 516 to 1,112 (115%). Community health workers identified 22,867 presumptive TB cases, of which 747 (3.3%) were diagnosed with TB (Table). This yield of TB cases among the presumptive TB cases suggests that community health workers have the capacity to correctly conduct TB screening. By the end of the year of implementation, about 8% of all reported TB cases in the project area were receiving treatment at community level which can help the TB patients for better treatment adherence.

**Conclusion:** Efforts to improve community-based TB control yielded promising results after just one year. Empowering the community and the community health workers and introducing operational tools for community-based TB care and health information systems to document the results are keys for the scale up of the community TB care.

### OAP-354-31 Self-care of TB patients: association between socio-demographic and clinical variables in a priority city for tuberculosis control, Brazil, 2012

BE Scatolin,<sup>1,2</sup> A Beraldo,<sup>1</sup> NH Orfao,<sup>1</sup> R Andrade,<sup>1</sup> A Wysocki,<sup>1</sup> T Arakawa,<sup>1</sup> MA Ponce,<sup>3</sup> TC Scatena villa.<sup>1</sup>

<sup>1</sup>College of Nursing of Ribeirão Preto – University São Paulo, Department of Maternal Child Nursing and Public Health, Ribeirão Preto, SP, <sup>2</sup>Barretos School of Health Sciences Dr. Paulo Prata, Department of FACISB, Barretos, São Paulo, SP, <sup>3</sup>São José do Rio Preto College of Medicine, Department of Nursing, São José do Rio Preto, SP, Brazil

**Background:** Being tuberculosis (TB) a chronic condition and a challenge for public health, WHO has recommended patient education for self-care (PAHO, 2006) in order to co-responsible individuals for the care to their health, evolving them in care and its outcomes.

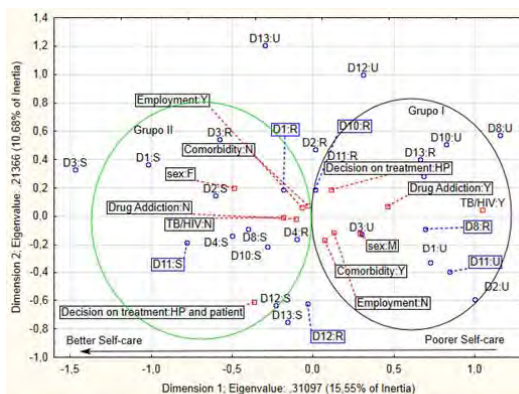
**Aim:** To analyze the association between self-care of patients with TB and individuals sociodemographic and clinical variables.

**Design/Methods:** Exploratory study conducted in São José do Rio Preto between november 2011 to october 2012. A total number of 106 TB patients in treatment for at least 3 months or more, aged above 18 years, outside prisional system and without limits of cognitions. For data collection, a structured questionnaire, based on the self-care concept, as defined in Mendes (2011). The

questionnaire is composed by a Likert 11-scale questions ranging from zero, being this the worst classification, to ten, the best classification. The association between patients sociodemographic and clinical data (considered as supplementary variables) with self-care variables (active variables) was tested by Multiple Correspondence Analysis (MCA).

**Results:** Two groups of TB patients were observed. The first group had a higher proportion of patients with the following features: drug addiction, HIV co-infection, male, comorbidities, and unemployed. This was associated with poor self-care in "knowledge about TB and the treatment", "search for information about TB", "participation in decisions about treatment", "search for a health service in case of doubts", "to know what to do in case of worsening of symptoms" and "time to take care of him/herself". The second group present the following characteristics: no drug addiction, no HIV, female, without comorbidities, employed and were associated with regular and satisfactory self-care items (Figure 1).

**Conclusion:** The results provide an alert to healthcare professionals regarding the profile of TB patients requiring emergent efforts to achieve well-being. We highlight the profile of little knowledge of the disease and treatment, participation in treatment decisions, and characteristics of drug addiction, HIV coinfection, comorbidities and unemployment.



**Figure 1** – Factorial plan regarding the association between self-care and patient sociodemographic characteristics, clinical and lifestyle data, São José do Rio Preto, 2012.

**Subtitle:** active variables: D1 - Knowledge about TB; D2 - Knowledge about treatment; D3 - Search for information in books or in the internet; D4 - Patient participation in decisions about their treatment; D8 - Search for a health service in case of questions regarding treatment; D10 - To know what to do if symptoms worsen; D11 - Dedication of time to take care of his/her health; D12 - Avoid consuming cigarettes; D13 - Avoid consuming alcohol. Categories of active variables responses (S = satisfactory, R = regular, U = unsatisfactory). Additional variables, HIV co-infection (TB/HIV: Y=yes, N=no), comorbidity (Y = yes, N=no), sex (F=female; M=male), Employment (Y=yes, N=no), Drug Addition (Y=yes, N=no), Decision on how the treatment would be (HP=health professional; HP and patient= health professional and patient).

## OAP-355-31 Factors contributing to good TB treatment adherence among patients in north-west region of Cameroon

W Mbacham,<sup>1</sup> M Sander,<sup>2</sup> L Ayuk,<sup>3</sup> A Z Achidi,<sup>3,4</sup>

I Ndong,<sup>4</sup> P Aseh.<sup>4</sup> <sup>1</sup>Laboratory of Public Health Research Biotechnology Centre, University of Yaoundé, Yaoundé, <sup>2</sup>Tuberculosis Reference Laboratory Bamenda, National Tuberculosis Control Program, Bamenda, <sup>3</sup>Regional Unit for TB control, North West Region, National Tuberculosis Control Program, Bamenda, <sup>4</sup>Department of Health Economics, Policy and Management, Catholic University of Cameroon,, Bamenda, Cameroon. Fax: (+237)33 36 11 04. e-mail: azachidi@yahoo.com

**Aim:** To investigate aspects of patient and healthcare worker knowledge and behaviour that is contributing to high adherence to TB treatment in the Northwest region of Cameroon, where only 3% of patients are lost to follow-up as compared to the national average of 8% (NTP data).

**Methods:** A convenient sample of 38 adult TB patients and 18 TB treatment nurses were recruited in the study. In-depth semi-structured interviews were conducted for all study participants. In addition, four focus group discussions (FGDs) were held for three groups of 10 patients each and one group of 10 TB nurses.

**Results:** From this qualitative assessment, several factors were identified that may potentially contribute to the relatively high TB treatment adherence in this region. From the in-depth interviews administered to TB patients, a majority of patients reported taking their medicine on their own, without a designated treatment supporter, by using an alarm system to remind them of the time to take their treatment (21 of 38 respondents). In addition, the TB nurses surveyed indicated a high level of knowledge about the correct administration of TB treatment including the importance of TB treatment adherence. The patients surveyed also had good knowledge of most aspects of tuberculosis treatment reported little or no feeling of stigmatization by their families or communities due to the disease and reported a good patient-health service staff relationship during the FGDs.

**Conclusion:** These results suggest that in similar settings where TB treatment administration is not directly supervised by a healthcare worker, high rates of treatment adherence and completion may be achieved by other methods, including patient use of mobile phone alarms as treatment reminders and strong engagement by health care workers in patient education at treatment initiation.

### OAP-356-31 Community care improves TB Conversion rates in sub-district C in the Nelson Mandela Metro District (NMB) in the Eastern Cape in South Africa

T Dayimani,<sup>1</sup> L Canzibe,<sup>1</sup> B Mpini.<sup>2</sup> <sup>1</sup>Health, University Research Corporation, Port Elizabeth, <sup>2</sup>Health, Mfesane NGO, Port Elizabeth, South Africa. Fax: (+27) 1248 49376. e-mail: thanekad@urc-sa.com

**Background and Challenges** NMB Health District in EC is seen as one of the District with a high TB Crisis in South Africa. Sub District C in NMB was identified with a challenge of high of treatment interruption where TB positive clients do not report to facilities for 2/3 months sputum conversion. Mfesane a Not for Profit Organization (NPO) a USAID TB Programme sub- grantee implemented a community based approach through employment of community based care health workers (CHCWs) to assist 10 Health facilities to trace treatment interrupters and ensure TB positive clients report back to facilities for their 2<sup>nd</sup>/3<sup>rd</sup> months sputum conversion (SC).

**Interventions/Response** Mfesane appointed community based members as CHCWs and placed them at facilities where they were allocated a number of positive TB clients to follow up and ensure they stay on treatment until the end of treatment period using the DOTS strategy. These CHCWs lived in within the same communities of their clients to allow for easy access and follow up. The CHCWs traced the clients, accompanied them to facilities to continue with treatment and followed them up at their homes and ensured treatment and sputum is collected for conversion. Using the TB Diaries CHCWs ensured that clients were followed up and reported timeous to facilities for their sputum conversion dates.

**Results and Lessons learnt** In the period that Mfesane CHCWs intervened there was a marked improvement. In Q4/2012, SC rate was 51.25% and in Q1/2013 it was 47.7% and it improved as follows: 100 % Q2/2013; 99% in Q3/2013 and 96% in Q4/2013.

**Conclusion** Having CHCWs living in the same neighborhood as same as the clients who need follow up increases the chances of success of the DOTS strategy. Use of TB diaries ensures timeous follow up of clients for SC and prevent loss to follow up and treatment interruption.

### OAP-357-31 The factors supporting self care by clients under treatment for pulmonary tuberculosis (PTB) in Depok, west Java, Indonesia

AY Nursasi,<sup>1</sup> V Williams,<sup>2</sup> Budi Keliat.<sup>3</sup> <sup>1</sup>Community Health Nursing, Faculty of Nursing Universitas Indonesia, Depok, Indonesia; <sup>2</sup>ICN TB Project, International Council of Nurses, Geneva, Switzerland; <sup>3</sup>Mental Health Nursing, Faculty of Nursing Universitas Indonesia, Depok, Indonesia. e-mail: fian\_3121@yahoo.ca

**Background:** This study aims to determine the factors related to the client's level of self-care in relation to PTB

in order to achieve full adherence to treatment and recovery from the disease. The researcher wanted to assess the relationship between the client's potential for self-care and his/her age, gender, level of knowledge, and perception of support offered by family, community volunteers and nurses.

**Design/Methods:** The study design was cross-sectional. Measurement of dependent and independent variables was done at the same time. The sample includes 81 clients with TB from 17 health centers in Depok city. Purposive sampling was used to select clients with smear positive TB who were undergoing treatment. Clients were given a structured questionnaire about level of independence in caring for themselves based on medication adherence, compliance with nutrition, rest/sleep, activity, efforts to overcome the side effects and self-protection efforts. In addition, clients were asked to answer questions about demographic data, knowledge of pulmonary TB, their perception of support from family, community volunteers and nurses during treatment. Ability to self-care was assessed according to the client's ability to adhere to treatment, manage side effects, fulfill nutrition needs, undertake activity/exercise, sleep and to prevent transmission using mask and cough etiquette. Client's responses were scored with a possible total of 120. If the score was less than 50, it was categorized as poor/low level of self-care.

**Results:** 43 clients (53.1 %) scored below 50 which suggested that the 38 (46.9 %) had a good potential for self-care.

**Results** of logistic regression analysis showed there is association between the patient's level of self-sufficiency with level of knowledge of the client (POR = 2.68; CI = 1.06 to 6.81, p-value = 0.038), and perceptions of nurses support (POR = 2.93 CI = 1.13 to 7.59, p-value = 0.027. PTB client with low level of self-care needs nursing intervention to support the achievement of treatment outcome.

**Conclusion:** The potential of clients to self-care is still not good. The role of the nurse and the client's increased knowledge of TB treatment are very important in increasing client independence in order to achieve a full recovery.

Table 1  
Association between Client's Level of Self Care Sufficiency with Level of Knowledge and Perceptions toward Nurses Support in Depok, West Java, Indonesia 2013

Variable	Level of self-sufficiency		OR	CI 95%		
	Low	High		Lower	Upper	p-value
Level of knowledge of the client						
Low	26 (60.5%)	17 (36.8%)	2.68	1.06	6.81	0.038
High	17 (39.5%)	24 (63.2%)				
	100%	100%				
Perceptions toward nurses support						
Poor	31 (72.1%)	18 (47.4%)	2.93	1.13	7.59	0.027
Good	12 (27.9%)	24 (52.6%)				
	100%	100%				



### OAP-358-31 Innovative patient's diary tool improves patients' adherence

V Gultai,<sup>1</sup> M Dolynska,<sup>1</sup> O Kheylo.<sup>1</sup> <sup>1</sup>USAID Strengthening Tuberculosis (TB) Control in Ukraine Project, USAID Strengthening Tuberculosis (TB) Control in Ukraine project, Kyiv, Ukraine. e-mail: vgultai@stbcu.com.ua

**Background and challenges to implementation:** The system of outpatient TB treatment is still being developed in Ukraine. Low treatment adherence and skepticism among doctors and patients towards DOT-based treatment continues to impede successful TB treatment in the country.

**Intervention or response:** Involvement of the Ukrainian Red Cross (URC) in outpatient follow-up is one of the achievements of projects funded by USAID and the Global Fund to Fight AIDS, Tuberculosis and Malaria. Looking for new approaches to improve treatment adherence, the USAID Strengthening Tuberculosis Control in Ukraine project and URC developed an innovative Patient's Diary publication, which provides patients with wider tools for self-observation and increases awareness of risks and possible outcomes caused by TB, helping to improve patients' commitment to TB treatment.

**Results and lessons learnt:** The publication consists of both text boxes with important TB-related recommendations, and chapters to be filled by a patient. Chapters include "My questions to health worker", "My next visit to hospital", "My observations", "Body weight" and "Body temperature" diagrams, a weekly diary, physician's and patronage nurse's contacts, administered treatment regimens, and a calendar for treatment monitoring. The diary also offers a special section designed for reading together with the patient's family members, e.g., related to infection control in households, contact tracing, and family planning. The tool is meant to be used by a patient on his or her own, although the assigned case worker can supervise and provide assistance in maintaining the Diary during the whole treatment period.

**Conclusions and key recommendations:** In addition to its informative function, the USAID project-developed Patient's Diary encourages patients to self-observe and communicate with their healthcare providers. Active and informed participation of patients in the TB treatment process results in better treatment adherence and thus better TB treatment outcomes.



### OAP-359-31 Engaging corporate social responsibility (CSR) for extensively drug-resistant (XDR) tuberculosis patients in Mumbai

M Khetarpal,<sup>1,2</sup> S Kumta,<sup>2</sup> A Bamne,<sup>1</sup> S Kunte,<sup>1</sup> S Deshmukh,<sup>1</sup> V Venkat,<sup>3</sup> C Mehra,<sup>3</sup> A Nayyar.<sup>3</sup> <sup>1</sup>Health - Tuberculosis, Municipal Corporation of Greater Mumbai, Mumbai, <sup>2</sup>Tuberculosis, Bill and Melinda Gates Foundation, New Delhi, <sup>3</sup>Tuberculosis, Global Health Strategies, New Delhi, India. e-mail: sameer.kumta@gatesfoundation.org

**Background and challenges to implementation:** India's Corporate Social Responsibility (CSR) law of 2013 uniquely requires all major corporates to put 2% of earnings into CSR, yet very little contribution to TB has been seen till date. As an initial foray into harnessing CSR for TB, Municipal Corporation of Greater Mumbai (MCGM) pursued CSR for social needs of extensively drug-resistant (XDR) TB patients in Mumbai. Setting: As of April 2014, 120 cases of XDR TB had been registered in Mumbai by the MCGM. Nearly all of these patients were under-resourced, undernourished, and had little access to proper nutrition and sanitation. Nutrition plays a key role in the recovery for TB patients, who are often unable to work and earn money to buy food for themselves and families. Awareness of simple and feasible infection control measures was limited. A patient support kit was envisaged to prevent further transmission through infection control and awareness; encourage adherence to treatment and immunity building for faster recovery.

**Intervention or response:** Eight companies were approached with the idea to make XDR-TB patient support kits available for all registered patients, over the course of their treatment. One company agreed and provided financing and goods including masks to the MCGM. Another company compiled the goods and co-ordinated the distribution of the kits. In March 2014, monthly patient supports kits containing nutritional supplements, face masks, tissues, hand sanitizers, handkerchiefs and patient information booklets, were prepared and distributed to 99 XDR-TB patients. The kit aims to build a relationship with the patient over and above the engagement with the National TB Programme and encourage treatment adherence.

**Discussion:** The first formal CSR support for TB patients in Mumbai has been deployed; the challenge is expanding from this small first step to more comprehensive CSR engagement and to be able to tap the unlimited resources available in the city. For starters, the patient kit can be scaled up for all TB patients in Mumbai. MCGM will look more intensively at CSR for financing larger demand generation campaigns.

## SYMPOSIA: THURSDAY 30 OCTOBER 2014

### 01. PROGRESS IN CLINICAL TRIALS FOR DRUG-SUSCEPTIBLE TB: 2014

#### The role of fluoroquinolones in treatment of drug-susceptible TB: what have we learnt from recent phase 2 and phase 3 trials?

R E Chaisson. Center for TB Research, Johns Hopkins University School of Medicine, Baltimore, MD, USA

**Background:** Fluoroquinolones (FQs) have marked antimicrobial activity against *Mycobacterium tuberculosis*, but their role in treating drug-susceptible tuberculosis is unclear, with mixed results from recent trials.

**Design/Methods:** Results from several recent Phase 2 and Phase 3 studies were assessed, and earlier results from animal models reviewed.

**Results:** Two of four Phase 2 trials showed improved culture conversion at 8 weeks when moxifloxacin was substituted for ethambutol, but negative results were found in two other trials. On the basis of the positive trials, two large Phase 3 trials using gatifloxacin (OFLOTUB) and moxifloxacin (ReMOX) were performed and showed that adding a FQ to standard therapy did not allow treatment shortening to 4 months. In addition, the RIFAQUIN study showed that moxifloxacin and rifapentine given twice weekly in the continuation phase did not allow treatment shortening to 4 months. A review of animal model studies suggests that the ability of FQs to shorten treatment may have been overestimated, however. The recent RioMAR trial found that the combination of low-dose rifapentine and moxifloxacin was associated with better culture conversion over two months than standard therapy, suggesting that FQs given with a more potent rifamycin may improve treatment outcomes. Additionally, the RIFAQUIN trial showed that high-dose rifapentine and moxifloxacin given once weekly for four months during the continuation phase was non-inferior to daily standard of care, whereas the earlier TBTC Study 22 found rifapentine and INH (without an FQ) during the continuation phase was considerably less potent.

**Conclusion:** FQs have potent bactericidal activity but may not be sufficient to shorten tuberculosis therapy. Recent data suggest that adding FQs to more potent sterilizing drugs like rifapentine could potentially shorten tuberculosis treatment duration.

#### The potential impact of 3-and 4-month regimens: insights from modelling

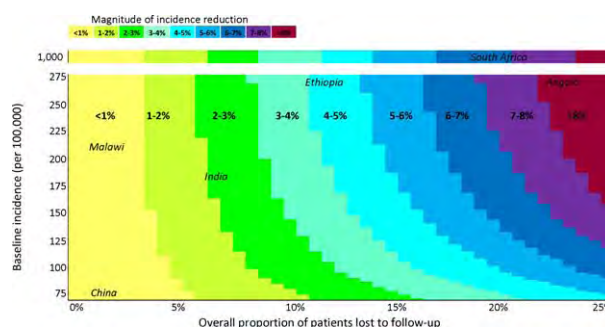
D W Dowdy. Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

**Introduction:** Despite current control efforts, global tuberculosis (TB) incidence is decreasing slowly. New

regimens that can shorten treatment hold promise for improving treatment completion and success, but their impact on population-level transmission remains unclear. Earlier models projected that a four-month regimen could reduce TB incidence by 10% but assumed that an entire course of therapy must be completed to derive any benefit. **Methods:** We constructed a dynamic transmission model of TB to evaluate the likely population-level impact of regimens that could reduce the current six-month course of therapy to three or four months, with equivalent efficacy. We used data from clinical trials of early short-course regimens to account for the partial efficacy of treatment courses that were not fully completed. Our primary outcome was the projected population-level incidence and mortality of TB over ten years, comparing standard six-month therapy to hypothetical regimens that could be completed in four months.

**Results:** The impact of hypothetical four-month regimens on TB incidence after 10 years was smaller than estimated in previous modeling analyses (1.9% [95% uncertainty range 0.6–3.1%] vs. 10%). Impact on TB mortality was larger (3.5% at 10 years) but still modest. Transmission impact was most sensitive to the proportion of patients currently completing treatment and the overall TB incidence. In settings where 95% or more of patients are already successfully completing the existing six-month regimen, newer 3–4 month regimens are unlikely to reduce TB incidence by more than 1% over ten years. By contrast, in settings with TB incidence of >250 per 100,000/year and 25% loss to follow-up on the current regimen, novel regimens can reduce population-level TB incidence by 8% or more over the same time period. The figure shows the projected 10-year reduction in incidence (as a percentage of total incidence) as a function of overall TB incidence and proportion of patients lost to follow-up. These findings remained robust under one-way variation of other model parameters.

**Conclusion:** Novel regimens that shorten treatment duration may have only a modest effect on TB transmission except in settings of high TB incidence coupled with very low treatment completion.



### Rifamycins for latent TB: perspectives from settings of low-and high-incidence

R Belknap.<sup>1</sup> <sup>1</sup>Denver Public Health, Denver Health and Hospital Authority, Denver, CO, USA

**Background:** Treating latent TB infection (LTBI) is a cornerstone of TB prevention. Isoniazid is effective but is limited by the long duration of treatment and side effects that result in early discontinuation.

**Design/Methods:** This talk will review the safety and efficacy of rifampin and rifapentine plus isoniazid for LTBI treatment in low and high burden settings.

**Results:** Daily Rifampin and once-weekly rifapentine plus isoniazid are effective shorter course regimens for LTBI treatment. Treatment completion using rifamycin-based therapy for LTBI is > 80% which is higher than achieved with daily INH alone. Rifamycins increase the metabolism of many medications and drug-drug interactions are an important limiting factor for these medications.

**Conclusion:** Rifamycin-based LTBI treatment regimens are more effective for TB prevention and should play an important role in programmatic strategies to control and eliminate TB.

### High-dose rifamycins: insights into kinetics, adverse effects and drug interactions

R Savic,<sup>1</sup> K Dooley.<sup>2</sup> <sup>1</sup>Department of Bioengineering and Therapeutic Sciences, University of California at San Francisco, San Francisco, CA, <sup>2</sup>Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA

Rifamycin antibiotics drive tuberculosis treatment response, and current doses are on the steep part of the dose response curve. Of treatment shortening strategies for drug-sensitive TB, optimization of rifamycins is among the most promising. In this talk, the pharmacology of high-dose rifampin and rifapentine, including insights into food effects, exposure-response relationships, dose-toxicity associations, and drug interactions will be presented. Results from mathematical modeling assessing concentration-effect relationships will be discussed along with ways to use pharmacology and PK/PD assessments as tools for selecting doses for definitive treatment-shortening trials. The potential impact of higher-dose rifamycins on concentrations of companion drugs, like antiretrovirals used to treat HIV, will also be discussed.

## 02. PREPARING FRONTLINE HEALTH WORKERS FOR COMMUNITY-LED CHANGE

### Teaching health care workers a patient-centred mindset in a technical world

T Fedotkina,<sup>1</sup> S Mishustin,<sup>1</sup> V Williams,<sup>2</sup> V Sarkisova,<sup>3</sup> O Ponomarenko,<sup>4</sup> A Solovieva.<sup>4</sup> <sup>1</sup>Nursing, Tomsk Oblast TB Dispensary, Tomsk, Russian Federation; <sup>2</sup>TB Program,

International Council of Nurses, Geneva, Switzerland; <sup>3</sup>TB, Russian Nurses Association, St Petersburg, <sup>4</sup>Tomsk TB Program, Partners in Health, Boston, MA, USA

**Background:** In spite of having the clinical means to diagnose and treat TB many patients continue to face challenges in adhering to a full course of treatment. Education regarding the clinical aspects related to diagnosis and treatment is often a case of passing on current theory and good clinical practice. Patient-centred care requires a more participatory approach in order to consider the variable impact a TB diagnosis and the associated treatment has on each patient.

#### Design/Methods:

According to a survey done among 187 TB patients in Tomsk oblast, the attention they receive from health care workers was regarded by most respondents (58,7%) as the main reason to adhere to treatment. A training program for health care professionals should be built on principles of peer education, client-centered approaches, best care practices and use teaching methods which require active student participation. Discussion topics should be broad - clinical knowledge of TB, treatment monitoring and side effects management, adult learning methods, conflict management, interpersonal communication skills, psychological and social care for TB patients and many others. TB service workers need to be systematically taught to provide patient-centered care, viewed as the ability to satisfy individual patient's needs while meeting the clinical standards of TB care.

**Results:** Experience of running 16 workshops using these techniques with nurses in various parts of Russia and 9 in Kazakhstan have raised serious issues that nurses face in delivering patient-centred care - understaffing, low profile of nursing, poor remuneration, other issues. In spite of this there are signs that this type of training has had a positive effect with the implementation of a patient-centred approach achieving

- better quality nursing care
- reduced defaults and treatment interruptions
- prevention of MDR and XDR TB greater trust in health care workers
- Development of community-based care: day hospitals, home care
- Better outcomes of TB Programmes

**Conclusion:** TB patients are in need of care and support throughout TB treatment, which is best provided by nurses trained in patient-centered care. Such nurses can be regarded as an effective resource within a health care system.

### Empowered community health care workers for improved results

S Neri,<sup>1</sup> S Dalebout,<sup>1</sup> C Whalen,<sup>1</sup> L Petersen,<sup>2</sup> D Moongo,<sup>2</sup> R Indongo,<sup>3</sup> F Mayhunga,<sup>4</sup> T N Shilongo.<sup>4</sup>

<sup>1</sup>Global Health, Project HOPE, Millwood, VA, USA; <sup>2</sup>Namibia, Project HOPE, Windhoek, <sup>3</sup>Namibia, USAID, Windhoek,



<sup>4</sup>National TB and Leprosy Programme, Namibia Ministry of Health and Social Services, Windhoek, Namibia.

**Background** Field Promoters (FP) in Namibia are the front lines of the National TB and Leprosy Programme's (NTLP) Community TB Care Strategy. Because they are trusted members of the communities that they serve, FPs are able to positively influence patients and the surrounding community and provide a strong conduit between the primary health care facilities and the surrounding community.

**Objective** To review challenges and recommendations for effectively sustaining FPs in Namibia.

**Intervention** The MoHSS works hand in hand with NGOs to hire, train and manage FPs. The strategy recognizes the strength of the NTP as a strategic and technical lead and NGO capacity to reach communities and supervise and manage FPs.

**Results** Training and supervision of FPs over the past 8 years has resulted in a tremendous capacity and depth of knowledge, resulting in improvements in cure and reduction of deaths from TB. National Treatment Success Rate increased from 69% for the 2003 cohort to 82% in the 2008 cohort, accompanied by a decrease in the combined default and transfer-out rate from 21% to 9%. Key challenges include: Adopting a health care worker with a stipend has yielded strong results but it is an expensive program model to sustain. NGOs have different salary scales and management systems and training funds are limited. Dual accountability of FPs to the Health Facility nurse and NGO. Country under transition for significant decrease in multi and bilateral funding. Limited human resources at district and clinic levels cause FPs to get pulled into "facility" based work, when they are most productive in the communities. FPs are not currently considered for long term employment in the MoHSS.

**Conclusions/Recommendations** Negotiation and clear communication are essential to ensuring long term sustainability of FPs, an effective support to ensuring treatment success in Namibia. FP training should ensure they have the skills so they can be absorbed into various future roles (Health Extension Program) and negotiate with the government for public health career paths for FPs. The MoHSS in coordinating/managing NGO sub-grant can ensure consistent country-wide management and salaries. NGOs need to motivate the donor community to allow for decentralized training and deliver strong results to incentivize donor investment. Engage with the regional and district health teams so that they understand clearly the opportunity cost of pulling field workers into the facility.

### The link between working conditions and the quality of care

K Mdolo.<sup>1</sup>, Democratic Nursing Organisation of South Africa (DENOSA), Pretoria, South Africa.

The aim of this study was to show the relationship between the concept of 'quality of care' and the prevailing working conditions within which health

professionals are subjected. Donabedian (1997) articulates that the concept 'quality of care' has linkages among three aspects which are 'the structural attributes in which care occurs, the processes of care, and the outcomes of care'. In her research study, Manojlovich (2005) concluded that practice environment has a direct contribution to 'nursing job satisfaction' and that favourable practice environment improves "both nurses perceptions of their commination and their job satisfaction" (2005:367) This study is going to highlight contributory factors to the improvement of quality of care at the two TB/MDR facilities in South Africa. The analysis revealed that there is a direct link between conditions of service and quality of care. It can be concluded that positive practice environment improves and enhances quality of care.

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### 03. HOW MULTI-SECTORAL APPROACH AND COMMUNITY ENGAGEMENT MAY STRENGTHEN PROGRAMMATIC MANAGEMENT OF TB IN PRISONS

#### Interagency collaboration between civilian and penitentiary TB control services in Tomsk region of the Russian Federation

S Mishustin,<sup>1</sup> E Andreev,<sup>2</sup> I Gelmanova.<sup>3</sup> <sup>1</sup>Tomsk TB & Pulmonary Medical Center, Tomsk TB & Pulmonary Medical Center, Tomsk, <sup>2</sup>Medical Department, Tomsk Oblast penitentiary system, Tomsk, Russian Federation; <sup>3</sup>Representative office in the Russian Federation, Partners In Health, Boston, MA, USA

**Background:** In 1999 an estimated 25% of all newly diagnosed persons with TB in the Russian Federation were in the penitentiary system. However, many started treatment in prison but were released into the civilian sector before treatment completion. In addition, some civilians got arrested while on active TB treatment. TB treatment in the penitentiary sector was provided by medical providers employed by the Ministry of Justice, while TB services in civilian sector were under the Ministry of Health. The links between both sectors were weak, thus a number of persons were not followed up after being released/ arrested. In 1999–2000 the Tomsk penitentiary and civilian sectors launched a system of collaboration. Design: The following interventions were performed to improve collaboration between two sectors In Tomsk regions:

- A coordinating body was set up that meets regularly and includes TB specialists from both sectors.
- Clinical trainings have been organized with participation of medical and laboratory staff from both sectors.

- A centralized stock of second-line drugs has been established.
- An advanced notification system about planned releases was developed.
- Civilian doctors, psychologists and social workers visit persons before their release to facilitate their transfer to treatment in the civilian sector. Inmates are provided with the information about TB offices and social support services in the Tomsk region.
- When a prisoner with active TB is freed, his medical file is sent to the local TB dispensary in the area where he will live. MDR TB prisoners are escorted to a state TB hospital or TB dispensary upon release.
- Priority of providing psychosocial support to patients from prison for the development of adherence to treatment (daily package of incentives worth \$5–10).
- Treatment results of transferred persons are reported back to the penitentiary and civilian sector.

**Results:** Between 1998–2013 the Tomsk penitentiary system released 2,860 persons with TB into the Tomsk civilian sector. The proportion of persons who continued treatment in the civilian sector was 57.8% (CI: 54.7%–61.0%) during 1998–2000 and rose to 73.4% (CI: 71.4%–75.4%) during 2001–2013.

**Conclusion:** Improved collaboration between the penitentiary and civilian sector was associated with a statistically significantly higher proportion of persons with TB on treatment continuation over the ten years that the program was in effect, compared to before the collaboration.

#### 04. TUBERCULOSIS AND DIABETES: FROM EVIDENCE TO ACTION

##### Possible mechanisms underlying increased susceptibility of diabetes patients to TB

R Van Crevel,<sup>1</sup> M Beiger,<sup>2</sup> TH Ottenhoff,<sup>3</sup> H Dockrell,<sup>4</sup> K Ronacher,<sup>5</sup> V Kumar.<sup>6</sup> <sup>1</sup>Medicine, Radboud University Medical Centre, Nijmegen, Netherlands; <sup>2</sup>Immunology, Max Planck Institute for Infection Biology, Berlin, Germany; <sup>3</sup>Infectious Diseases, Leiden University Medical Centre, Leiden, Netherlands; <sup>4</sup>Immunology and Infection, London School of Hygiene and Tropical Medicine, London, UK; <sup>5</sup>Immunology Research Group, Stellenbosch University, Stellenbosch, South Africa; <sup>6</sup>Genetics, University Medical Center Groningen, Groningen, Netherlands.

Epidemiological studies have shown that Type 2 diabetes mellitus (DM) patients have a three-fold risk of developing active TB, and a worse outcome of TB treatment. DM is therefore responsible for an estimated 15% of TB cases globally, and this number will increase due to rapid growth of DM in TB endemic regions of Africa and Asia. Many epidemiological studies have been published on the link between TB and DM in recent years, but very few data are available on biological mechanisms underlying the increased TB susceptibility of DM patients. Therefore, many questions remain unanswered. For example, does DM exert its effects through altered function of macrophages, adipocytes, T cells, or

other cell types? Are these effects genetically determined, affected by hyperglycaemia or DM treatment? Hyperglycaemia, hyperinsulinaemia or use of DM drugs might affect macrophage function, M tuberculosis killing capacity, or T-cell activation, thereby lowering the innate or adaptive immune response to tuberculosis. In addition, adipocytes in fat tissue might act as a reservoir ('sanctuary site') for M tuberculosis infection. From a genetic point of view, common genetic variants known to increase susceptibility to type 2 diabetes might be associated with an increased risk of tuberculosis, while rare genetic variants might exist that affect both susceptibility to TB and diabetes. Increased pathophysiological understanding of the link between TB and DM may help identify those individuals with DM that are most at risk for TB, or develop more effective preventive or therapeutic strategies for diabetes-associated TB. In this lecture, an overview of the existing knowledge base on this topic will be presented, and possible approaches for further research will be discussed.

##### TB-diabetes collaborative activities—from evidence to action

A D Harries.<sup>1,2</sup> <sup>1</sup>Operational Research, International Union Against Tuberculosis and Lung Disease, Paris, France; <sup>2</sup>London School of Hygiene and Tropical Medicine, London, UK

The global burden of diabetes mellitus (DM) is immense and increasing, with the numbers expected to rise to over 550 million by 2030. Countries in Asia, such as India and China, will bear the brunt of this unfolding epidemic. Persons with DM have a risk of developing active tuberculosis (TB) that is two to three times higher compared with persons without DM. This presentation reviews the epidemiology and interactions of these two diseases and discusses the World Health Organization and International Union Against Tuberculosis and Lung Disease Collaborative Framework for the care and control of TB and DM. The three recommended collaborative activities are: a) to establish mechanisms for collaboration; b) to detect and manage TB in persons with DM; and c) to detect and manage diabetes in patients with TB. The collaborative framework provides a template for action. This talk will briefly look at the evidence that has been acquired to date, the actions that have been taken, the gaps in knowledge and the priority research areas which need to be addressed in order to build a firm foundation for the scaling up of interventions that work and are effective in tackling the dual burden of disease.

##### TB-diabetes collaborative activities in China

Y Lin. China Office, International Union Against Tuberculosis and Lung Disease, Beijing, China.

Diabetes is a well known risk factor for tuberculosis (TB). In screening reports, TB prevalence and incidence are consistently higher in people with diabetes than in either the general population or in non-diabetes controls.

In order to get early diagnosis and treatment for both TB and diabetes, WHO and the Union have recommended bi-directional screening as one of the important activities in the Collaborative Framework for the Care and Control of Tuberculosis and Diabetes. During the past 3 years after publication of the Framework, there have been several published studies exploring different ways of implementing bi-directional screening in the routine health service in China. The study sites were largely tertiary hospitals where it was found that the screening models are feasible. However, it is still not known whether the same screening models would work well in community settings. From June 2013 to April 2014, the Union, in collaboration with Family Health International (FHI) and Yunnan Provincial TB Center, has implemented screening of diabetes patients for TB in routine community health services. This presentation will describe implementation, results and challenges of the screening process.

### **TANDEM field studies on TB and diabetes mellitus in Peru, South Africa, Romania and Indonesia**

R Ruslami,<sup>1</sup> C Ugarte-gil,<sup>2</sup> G Walzl,<sup>3</sup> M Ioana,<sup>4</sup> P Hill,<sup>5</sup> J Critchley,<sup>6</sup> H Dockrell,<sup>7</sup> R Van Crevel.<sup>8</sup> <sup>1</sup>Pharmacology and Therapy, Faculty of Medicine, Universitas Padjadjaran, Bandung, Indonesia; <sup>2</sup>Public Health, Universidad Peruana Cayetano Heredia, Lima, Peru; <sup>3</sup>Immunology Research group, Stellenbosch University, Stellenbosch, South Africa; <sup>4</sup>Molecular Genetics, Universitatea de Medicina si Farmacie, Craiova, Romania; <sup>5</sup>Center for International Health, University of Otago, Dunedin, New Zealand; <sup>6</sup>Epidemiology Research Institute, St. George's University of London, London; <sup>7</sup>Infectious and Tropical Disease, London School of Hygiene and Tropical Medicine, London, UK; <sup>8</sup>Internal Medicine, Radboud University Nijmegen Medical Center, Nijmegen, Netherlands.

The alarming growth of type-2 diabetes (DM), which triples the risk of TB, poses a serious threat to TB control worldwide. Awareness about this problem is increasing, but many questions remain unanswered. For instance, what is the best way to screen TB patients for DM and vice versa? Also, DM is associated with more TB treatment failure, relapse and death, but it is uncertain whether optimal glucose control can reduce these effects, and how optimal glycemic control is best achieved, as both TB itself and anti-TB drugs can hamper glucose control in DM. In addition, no study has examined treatment needs of newly diagnosed DM once TB treatment is completed. TANDEM, which stands for Tuberculosis and Diabetes Mellitus ([www.tandem-fp7.eu](http://www.tandem-fp7.eu)) is a project funded by EU that will address some of these gaps in knowledge, hopefully contributing to the evidence for policy and patient management, as well as better understanding of biological pathways underlying the association between TB and DM. TANDEM's first main objective is to identify optimal ways to screen TB patients for DM, and vice versa, and to develop evidence-based screening algorithms. TANDEM will also focus on the combined treatment of TB and DM, and the

requirements, feasibility and cost-effectiveness of different strategies. In a pragmatic clinical trial we will evaluate the benefits of intensifying counseling for DM, increasing the frequency of glucose monitoring, and using standardized protocols for glycemic control during TB treatment. TANDEM will also examine the relationship between DM control and TB treatment outcome, as well as the long-term requirements for management of DM in this group. Field studies take place in four countries with different healthcare systems and population demographics (Peru, South Africa, Romania, and Indonesia), all characterized by a high burden of TB and a growing prevalence of DM. Field studies will be combined with biomarker, in-vitro and genetic studies to understand the causal mechanisms underlying the increased susceptibility and worse outcome of TB in DM patients. TANDEM aims to will hopefully improve prevention and therapeutic management of combined TB and DM, and expand basic knowledge on the link between the two diseases. This presentation will give a brief overview of the objectives, methods, and initial results of the TANDEM program.

### **Beyond screening: clinical management of concurrent TB and diabetes**

F Pearson,<sup>1</sup> J Critchley,<sup>1</sup> C Ugarte-Gil,<sup>2,8</sup> B. Alisjahbana,<sup>3</sup> P Hill,<sup>4</sup> A Riza,<sup>5,7</sup> D Moore,<sup>6</sup> R Van Crevel.<sup>7</sup> <sup>1</sup>Population Health Research Institute, St Georges University London, London, UK; <sup>2</sup>Universidad Peruana Cayetano Heredia, Lima, Peru; <sup>3</sup>Center for TB-HIV research, Medical Faculty, Padjadjaran University, Hasan Sadikin Hospital, Bandung, Indonesia; <sup>4</sup>Centre for International Health, Faculty of Medicine, Otago University, Otago, New Zealand; <sup>5</sup>Human Genomics Laboratory, University of Medicine and Pharmacy of Craiova, Craiova, Romania; <sup>6</sup>London School of Hygiene and Tropical Medicine, London, UK; <sup>7</sup>Internal Medicine, Radboud University Medical Center, Nijmegen, Netherlands; <sup>8</sup>International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

Diabetic patients are at a threefold higher risk of tuberculosis infection, which suggests that the growing burden of type 2 diabetes will contribute to sustaining the existing tuberculosis epidemic. To meet this intricate health problem, bidirectional screening has been recommended. There is little proof though on the performance of specific screening tests for diabetes in patients with tuberculosis, and tuberculosis in individuals with diabetes. Also, evidence on the need for preventive therapy for latent tuberculosis infection in individuals with diabetes is also lacking. Clinical management of patients with both diseases can be difficult. Anti-tuberculous drugs have an increased toxic effect in individuals with diabetes. Good glycaemic control improves long-term diabetes complications. Though it could possibly also improve tuberculosis treatment outcomes, it may be difficult to attain due to chronic inflammation, drug-drug interactions, suboptimal adherence to tuberculosis treatments, and other factors. In addition to drug treatments for tuberculosis and diabetes, other interventions might be needed, especially for patients with newly



diagnosed diabetes or those who need insulin. These patients would benefit from integrated counselling and education, long-term lifestyle interventions, as well as antihypertensive, lipid-lowering, antiplatelet and other medication, in some patients. After completion of tuberculosis treatment, individuals with diabetes need continued diabetes management and heightened alertness for tuberculosis symptoms as relapse is more common. From a health systems point of view, delivery of optimal care and integration of services to manage concurrent tuberculosis and diabetes is a huge challenge in many countries. Lessons learned from the combined tuberculosis and HIV/AIDS epidemic could serve as example, but more studies focused on the economic assessment of both screening methods and health systems are needed. This presentation will focus on clinical management challenges of the patient with concurrent diabetes and tuberculosis, as both drug treatments may need adjustment, monitoring may need to be intensified, and other interventions should be considered. An elaborate review of these issues was published in *Lancet Diabetes and Endocrinology* 2014 (September).

## 05. NEXT GENERATION OF EHEALTH FOR TB: SYSTEMS THAT COMMUNICATE

### Video-Directly Observed therapy (VDOT): a solution for monitoring TB treatment adherence

R Garfein,<sup>1</sup> K Collins,<sup>1</sup> F Munoz,<sup>1</sup> J Cuevas-mota,<sup>1</sup> J L Burgos,<sup>1</sup> K Moser,<sup>2</sup> G Rangel,<sup>3</sup> K Patrick.<sup>4</sup> <sup>1</sup>Department of Medicine, University of California San Diego, La Jolla, CA, <sup>2</sup>Tuberculosis and Refugee Health, San Diego County Health and Human Services Agency, San Diego, CA, USA; <sup>3</sup>Departamento de Estudios de Población, El Colegio de la Frontera Norte, Tijuana, Mexico; <sup>4</sup>Department of Family and Preventive Medicine, University of California San Diego, La Jolla, CA, USA

**Background:** Over 8.8 million people become ill and 1.4 million people die annually from tuberculosis (TB) worldwide. TB is treatable with antibiotics; however, poor adherence to daily medication regimens lasting >6 months leads to ongoing disease transmission, higher mortality, and development of antibiotic resistant bacteria. "Directly observed therapy" (DOT) is recommended to minimize these problems by having health workers watch patients take each medication dose. While effective, DOT is costly, time consuming, invasive, and impractical for some patients. Thus, some TB programs have begun teleconferencing with patients using analogue or digital devices. However, DOT records are still maintained in paper form or local databases making analysis of medication adherence and outcomes difficult.

**Intervention or response:** We developed and pilot-tested the Video DOT (VDOT) System whereby patients use mobile phones to record and securely transfer time-stamped videos of them taking their medications, which are then viewed remotely by a health worker who

documents doses observed in the system's database. TB patients were enrolled in San Diego, California (43) and Tijuana, Mexico (9) to test the feasibility and acceptability of VDOT. Participants were interviewed at baseline and at treatment completion.

**Results and lessons learnt:** Overall, participants ages ranged from 18 to 86 years, 54% were male, and 77% were non-white. Participants used VDOT a mean of 5.5 months (range: 1–11 months); 7 (13%) returned to in-person DOT. Treatment adherence was excellent in San Diego (93%) and Tijuana (96%). Post-treatment interview responses were similar across cities. Overall, 89% of patients reported never/rarely having problems recording videos, 92% preferred VDOT over in-person DOT, 81% thought VDOT was more confidential, and 100% would recommend VDOT to others. Three non-compliant participants were returned to in-person DOT, suggesting the need for both options. Data collected in this common database were easily analyzed.

**Conclusions:** VDOT provides a promising mobile solution to the high cost and burden of in-person DOT for monitoring TB and other conditions that require strict treatment adherence. Once scaled, standardized medication adherence data from multiple TB control programs may be analyzed quickly and efficiently. Data may also be used to generate health insurance reimbursement requests as telehealth becomes more accepted by insurers.

### Harnessing the power of information systems for strategic decision-making: summary from five diverse countries

L G Bastos,<sup>1</sup> N Konduri,<sup>1</sup> A Zagorski.<sup>1</sup> <sup>1</sup>Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program, Management Sciences for Health (MSH), Arlington, VA, USA

**Background:** E-TB Manager integrates data across key aspects of TB control, including information on patients, medicines, laboratory testing, diagnosis, treatment, and outcome. Globally, 2,385 active users covering 2,411 sites in 10 countries are managing 223,021 TB cases, DR-TB cases and presumptive TB individuals.

**Objective:** To highlight program implementation experience from 5 diverse countries - Ukraine, Indonesia, Bangladesh, Namibia and Brazil - in terms of population (e.g. sparsely populated v/s densely populated), TB health systems organization (e.g. central v/s decentralized), and extent of domestic versus donor funding.

**Findings:** After TB programs institutionalized e-TB Manager following pilot phase, users reported timely and more accurate reporting rates, better monitoring of patient treatment and medicine stock levels countrywide. The system provides accurate information for medicines procurement processes, including possibility of different scenarios, costs and program changes. Access to real-time information contributed to the reduction of stock-outs. Compared to paper based processes, the system contributed to significant time reduction between release of laboratory results and start of treatment regimen. The

system has assisted in organizing the TB referral network, in strict control of medicine dispensing and in the overall quality of TB surveillance. Due to the wide access permitted in the system, transparency and accountability measures are established according to individual country needs. Users reported feeling empowered and motivated in accessibility of data while central TB program staff reported confidence in review of program performance and analysis. Progressively, use of e-TB Manager showed potential for better decision making while contributing to better treatment outcome rates. We are using our program experience to develop an interim framework to evaluate the impact of e-TB Manager and synthesize lessons learned, challenges and recommendations. Additional program experience will be presented during the symposium.

**Conclusion:** An electronic system such as e-TB Manager allows wider availability and easier access to TB information at all levels, which may contribute to better analysis of data and decision making that culminates in improved program performance.

### **TB data exchange with private sector providers using eHealth solutions in Pakistan**

**A Habib.** Software Development, Interactive Health Solutions, Karachi, Pakistan.

**Background:** The different aspects of TB control often involve disparate systems that don't communicate with each other. For example, labs may have specialized systems that don't deal with treatment or registration information. This means that an integrated patient record (even just for TB) is a difficult proposition, making health information exchange a complicated matter. The solution described here provides the informatics system for a social business aimed at screening, diagnostics, and treatment for TB and Lung Disease in Pakistan. A similar system is in use in Bangladesh and Indonesia.

**Methods:** An OpenMRS based electronic medical record system (EMR) was set up to provide a centralised store for patient information. Access to this system is via an Android application or a web-based interface accessible over a desktop, laptop or tablet computer. All patient data including screening, test results, and treatment information is stored and accessed using this system. Care providers with accounts on the system can access this data and view, edit, or delete data as per the role assigned to them. Additionally, GeneXpert test results are automatically stored in the EMR and sent to care providers as SMS alerts to ensure prompt delivery of information that is critical to patient care. This is done using the XpertSMS system which has been integrated with OpenMRS. Screeners can enter screening data using their smartphones, and can view their own performance using mobile reports. Similarly, those managing the program can see performance statistics on web-enabled dashboards.

**Results:** This system is currently in use by nearly 160 field personnel as well as nearly 40 research and project

management staff in Karachi with plans to expand other parts of Pakistan. The use of a central medical record system allowed data exchange with external parties (phones, GeneXpert machines, screening center staff, doctors) over a single interface. The system of rights and privileges means that levels of access can be provided as needed to different types of users.

**Conclusion:** The integration of smartphone applications and SMS alerting systems with the central EMR underscores the importance of open platforms and standards towards building systems that communicate. This system can be further extended to incorporate other diseases (e.g. HIV or Malaria) with minimal effort and potentially scaled up into a single integrated system for patient care across disease and health system areas.

### **From data collection to data analysis: a fully digital TB prevalence survey in Zambia using barcode scanning for identification**

**P Chanda,<sup>1</sup> C Silavwe,<sup>1</sup> E Chizema,<sup>1</sup> N Kapata,<sup>2</sup> N Kalisvaart,<sup>3</sup> E Klinkenberg.<sup>4</sup>** <sup>1</sup>Disease Surveillance Control and Research, Ministry of Health, Lusaka, <sup>2</sup>National TB/ Leprosy Control, Ministry of Community Development Mother and Child Health, Lusaka, Zambia; <sup>3</sup>Data Management, KNCV Tuberculosis Foundation, The Hague, <sup>4</sup>Regional Team Africa, KNCV Tuberculosis Foundation, The Hague, Netherlands.

**Background:** The national tuberculosis prevalence survey was conducted for the first time in Zambia. The aim was to estimate in a nationwide representative survey the adult (15years and older) prevalence of bacteriological confirmed pulmonary Tuberculosis (PTB) in 2013–2014 in the country. The survey will provide information on the burden of PTB among adults in Zambia. The survey will also form as a baseline for future TB prevalence surveys to measure progress and impact of TB interventions. The survey will also provide invaluable information on the TB-HIV co infections. The primary objectives were: 1) To estimate the prevalence of sputum positive pulmonary TB 2) To estimate the prevalence of culture positive pulmonary TB. The national prevalence survey provides an opportunity for population based estimates for pulmonary TB in the population aged 15 years and above in Zambia. In order to improve the efficiency and quality of the data, digital systems for data collection and management were applied.

**Design/Methods:** This was a nationally representative cross sectional survey among households in the selected 66 clusters from all the 10 provinces of Zambia. At field level, Personal Digital Assistants (PDAs) were preloaded with all the pre-survey and survey questionnaires. Unique Personal Identifier Codes (UPIC) were generated at household level and saved on the PDA for use at the different stages of the survey. The field X-rays were taken using digital radiographs and transmitted via satellite to the central chest x-ray using the Picture Archiving and Communication System (PACS). Field level data was extracted and merged from different PDAs and sent by email to the central data management unit daily. Data from central reference laboratories and central x-ray was

emailed to central data management unit for merging and storage. Back up systems were employed.

**Results:** Data from the field was digitally transmitted to the central reference laboratories, central radiology and central data management unit using available electronic technological approaches. Monitoring of the data quality at field and central level was enhanced.

**Conclusion:** The digitalisation of data collection and management procedures should be prioritised in future TB prevalence surveys if efficiency and quality is to be achieved. Digital data collection systems have the potential for application in routine TB surveillance.

## 06. EMPIRICAL TREATMENT FOR TB AMONG HIV-POSITIVE PEOPLE: WHO, WHEN, HOW? UPDATE ON TRIALS IN PROGRESS

### The STATIS trial

F-X Blanc.<sup>1,2</sup> <sup>1</sup>Pneumology, INSERM UMR 1087, CNRS UMR 6291, L'Institut du Thorax, on behalf of the ANRS 12290 STATIS team, <sup>2</sup> Nantes University, Nantes, France.

**Background:** Morbidity and mortality linked to tuberculosis (TB) remain unacceptably high in HIV-infected adults. In severely immunocompromised patients, mortality during antiretroviral therapy (ART) is remarkably higher during the first months of treatment in resource-limited settings, contrasting with the pattern of mortality in industrialized countries. On one hand, diagnosis of TB in ART services is a huge challenge and a fundamental weakness that undermines the ability to address HIV-associated TB deaths, even with recently point-of-care (POC) diagnostic tools. On the other hand, systematic empirical TB treatment could help treating patients with underlying, not recognized TB, reduce invasive bacterial infections and allow passing these first months of ART. Thus, we designed a multicentre, two-arm, unblinded randomized trial to compare a strategy of extensive TB screening using rapid diagnostic POC tools to a more simple approach using systematic TB treatment.

**Design/Methods:** The primary objective of the STATIS (ANRS 12290) trial is to compare the 24-week risk of death or occurrence of invasive bacterial infection between 2 experimental strategies in adults who are ready to start ART with CD4 <100/mm<sup>3</sup>: continuous extensive TB testing using chest X-ray, Xpert MTB/RIF and urine lipoarabinomannan (LAM), vs. systematic empirical TB treatment. The trial will be conducted in 4 countries: Cambodia, Côte d'Ivoire, Uganda, and Vietnam. From end 2014 to 2016, 1050 patients (525 per arm) will be recruited. Eligibility criteria include: HIV-1 infection; age ≥18 years; CD4 <100 cells/mm<sup>3</sup>; no history of ART, except transient ART for PMTCT. Exclusion criteria are: AST or ALT >5 times the upper limit of normal; creatinine clearance <50 ml/min; overt evidence that TB treatment should be started immediately; history of TB treatment in the past 5 years; ongoing TB chemoprophylaxis; any condition that would lead to

differ ART initiation (e.g. acute condition requiring investigations prior to ART initiation); pregnancy or breastfeeding. At inclusion, patients who will not start TB treatment because of negative POC tests will start ART immediately, while those who will start TB treatment either because of a positive test or randomization in the systematic TB treatment arm will start ART 2 weeks later. ART regimen will be TDF-FTC + efavirenz or AZT-3TC + efavirenz. Each patient will be followed 48 weeks. During follow-up, participants will be monitored for safety, mortality, ART efficacy and serious morbidity. The primary analysis will be an intention-to-treat one using the Kaplan-Meier method and the log-rank test.

**Results:** Expected in mid-2017.

**Conclusion:** The STATIS trial will hopefully help clinicians to better manage HIV-infected adults with CD4 <100/mm<sup>3</sup> and no overt evidence of active TB when initiating ART. Whether extensive TB tests or systematic TB treatment should be offered to reduce early mortality remains to be determined.

### Overview: why does empirical TB treatment matter?

**A Grant.** Clinical Research, London School of Hygiene & Tropical Medicine, London, UK

**Background:** Empirical TB treatment, meaning initiation of treatment without bacteriological confirmation, is inevitably necessary while diagnostic tests for TB have suboptimal sensitivity. Empirical TB treatment is particularly relevant in groups among whom TB is hard to diagnose, and the risk of mortality is high if active TB remains untreated, notably people with advanced HIV disease. This problem is illustrated by continuing high mortality among people starting ART in resource-constrained settings, among whom TB remains the most important cause of death. The challenge: The roll-out of Xpert MTB/RIF, and recent trials of Xpert such as TB NEAT and XTEND, have highlighted that empirical TB treatment is common practice. Advantages of empirical TB treatment include rapid treatment initiation, which could reduce morbidity and mortality; patient convenience; reduced investigation costs; and in some cases reduced delay in initiation of antiretroviral therapy. Disadvantages include inappropriate initiation of TB treatment among people who do not have active TB, carrying risks of unnecessary adverse effects and drug interactions; delay in diagnosis of drug-resistant TB; failure to diagnose other treatable conditions; and increased difficulty interpreting routine data based on number of cases treated. Empirical TB treatment should ideally be targeted to those most likely to benefit. Currently this is based on clinical judgement, often requiring a doctor's decision. If evidence-based criteria could be established to identify groups of patients among whom the benefits of empirical treatment outweigh the risks, this would promote rational use of this intervention across a range of health care settings, and enable a



wider range of health professionals to initiate empirical treatment in primary care clinics.

**Conclusion:** Trials are needed to define groups of patients among whom the benefit of empirical TB treatment outweighs the risk. Subsequent presentations in this symposium will outline trials addressing this question.

### The TB Fast Track trial

M Tlali,<sup>1</sup> S Charalambous,<sup>1</sup> G Churchyard,<sup>1,2,6</sup> A Karat,<sup>2</sup> A Grant,<sup>2</sup> K Fielding,<sup>3</sup> C Hoffmann,<sup>4</sup> S Johnson.<sup>5</sup>

<sup>1</sup>Epidemiology, The Aurum Institute, Johannesburg, South Africa; <sup>2</sup>Clinical Research Unit, and <sup>3</sup>Medical Statistics & Epidemiology, London School of Hygiene & Tropical Medicine, London, UK; <sup>4</sup>Medicine, Division of Infectious Diseases, Johns Hopkins School of Medicine, Baltimore, MD, USA; <sup>5</sup>Technical Support, The Foundation for Professional Development, Pretoria; <sup>6</sup>School of Public Health, The University of Witwatersrand, Johannesburg, South Africa.

**Background:** New tools are urgently needed to identify TB in HIV positive individuals' at highest risk of mortality. The TB Fast Track cluster-randomised trial evaluates the effect on mortality of a novel, risk-based algorithm aiming to identify adults with advanced HIV disease who are also at highest risk of TB to facilitate rapid initiation of TB treatment and/or ART. We describe the baseline characteristics of participants and early outcomes of the study algorithm.

**Methods:** Among participants enrolled to the intervention arm by 30 April 2014, we assessed the proportion of those assigned to a high probability (ANY OF; positive point of care (PoC) LAM test, haemoglobin (Hb) <10 or body mass index (BMI) <18.5), medium probability (no high probability criteria BUT TB symptoms) or low probability (no high probability criteria AND no TB symptoms) of TB and the proportion started on TB treatment.

#### Results:

**Probability of TB:** 1008 participants (53% female, median age 38 [interquartile range, IQR 32–44] years) and median CD4 74 [IQR 35–113] were included. 458/1008 (45%) were assigned high probability and the most frequent criterion was a low Hb in 290/1008 (63%), with low BMI and positive LAM contributing 222/1008 (48%) and 113/1008 (24%) respectively. 319/1008 (32%) were assigned medium probability; weight loss was the most commonly reported TB symptom in 292/319 (92%). Cough, night sweats and fever were reported in 157 (49%), 122 (38%) and 77 (24%) individuals assigned as medium probability respectively. 231/1008 (23%) were assigned low probability.

**TB treatment started:** By 2 months 584/1008 (58%) of participants started TB treatment based on the algorithm: 442/458 (97%) of the high probability, 133/319 (42%) of the medium probability and 9/231 (4%) of the low probability. TB treatment was started within 7 days of enrolment in 413/442 (93%) of high probability and 92/133 (69%) of medium probability participants.

**Conclusion:** Tools combining PoC tests for TB and simple clinical criteria, which can be utilised in nurse-led

primary health care clinics, have the potential to rapidly identify those at highest risk of TB in severely immunocompromised individuals allowing for faster initiation of treatment. The TB Fast Track trial will evaluate the sensitivity and specificity of this novel risk-based algorithm and its effect on mortality compared to routine management.

## 07. COMMUNITY ENGAGEMENT AND RELIEF OF SUFFERING IN PALLIATIVE CARE

### Palliative care in drug-resistant TB: guiding principles

S Connor. Advocacy, Worldwide Palliative Care Alliance, London, UK

**Background:** Palliative care is a necessary addition to the continuum of care in management of drug resistant TB

**Design/Methods:** Presentation of major principles of palliative care in the care of DR-TB patients and families.

**Results:** Inclusion of palliative care improves quality of life for patients and families living with drug resistant TB.

**Conclusion:** In this session participants will gain an understanding of the role of palliative care in the continuum of care for people living and dying with drug-resistant TB. The major principles of palliative care will be shared along with guidance on how palliative care can be applied to help improve treatment as well as ease suffering at the end of life.

### Community based care for DR-TB patients in South Africa

R Matji. Health, University Research Company, Pretoria, South Africa.

The South African Government adopted Community Based Care management of MDR TB as a national strategy in 2009. The number of MDR TB cases has increased in the past 10 years and also the number of chronic patients is also increasing. Options for treatment are limited and for such patients treatment is terminated and patients are discharged back to the community still highly infectious. Patients can survive for up to 2 years from the time that treatment is terminated and go through severe suffering and pain, therefore Palliative care is essential for such patients. Currently there is very limited link between existing NGO's that manage terminally ill patients with nearby clinics and there is also weak guidance on how to manage such patients The USAID TB project managed by University Research Company, funded by USAID provides technical support to the National TB Control Programme on all key aspects of TB control. One of the objectives of the project is to provide grants to NGO's that provide services at community level. One of the organizations supported is Hospice Palliative Care Association (HPCA). With increasing number of M/XDR TB patients managed at community level and also increasing number of patients

who fail treatment, it is necessary to work with NGO's that can provide support to such patients. Such NGOs should be at closest proximity to the patients to be able to provide regular home visits and to provide the necessary care and continuous counselling to the patients and the families that live with such patients. The project has therefore identified an essential need to guide NGO's on how to provide palliative care to terminally ill TB patients. It is therefore important that Palliative care is provided closest to the patient's family and staff at both clinic and community levels are trained. Recommendations: It is recommended that NGO's that provide such support to patients should be supported by Government to ensure sustainability NGO's should be provided with training and all necessary counselling skills in order to support patients Infection control should always be emphasised and practiced in order not to put Community Health Care Workers at risk of contracting TB

### **The inseparable work of caring and curing: a community-based model of integrated TB treatment**

A Solovyeva,<sup>1</sup> D Taran,<sup>1</sup> I Gelmanova,<sup>2</sup> V Berezina,<sup>3</sup> S Keshavjee.<sup>4,5</sup> <sup>1</sup>Partners in Health, Moscow, Russian Federation; <sup>2</sup>Partners in Health, Boston, MA, USA; <sup>3</sup>Administration, Tomsk Oblast Tuberculosis Services, Tomsk, Russian Federation; <sup>4</sup>Department of Medicine, Brigham and Women's Hospital, Division of Global Health Equity, Boston, MA, <sup>5</sup>Program in Infectious Disease and Social Change, Department of Global Health and Social Medicine, Harvard Medical School, Boston, MA, USA

**Background:** A novel patient-centered tuberculosis (TB) treatment delivery program, 'Sputnik', with a strong palliative care component, was introduced for patients who were at high risk of treatment default or failure due to non-adherence in Tomsk City, Russian Federation.

**Design/Methods:** Supportive Sputnik team provided patients with a choice of place and time for supervised medications intake; side effects and co-morbid illnesses were closely monitored and all required ancillary medications were provided. Specialists' consultations including drug addiction expert were organized at patients' homes if necessary. Daily food sets and other forms of social support were delivered. Patients and their family members met regularly with a psychologist.

**Results:** Among 138 patients referred to the program from Nov 2006 till Dec 2012 one-hundred-four (75%) had multi-drug resistant TB; 111 (80%) suffered from chronic alcoholism, 49 (36%) were drug abusers; 63 (46%) had hepatitis, 6 (4%) were HIV-positive and 7 (5%) suffered from psychiatric diseases. Seven 9 (7%) patients either refused any TB treatment or Sputnik personnel was not able to find them. Among those 129 patients who took at least one pill while on program 93 (72%) were eventually cured, 14 (11%) failed, 14 (11%) defaulted; 3 (2%) were transferred out of the region and 5 (4%) died of causes not related to TB;

**Conclusion:** Palliation of side effects and co-morbid illnesses was a critical component of the Sputnik intervention and contributed to the successful commu-

nity-based treatment of previously non-adherent TB patients.

### **Community engagement in a mainstream TB programme: how palliative care enhances community involvement**

L Kuksa. MDR TB, Riga East University Hospital; TB and Lung Disease Clinic, Riga, Latvia.

MDR TB program was introduced in 1997. Two years later in 1999, as a part of holistic approach palliative care was introduced to sustain the quality of life of patients and secure infection control measures. Initially we favored hospital model inherited from actual health care system and learned by doing through experiences from other health care programs like lung cancer, chronic obstructive lung disease etc.. It was important to find causes for existing and increasing pool of chronic patients. To be able to find reasons for ongoing infection in the community and understand patient needs, emotional and social status OR was carried. Findings showed that patients are afraid of: isolation and loneliness; to burden someone; ignorance and inability to take care for themselves. In the same time 70% patients wanted to be involved in leisure time activities during their hospitalization. Activities within project "Patient to patient" were launched.\* structured information sessions were held on MDR TB and palliative care and psychological peer support through discussions, and testimonies; psychological support was given to patients and their family members; hospital library and gym were renovated and upgraded to enable self- development; computer literacy courses organized; civil and faith-based organizations and individuals were involved in delivery of psychological support; patients were involved in hospital management activities. As NTP gained practical experience in organizing palliative care topic has been included in World Health Organization Collaborative Centre (WHO CC) Latvia training programs on PMDT since 2006. In March 2014 WHO CC launched and implemented 5 days course "Role of Palliative care in M/XDR-TB management". During the course participants from Armenia, Georgia, Russia, Tajikistan and Ukraine were asked about community involvement in their countries. Almost all respondents said that they have some practices as social and psychological support from Red Cross based on NTP strategic plans and budgets. Some countries lack basic data on availability and need for palliative care.

**Conclusion :** Palliative care protocols need to include use of medication and organization of psychological, social support through medical and community based organizations.

\*TA and financial support received from "Swedish Lung and Heart Disease Patient Association" 1999 –2009.

## 08. CHILD PNEUMONIA: INNOVATIVE SOLUTIONS FOR THE NEXT GENERATION

### PERCH: causes of child pneumonia in high burden settings

JAG Scott,<sup>1,2</sup> for the PERCH Study Group <sup>1</sup>Infectious Disease Epidemiology, London School of Hygiene & Tropical Medicine, London, UK; <sup>2</sup>Epidemiology & Demography, KEMRI-Wellcome Trust Research Programme, Kilifi, Kenya.

**Background:** Changes in antibiotic availability and resistance, new vaccine introduction, HIV prevalence and urbanization are impacting on the pattern of childhood pneumonia and its causes. PERCH aims to describe the aetiology of hospitalized pneumonia in children aged 1-59m across Africa/Asia, to estimate the preventable fraction of pneumonia attributable to pathogens for which vaccines are under development and to estimate the role of other known but poorly quantified causes. It also aims to measure the risk factors for pneumonia in children.

**Methods:** PERCH is a 7-site case-control study of pneumonia aetiology. Sites were selected in The Gambia, Mali, Zambia, South Africa, Kenya, Bangladesh and Thailand. Cases were hospitalized children with WHO-defined severe and very severe pneumonia. Controls were age-matched children randomly selected from the background population. The case definition and investigations were standardized and controlled by recurrent visits and quality control indicators. Blood, induced sputum and lung aspirate samples were taken from cases for culture. NP/OP swabs and urine were taken from cases and controls. All respiratory and blood specimens were investigated with quantitative PCR against 32 putative pathogens. Aetiology was ascribed by a Bayesian quantitative, integrated model based on latent class analyses of case specimens and probabilistic inferences from case-control specimens incorporating prior knowledge of test sensitivities and specificities.

**Results:** 4,232 cases and 5,325 controls were recruited between August 2011 and March 2014. The proportion of cases with very severe disease varied from 10–52% by site. Case fatality ratios for very severe cases varied from 3.7–35.4%. HIV infection was rare among cases except in Zambia (17%) and S. Africa (12%). Blood cultures were obtained in 4,177 cases and pathogens were cultured 176. The leading pathogens were *S. pneumoniae*, *H. influenzae* and *S. aureus*. NP/OP swabs were obtained in >99% of participants yielding 3.9 and 3.6 different pathogens per case and control, respectively. Pathogens with the greatest relative odds of detection among cases were RSV and parainfluenza viruses.

**Conclusion:** Preliminary conclusions from the examination of these raw data suggest that there is considerable variation in the pattern and severity of disease by site and that the attribution of causality among multiple infecting pathogens is complex. The integrated analysis of PERCH results will be available in 2015.

### Biomarkers: towards point of care diagnosis

Q Bassat.<sup>1,2</sup> <sup>1</sup>Barcelona Centre for International Health Research (CRESIB), Instituto de Salud Global (ISGlobal), Barcelona, Spain; <sup>2</sup>CISM, Centro de Investigação em Saúde de Manhiça, Manhiça, Mozambique.

**Background:** Malaria, bacterial pneumonia and viral pneumonia contribute substantially to the disease burden of children in developing countries. Clinical differentiation of these infections is complicated by overlapping symptoms of respiratory distress, fever and cough. Misdiagnosis (especially over-diagnosis of malaria) is thought to be frequent, resulting in children receiving incorrect or multiple treatments. This inaccuracy contributes to antimalarial and antibiotic drug resistance, increased morbidity and mortality, and exposure to side-effects of unnecessary medication. We will present preliminary results of an ambitious project aimed at identifying host biomarkers in peripheral whole blood which could reliably distinguish between these three infections in paediatric patients meeting the World Health Organization defined criteria for clinical pneumonia.

**Design/Methods:** Accurate classification of patients into clinical categories (1. Malaria; 2. Bacterial pneumonia; 3. Viral pneumonia and 4. Healthy community controls) was based on signs and symptoms of infection combined with radiology and a series of laboratory tests including full blood counts, parasitology, RT-PCR viral antigen testing, blood culture, and a PCR panel capturing the species most frequently responsible for bacterial pneumonia. Biomarkers were pursued using a candidate gene approach. Affymetrix mRNA profiling was used to identify genes of interest. Additionally, plasma chemokine and cytokine levels were assessed using Luminex immunoassays.

**Results and discussion:** We will present preliminary results that suggest that the different infections may be readily distinguishable using the expression patterns derived from the host blood. Such gene product(s) would therefore eventually be targeted and quantified using mass spectrometry with the intention of identifying proteins and/or peptides which could become the basis of new rapid point-of-care diagnosis tests, practical in areas where laboratory facilities are scarce. Additionally, we will discuss other potential diagnostic tools based on the use of minimally invasive post-mortem sampling techniques which could be of great utility in the developing world for cause of death investigation (including pneumonia and tuberculosis) in places where the feasibility and acceptability of routine autopsic procedures is seriously compromised.



## 09. INTEGRATING COMMUNITY-BASED TOBACCO CONTROL ACTIVITIES IN TB PROGRAMMES: EXPERIENCE FROM MULTIPLE COUNTRIES

### TB and tobacco: joint community-driven intervention and evaluation needs for two global epidemics

T Novotny,<sup>1</sup> S Shin,<sup>1</sup> R Lindsay,<sup>2</sup> A Sereno.<sup>3</sup> <sup>1</sup>Graduate School of Public Health, San Diego State University, San Diego, CA, <sup>2</sup>Health Sciences Program, Idaho State University, Meridian, ID, USA; <sup>3</sup>Pulmonary Medicine, Federal University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil.

**Background:** Tuberculosis (TB), HIV/AIDS, and tobacco use together account for over seven million early deaths and an even greater burden of ongoing morbidity worldwide. In 2012, there were 8.6 million new cases and nearly 1.3 million deaths worldwide from TB, as well as 2.3 million new HIV infections and 1.3 million AIDS deaths. Tobacco use is currently responsible for almost six million deaths annually, and that figure is projected to continue to rise in the coming years. These colliding epidemics have so far been addressed almost entirely independently through separate and distinct intervention programs. Implementation research is critically needed on interventions that integrate new tobacco control approaches within TB as well as with HIV/AIDS treatment programs.

**Design/Methods:** We have reviewed the evidence on the relationship between TB and tobacco use, and between HIV/AIDS and tobacco use. In addition, we reviewed tobacco use interventions that have been applied in TB treatment programs and the design of effective community-based tobacco control programs.

**Results:** According to the 2014 Report of the US Surgeon General, the evidence is sufficient to infer a causal relationship between smoking and an increased risk of TB disease. The evidence is also sufficient to infer a causal relationship between smoking and mortality due to tuberculosis. While understanding of the influence of tobacco use on HIV acquisition, progression, and mortality remains limited, there is sufficient evidence that tobacco use influences HIV outcomes which, in turn affect TB infection and disease. We have found that, although there is evidence for some success of targeted cessation programs, more comprehensive, community-based approaches may be needed in order to reduce the significant tobacco-attributable morbidity and mortality among persons with TB and especially among those with HIV co-infection.

**Conclusion:** TB and HIV treatment programs must include effective tobacco control interventions. However, offering only behavioral cessation interventions is insufficient, and more comprehensive, community-based interventions are necessary to impact the global tobacco/TB disease burden. These include public information campaigns, financial incentives or disincentives, home smoking bans, cessation assistance and pharmaceutical treatment, monitoring/evaluation, and incorporation of

these interventions as standard practice for global TB and HIV treatment programs.

### Community-based interventions of intensive TB case finding among high-risk smokers in a poor province in China

X Wei,<sup>1</sup> X Lin.<sup>2</sup> <sup>1</sup>School of Public Health and Primary Care, Chinese University of Hong Kong, Hong Kong, <sup>2</sup>TB Control, Yunnan Provincial Centre for Disease Control, Kunming, China.

Tobacco is one of the most detrimental factors to public health and a proven risk to TB control. Compared with non-smokers, smokers are more likely to be infected with TB, progress with serious symptoms, default and develop multi-drug resistant TB. However, there is no intensified TB case finding strategy for the smoking population. The study was conducted in the suburb of Kunming, Yunnan Province. Yunnan is a poor and ethnically rich province in China with relatively high TB prevalence. It also holds the largest tobacco company in China. The intervention was conducted in two communities with a population around 100,000 from September 2013 for six months. Another two comparable communities with similar population were chosen as the control group. We have developed the guideline for intensified TB case finding for GPs and TB doctors. After training, GPs in the intervention group identified high risk smokers (e.g. smokers who are diabetes, TB symptomatic, older than 60s, close contact with TB patients) through annual health examination, outpatient visits, and review of patients with hypertension and diabetes, and referred them to TB dispensaries. During the six months intervention in 2013/14, 883 smokers with high risk were examined, of which 295 were successfully referred to TB dispensaries. A total of 26 new TB patients were identified with a yield rate of 1.35% in the intervention group. The intervention group had significant higher TB notification rates compared with that of the control group (29 vs. 10 per 100,000,  $P < 0.05$ ). The project demonstrated the feasibility of screening high risk smokers for TB case finding in routine practice of primary care.

### Integrating tobacco control with community based TB services in improving TB cure rates and tobacco quit rates in peri-urban centres in Bangladesh

S Islam,<sup>1</sup> M Akramul Islam,<sup>1</sup> MAKB Basher,<sup>1</sup> A Khan,<sup>2</sup> MA Husain.<sup>2</sup> <sup>1</sup>TB Control Program, BRAC, Dhaka, <sup>2</sup>National TB Control Program, Dhaka, Bangladesh.

**Background:** Tobacco smoking has increased substantially over the past few decades, especially in developing countries like Bangladesh. BRAC an international organization started integration of smoking cessation intervention into Directly Observed Therapy (DOTS) programs in 17 DOTS Centers of Dhaka peri-urban since May 2011. Tobacco smoking is associated with tuberculosis (TB) and tobacco use may decrease the effective-

ness of TB treatment. The objectives of the initiative are to identify current smokers among TB patients, to see the effectiveness of smoking prevention and cessation on TB outcomes.

**Design or Response:** BRAC supported 17 peri-urban TB centers of Dhaka with 2.8 million population were selected for intervention. TB programme staff were trained on tobacco control with particular focus on harmfulness of smoking, second-hand smoking and its impact on TB, introduce counseling methods and documentations. All tools were developed based on the guideline “Smoking Cessation and Smoke-free environment for TB patients” of the Union. The tools were translated in Bengali and shared with staff. Counseling is given to TB patients for smoking cessation during initiation of treatment and subsequent visits to DOTS centre. A brief counseling is done by Shasthya Shebika (frontline community health worker) during DOT. Results and lessons learnt: From May 2011 to December 2013, a total of 9,680 TB patients were enrolled in the intervention areas. Among them, 22% patients were smokers where 98% were male and 2% female. The level of addiction was high in 29% cases and low in 71% cases. Among the TB patients registered from May 2011 to December 2012, 21% was smokers and among smokers 68% quitted smoking. Treatment success rate was 90% among the smokers whereas 93% among the nonsmokers. Treatment outcome is much better (96%) among the TB patients who has quitted tobacco after counseling and remain quitted up to 5 months of total treatment period. All the 17 health centers were declared as smoke-free and ‘No smoking’ signage is placed at the entrance of these centers.

**Conclusion:** Patients with TB should receive counseling and assistance in stopping tobacco use and it is found effective. Health professionals working in TB care can do cessation counseling systematically within a DOTS-based programme which is also effective.

### **Building local initiative to facilitate integration of tobacco cessation intervention into national TB programme in China**

G Zou,<sup>1</sup> X Wei,<sup>2</sup> J D Walley.<sup>3</sup> <sup>1</sup>China Program, University of Leeds COMDIS Health Service Delivery Research Consortium, Shenzhen, <sup>2</sup>School of Public Health and Primary Care, Chinese University of Hong Kong, Hong Kong, China; <sup>3</sup>Nuffield Centre for International Health and Development, University of Leeds, Leeds, UK

**Background:** The association between smoking and tuberculosis (TB) has been reported substantially. However, it is unclear to what extent such association exists among the Chinese population, especially to what extent tobacco control measures have been integrated into TB control in China.

**Objectives:** To review evidence of the relationship between tobacco smoking and TB, and integration of smoking cessation interventions in TB treatment in China.

**Methods:** Three databases (Medline, Pubmed, Web of Science) and Google Scholar were searched for relevant

articles published between 2000 and 2014 regarding studies conducted in China. Key words were used such as: “tuberculosis”, “TB”, “smoking”, “smoking cessation”, “smoke\*”, “risk factors”, “China”, “Hong Kong”, “Taiwan” and “Macao”. Grey literature and Chinese Baidu were also searched. In total, 17 primary studies were included.

**Results:** All are observational studies, all of which but one provided evidence of a strong relationship between smoking and TB. Smokers had a higher risk for TB compared to never/former smokers. In addition, two studies found that those who smoked more cigarettes per day had an increased risk for TB. These studies revealed that smoking cessation could benefit TB control by reducing their risk of developing TB, improving adherence to TB treatment, reducing TB relapse and mortality. Indeed, a modelling study estimated that when 20% DOTS coverage was sustained, complete cessation of smoking and solid fuel use would result in a 33–71% reduction of the projected annual TB incidence by 2033. However, a qualitative study found that TB patients’ attempts to quit smoking could be weakened by the presence of non-smoke free TB facilities and physicians’ poor knowledge of smoking-TB association and reluctance to integrate smoking cessation into TB treatment. Little study concerning integration of smoking cessation among TB treatment was identified from the English Databases.

**Conclusion:** Given the strong association between smoking and TB, efforts should be made to integrate tobacco control measures in TB control programs in China. Further research is needed to explore feasible interventions such as community-based intensive case finding from smokers, e.g., through routine health checkup, and conducting effective health education among TB smokers in primary healthcare. Implementing such initiatives requires strong collaboration between TB program, health systems and governments.

### **Developing capacity for integrating tobacco dependence treatment with TB treatment in primary care facilities: the South African experience**

AO Ayo-Yusuf,<sup>1,2</sup> G Louwagie.<sup>1</sup> <sup>1</sup>School of Health Systems & Public Health, University of Pretoria, Pretoria, <sup>2</sup>Office of the Director: School of Oral Health Sciences, University of Limpopo MEDUNSA Campus, Pretoria, South Africa.

**Background:** South Africa, as with many other countries in Africa, has high burden of TB mortality that is closely linked to HIV co-infection and made worse by tobacco smoking. However, only limited capacity exists to treat tobacco dependence in TB patients. This paper sought to describe findings from training health workers in a number of African countries and patient smoking cessation outcomes following motivational interviewing offered by a subset of trainees - lay or community health care workers, as compared to nurses who offered only a brief advice.

**Design/Method:** A healthcare alliance for treatment for tobacco dependence treatment (TDT) – the Global bridges – was launched in the Afro region during 2011 with the aim of building regional capacity for TDT. The Global bridges provided 2-day (16 hours) trainings on policy advocacy and treatment for tobacco dependence to health care workers, among whom were health workers working in TB treatment facilities. The programme included didactic experiences as well as applied training in which participants participated in video recorded role-plays to develop skills in brief motivational interviewing (MI) counselling style. Participants completed pre- and post-training evaluation that tested any change in their level of confidence in offering TDT. For the subset of lay health care workers (LHCW), the quit rates of patients seen at 1-, 3- and 6-months by these LHCW was compared to those of nurses that offered only a brief advice following a random assignment of about equal number of patients to the two groups (total patients = 420).

**Results:** About 289 health providers were trained over 2 years, which included 11 LHCW that offered MI to TB patients seeking treatment. The 5-item scale on confidence for TDT ( $\alpha=0.71$ ) showed that for all those trained, the confidence to offer TDT significantly improved after the training. Furthermore, one session of brief motivational interviewing offered by trained LHCW approximately doubled 6-month sustained abstinence compared to brief advice alone offered by trained nurses (RR 2.29, 95% Confidence Interval 1.34; 3.92; Quit rates= 21.5% vs. 9.3%).

**Conclusion:** While there were challenges in training LHCW, this study established the feasibility of training of LHCW for TDT in South Africa and other Sub-Saharan African countries.

## 10. SHORTENED TREATMENT REGIMENS FOR MDR-TB: RESULTS FROM THE FIELD AND FUTURE DIRECTION

### STREAM: a multi-country clinical trial evaluating the shortened MDR-TB regimen

A Nunn. Clinical Trials Unit, Medical Research Council, London, UK

The need for shorter, safer and more effective treatment regimens for MDR-TB is universally recognised. Results from a cohort of patients receiving a 9-month regimen in Bangladesh are very encouraging and have led to the establishment of similar cohorts in several other settings. There are however no data available from randomised clinical trials comparing a 9-month regimen with the longer WHO-recommended regimen. The primary efficacy objective of STREAM is to assess in a randomised clinical trial whether the proportion of patients with a favourable outcome on a 9-month study regimen is not inferior to that on the control (locally-used WHO approved MDR-TB) regimen. The 9-month regimen is the same as that used in Bangladesh with the exception

that high dose moxifloxacin replaces high dose gatifloxacin which can no longer be easily obtained. Safety is assessed by comparing the proportion of patients who experience grade 3 or greater adverse events, during treatment or follow-up in the two regimens. Patients with resistance on line probe assay to quinolones or second-line injectables are ineligible. Funding for the trial is through the USAID-funded TREAT TB initiative with additional support from the British Medical Research Council. All patients are followed for a minimum of 27 months following randomisation; a favourable outcome requires that they are culture negative at their 27-month assessment not having required a major change or extension of treatment for failure, relapse or adverse drug reactions. Treatment on the 9-month regimen can be extended to 11 months if sputum-smear conversion is late. A total of 400 patients are required on the assumption that a favourable outcome of 70% will be obtained on the control regimen and 75% on the 9-month regimen. A 10% margin of non-inferiority is considered acceptable given the considerably reduced pill burden and duration of treatment. To date over 300 patients have been enrolled from five sites in Ethiopia, South Africa and Vietnam; enrolment is expected to be completed by late 2014 or early 2015 and results available late 2017. An opportunity to include additional regimens in the STREAM trial has arisen and discussions are at an advanced stage to consider how the 9-month regimen could be further simplified, in particular whether the regimen could be made fully oral by substituting bedaquiline for the injectable which frequently leads to severe side-effects including ototoxicity.

### Expanding shortened MDR-TB treatment: the West African experience

A Trébucq,<sup>1</sup> V Schwoebel,<sup>1</sup> C Kuaban,<sup>2</sup> Z Kashongwe Munogolo,<sup>3</sup> V Fikouma,<sup>4</sup> A Bakayoko,<sup>5</sup> T Ndikumana,<sup>6</sup> S Hassane Harouna.<sup>7</sup> <sup>1</sup>TB, The Union, Paris, France;

<sup>2</sup>University of Yaoundé, Faculty of Medicine and Biomedical Sciences, Yaoundé, Cameroon; <sup>3</sup>Pneumology Department, University School of Medicine, Kinshasa, Democratic Republic of Congo; <sup>4</sup>Hôpital Communautaire, Service de Médecine Interne, Bangui, Central African Republic; <sup>5</sup>CHU Treichville, Service de Pneumo-phthisiologie, Abidjan, Côte d'Ivoire; <sup>6</sup>Ministry of Health, NTP Manager, Bujumbura, Burundi; <sup>7</sup>Tuberculosis, Action Damien, Niamey, Niger.

**Background:** A 9-month regimen (4KmMfxPtoHCfzEZ / 5MfxCfzEZ) for multidrug-resistant tuberculosis (MDR-TB) has proven successful in Bangladesh. We report preliminary results from an observational cohort study coordinated by The Union which aims to evaluate the effectiveness and tolerance of this regimen in 9 countries of francophone Africa.

**Design/Methods:** The study started in 2013 in Benin, Burundi, Cameroon, Côte d'Ivoire, Niger, Central African Republic and Democratic Republic of Congo. Patients receive treatment under strict daily observation after giving informed consent and undergoing standard clinical and laboratory examinations. Follow-up is monthly until treatment completion and 6-monthly



thereafter for two years. Number of MDR patients detected and enrolled, and drug stocks are monitored quarterly. Adverse drug events and response to treatment are monitored through individual anonymous databases maintained in each country and controlled for quality by The Union. These data were used to describe patient characteristics, sputum conversion, and adverse drug events among patients enrolled in 2013.

**Results:** As of 1st April 2014, 361 patients had been enrolled. Among the 208 patients enrolled in 2013, 25% were HIV-positive, the median body mass index was 18.1 (range 11.7 – 26.6). Rifampicin resistance was detected by molecular test in 92%. The majority of patients (59%) had prior treatment failure, 31% had relapsed, and 10% were new cases. All had pulmonary TB. At month 4 (M4), the median weight gain was 5 kg; microscopically 74% had negative smears, 13% rare bacilli, 9.5% 1+, and 3.5% 2+ positive smears. By culture, 96% were negative at M4. Twelve patients (5.7%) died, 75% of whom within 2 months of treatment start and 6 of them were HIV-positive. Mild gastric discomfort or vomiting was reported by 43% at M1, with a substantial decrease after M2. Hearing loss  $\leq 70$  decibels (dB) was detected in 16/92 patients, and  $>70$  dB in 9/92 at M4. An abnormal audiogram at baseline was associated with a higher probability of hearing loss at M4. Updated data will be communicated at the conference.

**Conclusion:** These preliminary results are consistent with a high regimen effectiveness. It shows that follow-up can be managed successfully within the national tuberculosis programme. Among the reported adverse events, hearing loss was the most prominent. Measures were taken for early detection to allow kanamycin dosage reduction where indicated.

### Community involvement in shortened MDR-TB regimen implementation

S Hamid,<sup>1</sup> K Jahan,<sup>1</sup> Khan Ahmed Hussain,<sup>1</sup> M Siddiqui,<sup>2</sup> Mong Aprue,<sup>3</sup> - Maug.<sup>4</sup> <sup>1</sup>TB, National Tuberculosis Control Programme, Dhaka, <sup>2</sup>TB, BRAC, Dhaka, <sup>3</sup>TB, Lepira Bangladesh, Dhaka, <sup>4</sup>TB, Damien Foundation, Dhaka, Bangladesh.

**Aim:** To determine whether facilitating delivery of MDR TB services through community involvement is contributing to the patient compliance and treatment outcome of MDR TB.

**Methods:** Shorter regimen is implemented in the 26 districts since 2008 by Damien Foundation, BRAC and Lepira. Although all implementing partners are following same guidelines for the diagnosis and treatment of MDR TB, but the community providers differ for one partner to another. DF uses village doctors; BRAC uses Sabika (village nurse) and Lepira uses Government community health workers. Data from All partners were collected based on the designed questionnaire.

**Results:** Over 98% of MDR TB patients initiated treatment from hospitals. Once the patients are in the community, DOT is provided by village doctors in Damien Foundation project areas, by Sabika in BRAC

supported areas and health worker/ village doctors in Lepira. DOT is ensured seven days per week. Only few (9) patients are treated from the zero day by village doctors in DF projects. In all settings patients and their family members received psychological support and importance of regular & complete treatment, disease transmission. Both providers and patient received financial supports monthly for proper nutritional and support for investigations during treatment period. Travelling Cost is also given to patients and one attendant to perform routine follow up culture and DST during treatment period and six monthly post treatment follow up for two years after successful completion. In all settings clinical monitoring is done by doctors and nurses while in hospital and by the health worker while in the community. In BRAC areas close contact with symptoms is screening by the same Community Health Worker routinely during their house hold visit. DOT provider's performances at field level are supervised by the respective NGO staff. 161 patients initiated treatment in BRAC and LEPIRA and 601 patients under DF projects in the community level after the initial 4 months in hospital at the community level with a treatment outcome of over 81% and 83% respectively.

**Conclusion:** Community care for MDR TB works well with all different providers, under a defined nation policy irrespective of provider type. However, acceptability of the village doctors is more because of the easy availability.

## 12. EXPLORING THE INTERSECTION BETWEEN TB AND MATERNAL AND NEONATAL HEALTH: FROM RESEARCH TO IMPLEMENTATION

### Diagnosing and treating tuberculosis in pregnant women: current practices and research opportunities

J Mathad. Medicine, Division of Infectious Diseases/ Center for Global Health, Weill Cornell Medical College, New York, NY, USA

Nearly 3 million women were diagnosed with tuberculosis last year, and over 400,000 died of the disease. Incidence peaks during a woman's reproductive years—due in part to the immune changes brought on by pregnancy—making tuberculosis a major cause of maternal-child mortality. Management of tuberculosis during pregnancy remains contentious, and national guidelines for screening and management vary widely owing to insufficient data. This presentation will review: 1) The global burden of tuberculosis in women of reproductive age; 2) How pregnancy and the postpartum period affect the course of tuberculosis; 3) How to screen and diagnose pregnant and postpartum women for active and latent tuberculosis; 4) The management of active and latent tuberculosis in pregnancy and the postpartum period, including the safety of tuberculosis medications, data on HIV/tuberculosis co-infection, and drug-resis-

tant tuberculosis; and 5) High-priority research areas for tuberculosis research in pregnant and postpartum women.

### TB case finding in antenatal care in Karonga district, Malawi

F Kayambo,<sup>1</sup> YG Yamikani Gumulira,<sup>1</sup> I Dambe,<sup>2</sup> S C Stender,<sup>3</sup> T Rashidi.<sup>4</sup> <sup>1</sup>HIV TB, Jhpiego, Lilongwe, <sup>2</sup>TB, NTP, Lilongwe, Malawi; <sup>3</sup>Regional HIV/TB Adviser, Jhpiego, Cape Town, South Africa; <sup>4</sup>CD (Technical Teamleader), Jhpiego, Lilongwe, Malawi.

**Background:** In Malawi, the prevalence of HIV among adults aged 15–49 is 10.6% (MDHS 2010) and incidence of TB is 163 per 100,000. The maternal mortality rate is 675 per 100,000 live births, and the TB/HIV co-infection rate is at 63%. Jhpiego/MCHIP piloted a program integrating TB screening into focused antenatal care (FANC) Karonga district. Intervention or response: TB symptom screening was integrated into routine antenatal care in five facilities with objective of early detection and treatment of TB. Activities included orientation of healthcare providers to screen TB in ANC; procurement and distribution of microscopes, training of laboratory personnel on TB microscopy; strengthening systems for transport of specimens; and modification of recording and reporting systems. Results or lessons learnt: The table below shows out of 3,920 women screened, 4 were found to have TB (0.1%), one of whom was HIV positive; all were initiated on TB treatment. Challenges faced include predominantly health systems issues. The clinics serve 45 to 50 pregnant mothers on a clinic day usually there is only one nurse, while other providers attend to ART and HTC clinics, no laboratory facilities in 3 of the 5 pilot facilities, as such they referred prepared sputum slides to district hospitals and turnaround time ranged from 1 – 3 weeks. TB treatment initiation does not occur in all clinics in Malawi, and challenges with transport of patients to get to the district hospital for treatment initiation was also found to be a challenge. Recording and reporting was a continuous challenge, due to human resource shortages.

**Conclusion:** TB symptom screening in ANC is feasible, however the pilot does not provide adequate evidence on whether or not it should be advocated for without further assessment given the low yield. Several possible contributing factors, including low incidence of TB in the project district, poor data systems, low sensitivity of light microscopy, and lack of specificity of symptoms, particularly among pregnant women. There is need to Intensify and standardize supportive supervision at all levels to improve implementation, and facility should be fully engaged to ensure ownership and sustainability. Efforts to integrate contributed to general health system strengthening, including expanding laboratory services, improving referrals, human capacity development, improving M&E systems, and strengthening supportive supervision.

Total FANC attendees	5,474
Women screened for signs/symptoms (s/s) of TB in FANC	3,920 (71.6%)
Women with s/s of TB	68 (1.7%)
Women with s/s of TB diagnosed with TB	4 (5.9%)
Women with s/s of TB diagnosed with HIV	8 (11.8%)

### Maternal and infant outcomes from a study in Cape Town, South Africa

A Bekker,<sup>1</sup> H S Schaaf,<sup>1</sup> A Slogrove,<sup>1</sup> HR Draper,<sup>1</sup> A Hesselning,<sup>1</sup> M Kriel,<sup>2</sup> G Walzl.<sup>2</sup> <sup>1</sup>Paediatrics and Child Health, Desmond Tutu TB Centre, Stellenbosch University, Cape Town, <sup>2</sup>Division of Molecular Biology and Human Genetics, DST/NRF Centre for Biomedical Tuberculosis Research, Stellenbosch University, Cape Town, South Africa.

**Background:** HIV and tuberculosis (TB) are leading infectious causes of morbidity and mortality in pregnant women and adversely impacts on perinatal outcomes.

**Design/Methods:** A prospective cohort study of maternal-infant pairs at Tygerberg Hospital, a tertiary hospital, Cape Town, January 2011-January 2012. Data was collected on maternal TB and HIV disease spectrum, maternal TB treatment outcomes and infant birth status.

**Results:** Seventy-four pregnant women with TB were consecutively enrolled, 53(72%) HIV co-infected (median CD4 count 155 cells/mm<sup>3</sup>, range 11–565); 38/53 (72%) on HAART; a median of 2 months antepartum HAART duration confirmed for 29 HIV-co-infected women. Newborns had a median gestation of 36 weeks and birth weight 2197 grams. Twenty-two (30%) women were retreated for TB and in 33 (45%) the TB diagnosis was made intra- or post-partum; 60/74 (81%) had pulmonary and 14 (19%) extrapulmonary TB. In 49 (66%) the diagnosis was bacteriologically confirmed; 23 sputum smear-positive and 37 culture-positive for *Mycobacterium tuberculosis*, 6/37 culture-confirmed cases had MDR-TB. Forty-one (55%) women had favourable TB treatment outcome (cure/treatment completion), 13 (18%) were lost to follow-up (LTFU) before entering the clinic TB registry, 13 (18%) were LTFU at the end of the treatment period, 2 (2%) had treatment failure and 5 (7%) died. All maternal deaths were classified as TB-related and all women who died were HIV-infected (3 disseminated TB, 1 TB meningitis and 1 pulmonary TB). All 5 (7%) newborn deaths and 4 intra-uterine deaths (IUDs) were amongst infants born to HIV-infected women.

**Conclusion:** The HIV prevalence is high amongst South African pregnant women with TB at the hospital referral level. They present with severe HIV-associated immune deficiency and delayed TB diagnosis. Two-thirds of newborns were premature and had low birth weight. TB treatment outcomes in pregnant women are poor and there is high maternal and newborn mortality associated with maternal HIV infection.

### Education and performance of nurses and midwives in essential TB tasks in Lesotho: results from a task analysis

A Christensen,<sup>1</sup> L Hart,<sup>2</sup> L Skolnik,<sup>3</sup> S C Stender.<sup>4</sup> <sup>1</sup>HIV/AIDS Technical Leadership Office, Jhpiego an affiliate of Johns Hopkins University, Dar es Salaam, United Republic of Tanzania; <sup>2</sup>Global Learning Office, Jhpiego, Washington DC, USA; <sup>3</sup>Global Programs, Jhpiego, Washington DC, USA; <sup>4</sup>HIV/AIDS Technical Leadership Office, Jhpiego, Cape Town, South Africa.

**Background:** In an effort to efficiently characterize the reality of local practice—to produce appropriate nursing and midwifery graduates—it is important to understand the job duties or tasks performed by health workers at the work site. Jhpiego has modified task analysis for international public health work in order to highlight current education gaps, prioritizing curriculum content, re-define scope and standards and ensure graduates are appropriately trained for the communities they will serve.

**Methods:** The study targeted practicing nurses/midwives (n=154) early in their careers or new to their workplace. The methodology entailed seeking responses from nurses/nurse-midwives in four key measurement areas, by task: FREQUENCY at which the task is performed; CRITICALITY of the task to patient/public health outcome; setting where the provider received EDUCATION/training on the task; and the provider's self-perceived level of competence in PERFORMANCE of the task.

**Results:** Despite TB being the fifth leading cause of years of lives lost in Lesotho, respondents indicated there were gaps in their TB education inclusive of community interventions. TB screening is one of two tasks that were reported by most as highly critical (92.2%) with only a low percentage of participants reporting training during pre-service. While 92.2% of participants rate "screening for TB based on patient symptoms" as highly critical, only about half (51.9%) reported pre-service exposure. Health center participants, the individuals most likely to deliver continuous services for people living with TB, rated all TB-related tasks as having high criticality, yet these tasks are some of the most frequently reported as not being covered in pre-service. Similarly 16.9% respondents reported never being trained in "contact tracing of TB-positive patient family members" and "tracing [TB] defaulters within the community".

**Conclusions:** Given Lesotho has TB prevalence of 632/100,000 all nurses and nurse-midwives must have comprehensive knowledge to appropriately screen, diagnose, promptly initiate and support patients to adhere to treatment. TB related education and services need to be strengthened across cadres and in health facilities. A key component is strengthening the community involvement in TB care and treatment and incorporating services into the community. It is vital that providers have knowledge to minimize occupational exposure and understand environmental and personal protective controls.

## 14. OUTSTANDING ISSUES IN HIV/AIDS

### PLHIV should be given longer duration of IPT to achieve an impact at the programmatic level.

T Samandhari.<sup>1</sup> <sup>1</sup>DTBE/IRPB, Centers for Disease Control and Prevention (CDC), Atlanta, GA, USA

Isoniazid preventive therapy (IPT) has been demonstrated to prevent tuberculosis (TB) among persons living with HIV (PLWH) in multiple settings. Whereas short courses (i.e., <12 months) of isoniazid prophylaxis appear to have a durable effect in settings where there are low to moderate incidences of TB, a more prolonged course may be necessary in settings with high TB incidences. In the present era, antiretroviral therapy programs are rapidly expanding in high incidence settings and in 2013 the World Health Organization recommended that antiretroviral therapy (ART) be initiated in PLWH with CD4+ lymphocyte counts  $\leq 500$  cells per microliter. While early ART initiation will be an important advance for PLWH, rates of TB in this population remain unacceptably high. Emerging evidence from cohorts receiving ART or with access to ART in high TB incidence settings, indicate that as an adjunct IPT is necessary and beneficial. Two randomized trials conducted in such settings that compared continuous (i.e., at least 36 month) IPT against 6 months IPT demonstrated the superiority of continuous IPT. It is unclear whether the benefit of continuous IPT was due to a more complete cure of baseline latent TB infection or the prevention of re-infection during the period of IPT receipt. Results from a recently published cluster-randomized trial of IPT among South African miners suggest that a high intensity of re-infection abolishes any observable benefit of IPT. An important modifying factor is that multiple studies have shown that only tuberculin skin test positive PLWH benefit from IPT. The speaker will review data about TB incidence after IPT cessation in TB endemic settings. A decision-analytic model showed that 36 months IPT in Botswana's ART program was more cost effective in reducing TB than provision of IPT without a TST, provision of only 6-months IPT, or expanding ART eligibility at high CD4 counts without IPT. The discussant will also present evidence and propose new studies for durable TB prevention among PLWH by including the following aspects: (1) whether the tuberculin skin test is necessary prior to the initiation of IPT; (2) whether IPT should precede, follow or begin at the time of ART initiation; and (3) the potential impact of alternative drug regimens for TB chemoprophylaxis.



## 15. SYSTEMATIC SCREENING FOR ACTIVE TB: FROM GUIDELINE TO IMPLEMENTATION

### Screening for TB in risk groups in Cambodia

T E Mao,<sup>1</sup> R-P Yadav.<sup>2</sup> <sup>1</sup>National Center for TB and Leprosy Control (CENAT), Ministry of Health, Phnom Penh, <sup>2</sup>Stop TB Unit, World Health Organization, Phnom Penh, Cambodia.

**Background:** The case finding has plateaued in Cambodia. The epidemic is concentrating in high risk groups. The country needs to maximize its resources by focusing on high risk groups, who are also the most vulnerable. They include the poor, elderly, HIV+, diabetics and contacts of TB cases. Systematic screening finds the missing cases by complementing the routine approach and by using newer approaches and tools (e.g., Xpert). The objective of this study was to conduct systematic screening among contacts of smear-positive cases of past two years, over a period of two years (2012–2014).

**Design/Methods:** We used quasi-experimental cluster randomized design with control and intervention arms. We covered 30 target operational districts (ODs) that have the poorest health access rates and highest household poverty rates. Out of these 30 ODs, 15 ODs were randomly allocated for intervention and 15 ODs were randomly allocated for control. In 2013–2014, we selected 30 more target ODs as intervention and control ODs. In the intervention arm, we identified all smear positive TB cases registered (index cases) in the past two years. Then, we visited all index cases and invited their household and neighbourhood contacts to the screening site. We screened using TB symptoms and chest X-ray. Those who were symptomatic or had abnormal radiography or both underwent Xpert MTB/RIF tests. In the control arm, routine national TB program activities continued using passive contact tracing and investigations.

**Results:** We were able to find 1,745 bacteriologically positive cases and 4,175 cases of all forms in the two years of the project, as yield. Compared to control districts, intervention districts found about 17% additional bacteriological positives and about 22% additional TB cases of all forms.

**Conclusion:** In an era of dwindling resources, programs need to maximize resources and programmatic outcomes. Systematic screening is an effective way of finding the missing cases, especially those among the most vulnerable populations who may not present to health facilities due to atypical symptoms or lack of access to services. When systematic screening uses multi-symptom screening with newer diagnostic tools like Xpert, the yield could be significant, as in the case of Cambodia.

## 16. COMMUNITY AS PARTNER: CREATING SUCCESSFUL COLLABORATIONS IN TB CONTROL

### The NTP perspective: overcoming challenges to community partnerships

J O Obasanya,<sup>1</sup> R Eneogu.<sup>1</sup> <sup>1</sup>National Tuberculosis and Leprosy Control Programme, Federal Ministry of Health, FCT Abuja, Nigeria.

**Background:** DOTS strategy was adopted and has been scaled up nationally with 5,389 DOTS centres and 1,602 AFB microscopy centres by the end of 2013, though with skewed distribution towards urban areas. Despite this achievement, case detection remains low. The result of the prevalence survey 2012 shows that Nigeria notifies approximately 17% of the incident TB cases. Furthermore about 73% of the diagnosed cases during the survey had typical TB symptoms, implying that TB remain a major problem in the community. The 2012 TB KAP survey also showed that awareness about TB in the general population remains low, with only 27% of the general population having good knowledge about TB. The structured involvement of community in routine NTBLCP activities was minimal.

**Design/Methods:** The NTBLCP organized a stakeholders meeting to plan for the engagement of the CSOs. This was followed by a dialogue with all factions of the CSOs to take a common position on the need to have greater community participation in routine TB control activities. Technical assistance was sought from PATH through USAID to provide TA on the best approach to engage the community/CSOs. Various sessions were held to assess the level of current community/CSO's participation, their expected roles and the strategy for the engagement. Joint plan for capacity building was developed and implemented. Community representatives are routinely invited to key programme management meetings

**Results:** The intervention resulted in improved trust between the NTBLCP and the CSOs. This led to better communication. There is better understanding of the roles of the community by the Programme and the community. Intra- and inter-community/network relationship improved tremendously putting the community in a stronger position to negotiate and engage the Programme constructively. There is better and structured involvement of CSOs in the planning, implementation and evaluation of activities of the TB programme at the national, state and local levels, development of the national TB Strategic Plan 2015–2020 which includes a robust community system strengthening and ACSM interventions. There is active contribution to the TBHIV Concept note. The community is spearheading the ongoing “intensified case finding activities” in various communities in 3 states.

**Conclusion:** Achieving satisfactory case detection requires that all care providers including communities are constructively engaged and empowered to function successfully

## 17. COMMUNITY-BASED APPROACHES TO ADDRESS LUNG HEALTH

### Community involvement and linkage to health service: accelerating the move towards prevention and control at community level

L Adams,<sup>1</sup> A Detjen.<sup>2</sup> <sup>1</sup>Medicine, Geisel School of Medicine at Dartmouth, Hanover, NH. <sup>2</sup>TB, International Union Against Tuberculosis and Lung Disease, New York, NY, USA

**Background:** Community-based care and integrated child health care services are necessary to address the burden of important lung diseases in children such as tuberculosis and asthma. Such approaches can extend the health services' reach and increase access for difficult to reach and marginalized populations. Community-based approaches are the ideal platform for tackling lung health in children and providing family-centered care.

**Methods:** A review of recent publications on the potential role of community-based approaches provided insights into the way forward of incorporating such approaches into child lung health including TB in children.

**Results:** Four main areas were identified as opportunities for improved care through community involvement and integration of services. 1) Early case detection. Through home-based visits, previously undiagnosed cases of TB may be identified. Environmental factors such as second-hand smoke exposure, which exacerbate lung diseases, can be assessed. Integrated child health algorithms in primary care departments can also improve detection of lung diseases in children who present to health facilities with unclear or multiple diagnoses. 2) Comprehensive TB contact investigations. These are rarely performed in high TB-burden countries and are a missed opportunity for reducing TB morbidity and mortality in children through secondary case detection and the provision of isoniazid preventive therapy (IPT). 3) Preventing future cases. Home-based care is the optimal setting for educating family members about child lung health and infection control in the household. 4) Treatment support. Provision of education and supportive treatment monitoring can be best achieved through home or community-based activities. This includes directly observed therapy for TB disease or monitoring IPT.

**Conclusions** The examples to follow in this symposium will illustrate best practices in a variety of settings and the benefits of community-based care and integration of child lung health into general pediatric care.

## 18. NON-TUBERCULOUS MYCOBACTERIAL INFECTIONS: DIAGNOSIS AND MANAGEMENT

### Epidemiology of non-tuberculous mycobacteria pulmonary disease: data and trends

D Wagner.<sup>1,2</sup> <sup>1</sup>Infectious Disease and Travel Medicine, and <sup>2</sup>Center of Chronic Immunodeficiency, University Hospital Freiburg, Freiburg, Germany.

Nontuberculous mycobacteria (NTM) are a grouping of over 140 different species that can cause a variety of infections in humans and animals. Similar to NTM lymphadenitis that is found mainly in young children, NTM lung disease (NTM-LD), the most frequent (65–90%) of all clinical NTM disease, must be distinguished from respective disease caused by *M. tuberculosis*: reports from African and Asian countries show that patients with NTM-PD may be treated for prolonged period as MDR-TB because of the lacking species identification of mycobacteria from respiratory samples. The NTM-NET world-map study indicates that the prevalence of NTM in respiratory specimen differs significantly in different parts of the world. The recently published NTM-NET study on prevalence estimates of NTM-PD support the hypothesis of significant prevalence differences between Japan, Europe, and United States. This study also uncovered the pronounced differences in treatment practices of NTM-PD in these countries indicating the need of prospective treatment studies and education of physicians treating patients with NTM-PD. The epidemiology of NTM is complicated by changing isolation frequencies of the different NTM species from respiratory specimen or in patients with cervical lymphadenitis over time. Part of these differences are explained by the better taxonomy of the genus *Mycobacterium*, but may also be related to changes in environmental exposure or decrease of cross-protection due to decrease of the TB prevalence or diminished use of BCG-vaccination. All in all evidence is growing that the incidence of NTM-LD and associated hospitalizations is on the rise, mainly in regions with a low prevalence of TB (United States, Canada, Taiwan, Germany). However, data from countries with a high prevalence of TB are lacking. Factors that may underlie this changing epidemiology are increases in the prevalence of the susceptible host, e.g. the number of patients with systemic (e.g. HIV infection, haematological malignancy, inheritable disorders of immunity, immunosuppressive drug use including TNF- $\alpha$  inhibitor therapy or systemic or inhalative corticoid therapy) or local immunosuppression (e.g. pre-existent pulmonary disease, e.g. cystic fibrosis patients, patients with chronic obstructive pulmonary disease (COPD)) has increased. In conclusion disease from NTM is a differential diagnosis in patients with suspected TB and physicians treating TB need to be educated to diagnose and treat NTM diseases.

## Molecular diagnosis and genetic diversity of non-tuberculous mycobacteria

D Starkova,<sup>1</sup> I Mokrousov,<sup>1</sup> A Vyazovaya,<sup>1</sup> O Narvskaya,<sup>1</sup> V Zhuravlev,<sup>2</sup> T Otten,<sup>2</sup> B Vishnevskiy.<sup>2</sup> <sup>1</sup>Laboratory of Molecular Microbiology, Pasteur Institute, St.Petersburg, <sup>2</sup>Laboratory of Etiological Diagnostics, Research Institute of Phthisiopulmonology, St.Petersburg, Russian Federation.

**Setting:** In recent 10 years, a steady increase of the cases of NTM infection has been observed in Saint Petersburg and vicinity.

**Goal:** Detection and identification of NTM human strains isolated from patients with lung disease in Saint Petersburg, Russia. Molecular typing of *M. avium* human strains isolated from 90 patients (including 27 HIV-positive) using two different methods (VNTR typing and IS1245 RFLP typing) to evaluate the genetic diversity of Russian strains.

**Methods:** A total of 450 NTM cultures (2011-13 years) were isolated from 359 patients with TB suspicion using solid media, BACTEC MGIT 960. In addition real-time PCR IS6110 was done for all cultures. For species identification GenoTypeCM/AS (HAIN Lifescience, Germany) were carried out. 38 patients (10.6%) had HIV co infection. The genetic diversity within the 90 *M. avium* human strains was studied by VNTR typing based on improved optimized scheme, included 13 most polymorphic loci from 8 and 15 loci proposed by Thibault et al. (2007) and Inagaki et al. (2009): TR292, TRX3, TR25, TR47, MATR-1, 4, 5, 6, 8, 11, 14, 15, 16. *M. avium* strains were typed according to IS1245-RFLP patterns.

**Results:** Following spectra of NTM strains were detected: *M. avium* (240 strains 53.3%), *M. intracellulare* 39(8.6%), *M. fortuitum* 38(8.4%), *M. chelonae* 38(8.4%), *M. abscessus* 23( 5.1%), *M. peregrinum* 19(4.2%), *M. lentiflavum* 19(4.2%), *M. gordonae* 15(3.3%), *M. kansasii* 5(1.1%), *M. malmoense* 5(1.1%), *M. xenopi* 3(0.6%), *M. celatum* 3(0.6%), *M. scrofulaceum* 2(0.4% ), *M. simiae* 1(0.2%). The VNTR-typing based on 13 polymorphic loci allowed for the detection of 36 patterns among 90 *M. avium* isolates. Among these, VNTR grouped 62 isolates into eight clusters, whereas 28 VNTR patterns were unique. VNTR showed one major genotype - 222223145443', which included 37 isolates (41.1%). The 72 strains possessed a truncated locus MATR-16 (allele 3') due to the 28 bp deletion in the third of three tandem repeats (GenBank accession no. KF479191). All strains clustered by VNTR-typing were analyzed by IS1245 RFLP-typing for further discrimination. As a result, all typed isolates produced 54 different IS1245-RFLP patterns. Among them 50 isolates had unique IS1245-RFLP patterns and 9 isolates were grouped into four clusters. The HGDI values was higher for reach for IS1245 RFLP-typing (0.996) method then for VNTR-typing (0.821).

**Conclusions:** The most common NTM species in our area is *M. avium*. The use of both typing methods is preferable for epidemiological studies.



## ABSTRACT PRESENTATIONS

### SATURDAY

### 1 NOVEMBER 2014

## e-POSTER SESSIONS

### 03. TB IN CHILDREN: MDR AND TRAINING

#### EP-125-01 Reported drug procurement patterns and formulation preferences expressed by providers caring for children with multidrug-resistant tuberculosis

J Furin,<sup>1</sup> L McKenna,<sup>2</sup> C Zen Ruffinen,<sup>3</sup> G Brigden.<sup>4</sup> <sup>1</sup>Case Western Reserve University, TB Research Unit, Cleveland, OH, <sup>2</sup>Treatment Action Group, New York, NY, USA; <sup>3</sup>International Office, Médecins Sans Frontières (MSF), Geneva, <sup>4</sup>Access Campaign, MSF, Geneva, Switzerland.  
e-mail: jjf38@case.edu

**Setting:** Although recent estimates show there are likely more than 33,000 cases of MDR-TB among children each year, less than 1% of these children are diagnosed and treated for the disease. One major barrier to treating children with MDR-TB is the lack of child-friendly formulations of DRTB medications. Further information is needed on the procurement practices and formulation preferences of health care providers and patients. A survey was done using a convenience sample of providers caring for children with MDR-TB. Twenty-five participants were contacted via email and asked to complete a survey on their procurement practices for obtaining second-line drugs as well as their preferences regarding new pediatric formulations; 17 (68%) of those surveyed responded, representing physicians, nurses and pharmacists.

**Results:** The respondents were from 17 countries (7 of which are high burden) and are providing care for more than 400 children combined. Twelve reported (70.6%) procuring TB medications exclusively from the Global Drug Facility (GDF), while three also reported procuring medications from in-country sources (17.6%). Two respondents (11.8%) reported procuring exclusively from the private market. All 17 respondents expressed problems with administering the current second-line TB drug formulations, and their stated preferences for improved pediatric formulations include (in order of preference): 1) dispersible tablets; 2) smaller and scored tablets; 3) syrups; and 4) granules with dosing spoons. Respondents also mentioned the need for fixed dose combinations (FDCs) of second-line drugs, pediatric formulations of the new TB drugs (including bedaquiline and delamanid), and the role of drug compounding for very small children.

**Conclusions:** A majority of providers procure their medications for pediatric MDR-TB from the GDF, and all of them expressed problems with the existing

formulations. Dispersible and smaller, scored tablets were preferred over syrups or granular formulations and respondents mentioned the need for FDCs, compounding, and pediatric formulations of new drugs. The results from this survey should be used along side future patient and guardian preference surveys to guide development of child-friendly formulations and to document the important role the GDF plays in procuring MDR-TB treatment for children.

#### EP-126-01 Nurse-led strategies to maximise pediatric TB diagnosis and linkages to care in Swaziland

G Mtetwa,<sup>1</sup> R Golin,<sup>1,2</sup> P Ustero,<sup>1,2,3</sup> K Ngo,<sup>3</sup> M Matshaba,<sup>1,2</sup> A Mandalakas.<sup>3</sup> <sup>1</sup>Tuberculosis, Baylor College of Medicine Children's Foundation Swaziland, Mbabane, Swaziland; <sup>2</sup>Pediatrics, Baylor College of Medicine, Houston, TX, <sup>3</sup>Global Tuberculosis Program, Baylor College of Medicine, Houston, TX, USA.  
e-mail: pustero@yahoo.es

**Background:** Baylor College of Medicine Children's Foundation-Swaziland (BCMCF-SD) offers comprehensive TB/HIV services since 2006. Currently more than 3000 children and adolescents are in care. TB services in 2006 included smear diagnosis and treatment with limited impact due to the scarcity of human resources. In 2012 BCMCF-SD leveraged WHO TB Reach funding to strengthen pediatric TB services via incorporation of GeneXpert TB/RIF (GXP) diagnostics, introduction of contact-tracing, and development of a high-quality comprehensive and nurse-led pediatric TB clinic.

**Intervention:** In order to realize this vision, complementary strategies were implemented: (i) build capacity for the charge nurse to deliver TB/HIV care, including initiation of TB treatment for sputum positive clients and ART initiation for HIV/TB co-infected clients, (ii) robust intensified case finding and contact tracing procedures, including home visits tailored to meet family needs, (iii) routine pediatric sample collection techniques with same day results, (iv) elimination of patient fees at the point of service to improve access to radiology which is the cornerstone of pediatric TB diagnosis, (v) implementation of IPT in TB contacts under 5 years of age, (vi) strategies to control DRTB, and (vii) establish a national educational center for childhood TB management.

**Results and Lessons Learned:** Infusing resources in our TB initiatives through empowering our TB nursing staff resulted in an increased number of children accessing TB services with doctors required only for complicated cases. In 9 months, we analyzed 802 GXP samples of which 13% and 40% were provided by children <5 years and 5–14 years, respectively. 19% of specimens were collected via gastric or nasopharyngeal aspiration, by the TB nursing staff. Nurses who have completed a TB attachment, feel empowered to start doing specimen collections.

**Conclusions:** In countries where doctors are scarce, task shifting provides a safe and high-standard environment to address TB in the pediatric population. Nurse-to-nurse

training on pediatric TB issues is breaking many barriers in management of a disease that used to be seen as doctor disease. Our program aims to become a model for pediatric TB care in Swaziland with context-adapted strategies that maximize resources.

### EP-127-01 Map the gap: missing children with MDR-TB and XDR-TB

C Rodriguez,<sup>1</sup> C Yuen,<sup>2</sup> S Keshavjee,<sup>1</sup> M Becerra.<sup>1</sup>

<sup>1</sup>Department of Global Health and Social Medicine, Harvard Medical School, Boston, MA, <sup>2</sup>Division of Global Health Equity, Brigham & Women's Hospital, Boston, MA, USA. e-mail: carly\_rodriguez@hms.harvard.edu

**Background:** Adult cases of multidrug resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) have been reported in 189 and 92 countries, respectively. However, surveillance and routine case notification are lacking for drug-resistant tuberculosis in children.

**Design/Methods:** To describe the gap between recognition of drug-resistant TB in children compared to adults, we compared countries in which MDR-TB or XDR-TB in children have been reported to countries in which MDR-TB or XDR-TB in adults have been reported. The latter set of countries was identified based on their routine reporting to WHO of MDR-TB and XDR-TB adult cases. Cases of children with MDR-TB and XDR-TB were identified through a systematic review of published peer-reviewed reports and conference abstracts.

**Results:** We found reports of  $\geq 1$  case of MDR-TB in a child in 40% of the 189 countries reporting adult cases of MDR-TB. We were unable to find any reports of MDR-TB in a child for 33% of the 27 countries with high burdens of MDR-TB. We were only able to find reports of XDR-TB in  $\geq 1$  child in 10% of the 92 countries that reported adult cases of XDR-TB.

**Conclusion:** The incongruence between the countries where child and adult cases of MDR-TB and XDR-TB have been documented points to a knowledge gap about the global extent of child cases of drug-resistant tuberculosis. Expanded efforts to diagnose and report drug-resistant tuberculosis among children will be required to quantify the true burden of pediatric MDR-TB and XDR-TB.

### EP-128-01 Taking up the challenge of childhood TB in Nigeria: from rhetoric's to action

A Awe,<sup>1</sup> J O Obasanya,<sup>2</sup> T Odusote,<sup>3</sup> J Kuye,<sup>2</sup> O Daniel,<sup>1</sup> E Oyama,<sup>1</sup> A F Omoniye,<sup>1</sup> M Gidado.<sup>4</sup> <sup>1</sup>TB, World Health Organization, Abuja, <sup>2</sup>TB, NTBLCP, Abuja, <sup>3</sup>TB/HIV, USAID, Abuja, <sup>4</sup>TB, TB CARE I, Abuja, Nigeria. Fax: (+234) 802 314 4120. e-mail: aweayo@yahoo.co.uk

**Background and challenges to implementation:** National TB case notification had been on the increase over the last 10 years from 55,765 in 2004 to 100,401 in 2013. It is however difficult to quantify the proportion of children 0–14 years notified among all forms of TB largely due to the inability of data collection tools to

disaggregate data on childhood TB for all forms of TB. The proportion of childhood TB among New smear positive TB(smr+) cases averages around 4%. Challenges with childhood TB include difficulty of TB diagnosis in children, low index of suspicion, poor engagement of pediatricians. This study was conducted to highlight actions taken by TB programme and the immediate results of these actions, the challenges and way forward. **Intervention or response:** Desk review was carried out to estimate the proportion of childhood TB among new Smr+ TB cases notified in the country in the last 5 years, and the quarterly proportion of TB cases among all forms of TB cases notified since the data tool was revised in 2012. The national TB programme developed a road map for scaling up management of childhood TB in the country. Elements implemented in 2012/2013 include: sensitization meeting of pediatricians from tertiary facilities, development of a desk guide on childhood TB, adoption of the new WHO regimen and dose for pediatric TB, revision of existing training documents on childhood TB, ToT workshop for pediatricians, cascading of the childhood TB training to the 6 zones, revision of existing R&R tool to capture the contribution of childhood cases to total TB notification

**Results and lessons learnt:** Proportion of childhood TB among new smr+ TB cases notified ranged from 3% in 2008 and peaked at 8% in 2009 but gradually declined to 2.4% in 2010. There was another spike to 7.2% in 2011 followed by a decline to 2.3% in 2012. In the quarterly analysis from quarter 1, 2012 to quarter 4, 2013, the childhood TB cases among all forms of TB notified in the country had stabilized at 3%.

**Conclusions and key recommendations:** Training must be cascaded to include all general health care workers. Some bottle necks in the diagnosis of TB such as the payment of chest X-ray needs to be addressed. Guidelines on the use of gene xpert for the diagnosis of TB in children should be speed up to address diagnostic challenges. The development of other simple tools to aid TB diagnosis in children will go a long way to improve childhood TB notification in resource limited areas.

### EP-129-01 Prevalence of TB disease and infection among child contacts of DR-TB patients in Karachi, Pakistan

F Amanullah,<sup>1,2</sup> A Malik,<sup>3</sup> F Khatoon,<sup>2</sup> A Parekh,<sup>3</sup> S Khowaja,<sup>3</sup> A Bhurgri,<sup>2</sup> A Khan.<sup>3</sup> <sup>1</sup>Pediatrics, The Indus Hospital, Karachi, <sup>2</sup>TB Control, The Indus Hospital, Karachi, <sup>3</sup>International Health, Interactive Research and Development, Karachi, Pakistan. e-mail: farhana.maqbool@irdresearch.org

**Background:** Investigation of child TB contacts allows early TB case detection and effective treatment including preventive therapy, however this global public health standard is rarely implemented in high TB burden settings. The problem is further compounded in contacts of DR-TB patients in whom no evidence from randomized controlled trials exists to guide the use of preventive therapy.

**Intervention or response:** A contact evaluation protocol was used to assess child contacts of newly registered adults with DR-TB. Health workers identified child contacts in the household and advised families to bring these children to the Indus Hospital, for assessment. All children that were brought in had the following, <5 year olds: History and physical, TST, CXR and a gastric aspirate if clinically indicated. All 5–14 year olds had a history and physical, TST and if symptomatic then CXR, sputum for AFB smear/culture.

**Results and lessons learnt:** A total of 192 child contacts were evaluated between Jan 2008– Jan 2013. Of these 59% were male and 55% were children of the index patient. 42% were severely underweight (z score <-2 SD). 33% had a PPD >10mm (n=130). Of all contacts evaluated 27% had one symptom (any of: cough, fever, night sweats, weight loss, adenopathy). TB disease was diagnosed in 9% (15/166) of which 40% (6/15) were culture confirmed to have DR-TB.

**Conclusions and key recommendations:** We found high prevalence of TB disease among child contacts of DR-TB patients after implementation of a contact evaluation protocol. All child contacts of DR-TB patients should be mandatorily evaluated at baseline and followed by health workers trained to conduct child TB symptom screens, for prevention, early diagnosis and treatment of TB in this vulnerable group.

### EP-130-01 Improving estimates of the burden of Childhood TB: diagnostic algorithms and age-disaggregated reporting

J Firth,<sup>1</sup> C Lijinsky,<sup>2</sup> T Arscott-mills,<sup>3,4,5</sup> B Phelps,<sup>1</sup> C Powell.<sup>6</sup> <sup>1</sup>Office of HIV/AIDS, United States Agency for International Development (USAID), Washington, DC, <sup>2</sup>Office of Sustainable Development, Bureau for Africa, USAID, Washington, DC, USA; <sup>3</sup>Pediatrics, Botswana-UPenn Partnership, Gaborone, Botswana; <sup>4</sup>Pediatrics, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, <sup>5</sup>Pediatrics, Children's Hospital of Philadelphia, Philadelphia, PA, <sup>6</sup>Office of Health, Infectious Diseases, & Nutrition, USAID, Washington, DC, USA. Fax: (+202)808-3742. e-mail: drjacquebup@gmail.com

**Background and challenges to implementation:** TB in children is more difficult to diagnose than TB in adults, leading to widespread under-diagnosis and poor estimates on the burden of TB disease in children. This is especially true among children with HIV. Pediatric TB diagnostic algorithms and recording of age-disaggregated data can help to address these issues but have not been universally implemented.

**Intervention or response:** We reviewed the TB and HIV guidelines from the eleven countries in Sub-Saharan Africa with the highest co-infection rates of TB and HIV (>40%) to determine how many countries currently have dedicated chapters on pediatric TB and specific algorithms for diagnosing TB in children. In addition, data collection tools were reviewed to determine if age-disaggregated data were being collected and reported to the national level.

Country	Co-infection Rate (WHO 2013)	Peds TB chapter in TB guidelines? (year of guideline)	Peds TB diagnostic algorithm?	Age disaggregation of data collected at district level?
Botswana	63%	Yes (2011)	TB guidelines: Yes HIV guidelines: No	Age reported, districts using electronic TB register
Lesotho	75%	Yes (2008)	TB guidelines: No HIV guidelines (2007): No	No
Malawi	59%	No (2007)	TB guidelines: No HIV guidelines: No	Age breakdown (0–4, 5–14) for case notification but not outcomes
Mozambique	58%	Yes (2008)	TB guidelines: No HIV guidelines (2014): Yes	Data collection forms not included in available TB guidelines
Namibia	47%	Yes (2011)	TB guidelines: No HIV guidelines: No	Age reported, districts using electronic TB register
South Africa	65%	Yes (2009)	TB guidelines: No HIV guidelines: No	Age reported, districts using electronic TB register
Swaziland	77%	Unable to access drug-susceptible TB guidelines	TB guidelines: N/A Pediatric HIV guidelines (2006): Score chart	Unable to access TB reporting forms
Tanzania	39%	Section only (2006)	TB guidelines: Score chart HIV guidelines: No	Age breakdown (<15, 15+) for case notification but no age disaggregation for outcomes
Uganda	50%	Section only (2010)	TB guidelines: No HIV guidelines: No (algorithm draft in progress)	Age breakdown (0–4, 5–14) for smear-positives only, and (<15, 15+) in cases registered & smear conversion
Zambia	54%	Yes (2008)	TB guidelines: No Pediatric HIV guidelines (2010): No	Age breakdown (<15, 15+) for smear pos, smear neg, EPTB, other previously treated and default/death
Zimbabwe	70%	Yes (2010)	TB guidelines: No HIV guidelines: No	Age breakdown (0–4, 5–14) for case notification but no age disaggregation for outcomes

**Results and lessons learnt:** Of the eleven countries whose TB and HIV guidelines were reviewed (Botswana, Lesotho, Malawi, Mozambique, Namibia, South Africa, Swaziland, Tanzania, Uganda, Zambia, Zimbabwe),



seven included specific chapters on pediatric TB and two had dedicated sections. We were unable to obtain the guidelines or data collection forms for drug-susceptible TB from Swaziland. Only one TB guideline and one HIV guideline included a specific pediatric TB diagnostic algorithm, while two countries used score charts for pediatric TB diagnosis. Eight countries collected age-disaggregated TB data on case notifications by age group (<15, 15+) at the district level for reporting to the national program, and two countries disaggregated treatment outcome and/or smear-conversion data. Only three countries disaggregated the <15 age group further (0–4, 5–14, 15+). Three countries using electronic TB registers collected age data for individual patients at the district level, which allows for age disaggregation of data on HIV-testing of TB patients and other relevant indicators at the national level.

**Conclusions and key recommendations:** Several countries have begun to recognize and address the challenge of pediatric TB through specific guidance on diagnosis of TB in children and collection of age-disaggregated data to guide estimates of burden and TB programming. However, more attention and support is needed to further the goal of diagnosing and treating all children with TB, and determining the burden of pediatric TB, especially among children with HIV.

**Disclaimer:** The authors' views expressed in this publication do not necessarily reflect the views of the U.S. Agency for International Development or the United States Government.

#### **EP-131-01 Improvement of paediatric TB case finding after the introduction of a national TB guideline and staff training at Mwenge military RCH facility**

E Chilolo,<sup>1</sup> R Mwanjela,<sup>2</sup> G Haverkamp,<sup>1</sup> J Rwezaura,<sup>1</sup> C Mwanziva,<sup>2</sup> S Mweri,<sup>2</sup> M Nyamkara.<sup>3</sup> <sup>1</sup>Health, PharmAccess, Dar es Salaam, <sup>2</sup>Health, Tanzania Peoples Defense Forces, Dar es Salaam, <sup>3</sup>Health, National TB/Leprosy Program, Dar es Salaam, United Republic of Tanzania. e-mail: echilolo@yahoo.co.uk

**Background:** Tanzania ranks 15<sup>th</sup> among 22 high burden Tuberculosis (TB) countries globally. The country has a TB prevalence of 295/100,000. Children contribute to 9% of the total TB notification (NTLP, 2012). Diagnosis of children with TB in Tanzania remains a great challenge. NTLP expects that children will contribute to 15–20% of total National TB notification when proper TB diagnosis in children is in place. In 2012 the Ministry of Health and Social Welfare (MOHSW) developed a childhood TB management guideline to improve pediatric TB services. PharmAccess, in collaboration with the Tanzania Peoples Defence Forces (TPDF), NTLP and National AIDS Control Program (NACP) conducts mentorship and trainings on pediatric TB to Health Care Workers (HCWs) in 63 TPDF clinics, including Mwenge military Reproductive and Child Health (RCH) facility in Dar es Salaam. Three HCWs were trained on pediatric TB in 2011, 5 in 2012, 6 in 2013, and five clinicians were trained on Chest X-Ray reading/interpretation in July 2013 (Fig.1).

**Objective:** Training and mentorship of HCWs on childhood TB management lead to an increase of TB suspects and TB case finding.

**Methodology:** A review of pediatric TB diagnosis data from TB unit registers, TB presumptive registers and TB contact registers logs from July 2011–March 2014 was conducted. The District TB Coordinator, TB DOT nurses and clinicians were interviewed using a structured questionnaire on the provision of pediatric TB services. The denominator data for children attending Mwenge RCH facility are not available.

#### **Results:**

- Pediatric TB notification for the period from July 2011, 2012, 2013 to March 2014 were 30, 38, 41 and 48 respectively. Children suspected with TB during the same period were 51, 63, 79 and 107 per year.
- From July 2011 to March 2014, 148 children were diagnosed with TB through a chest X-Ray; 9 children through sputum testing.
- 23% of the children diagnosed with TB were TB/HIV co-infected.

#### **Conclusions and key recommendations: Recommendations:**

- Training of HCWs regardless of their cadres as it has great effect on the increase of TB diagnosis in children.
- Integrate pediatric TB screening into RCH services.

#### **EP-132-01 Implementation of a multi-national childhood tuberculosis training targeting high-burden settings**

K Ngo,<sup>1</sup> P Ustero,<sup>1,2</sup> R Golin,<sup>1,2</sup> A Detjen,<sup>3</sup> B Naik,<sup>1</sup> B Dublin,<sup>4</sup> A Mandalakas.<sup>1</sup> <sup>1</sup>Pediatrics, Baylor College of Medicine, Houston, TX, USA; <sup>2</sup>Global TB program, Baylor College of Medicine Children's Foundation - Swaziland, Mbabane, Swaziland; <sup>3</sup>Child Lung Health, The International Union Against Tuberculosis and Lung Disease, Paris, France; <sup>4</sup>Global Health Initiative, Texas Children's Hospital, Houston, TX, USA. e-mail: katherine.ngo@bcm.edu

**Background:** In 2012, children carried 6% of the global TB burden, and 74,000 HIV-uninfected children died from TB. Well-recognized limitations of these estimates contribute to underestimation of the burden of childhood TB. To enhance identification, diagnosis, and treatment of TB in high burden settings, the Global Tuberculosis Program at Texas Children's Hospital conducted childhood TB training targeting physicians and nurses from Baylor International Pediatric AIDS Initiative (BIPAI) sites, their local partners, and National Tuberculosis Program (NTP) managers from 6 Sub-Saharan African countries.

**Intervention:** The Union's Desk Guide for Diagnosis and Management of TB in Children and the World Health Organization (WHO) and The Union joint Child TB Training Manual guided course development. Presenters adapted training materials to address topics highlighted by participants in pre-training evaluations including unique needs of HIV-infected children. Participants were divided into country-specific teams that engaged in problem-based learning. Pre- and post-course assessment measured participant knowledge. Each country team

developed work plans detailing gaps in national and local TB program activities and opportunities to bridge these gaps. Quarterly follow up with designated country representatives measured long-term impact.

**Results and lessons learnt:** Participants' comfort levels for diagnosis, interpretation, and treatment of TB increased following training. "Feeling comfortable with diagnosing pediatric TB" increased from 49% to 94%. 96% of participants "felt comfortable with explaining and prescribing IPT" post-training compared to 21% at baseline. The percentage of IPT questions answered correctly increased by 50% post-training. During follow up, over half of sites reported increased TB program activities including gastric aspiration training, TB journal clubs, partnering with NTPs to develop national pediatric TB guidelines, and utilization of course materials to build capacity in other community clinics.

**Conclusions:** Adaptation of course materials to the specific needs of the learner effectively support short and long term goals for knowledge retention and dissemination. Furthermore, children living with HIV display an increased risk for TB infection and subsequent morbidity and mortality. A childhood TB training course with an emphasis on TB/HIV is imperative to address the more complex and unique treatment needs of this vulnerable population.

#### EP-133-01 A simple intervention improves the reporting of hospital-diagnosed TB in children

K Du Preez,<sup>1</sup> H S Schaaf,<sup>1,2</sup> R Dunbar,<sup>1</sup> H Finlayson,<sup>2</sup> A A Swartz,<sup>3</sup> A Hesselning.<sup>1</sup> <sup>1</sup>Paediatrics and Child Health, Faculty of Medicine and Health sciences, Stellenbosch University, Desmond Tutu TB Centre, Cape Town, <sup>2</sup>Paediatrics and Child Health, Faculty of Medicine and Health sciences, Stellenbosch University, Tygerberg Hospital, Cape Town, <sup>3</sup>Health, Western Cape, Cape Town, South Africa. e-mail: karen\_dupreez@sun.ac.za

**Background:** Diagnostic challenges and limited investigations available at primary health care (PHC) level often result in children with tuberculosis (TB) being diagnosed at hospital level. In settings with decentralised TB services, continuity of TB care between hospital and PHC is challenging and recording and reporting of child TB cases often incomplete.

**Design/Methods:** In 2012 a dedicated TB referral service was established in the paediatric wards at Tygerberg Hospital, a large referral hospital in Cape Town, South Africa, to improve linkage of TB care for children. Allocated personnel completed 1) daily hospital and laboratory-based surveillance, 2) counselling of TB patient caregivers and 3) telephonic follow up with PHC-based TB personnel and caregivers to ensure continuation of care and TB treatment upon hospital referral. Matching of TB cases with the provincial TB registers compared reporting of child TB cases before and after the hospital-based intervention. Pre-intervention surveillance data was limited to culture-confirmed TB cases.

**Results:** During 2012, 408 children with TB (median age 29 months, IQR 12–64; 221 [54%] male) were identified

through hospital and laboratory surveillance. Of these, 285 (70%) children were referred to PHC clinics, 83 (20%) to TB Hospitals, 22 (5%) to secondary/primary level hospitals, 8 (2%) to medium-term care facilities and 10 (3%) died prior to referral. Only PHC clinic referrals were targeted by the intervention (n=285). Continuation of care was confirmed in 280 (98%) children; 225 (79%) were included in routine provincial reporting mechanisms, an increase from the pre-intervention period (125/183, 68%). Compared to pre-intervention, children with culture-confirmed TB were significantly more likely to be reported during the intervention period (125/183 (68%) vs. 83/105 (79%),  $p=0.050$ ). Recording and reporting of deaths prior to referral was also significantly more complete during the intervention period when compared to pre-intervention (0/10 (0%) vs 7/10 (70%);  $p=0.003$  (Fisher's exact test)).

**Conclusion:** A simple hospital-based TB referral service can improve continuity of care and improve recording and reporting of childhood TB in settings with decentralised TB services. Such efforts should be scaled up to improve estimates of TB burden and TB-related morbidity and mortality in children.

#### EP-134-01 Assessment of training to improve quality and quantity of TB screening and referral behavior of Qu'ranic school teachers for residential school pupils

N Shuaib,<sup>1</sup> H Tijjani,<sup>2</sup> B Musa,<sup>3</sup> T. Bot,<sup>4</sup> E H Mitchell,<sup>5</sup> M Gidado,<sup>6</sup> A Habib.<sup>3</sup> <sup>1</sup>Ministry of Health, Jigawa State TB and Leprosy Control Program, Dutse, <sup>2</sup>Ministry of Health, Kano State TB and Leprosy Control Program, Kano, <sup>3</sup>Medicine, Bayero University Kano, Kano, <sup>4</sup>Community Medicine, Ahmadu Bello University Teaching Hospital, Zaria, Nigeria; <sup>5</sup>Research, KNCV TB Foundation/TB CARE I project, Hague, Netherlands; <sup>6</sup>Program, KNCV/TB CARE I project, Abuja, Nigeria. e-mail: msnura@yahoo.com

**Background:** Few pediatric TB cases are diagnosed in Northern Nigeria relative to the magnitude of vulnerable children in the region. Tsangaya boarding Qur'anic schools are widely distributed across northern Nigeria and some parts of West Africa and house 9.5 million children between the ages of 7 and 18. The pupils often live in congregate, communal structures with meager sanitary, hygiene, and sleeping conditions conducive for the spread of communicable diseases including Tuberculosis. The school pupils (almajiris) are typically young, undernourished, poor, isolated from family, and have limited access to healthcare. This study assessed the effectiveness of childhood TB training of Qu'ranic school Teachers (massan) to improve recognition of TB, increase appropriate TB symptom screening and referral behaviour and collaboration with TB DOTS centres in Kano state, North-Western Nigeria. This is the first intervention to address TB in this vulnerable pediatric population.

**Design/Methods:** Multi-stage sampling was employed to randomly select 4 Local Governments Areas of Kano State, and 55 schools with the LGA. Within the selected schools the head teacher and two other teachers were

purposefully selected. Structured KAP questionnaires were administered to the Qu'ranic school teachers and their assistants before the intervention. A cross-over design was employed to train two cohorts of schools at distinct time intervals. Teachers were trained to identify presumptive TB cases and refer to DOTs centres.

**Results:** Islamic educational leaders were open to improving health conditions and training. A total of 148 teachers were trained in two time clusters from 54 schools serving over 16,000 almajiris. All the respondents were male aged between 18 and 75 years; 71% of them were married. Among the respondents, 77% heard of TB and the main source was radio 27.5%. About 16.9% know the cause of TB; 23.6% were aware of the cardinal symptoms of TB. Up to 59.5% of the respondents believed that there are cultural beliefs that prevent people from associating with TB patients, 86.4% of whom believed stigma as the major belief. There were 214 referrals out of which 61 (28.5%) were presumptive TB cases aged between 7 and 17 years.

**Conclusion:** Training Qu'ranic school teachers on presumptive TB cases and referral could improve the knowledge, attitude and practice of Qur'anic teachers and their suspicion and referral behaviour for their pupils to TB DOTS centres.

## POSTER DISCUSSION SESSIONS

### 45. TB IN CHILDREN: EPIDEMIOLOGY

#### PD-1014-01 Comparación entre las características socio-demográficas y clínicas de la tuberculosis infantil por el estado del HIV en Brasil: un análisis jerárquico

E Dias,<sup>1</sup> T Do Prado,<sup>1</sup> E Lima,<sup>1</sup> A Guimarães,<sup>1</sup> E L Noia Maciel.<sup>1</sup> <sup>1</sup>Enfermagem, Universidade Federal do Espírito Santo, Vitória, ES, Brazil. e-mail: eliasvix@gmail.com

**Background:** La tuberculosis (TB) infantil todavía es una de las enfermedades más prevalentes y preocupantes en el mundo, y es la responsable por el 20% de los casos notificados. El surgimiento del HIV, en el inicio de los años 80, ha traído un cambio en el perfil clínico y epidemiológico de la tuberculosis, ya que la infección por el HIV dificulta el diagnóstico en los niños porque los signos y síntomas de las dos enfermedades se superponen. Este estudio tuvo como objetivo comparar las características epidemiológicas de la TB infantil por el estado del HIV, notificados en el Sistema de Vigilancia Nacional.

**Design/Methods:** Analizamos individuos, menores de 15 años, co-infectados TB y HIV (TB - HIV) con aquellos que solo tenían TB, de 1 de enero de 2007 a 31 de diciembre de 2011. Un modelo de regresión logística jerárquica fue realizado, estableciendo un nivel de significancia de 5% e intervalo de confianza de 95%. Los paquetes estadísticos utilizados fueron el STATA 13.0.

**Results:** Comparamos 6091 individuos, donde 780 (12,80%) eran TB -HIV y 5.311 (87,20%) solamente TB. Los niños entre 10-14 años y que residen en la zona rural tienen menos chance de estar co-infectados TB-HIV (OR: 0,73) y (OR = 0,65), son menos probables de hacer el tratamiento supervisado (OR = 0,57). Son más probables de ser institucionalizados (OR = 2,22), tener tratamiento con recidiva (OR = 5,03), retorno pos-abandono (OR = 16,7), tener desenlaces desfavorables del tratamiento de la TB como abandono (OR = 2,85) y muerte por TB (OR = 2,76).

**Conclusion:** Este estudio pone de relieve la importancia del VIH entre los niños con tuberculosis en Brasil. Por otra parte, el análisis multivariado jerárquico permitió justificar las características que pueden explicar las diferencias en la tuberculosis TB-VIH. Puede proporcionar estrategias importantes para el desarrollo de intervenciones de salud pública

#### PD-1015-01 Burden, risk factors and public health implications of childhood TB in Kenya

A Brent,<sup>1,2,3</sup> C Nyundo,<sup>2</sup> J Langat,<sup>2</sup> C Mulunda,<sup>2</sup> J Wambua,<sup>2</sup> E Bauni,<sup>2</sup> M Levin,<sup>3</sup> JAG Scott.<sup>4</sup> <sup>1</sup>Medical Sciences Division, University of Oxford, Oxford, UK; <sup>2</sup>Department of Epidemiology & Demography, KEMRI-Wellcome Trust Research Programme, Kilifi, Kenya; <sup>3</sup>Department of Paediatrics & Wellcome Trust Centre for Clinical Tropical Medicine, Imperial College London, London, UK; <sup>4</sup>Department of Infectious Disease Epidemiology, London School of Hygiene & Tropical Medicine, London, UK. e-mail: dr.a.brent@gmail.com

**Introduction:** Children are at high risk of tuberculosis disease following infection, and may account for up to 40% of cases in high burden settings. However diagnosis is challenging and surveillance data limited. We established intensified case finding and state of the art TB diagnostics to investigate the epidemiology of childhood TB in Kenya.

**Methods:** The study was conducted at Kilifi District Hospital in Kenya, nested within the Kilifi Health & Demographic Surveillance Survey (KHDSS). Between 2009 and 2011 child household TB contacts and children presenting with features of TB were carefully investigated. Incidence estimates were derived using KHDSS denominator data, and adjusted for the sensitivity of hospital-based surveillance using notification, vital registration, verbal autopsy and spatial data. Epidemiological risk factors for TB were identified in a nested case control analysis.

**Results:** The estimated community incidence of microbiologically confirmed and clinically highly probable childhood TB was 46 per 100,000/year for Kilifi. Conservative estimates suggest official notification data underestimate the national burden of childhood TB in Kenya by about two thirds. Known close TB contact, HIV infection and malnutrition were all identified as risk factors. Half of all childhood TB cases were attributable to a known close TB contact.

**Discussion:** This is one of very few prospective incidence studies from high burden countries, the first from East



Africa, and the first to quantify the disease burden attributable to a known close TB contact. It suggests that most cases in Kenya are not currently diagnosed or notified, and that half of all cases are potentially preventable by implementing current recommendations for isoniazid chemoprophylaxis.

#### PD-1016-01 Evolución de la tuberculosis pediátrica 1991–2012

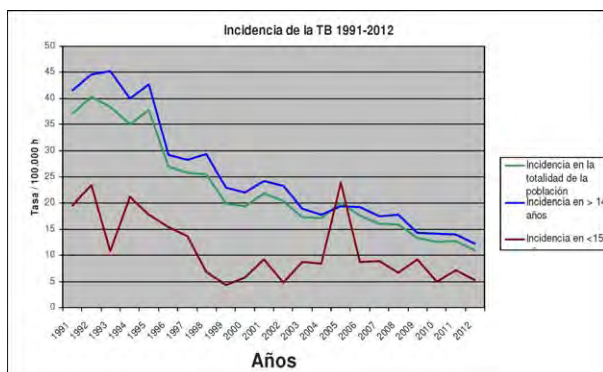
L Clotet,<sup>1</sup> J M Pina Gutierrez,<sup>1</sup> R Sala.<sup>1</sup> <sup>1</sup>Departament de Salut, Agència Salut Pública de Catalunya, Sant Cugat del Vallès, Spain. e-mail: laura-clotet@hotmail.com

**Objetivo:** La tasa de TBC en las comarcas de Vallès Occidental y Vallès Oriental, en el área metropolitana Norte de Barcelona (1.300.000 habitantes) en el período 1991-95 fue >30 casos /100.000 habitantes, mientras que en 2008-12 fue <20/100.000. El objetivo de este estudio es comparar la incidencia y características de la tuberculosis (TBC) pediátrica, enfermos menores de 15 años, en el período 1991–2012, y entre los dos períodos con valores de incidencia más diferenciados.

**Método:** Se han estudiado los casos de TBC declarados a la Unidad de Vigilancia Epidemiológica desde 1991 a 2012. Se ha calculado la incidencia global, en la edad pediátrica y en adultos. Se analizan los factores clínico-epidemiológicos comparando los dos periodos.

**Resultados:** La incidencia de tuberculosis en 2012 es la mas baja de todo el período estudiado tanto en adultos como en niños (figura).

En los casos pediátricos no se encontraron diferencias estadísticamente significativas entre los períodos de 1991-95 y 2008-12 según la edad, sexo, realización del estudio de contactos, localización de la tuberculosis o el cumplimiento terapéutico. Sin embargo se observaron diferencias en cuanto a la frecuencia de inmigrantes (21% en 2008-12 y 3% en 1991-95;  $p<0,001$ ), autóctonos hijos de inmigrante (64% vs 4%;  $p<0,001$ ), detección del caso índice (69% vs 37%;  $p<0,001$ ), y confirmación bacteriológica (33% vs 20%;  $p<0,001$ ).



**Conclusiones:** El descenso de la incidencia de la TBC pediátrica desde 1991 ha sido paralelo a la los adultos. En los años 2008-12 aunque ha disminuido la incidencia las características de los casos han variado respecto a los años de mayor incidencia (mayor frecuencia de inmigrantes), aunque ha aumentado la precisión diagnóstica y la detección de los casos índice, mejorando por lo tanto el

control de la enfermedad, y es de esperar que la incidencia siga disminuyendo.

#### PD-1017-01 Special intervention increases the detection of child TB

S Naha,<sup>1</sup> P Daru,<sup>1</sup> Z Siddique.<sup>1</sup> <sup>1</sup>TB CARE II Bangladesh, University Research Co., LLC, Dhaka, Bangladesh. e-mail: kchakraborty@urc-chs.com

**Background and challenges to implementation:** Though children contribute a significant proportion to the global TB burden, the notification of childhood TB in Bangladesh remains very low. In 2011, the detection of child TB was only 3.15% among all new TB cases detected nationally and it was only 1% in the intervention area. The detection is far behind the global estimation of 11%.

**Intervention or response:** The intervention includes functional linkages with the Graduate and Non-graduate doctors in the rural Sunamgonj district of Bangladesh, the project also extended financial support to the patients who needed investigation other than sputum microscopy. Graduate and non-graduate health practitioners were oriented and met together quarterly under the leadership of Upazila Health Manager (UH& FPO-Govt. Officer) to strengthen the referral system and thus increase the detection of smear negative, EP and child TB cases.

**Results and lessons learnt:** The program established referral linkages with 50 graduate and 246 non-graduate practitioners in 2012 and 2013. With this initiative we have minimized the gap in referral system and diagnostic ability of the patients. Before starting the intervention in 2012, the number of child TB detection in the project area was 136 (all forms). In 2012 and 2013, after implementation, the detection of the same was 185 and 162 respectively; an increase of 21% and 25% respectively compare to 2011. Though the detection of child TB increased in number compare to 2011, the proportion of detection among all the new cases remained same as 1%.

**Conclusions and key recommendations:** The intervention has greater impact in detection of adult Smear Negative and EP TB compare to the child TB detection. Further investigation/analysis needed to explore the specific reasons and design more effective intervention for the children.

#### PD-1018-01 Tuberculosis case finding based on symptom screening among children attending health facilities in southern Nigeria

C Ogbudebe,<sup>1</sup> J Chukwu,<sup>1</sup> C Nwafor,<sup>1</sup> A Meka,<sup>1</sup> N Ekeke,<sup>1</sup> D Oshi,<sup>1</sup> N Madichie,<sup>1</sup> J Ikebudu.<sup>1</sup> <sup>1</sup>Medical, German Leprosy and TB Relief association, Enugu, Nigeria. e-mail: dadasky22@yahoo.com

**Background:** Tuberculosis (TB) is one of the major causes of morbidity and mortality among children especially in the developing countries. In Nigeria the proportion of children among notified cases of tuberculosis remains consistently low at 6% compared to WHO estimate of 10–20%. This study assessed the yield of a tuberculosis

screening project based on symptom screening conducted for children attending public and private health facilities.

**Design/Methods:** Presence of symptoms suggestive of active tuberculosis was investigated by verbal screening in children presenting for any medical condition to 30 health facilities in 6 states in southern Nigeria from 1<sup>st</sup> July to 31<sup>st</sup> December, 2013. Children reporting at least one symptom were referred to a medical doctor/ paediatrician for diagnostic workup.

**Results:** Among 4349 children screened 2.4 per cent of whom were PLHIVs (median age 4.5 years; female 48.3 per cent), 1159 (26.6 per cent) reported at least one symptom suggestive of tuberculosis and were referred to a medical doctor/ paediatrician for diagnostic evaluation. Of them, 621 (53.6 percent) were evaluated for tuberculosis. The rest were not accounted for largely due to recording deficiencies. Tuberculosis was diagnosed in 98 children representing 2.3% of those screened and 15.8 per cent of those evaluated for tuberculosis. It is noteworthy that 20.4 per cent were smear positive TB. About 80 per cent (78) were diagnosed using X-ray and clinical features. All patients were promptly put on treatment.

**Conclusion:** The results show that scaling up TB diagnosis in children through active tuberculosis screening programme based on symptom screening improved detection of TB in children. There is a need to prioritize this strategy in the Nigeria programme.

#### PD-1019-01 Childhood tuberculosis is directly linked to the smear positive tuberculosis case notification rate: results from Amhara and Oromia regions, Ethiopia

B Girma,<sup>1</sup> M Melese,<sup>1</sup> Z Habtamu,<sup>2</sup> M Ligalem,<sup>3</sup> Y Kassie,<sup>1</sup> S Negash,<sup>1</sup> D Jerene,<sup>1</sup> P Suarez.<sup>4</sup> <sup>1</sup>Help Ethiopia Address the Low TB Performance (HEAL TB) Project, Management Sciences for Health (MSH), Addis Ababa, <sup>2</sup>Oromia Regional Health Bureau, Addis Ababa, <sup>3</sup>Amhara Regional Health Bureau, Bahir Dar, Ethiopia; <sup>4</sup>Management Sciences for Health (MSH), Arlington, VA, USA. e-mail: bgirma@msh.org

**Background:** Addressing childhood TB is a high priority area for Ethiopia's National TB Control Program (NTP), as it is in other countries with high burden of TB. However, there is limited information on the burden of childhood TB in Ethiopia. The objective of this analysis was to determine the magnitude of childhood TB in Ethiopia.

**Intervention:** As part of its routine program monitoring, the regional health bureaus with support from the USAID-funded Help Ethiopia Address the Low TB Performance (HEAL TB) project, conducted a descriptive analysis of program data to determine the magnitude of childhood TB 10 zones between July of 2012 and June of 2013. Among children, TB diagnosis is made using smear microscopy or TB diagnostic algorithms. The molecular techniques have very limited role. We used mid-year population estimates to calculate the case notification rate of sputum smear positive (SS+) TB cases

in each zone. We then conducted a Pearson correlation analysis of this data.

**Result:** Of the 35,059 TB cases notified, 12.7% were children ages 0 to 14. There was a wide variation in the proportion of childhood TB cases across the 10 zones. The highest proportion of childhood TB was noted in East Hararghe (18.5%) followed by West Hararghe (15.7%) and the lowest proportion was noted in South Wollo (5.9%). At the zonal levels, a significant positive correlation was found between the proportion of childhood TB cases and the overall SS+ TB case notification rate ( $p=0.01$ ). Although there is a clear correlation between high overall TB case notification and high childhood TB case notification, the zone's diagnostic capacity may contribute to this difference. Among the children with active TB, 2,145 (48.1%) had extra-pulmonary TB, 1,632 (36.6%) had sputum smear negative TB, and 691 (15.5%) had SS+ TB.

**Conclusion:** There was a high prevalence of childhood TB in areas where there was high overall SS+ TB case notification rate. The high rate of childhood TB indicates a high rate of TB transmission in these zones. The relationship between overall SS+ TB and childhood TB should be studied further so TB programs can develop tailored interventions to improve TB control among this vulnerable group.

Summary Table Zones	CNR SS+ TB	% Children among all notified TB cases
Arsi	47.1	13.1
East Gojam	38.7	14.5
East Hararghe	52.8	18.5
East Wollega	32.1	10.4
Jimma	43.8	12
North Gondar	46.8	13.2
North Wollo	22	7.9
South Gondar	26.4	11.1
South Wollo	29.7	5.9
West Hararghe	48.4	15.7
Total	40	12.7

#### PD-1020-01 Tuberculosis in children at BRAC-supported areas: a challenge in case detection

S Reza,<sup>1</sup> S Islam,<sup>1</sup> M Akramul Islam,<sup>1</sup> K Fatema,<sup>1</sup> V Begum,<sup>2</sup> M Hossain,<sup>3</sup> M Siddiqui,<sup>1</sup> MA Husain.<sup>4</sup> <sup>1</sup>HNPP, BRAC, Dhaka, <sup>2</sup>TB, WHO, Dhaka, <sup>3</sup>TB, URC, Dhaka, <sup>4</sup>TB, NTP, Dhaka, Bangladesh. e-mail: shayla.dhaka@gmail.com

**Background and challenges to implementation:** Tuberculosis is one of the public health concerns in Bangladesh. National tuberculosis control programme (NTP) along with partners has improved adult TB patients' diagnosis and treatment but diagnosis of child TB patients is not satisfactory. BRAC a non-government organization is jointly working with NTP to intensify TB services for these particular populations.

**Intervention or response:** In 2010, NTP developed child TB guideline and took new steps for orienting medical doctors of government and private medical doctors including pediatricians. These private medical doctors are oriented to ensure proper referral linkage. The

children who are TB symptomatic and close contact of smear positive TB patients are sent for examination. A child is diagnosed as TB cases after proper assessment done by qualified physician through the simple symptom based approach adopted by NTP. Diagnosed child TB patients are referred to treatment centers for treating under NTP guidelines. BRAC front line health workers ensured DOT and encourage parents to visit medical doctors if there are any complications. NTP also supplied child friendly dispersible drugs to all TB centers.

**Results and lessons learnt:** In 2013, a total of 121,239 TB cases were notified in BRAC supported areas. Of them, 2,865 (2.36%) were child TB cases with 53% female cases and 47% male cases. Among all child TB cases 501 (17%) were new smear positive (NSP), 784 (28%) were smear negative and 1,580 (55%) were extra pulmonary (EP) cases. A total of 1,064 cases were diagnosed in urban areas where around 30% of total population lives. On the other hand, a total of 1,801 cases were diagnosed in rural areas where 70% of total population lives. Available qualified physicians and easy access to diagnostic facilities may have potential impact on child TB case notification in urban areas.

**Conclusions and key recommendations:** The case notification rate of child TB is still low especially in rural areas. Strengthening of diagnostic facilities and capacity of health care providers regarding child TB case notification is essential. Involving the pediatricians in national tuberculosis control programme can contribute a lot in child TB diagnosis and management.

#### PD-1021-01 Urban trend and burden analysis of pediatric tuberculosis in Maharashtra, India: epidemiological trend analysis 2011–2013

O Bera,<sup>1</sup> B Pawar,<sup>2</sup> S Chadha,<sup>1</sup> S Nayak.<sup>1</sup> <sup>1</sup>Union South East Asia Office, International Union against Tuberculosis and Lung Disease, New Delhi, <sup>2</sup>State Tuberculosis Control Society, ADHS, Pune, Maharashtra, India.  
e-mail: oprakash@theunion.org

**Background:** The extent of Tuberculosis (TB) in children is reflection of the pool of infectious adult pulmonary tuberculosis cases in community and their ability to transmit infection. Childhood infection is acquired predominantly from adults. Infection and disease in young children are therefore a measure of recent TB transmission. The objective of the research paper is to analyse and establish burden and trend of Pediatric TB in urban reporting units. Spatial mapping of TB in this population will help design and target interventions for effective TB control.

**Method:** Epidemiological trend analysis was undertaken in all 78 RNTCP reporting units in Maharashtra state and data source was Revised National Tuberculosis Control Programme (RNTCP), Maharashtra quarterly performance reports generated at the units for routine reporting of data for the year 2011, 2012, 2013. Out of the 78 units, 45 are categorized as urban units. According to 2011 census, total population in Maharashtra is 115.3 million and that of urban and rural areas are 34.8 million

and 80.5 million respectively. All verified new TB cases having age less than equal to 14 years reported to the TB reporting units during this period were included in the study; calculated was the (i) proportion of pediatric new TB cases compared to all new TB cases (all ages) (ii) proportion of urban pediatric new TB case compared to all pediatric case Result: Despite urban areas having less than half the population of rural areas yet the pediatric TB case density is three times in urban (107.4 per million) than that of rural (36.8 per million). In the year 2011, 2012, 2013 the total new TB cases (adult & pediatric) were 105457, 105514 and 111450 respectively. Out of the total, pediatric TB cases were 7382(7%), 7386(7%) and 6687(6%) in the year 2011, 2012 and 2013 respectively. Of the pediatric TB cases, it is observed that 4029(54.5%), 3965(53.7%), 3738(55.8%) are from urban reporting units depicting clearly the increased percentage of pediatric TB in urban areas.

**Conclusion:** Although there is a marginal drop in incidence of pediatric TB in Maharashtra, yet gradually the proportion of pediatric TB cases in urban settlements is increasing. Felt need is for strategic urban TB planning and allocation of resources according to case load for improved positive outcomes in childhood TB control.

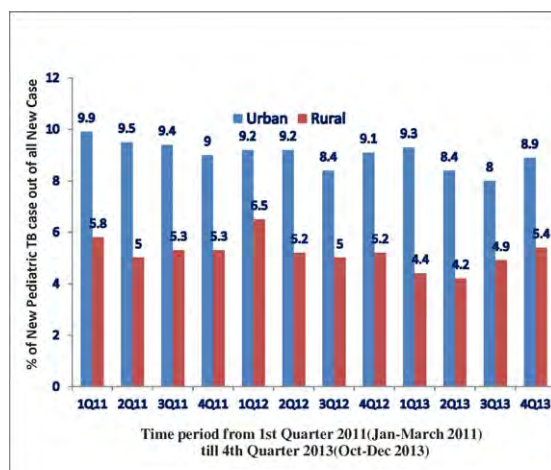


Figure: Burden and Trend of Pediatric TB in urban and rural area of Maharashtra, India (Jan2011-Dec 2013)

#### PD-1022-01 The epidemiological studies of tuberculosis in Latvian children

I Jansone,<sup>1</sup> A Nodieva,<sup>2</sup> I Ozere,<sup>3</sup> R Ranka,<sup>1</sup> I Pole,<sup>3</sup> G Skenders.<sup>3</sup> <sup>1</sup>Laboratory of Molecular Microbiology, Latvian Biomedical Research and Study Centre, Riga, <sup>2</sup>Infectology and Dermatology, Riga Stradins University, Riga, <sup>3</sup>Clinic of Tuberculosis and Lung Diseases, Riga East University Hospital, Riga, Latvia. Fax: (+371) 6744 2407.  
e-mail: intai@biomed.lu.lv

**Background:** Latvia is among the EU countries with relatively high incidence of tuberculosis (TB): 38.1 overall incidence, and 16.6 TB for children and adolescents in the 2013<sup>th</sup>. Taking into account that children TB develops within a year after infection, molecular analysis of their M.tuberculosis (MT) genotypes may give information about actual circulating MT



strains. Aim of this study was to characterize strains and local transmission dynamics of TB among children.

**Design/Methods:** 89 MT isolates (years 2001–2013) from children and all isolates from their suspected infectious contacts were genotyped using spoligo-typing and IS6110 restriction fragment length polymorphism (RFLP) or MIRU-VNTR.

**Results:** Identical genotypes were found for children and suspected adult patients in 55 cases, thus confirming infection transmission. In 20 cases of children isolates the possible infection source showed different genotype, indicating on the existence of undiscovered infection source in an appropriate social group. Absence of any clinical and X-ray positive data from 14 children led us to interpret these data as unclear and to exclude from further analysis. Most of the children's cases of TB were associated with one or two adults with active TB and were restricted only to family or relatives. This study has also revealed small outbreaks of TB, with four to eleven patients in each. From these epidemiologically linked cases following *M. tuberculosis* genotypes were detected: SIT766 is widely distributed genotype in Latvia, SIT50 is rare, while SP57 is not registered in the database SITVIT and was found only in the context of this project. The identified small outbreaks of TB were further analyzed for conditions and factors promoting development of TB in children.

**Conclusion:** About a quarter of children's TB sources are not related to close relatives, therefore there is a need for wider contact tracing.

#### PD-1023-01 Recent trends of childhood tuberculosis in Scotland between 2000–2011

K Lin,<sup>1</sup> L Brondi,<sup>1</sup> J Stevenson,<sup>2</sup> A Smith-Palmer.<sup>3</sup> <sup>1</sup>Centre for Population Health Sciences, University of Edinburgh, Edinburgh, <sup>2</sup>Health Protection Team, National Health Service, Lothian, Edinburgh, <sup>3</sup>NHS National Services Scotland, Health Protection Scotland, Edinburgh, UK.  
e-mail: karen.lin1987@gmail.com

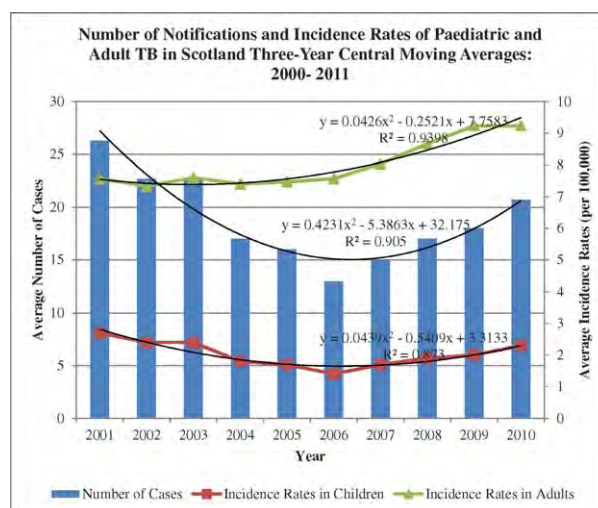
**Background:** Paediatric tuberculosis (TB) is an important and often neglected component of TB programs worldwide. In Scotland, a low TB incidence country, the trends of childhood TB are unique from the rest of the UK and therefore require special attention. We describe epidemiology and determine risk factors of paediatric TB in Scotland from 2000–2011.

**Method:** We describe trends in incidence rates of cases reported to the Scottish TB surveillance system. We also analysed demographic factors, source of infection, gender, region, and age of cases. Carstairs scores were used to determine deprivation by postcode sector. All analysis was conducted using SPSS 19.0.

**Results:** There were 239 cases of TB in children ages 0–15 years, 44.8% of these were under 5 years. Pulmonary TB was the most common presentation (81.5%), with the average age of nonpulmonary cases greater than pulmonary 9.50 years versus 5.9 years ( $p < 0.001$ ). 16.7% of cases were born outside the UK and entered the UK an average of 2.1 years prior to diagnosis. Data suggests age, deprivation, and being UK-born as risk factors for

childhood TB in Scotland. 59.4% of TB was identified through contact tracing with the household being the most common source (53.1%). 59.8% of TB cases had not received BCG vaccine and 90% of non-vaccinated cases were UK-born.

**Conclusions:** Despite low incidence of paediatric TB in Scotland, they are increasing. “UK-born” masks second generation immigration to the UK and are still at increased risk of TB. Areas with greater deprivation have more burden of childhood TB.



#### 46. CLINICAL TRIALS: DRUGS AND VACCINES

##### PD-1024-01 Construction of *Mycobacterium tuberculosis* antigen 85B and human Fc'1 as a fusion protein, to target Fc'R as a delivery system for a vaccine

S Soleimanpour,<sup>1</sup> M Taghiabadi,<sup>1</sup> R Rezaee,<sup>1,2</sup> H Farsiani,<sup>1</sup> A Mosavat,<sup>1</sup> F Sedighinia.<sup>1</sup> <sup>1</sup>Microbiology & Virology Research Centre, Bu-Ali Research Institute, Mashhad University of Medical Sciences, Mashhad, <sup>2</sup>HTLV-1 research centre, Ghaem Hospital, Mashhad University of Medical Sciences, Mashhad, Islamic Republic of Iran.  
e-mail: soleimanpours881@mums.ac.ir

**Background:** The only tuberculosis (TB) vaccine currently available is an attenuated strain of BCG. However, the efficacy of BCG vaccine continues to be debated. Therefore, a more effective vaccine against TB is urgently needed. The components of antigen 85 complex of *Mycobacterium tuberculosis*, due to their immunodominant and secretory nature, represent promising protective antigen candidates and have been used in numerous vaccine preparations.

**Design/Methods:** To construct the Ag85B:Fcγ1 and test our hypothesis, encoding region of Ag85B was PCR amplified from *M. tuberculosis* CDC1551 DNA. Unique XbaI and NotI sites were introduced into primers. Ag85B was cloned into a TA cloning vector and transformed

into DH5 $\alpha$  E. coli. Purified Ag85B then cloned into PDR2EF1 expression vector containing the C-terminal region of the Fc fragment of human IgG1 (Fc $\gamma$ 1). The Ag85B:Fc $\gamma$ 1 fusion protein is containing a linker site of 8 amino acids which had a cleavage site for Xa factor. The resulting fusion protein was expressed from stable CHO cells transfected with the expression vector. Finally the stable production of Ag85B:Fc $\gamma$ 1 fusion protein in engineered CHO cells was measured by immunofluorescence assay (IFA).

**Results:** Our sequencing data shown that Ag85B:Fc $\gamma$ 1 was out of any error and was in frame with Fc $\gamma$ 1 fragment. IFA results showed that Ag85B:Fc $\gamma$ 1 fusion protein was expressed in CHO cell line properly.

**Conclusions:** Fc $\gamma$ 1 fragment of the fusion protein allow APC to bind specifically through Fc $\gamma$ 1 receptors. This is the main point of the present study to understand the effect of selective entrance of antigen into APC. However, this construct should study more to see if the linker site (8 aa between Ag85 and Fc fragment), can affect on immunogenicity of the protein.

#### **PD-1025-01 Increasing engagement of China in tuberculosis (TB) clinical trials: China tuberculosis clinical trial consortium (CTCTC) baseline site assessment**

C D Hamilton,<sup>1</sup> L Li,<sup>2</sup> Y H Liu,<sup>2</sup> Y Zhang,<sup>1</sup> J Bao,<sup>3</sup> R Hafner,<sup>3</sup> S Xu,<sup>2</sup> S Williams.<sup>3</sup> <sup>1</sup>GHPN, FHI 360, Durham, NC, USA; <sup>2</sup>Clinical Center on Tuberculosis, Chinese Center for Disease Control and Prevention, Beijing, China; <sup>3</sup>Division of Allergy and Infectious Diseases, US National Institutes of Health, Bethesda, MD, USA. Fax: (+1) 919 544 7261. e-mail: chamilton@fhi360.org

**Background:** High quality clinical trial sites are urgently needed worldwide to improve the effectiveness of TB treatment strategies. Facilitating development of additional research capacity in emerging markets, such as China, represents a crucial opportunity to promote progress. However, challenges remain in terms of establishing Good Clinical Practice (GCP), research ethics standards, and accredited microbiology laboratories.

**Methods:** The CTCTC is a network with 12 specialized TB hospitals across China and met initially in September 2013 and again in February 2014. Formation of the CTCTC is supported by member hospitals and facilitated by the US NIH (NIAID/DAIDS) which funds FHI 360 (Durham, NC, USA) through Leidos Biomedical Research, Inc. to provide mentoring and training for Network and site capacity building (funded by NCI Contract No. HHSN261200800001E).

**Results:** In preparation for training and capacity building, FHI 360 performed baseline site and TB laboratory assessments based on ICH GCP criteria at 6 CTCTC member hospitals during January 2014. During 2013, a total of 29,336 first-visit pulmonary TB cases were reported from 6 sites assessed, ranging from 2500–6437 cases per site. Multiple-drug resistant cases accounted for 5–15% of TB admissions (Table). All 6 sites have an established ethics committee and have

received GCP training; 5 sites are certified by China FDA to conduct clinical trials of investigational new TB drugs. All sites have been involved in phase IV TB clinical trials funded by the Ministry of Science and Technology of China, while 3 sites have been engaged in multi-center international trials of new TB drugs.

**Conclusion:** Based on the assessments and debriefings from previous TB trial successes and challenges, the development focus will be on training and ongoing monitoring/mentoring to ensure adherence to ICH GCP, research ethics, and Good Clinical Laboratory Practice, with special emphasis on mycobacteriology methods and quality assurance. In addition, work with CTCTC leadership is ongoing to develop Consortium-wide scientific leadership and expertise, as well as an efficient network infrastructure. Development of standards, policies, SOPs and relevant trainings are scheduled during 2014, enrollments to follow.

Site	#1st-visit PTb, 2013	MDR of hospitalized	Children	Living nearby
1	2500	8%	30%	40%
2	6190	15%	5%	60%
3	5198	6%	4.4%	35%
4	2543	12%	0	85%
5	6432	7%	5.5%	58%
6	6473	5%	2.1%	24%

#### **PD-1026-01 PanACEA capacity development: developing self-sustainable clinical TB research sites in sub-Saharan Africa**

A-M Mekota,<sup>1</sup> T Jana,<sup>2</sup> S Lakhi,<sup>3</sup> A Okwera,<sup>4</sup> A Alabi,<sup>5</sup> E Amukoye,<sup>6</sup> G Plemper Van Balen,<sup>7</sup> M Boeree.<sup>7</sup>

<sup>1</sup>Department for Infectious Diseases & Tropical Medicine, Klinikum of the University of Munich (LMU), Munich, Germany; <sup>2</sup>Kilimanjaro Christian Medical Centre, Kilimanjaro Clinical Research Institute (KCRI) Moshi, Moshi, United Republic of Tanzania; <sup>3</sup>Institute for Medical Research and Training, University Teaching Hospital Lusaka, Lusaka, Zambia; <sup>4</sup>Mulago Hospital, Makerere University, Kampala, Uganda; <sup>5</sup>Medical Research Unit, Centre de Recherches Medicales de Lambarene (CERMEL), Lambarene, Gabon; <sup>6</sup>Medical Research Unit, Kenya Medical Research Institute (KMRI), Nairobi, Kenya; <sup>7</sup>Medical Center, Radboud University Nijmegen, Nijmegen, Netherlands. e-mail: mekota@lrz.uni-muenchen.de

**Background:** The PanAfrican Consortium for the Evaluation of Anti-Tuberculosis Antibiotics (PanACEA) is a network of 3 European research institutions and 11 sub-Saharan clinical trial sites. Its objective is predicated on building clinical TB trial capacity while conducting high standard, GCP-conform clinical trials to shorten and simplify treatment. A crucial part of its program is capacity development for bringing together centers from across Africa with diverse infrastructure and training needs. In 2011, a capacity development program, funded by the European & Developing Countries Clinical Trials Partnership (EDCTP), was launched to aid and strengthen the collaborating sites to reach the ultimate goal of achieving self-sustainable TB study sites.

**Intervention:** All centers, in 6 sub-Saharan TB-endemic countries (Gabon, Kenya, South Africa, Tanzania, Uganda and Zambia), self-assessed their requirements for capacity development. Support provided by PanACEA included: 1) Networking: to foster development by implementing activities and platforms to consolidate South-South and North-South collaboration, 2) Training: to strengthen expertise by funding of MSc and PhD students, and conducting a local monitor training program, thereby establishing a central monitoring pool, 3) Conducting Studies: to conduct, mentor and monitor observational and clinical studies (ReMox, MAMS, OEBA, PANEPI, CONFIRM), and 4) Upgrading of Sites: to refurbish laboratory and/or clinical sites.

**Results:** During these 4 years, the program refurbished 6 sites (wards, clinics, laboratories and pharmacies), conducted a monitoring training program for 11 learners, funded 3 master students and 2 PhD students, conducted various epidemiological studies, supported the sites to conduct phase II studies and formed a solid and wide-stretching network for TB research (panacea-tb.net). Our experience has shown, that through our capacity development activities, research sites can be supported and mentored to perform GCP-compliant clinical TB trials, but this depends on sound physical infrastructure, trained and experienced personnel and strong on-site leadership qualities and commitment.

**Conclusion:** We believe that gaining experience through actually conducting clinical TB trials while having the possibility to be mentored, monitored and trained is the best impetus for future self-sustainable research centers.

#### PD-1027-01 Clinical trial with the food supplement Nyaditum resae®: a new tool to reduce the risk of developing active tuberculosis

E Montané,<sup>1,2</sup> AM Barriocanal,<sup>2,3</sup> AL Arellano,<sup>1</sup> A Valderrama,<sup>1</sup> Y Sanz,<sup>1</sup> P Cardona,<sup>4,5</sup> C Vilaplana,<sup>4,5</sup> PJ Cardona.<sup>4,5</sup> <sup>1</sup>Clinical Pharmacology, Hospital Universitari Germans Trias i Pujol, Badalona, <sup>2</sup>Farmacologia, Terapèutica i Toxicologia, Universitat Autònoma de Barcelona, Bellaterra, <sup>3</sup>Unitat Polivalent d'Investigació Clínica (UPIC), Fundació Institut Germans Trias i Pujol, Badalona, <sup>4</sup>Unitat de Tuberculosi Experimental (UTE), Fundació Institut Germans Trias i Pujol, Badalona, <sup>5</sup>Genètica i Microbiologia, Universitat Autònoma de Barcelona, Bellaterra, Spain. e-mail: cvilaplana@gmail.com

**Background:** Based on the basic studies of the Experimental Tuberculosis Unit pointing out an exacerbated inflammation (with massive infiltration of neutrophils and pro-inflammatory cytokines) as a key factor in active tuberculosis (TB) development (PMID: 24291066), Nyaditum resae® has been patented and developed as a new tool to reduce the risk to develop active pulmonary TB through immunomodulation induced by oral tolerance. Nyaditum resae® is manufactured based on a heat-killed environmental mycobacteria (*Mycobacterium manresae* –new proposed specie-). With a wide portfolio of successful preclinical studies, a clinical trial has been

launched to confirm the safety and the immunomodulation of the product in healthy humans.

**Design/Methods:** A double blind, randomized, placebo-controlled CT (ClinicalTrials.gov Identifier: NCT02076139) has been performed with the aim to evaluate the safety and the immunogenicity (specific regulatory T-cells production) of two doses of Nyaditum resae® given orally daily during 2 weeks. A total of 60 healthy volunteers with and without tuberculosis infection (TST+ (n=30) and TST- (n=30)) were enrolled at the Hospital Universitari Germans Trias i Pujol. The correspondent Nyaditum resae® dose or matched placebo was administered and the volunteers followed-up during 6 weeks (with blood samples extracted at days 0, 7, 15 and 42). The primary endpoints were the adverse events and immunogenicity. The statistical analysis is done with SPSS 15.0, by comparing the results between time-points and groups. The protocol and all the procedures were submitted to review and approved by the Ethics Committee of the Hospital.

**Results:** The trial started on March 2014. Safety preliminary results have shown good tolerability of Nyaditum resae®, although some mild gastrointestinal effects have been reported.

**Conclusion:** Preliminary data supports the good tolerability of Nyaditum resae®. The complete definitive data will be presented during the 45<sup>th</sup> Union World Conference on Lung Health, opening a new way to reduce the risk of developing active TB.

**Acknowledgements:** Manremyc (www.manremyc.cat), ISCIII (FIS11/0782, CP13/00174).

#### PD-1028-01 Potential impact of spatially targeted tuberculosis vaccine strategies in Gujarat, India

S Shrestha,<sup>1</sup> S Chatterjee,<sup>2</sup> K Rao,<sup>3</sup> D Dowdy.<sup>1</sup>

<sup>1</sup>Epidemiology, Johns Hopkins School of Public Health, Baltimore, MD, USA; <sup>2</sup>Public Health Foundation of India, New Delhi, India; <sup>3</sup>International Health, Johns Hopkins School of Public Health, Baltimore, MD, USA. e-mail: sshres14@jhu.edu

**Background:** As novel vaccines for tuberculosis (TB) are being developed, it is important to understand how such vaccines might be most efficiently scaled up. For TB vaccines that target adolescents and adults, vaccination of an entire population at high coverage is not feasible. Spatially targeted delivery of a vaccine to geographic “hotspots” of high TB incidence may be one method to optimize the impact of a novel TB vaccine.

**Methods:** We conducted a demonstration study in the state of Gujarat, India, to evaluate the degree of heterogeneity in TB incidence at the level of the “TB Unit” (~500,000 population). We constructed a dynamic transmission model to project the impact of a vaccine with 60% efficacy and 10-year duration of effect, comparing an untargeted vaccination (UTV) strategy in which vaccine is delivered randomly to 8% of the adult population (>20 yrs) in a single mass campaign to a spatially targeted vaccine (STV) that is preferentially delivered to 80% of the adult population in the 10% of



Gujarati TB Units with the highest TB incidence between 2009 to 2012. Both strategies included the same number of total vaccine doses and were augmented by vaccination of 80% of all adolescents turning 10 years old.

**Results:** The TB incidence in the highest decile of Gujarati TB units (i.e., the “hotspot”) was 340 per 100,000/year, versus 229 in the other 90% of the population. The untargeted vaccination strategy reduced TB incidence by 25% after 10 years, whereas the spatially targeted vaccine reduced TB incidence by 27–32%, or an 6–25% additional increase in impact, relative to UTV. The added value of spatial targeting depended largely on the extent of spatial heterogeneity and the level of mixing between the “hotspot” and general population. If a sub-population (10% of the total population) could be identified that had three times the TB incidence of the general population, and in which 5% of all respiratory contacts were shared with the general population, the spatially targeted vaccine had 1.6 times the impact on TB incidence as the untargeted strategy.

**Conclusions:** In Gujarat, a high-burden setting with relatively little spatial heterogeneity at the TB Unit level, spatial targeting of TB vaccines can bring modest but potentially important additional benefits. The benefits could be augmented by identifying populations at higher risk with more daily mixing, perhaps by using smaller spatial scales.

#### **PD-1029-01 Regional prospective observational research for tuberculosis (RePORT) consortia using a common protocol to collect specimens for biomarker research**

C D Hamilton,<sup>1</sup> J Ellner,<sup>2</sup> S Swaminathan,<sup>3</sup> D Christopher,<sup>4</sup> A Gupta,<sup>5</sup> T Sterling,<sup>6</sup> V Cavalcanti Rolla,<sup>7</sup> S Stoszek.<sup>8</sup> <sup>1</sup>GHPN, FHI 360, Durham, NC, <sup>2</sup>Infectious Diseases, Boston University School of Medicine, Boston, MA, USA; <sup>3</sup>HIV/AIDS, National Institute for Research in Tuberculosis, Chennai, <sup>4</sup>Pulmonary Medicine, Christian Medical College, Vellore, India; <sup>5</sup>Center for Clinical Global Health Education, Johns Hopkins University Bloomberg School of Public Health, Baltimore, MD, <sup>6</sup>Infectious Diseases, Vanderbilt University, Nashville, TN, USA; <sup>7</sup>Clinical Research Laboratory on Mycobacteria, National Institute of Infectious Diseases, Fiocruz, RJ, Brazil; <sup>8</sup>Clinical Trials, Westat, Rockville, MD, USA. Fax: (+1) 919 544 7261. e-mail: chamilton@fhi360.org

**Background:** Progress in tuberculosis (TB) clinical research is hampered by a lack of reliable biomarkers that predict progression from latent to active TB, and subsequent cure, relapse or failure. Culture-based results have been the gold standard for predicting efficacy of new candidate vaccines, drugs, and regimes, but are time-consuming. Well-curated samples collected in a standardized fashion with concomitant phenotypic and genotypic metadata could significantly accelerate progress in the development of appropriate biomarkers.

**Methods:** The Indo-US Vaccine Action Program and the US NIH are co-funding 5 teams of India- and US-based investigators, to implement individual cohort studies of active and latent TB in India. Concurrently, Brazil and

the US are co-funding a team of Brazil- and US-based investigators to implement similar studies in Brazil. Though each project carries distinct research aims in its parent protocol (PP), the RePORT project provides a platform for coordinated approaches to clinical TB research. In addition, RePORT researchers have developed an overarching Common Protocol (CP) that defines processes for each observational cohort to collect in-country biorepository specimens. In addition to populating the biorepository with carefully curated specimens, independent regional cohorts linked through the CP should lead to increased clinical TB research capacity.

**Results:** The CP uses standardized TB data elements when available. The CP is patterned on the Global TB Alliance’s CTB<sup>2</sup> protocol to encourage future data sharing. Each site’s PP has been harmonized with the CP to promote efficiencies. RePORT-India anticipates enrolling 5500 active and over 14,000 household contacts (HHC) in parent and CPs. This will yield approximately 275–550 relapse or failure cases and 1300–2500 active TB cases among HHC. RePORT-Brazil will enroll 900 active TB cases and 2700 HCC, anticipating 45–90 relapse or failure cases and 54–540 active TB cases among HHC.

**Conclusion:** The RePORT consortia aim to promote global cooperation among biomarker and clinical investigators for data and specimen meta-analyses. This unique collaboration is being leveraged by other sponsors (e.g., NIH/NICHD and the Bill & Melinda Gates Foundation) to further the development of pediatric and vaccine-related biomarker research.

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#### **PD-1030-01 Urine colorimetry to detect low rifampicin bioavailability: a proof-of-concept study**

L Khensouvann,<sup>1</sup> M Kutzler,<sup>1</sup> P Jotam,<sup>2</sup> T Gumbo,<sup>2</sup> H Schlecht,<sup>1</sup> G Bisson,<sup>3</sup> C A Peloquin,<sup>4</sup> C Vinnard.<sup>1</sup>

<sup>1</sup>Medicine, Drexel University College of Medicine, Philadelphia, PA, <sup>2</sup>Office of Global Health, UT Southwestern Medical Center, Dallas, TX, <sup>3</sup>Medicine, University of Pennsylvania, Philadelphia, PA, <sup>4</sup>Infectious Disease Pharmacokinetics Lab, University of Florida, Gainesville, FL, USA. Fax: (+1) 215 762 3031. e-mail: christopher.vinnard@drexelmed.edu

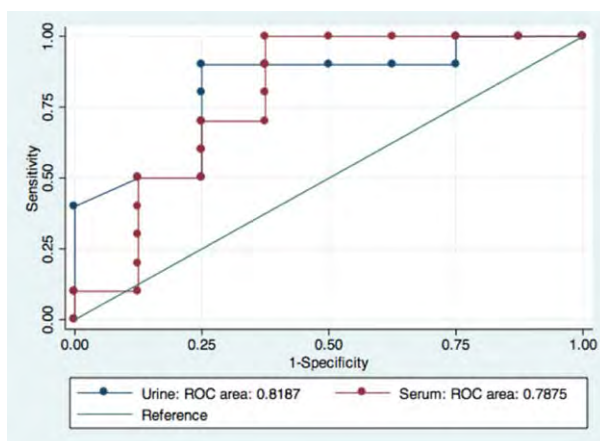
**Background:** Pharmacokinetic (PK) variability of anti-tuberculosis (TB) drugs has been linked to delayed sputum sterilization and the emergence of drug-resistant mutants. Standard approaches for therapeutic drug monitoring during TB treatment are infeasible for many resource-constrained settings. Our objective was to determine whether a simple colorimetric test of urine can identify subjects with low rifampicin bioavailability, defined as either a low maximum serum concentration (C<sub>max</sub>) or a low area under the concentration-versus-time curve (AUC).

**Design/Methods:** We performed a single-dose, non-randomized, open-label, cross-over study of the first-line

anti-TB drugs (rifampicin, isoniazid, ethambutol, pyrazinamide) in 6 healthy volunteers. Each subject completed 3 study visits, corresponding to 3 different anti-TB drug dose sizes (for rifampicin, 150 mg, 300 mg, and 600 mg), and each study visit separated by a wash-out period of at least 1 week. Serum samples were obtained 0, 1, 2, 4, 6, and 8 hours after dosing. Urine samples were collected throughout each study visit, with timed samples at 4 and 8 hours after dosing. For the timed urine sample obtained 4 hours post-dosing, absorbance was read at 475 nm using a Beckman Coulter DU 720 spectrophotometer. Serum PK parameters were estimated by nonparametric analysis using a one compartment model with the ADAPT algorithm Maximum-Likelihood Solution via Expectation Maximization.

**Results:** For the 150 mg dose visit, the mean rifampicin AUC<sub>0-24</sub> was 17.86 mg-hr/L, for the 300 mg dose visit the mean rifampicin AUC<sub>0-24</sub> was 35.45 mg-hr/L, and for the 600 mg dose visit the mean rifampicin AUC<sub>0-24</sub> was 84.01 mg-hr/L. The correlation coefficient (*r*) corresponding to the 475 nm absorbance of a timed urine 4 hours post-dosing and rifampicin AUC<sub>0-24</sub> was 0.78. At a C<sub>max</sub> threshold of 4 microg/ml, the area under the receiver-operating-characteristic (ROC) curve was 0.83, with 89% sensitivity at a specificity of 78%. At an AUC<sub>0-24</sub> threshold of 35 mg-hr/L, the area under the ROC curve was 0.82 (Figure). For comparison, a single serum concentration obtained 2 hours post-dosing had an ROC area of 0.83 to detect rifampicin C<sub>max</sub> < 4 microg/ml, and an ROC area of 0.79 to detect rifampicin AUC<sub>0-24</sub> < 35 mg-hr/L (Figure). Two serum samples obtained 2 hours and 6 hours post-dosing correctly classified all subjects at this AUC<sub>0-24</sub> threshold.

**Conclusion:** Absorbance at 475 nm of a single urine specimen obtained 4 hours post-dosing provided reasonable diagnostic accuracy to detect low rifampicin C<sub>max</sub> and AUC among healthy subjects receiving varying rifampicin dose sizes, performing similarly to a single serum concentration obtained 2 hours post-dosing. In future work we will determine whether pre-analytic extraction of rifampicin and its metabolites from urine can improve diagnostic performance, and validate this approach among TB patients dosed with rifampicin according to standard weight-based bands.



## PD-1031-01 Lipid-body containing, "fat and lazy" *M. tuberculosis* cells increase in the first two weeks of antituberculosis treatment

S Friedrich,<sup>1</sup> XA Kayigire,<sup>1</sup> L Van Der Merwe,<sup>1</sup> A Diacon.<sup>1</sup>

<sup>1</sup>Biomedical Sciences, Stellenbosch University, Cape Town, South Africa. e-mail: svenf@sun.ac.za

**Background:** "Fat and lazy" *M. tuberculosis* cells are characterized by accumulation of intracellular lipid bodies that stain with Nile Red. These cells are believed to represent metabolically less active bacteria that have become tolerant to antibiotics, are hard to grow in culture and require antituberculosis treatment to be continued beyond sputum culture conversion to achieve clinical cure. Little is known about the dynamics of these cells in sputum during treatment.

**Methods:** We collected daily 16-hour sputum samples from 42 patients participating in a 14-day early bactericidal activity study. Smears were heat-fixed, stained with Auramine and Nile Red and examined with high-resolution fluorescence microscopy to count the total number and the number of cells with lipid bodies. The viable bacterial sputum load was determined with colony forming unit (CFU) counts and time to culture positivity (TTP). We correlated cell counts, TTP and CFU with a statistical model adjusting for baseline values.

**Results:** Average total cell count, Nile Red positive cell count, TTP and CFU did not significantly differ between baseline days. After initiation of treatment average TTP increased and average CFU decreased. The average cell count per field dropped significantly upon start of treatment and remained around two thirds of baseline during treatment. The proportion of Nile Red positive cells increased from 3.5% at baseline to just below 50% of the total cell count on day 14 (daily increase of Nile Red positive cells: 17%; 95% CI: 16% to 19%). The increasing proportion of Nile Red positive cells was associated with significantly reduced CFU and increased TTP independent of the total number of cells.

**Conclusions:** Nile Red positive, "fat and lazy" *M. tuberculosis* cells are present in sputum at diagnosis, increase after treatment initiation, and are associated with reduced viable cell recovery in culture. This is, to our knowledge, the first clinical observation of the dynamics of *M. tuberculosis* cells linked to dormancy.

## PD-1032-01 Reporting of outcomes in phase II studies of drug-sensitive tuberculosis

L Bonnett,<sup>1,2</sup> G R Davies.<sup>1</sup> <sup>1</sup>Clinical Infection, Microbiology & Immunology, University of Liverpool, Liverpool,

<sup>2</sup>Biostatistics, University of Liverpool, Liverpool, UK. e-mail: L.J.Bonnett@liv.ac.uk

**Background:** Tuberculosis (TB) remains a major killer amongst infectious diseases. Current treatment involves a four-drug regimen for at least six months. Clinical development of a single novel TB drug is expected to take at least six years. A completely novel combination regimen would require twenty years or more. New drugs and regimens are required to shorten treatment duration, reduce toxicity and combat drug resistance. The optimal

methodology to define the critical path for these regimens is not well-defined. We reviewed historic phase II trials of pulmonary TB in newly diagnosed patients to quantify and rank the efficacy of combinations of seven drugs of interest - ethambutol (E), isoniazid (H), pyrazinamide (Z), rifampicin (R), streptomycin (S), thiacetazone (T), and para-aminosalicylic acid (P), according to endpoints reported in these trials.

**Methods:** Phase II trials of combinations of seven agents for drug sensitive individuals with TB were included in our review. Early clinical endpoints incorporated proportion culture negative at eight weeks and early bactericidal activity (EBA) over two, seven and 14 days. Pooled estimates were obtained via the generalised inverse variance method. In cases where a measure of spread was unavailable, we used the proportion of patients contributed by each study, per drug combination, to estimate a standard error.

**Results:** 49 phase II studies were identified presenting data on 24 drug combinations. 18 studies contributed to the eight week culture negativity results with most evidence being available for the combination EHRZ - nearly 80% of patients will achieve culture negativity by eight weeks according to solid culture results. This is the highest result for any combination considered. 63 studies contributed to the EBA 0–2 day results with most evidence being available for patients on H monotherapy. The pooled result in this case is approximately 0.4 log<sub>10</sub>CFU/ml/sputum although it was difficult to rank the combinations due to the relatively low number of trials. Only eight studies contributed to the EBA 0–7 results and to the EBA 0–14 results and the quality of reporting in these studies was poor.

**Conclusion:** Due to the poor quality of reporting and limited data on the drug combinations of interest, in the absence of individual participant data (IPD), this is the best summary currently available. However, requests for IPD are ongoing. An update with more precise and accurate estimates can be expected in the near future.

#### PD-1033-01 Measles vaccination in children with various forms of tuberculosis infection

S. Kharit,<sup>1</sup> T. Drozdenko,<sup>1,2</sup> I. Dovgaluk,<sup>2</sup> A. Starshinova.<sup>2</sup>  
<sup>1</sup>Vaccination, St. Petersburg Research Institute of Children's Infections, St. Petersburg, <sup>2</sup>Phthiopulmonology, St. Petersburg Research Institute of Phthiopulmonology, St. Petersburg, Russian Federation. Fax: (+812) 591 5788. e-mail: starshinova\_777@mail.ru

**Objective:** Assessment of clinical and immunological characteristics after measles vaccination in children with tuberculosis of intrathoracic lymph nodes.

**Design/Methods:** In department of children's in institute of phthiopulmonology during the period of time 2006–2012 were examined 30 patients age from 3 – 14 years with various manifestations of tuberculous infection. Diagnostic complex included: Diaskintest ® (DST), QuantiFERON-TB Gold (QFT-G) and multislice computer tomography (MCT). After examination were divided children in two groups: I group (n=17) - infected by *Mycobacterium tuberculosis* according tuberculin test

(TT), II group (n=13) - patients with tuberculosis of intrathoracic lymph nodes. All of them were vaccinated against measles vaccine combined live vaccine (measles, mumps, rubella). The vaccination was carried out after 4 months of treatment. We assessed: leucocytes' subsets, the level of cytokine-induced (IL1β,4,6, IFN-γ, TNF-α), common pool of circulating immune complex the phagocytic activity of neutrophils, Ig, antibodies to measles were detected before the vaccination, on the 14th, and 30–45th days after the vaccination.

**Results:** In both groups, the increase was determined by CD16 + cells to the 45Day, in Igroup with 10.0% (CI95% 4–13) to 11 % (CI95% 8.5–16.5), p = 0.02 in IIgroup with 11 % in group (CI95% 10–16) to 14% (CI95% 9–17), p = 0.05. Increase the IgG to day 14 with 7.9 g / L (95 % CI 7.2–9.8) to 10,9 g / L (95 % CI 9.9–11.8), p = 0.01 correlated with the maximum of antibody in these terms. In general, for any one group is not revealed immunosuppressive changes in post-immunization period. Increase in the number of natural killer cells in tuberculosis infection which is characterized by the suppression of T-cell immunity is a positive, as it is directed at the elimination of the pathogen from the body.

**Conclusion:** In children with tuberculosis aggravation of TB infection was not determined, which confirms the immunological safety of vaccination in this group of children. No significant differences in immunological and clinical parameters after vaccine process is not detect in children with infected by *M. tuberculosis* and TB patients.

#### PD-1034-01 Assessment of messenger RNA of *Mycobacterium tuberculosis* as a marker of cure in patients with pulmonary tuberculosis

R. Montenegro,<sup>1</sup> K. Guarines,<sup>1</sup> L. M. Montenegro,<sup>1</sup> L. Lira,<sup>1</sup> J. Falcão,<sup>1</sup> F. Lopes,<sup>1</sup> Fulco Santos,<sup>1</sup> H. Charifker Schindler.<sup>1</sup>  
<sup>1</sup>Imunology, Aggeu Magalhães Research Center - Fiocruz, Recife, PE, Brazil. e-mail: rosana.amontenegro@gmail.com

**Background:** Tuberculosis (TB) is a major public health problem worldwide due to their high rates of morbidity and mortality and transmission rates, although it has an effective treatment and control of the disease. Early diagnosis combined with appropriate therapy is essential for effective control of public programs. The diagnostic techniques, microscopy and culture, used for routine detection of *Mycobacterium tuberculosis* in clinical specimens are lacking in sensitivity and delay in obtaining results, respectively. Culture is considered the gold standard to assess the viability of the bacillus in patients with tuberculosis in the presence of specific treatment, however, being laborious and requires at least 4 weeks for growth of the bacillus, very difficult clinical monitoring and response the patient to antituberculosis drugs. In this context, molecular methods have been developed especially for the technology of polymerase chain reaction (PCR) highlighting the reverse transcription followed by real-time quantitative PCR (RT-qPCR)



using the messenger RNA that expresses well bacillus viability.

**Design/Methods:** The system was evaluated in 98 patients with signs of pulmonary TB were selected: 56 were considered infected with *Mycobacterium tuberculosis* they had positive cultures or evident clinical response to anti-TB treatment. Patients with pulmonary tuberculosis were evaluated by culture and RT-qPCR for a 30-day specific treatment.

**Results:** It was found that both tests demonstrated a decline in viable bacilli at 15 and 30 days after the beginning of the therapy in most of the patients. The quantification of the 85B mRNA target was performed in 52 patients who had initially shown positive results by RT-qPCR and who were followed on the days 15 and 30 after the specific treatment. Thus 85B mRNA was detectable in sputum samples in 52 patients with a confirmed diagnosis of pulmonary tuberculosis on day 0. During the specific treatment the 85B mRNA was detectable in 13 patients on day 15 and in only three patients on day 30.

**Conclusion:** *M. tuberculosis* mRNA in the sputum is a useful prognostic marker and its quantitation, an early and reliable indicator for monitoring response to treatment, drug resistance, re-infection and relapse.

#### **PD-1035-01 The pleiotropic transcriptional response of *Mycobacterium tuberculosis* to vitamin C overlaps with bacterial response to intracellular stresses**

J Tyagi,<sup>1</sup> K Sikri,<sup>1</sup> S Dhingra,<sup>1</sup> M Nandi,<sup>1</sup> N Taneja.<sup>1</sup>

<sup>1</sup> Biotechnology, AIIMS, New Delhi, India. Fax: (+11) 265 88663. e-mail: jstyagi@gmail.com

**Background:** The success of *M. tuberculosis* as a pathogen is attributed to its ability to exist in a persistent state of 'dormancy' resulting in a lifelong latent TB infection. An understanding of bacterial adaptation during dormancy will help to devise approaches to counter latent TB infection. Although in vitro models have provided valuable insights into bacterial adaptation, these models do not disclose the bacterial response in totality to the complex intracellular environment during infection. Here we describe the bacterial response in the vitamin C model of dormancy developed in our laboratory.

**Design/Methods:** We analyzed the global gene expression changes that occur in in vitro *M. tuberculosis* cultures upon exposure to vitamin C by transcriptomics. Subsequently we compared the bacterial response to vitamin C with the bacterial response to numerous intracellular stresses.

**Results:** Vitamin C mediates rapid and extensive changes in gene expression. A total of 280 and 283 genes were up- or down-regulated by  $\geq 1.8$  fold ( $P$  value  $\leq 0.05$ ), respectively. The up-regulated genes were more represented in lipid metabolism, intermediary metabolism and respiration and regulatory protein categories while the down-regulated genes majorly belonged to the virulence,

detoxification and adaptation, information pathways and cell wall and cell wall processes categories.

**Conclusion:** The differential gene expression data from the vitamin C 'dormancy' model was compared with the bacterial response in in vitro models mimicking various intracellular stresses faced by *M. tb* including hypoxia, oxidative and nitrosative stresses, iron limitation, nutrient starvation and exposure to gaseous stresses such as nitric oxide and carbon monoxide and also in the macrophage infection model. This comparative analysis reveals that vitamin C generates a multi-stress environment in axenic bacterial cultures that resembles a macrophage-like scenario and leads to gene expression patterns consistent with those reported in in vitro dormancy models. A detailed characterization of *M. tb* adaptation in the vitamin C 'dormancy' model is expected to suggest useful strategies to counter the adaptive mechanisms essential to dormancy.

#### **47. TB MOLECULAR EPIDEMIOLOGY: FROM LABORATORY DIVERSITY TO OUTBREAK**

##### **PD-1036-01 Genetic diversity and transmission dynamic of *Mycobacterium tuberculosis* causing pulmonary- and extra-pulmonary tuberculosis in Thailand**

A Chaiprasert,<sup>1</sup> P Srilohasin,<sup>1</sup> K Tokunaga,<sup>2</sup> N Nishida,<sup>3</sup> T Prammananan,<sup>4</sup> N Smittipat,<sup>4</sup> S Mahasirimongkol.<sup>5</sup>

<sup>1</sup>Microbiology, Mahidol University, Bangkok, Thailand;

<sup>2</sup>Human Genetics, The University of Tokyo, Tokyo, <sup>3</sup>Research Center for Hepatitis and Immunology, National center for Global Health and Medicine, Chiba, Japan; <sup>4</sup>National Center for Genetic Engineering and Biotechnology, National Science and Technology Development Agency, Pathum Thani,

<sup>5</sup>Medical Sciences, National Institute of Health, Nonthaburi, Thailand. Fax: (+662) 418 2094.

e-mail: angkana.cha@mahidol.ac.th

**Background:** Determination of heterogeneity and the transmission dynamics of circulating *M. tuberculosis* in BCG vaccination country should be benefit for further tuberculosis (TB) vaccine development and TB control strategies. Our study was the first to unveil genetic diversity and transmission dynamic of *M. tuberculosis* after 58 years of BCG vaccination in Thailand.

**Design/Methods:** A total of 1,414 culture-positive *M. tuberculosis* from 1,282 pulmonary TB (PTB) and 132 extrapulmonary TB (EPTB) patients collected during 1998–2011 in Thailand were characterized in this study. All purified genomic DNAs of *M. tuberculosis* strains were typed by developed DNA chip with 51 Single Nucleotide Polymorphism (SNPs) based on DigiTag2 assay under optimized multiplex PCR and hybridization conditions and analyzed the results by comparing with the conventional typing techniques such as large sequence polymorphisms (LSP), spoligotyping and SNP typing. Association between bacterial genotypes among

PTB and EPTB was evaluated using a Chi square test. P value of  $\leq 0.05$  was considered statistically significant. **Results:** 1,414 *M. tuberculosis* clinical isolates were classified into 19 reported Sequence Types (STs) and 9 novel STs belonging to 6 SNP Cluster Groups (SCGs). The SCG2 (44.1%) which included Beijing (BJ) genotype and SCG1 (39.4%) or East-African-Indian (EAI) genotype were predominate in Thailand. Comparing between *M. tuberculosis* causing PTB and EPTB showed similar prevalence trend of *M. tuberculosis* genotypes but genetic diversity was higher in PTB patients. The finding of 10 reported STs and 3 novel STs was considered to be a preferential expansion of SCG2 or Beijing (BJ) genotype especially modern ST10 and ancestral ST19 in Thailand. **Conclusion:** Evidence of an association of the highest prevalence SCG2 (44.1%) and SCG1 (39.4%) with the different age groups of patients implied the presence of difference and genetic advantages among bacterial populations in Thai. The results revealed the significantly increasing cases of patients who were infected with *M. tuberculosis* SCG2 and SCG5 during BCG vaccine implementation, contrasting with the reduction of SCG1.

**PD-1037-01 Tuberculosis among foreign-born persons in Japan: whole genome sequencing analysis of *Mycobacterium tuberculosis* isolates from residents in Tokyo**

N Kobayashi,<sup>1</sup> M Kato,<sup>2</sup> T Miyoshi-akiyama,<sup>2</sup> J Takasaki,<sup>3</sup> M Okada,<sup>4</sup> T Kirikae.<sup>2</sup> <sup>1</sup>Respiratory Medicine, National Hospital Organization Tokyo National Hospital, Kiyose, <sup>2</sup>Infectious Diseases, Research Institute, National Center for Global Health and Medicine, Tokyo, <sup>3</sup>Respiratory Medicine, National Center for Global Health and Medicine, Tokyo, <sup>4</sup>Clinical Research Center, National Hospital Organization Kinki-Chuo Chest Medical Center, Sakai, Japan. e-mail: kobayashin@tokyo-hosp.jp

**Background:** In Japan, the incidence of tuberculosis (TB) has been constantly declining, but the proportion of foreign-born TB cases is gradually increasing (5.2% of all TB patients in 2012). To determine the clinical and epidemiological characteristics of TB in foreign-born populations, we investigated clinical features of foreign-born patients and performed genotypic analysis of *M. tuberculosis* isolates.

**Design/Methods:** We analyzed clinical and microbiological data on foreign-born TB patients treated in National Center for Global Health and Medicine from 2007 through 2012, and determined full genome sequences of 259 *M. tuberculosis* clinical isolates obtained from foreign-born and Japanese-born patients in Tokyo.

**Results:** One hundred seventy eight foreign-born patients with active TB originated mainly from Asia, especially from China, Korea and Philippines. Approximately 30% of them were students including Japanese language school students. Compared with Japanese patients, foreign-born patients are younger and female predominant. Rifampin resistance and multi-drug resistance were more prevalent in foreign-born patients than in Japanese-born patients (2.3% vs 0.3%,  $p=0.002$ ; 1.5% vs 0.2%,  $p=0.018$ , respectively). A phylogenetic tree constructed

by concatenated SNP sequences were clustered into four clades; including East Asian lineage ("Beijing" genotype), Euro-American lineage, Indo-Oceanic lineage and East African-Indian lineage. The proportion of the East Asian lineage isolates from foreign-born patients was significantly smaller than that from Japanese-born patients (47.3% vs 82.7%), whereas that of the Indo-Oceanic lineage from foreign-born patients was significantly larger than that from Japanese-born patients (20.9% vs 2.4%). Of the 259 isolates, 239 had a strain-specific SNP(s). The numbers of strain-specific SNPs of isolates from foreign-born patients were significantly larger than those from Japanese-born patients.

**Conclusion:** *M. tuberculosis* isolates from foreign-born patients are more often rifampin-resistant and multidrug-resistant compared with those from Japanese patients. Whole genome sequencing analysis demonstrated that *M. tuberculosis* isolates from foreign-born patients had more genetic diversity than isolates from Japanese-born patients. Analysis with concatenated SNP sequence will provide a useful tool of TB epidemiology with the combination of conventional genotyping using LSP and SNP markers and IS6110.

**PD-1038-01 Association between the *rpo* gene mutations and multidrug-resistant tuberculosis transmission**

YM Deng,<sup>1</sup> P-C Chuang,<sup>1</sup> WL Huang,<sup>1</sup> LC Kao,<sup>1</sup> R Jou.<sup>1,2</sup>

<sup>1</sup>Reference laboratory of Mycobacteriology, Centers for Disease Control, Taipei, <sup>2</sup>Institute of Microbiology and Immunology, National Yang-Ming University, Taipei, Taiwan. Fax: (+886) 2-2653-1387. e-mail: rwj@cdc.gov.tw

**Background:** Approximately 50–60% of confirmed multidrug-resistant tuberculosis (MDR-TB) is new cases in Taiwan, and the courses remain elusive. The objective of this analysis was to examine the association of putative compensatory mutations in the *rpoA* and *rpoC* genes of rifampin-resistant *Mycobacterium tuberculosis* on MDR-TB transmission.

**Design/Methods:** We analyzed 63 MDR *M. tuberculosis* Isolates of 17 confirmed clusters and 56 representative MDR isolates with unique genotypes selected from our database. Whole genomes of the *rpoA* and *rpoC* genes and a hot-spot region of the *rpoB* gene were sequenced. Isolates were genotyped by spoligotyping and IS6110 RFLP fingerprinting. A cluster was defined as at least 2 isolates having identical RFLP patterns and confirmed epidemiological links. Statistical analyses were performed using the Fisher's exact test.

**Results:** In this study, no *rpoA* mutation was found in 63 clustered isolates, while 5.6% (3/53) non-clustered isolates had concurrent *ropB* S531L and *rpoA* mutations. Moreover, we found 84.1% (53/63) of *ropB*-mutated clustered isolates, and 90.4% (47/52) of *ropB* S531L-clustered isolates carried at least one nonsynonymous mutation in the *rpoC* gene.

**Results** revealed that 29.3% (5/17) of 17 clusters had mutation at codon 483 of the *rpoC* gene. Among 56 non-clustered isolates, 71.4% (40/53) had *rpoB* S531L and

43.3% (23/53) had concurrent rpoC mutations. Whereas only 3.8% (2/53) of isolates with other rpoB mutations harboring rpoC mutations. Among non-clustered isolates, the rpoB S531L was associated with rpoC mutations ( $p=0.003$ ). Preliminary results showed that non-clustered isolates harbored diversified nonsynonymous mutations in the rpoC gene. Putative compensatory mutations at codons 172, 433, 483 and 491 of the rpoC gene were found in both clustered and non-clustered isolates. Furthermore, the rpoC A172V might be an EAI lineage-specific marker.

**Conclusion:** High proportion of non-clustered isolates harboring rpoC mutations might indicate possible future transmission and genetic information could be useful for guiding contact tracing.

#### PD-1039-01 Isoniazid resistance-associated gene mutations and ethionamide resistance among Beijing and non-Beijing genotypes of *Mycobacterium tuberculosis*

WL Huang,<sup>1</sup> KF Chen,<sup>1</sup> R Jou.<sup>1,2</sup> <sup>1</sup>Reference Laboratory of Mycobacteriology, Centers for Disease Control, Taipei, <sup>2</sup>Institute of Microbiology and Immunology, National Yang-Ming University, Taipei, Taiwan. Fax: (+886) 2-2653-1387. e-mail: rwj@cdc.gov.tw

**Background:** To determine association between isoniazid (INH) resistance-associated mutations and ethionamide (ETH) resistance among Beijing and non-Beijing genotypes of multidrug-resistant (MDR) *Mycobacterium tuberculosis*.

**Design/Methods:** MDR *M. tuberculosis* clinical isolates were identified by a standardized drug susceptibility testing (DST) utilizing the agar proportion method.

**Results** of DST to INH and ETH were used for this study. A molecular line probe assay, the GenotypeMTBDRplus test, was performed to identify inhA C-15T and katG S315T gene mutations that conferring INH resistance. We excluded isolates having more than one mutation for this analysis. Spoligotyping was performed to determine Beijing and non-Beijing genotypes. Statistical analyses were performed using the Fisher's exact test.

**Results:** Of the 284 MDR *M. tuberculosis* isolates analyzed, 133 (46.8%) were Beijing and 151 (53.2%) were non-Beijing genotype isolates. We found 76.2% (115/151) of non-Beijing isolates showed high-level INH resistance and 33.1% (50/151) were ETH resistant. Of the 133 Beijing isolates, 71.4% (95/133) of isolates were resistant to high-level INH, and 45.1% (60/133) of isolates were resistant to ETH. Non-Beijing isolates showed high- and low-level resistance to INH were respectively resistant to ETH with inhA C-15T ( $P<0.005$ ) and katG S315T ( $P<0.001$ ) mutations. While Beijing isolates showed high-level resistance to INH were resistant to ETH with inhA C-15T ( $P<0.05$ ) mutation. Moreover, Beijing isolates showed low-level resistance to INH, both inhA C-15T ( $p=0.492$ ) and katG S315T ( $P=0.276$ ) mutations were not associated with ETH resistance.

**Conclusion:** Both inhA C-15T and katG S315T gene mutations could be used to predict cross resistance between INH and ETH among non-Beijing genotype MDR *M. tuberculosis* isolates. Whereas, only the inhA C-15T mutation could predict ETH resistance among Beijing genotype MDR isolates.

#### PD-1040-01 Insights into the population structure of *Mycobacterium tuberculosis* using spoligotyping and RDRio in a prison unit in south-east Brazil

MH Saad,<sup>1</sup> Fe Huber,<sup>1</sup> A Sanchez,<sup>2</sup> S Vasconcellos,<sup>3</sup> S Machado,<sup>1</sup> H Gomes,<sup>3</sup> B Larouze,<sup>4</sup> P Suffys.<sup>3</sup>

<sup>1</sup>Laboratory of Cellular Microbiology, Oswaldo Cruz Institute (IOC), Fiocruz, Rio de Janeiro, RJ, <sup>2</sup>State Department of Corrections, Tuberculosis Control Program and Coordination Management in Prison Health, Rio de Janeiro, RJ,

<sup>3</sup>Laboratory of Molecular Biology Applied to Mycobacteria, Oswaldo Cruz Foundation (IOC), Rio de Janeiro, RJ, Brazil;

<sup>4</sup>Department of Social Epidemiology and Public Health, INSERM, UMR\_S 1136, Pierre Louis Institute of Epidemiology, Paris, France. Fax: (+55) 21 2562 1598. e-mail: saad@ioc.fiocruz.br

In a prison unit in Rio de Janeiro city (RJ), southeast Brazil, with an incidence of 8,185/100,000 tuberculosis cases in 2005, the disease poses a threat to health. A total of 108 *Mycobacterium tuberculosis* complex strains, isolated from 102 inmates as part of a previous TB survey that was realized from 2005–2006, were genotyped using spoligotyping and analysis of the presence of RD<sup>Rio</sup> and LigB<sup>1212</sup> SNP. Spoligotyping identified Latin American Mediterranean (LAM) as being the most prevalent genotype (66.7%,  $n=72$ ) and additional typing of RD<sup>Rio</sup> and LigB<sup>1212</sup> slightly increase this frequency to 69.4%. The LAM2 lineages SIT17 ( $n=23$ ) and SIT179 ( $n=12$ ) comprised one third of all isolates; followed by genotypes Haarlem (11.5%,  $n=12$ ), T (8.7%,  $n=9$ ) and X (5.7%,  $n=6$ ). Strains with unknown signatures represented 5.5% ( $n=6$ ) and four (3.7%) did not match to any lineage. Spoligotyping clustering strains was high (79.6%,  $n=86$ ) composed of 14 clusters and when combined with IS6110-RFLP data, remained high (62%,  $n=67$ ). We observed RD<sup>Rio</sup> among 64/108 (59.2%) isolates and 54 (50%) were of the LAM isolates. In particular, the LAM2/RD<sup>Rio</sup> lineage was significantly associated with clustering ( $p=0.02$ ). Eight strains presented mixed genotypes of RD<sup>Rio</sup> and wild type and calls for attention to superinfection that not necessarily would have been detected by other genotyping assays. Our data show a high frequency of LAM/RD<sup>Rio</sup> in the prison population when compared to that of the general TB cases in RJ and this might be related to the particular conditions related to spread of tuberculosis in this prison. The high clustering found claim for adequate resources for TB control in the prison. Because the risk of developing active tuberculosis is greater among inmates, it is essential that prison medical staff increase their index of suspicion for tuberculosis in inmates with respiratory symptoms, and undertake rapid evaluation of any



suspected cases, and it is essential a structural changes to provide a more friendly environments.

#### PD-1041-01 Genetic diversity of *Mycobacterium tuberculosis* isolates in Cuba, 2009–2010

Y Herrera Avila,<sup>1</sup> D Lemus,<sup>1</sup> C Fonseca,<sup>1,2</sup>

A Marrero Figueroa,<sup>3</sup> R Díaz Rodríguez.<sup>1</sup> <sup>1</sup>National Reference Laboratory of Tuberculosis and Mycobacteria, Institute of Tropical Medicine Pedro Kouri (IPK), Havana, <sup>2</sup>Hospital, IPK, Havana, <sup>3</sup>National Tuberculosis Control Program, Ministry of Public Health, Havana, Cuba. Fax: (+537) 204 6051. e-mail: raul.diaz@infomed.sld.cu

**Background:** The acknowledge of the prevalent *Mycobacterium tuberculosis* lineages is important to understand the origin, evolution and dissemination of the bacterium in a certain geographic area.

**Methods:** A total of 308 *M. tuberculosis* isolates, from all provinces of Cuba and obtained in the 2009–2010 period, were characterized by spoligotyping. The resulting profiles were classified according to the international database SPOLDB4 and using the online bioinformatics tool MIRU-VNTRplus. The changing of genotypes in the time was determined by comparison to the genotypes from 1993–1995 period in the National Spoligo Database.

**Results:** Seventy-nine different Spoligo patterns were found, including 46 no already registered in SPOLDB4. The five most predominant lineages observed were: Beijing (25.6%), S (19.2%), the Latin-American Mediterranean (LAM, 16.9%); Haarlem (16.9%); and T (5.8%). By region, there was a clear predominance of S (West), Beijing (Centre) and LAM (East) genotypes. In relation to the 1993–1995 period, Haarlem and T lineages diminished 13.5% and 18.2%, respectively. There was a dramatic increase of Beijing (14.2%) and S (16.7%) genotype.

**Conclusions:** A high genetic diversity of Cuban *M. tuberculosis* isolates from 2009–2010 was found. The prevalence of *M. tuberculosis* genotypes varied among geographic regions. The genetical population of *M. tuberculosis* in Cuba has changed in the time with an increase of S genotype and the globally-emerging Beijing/W genotype family.

#### PD-1042-01 Correlación entre el estudio genético de las mutaciones de resistencia frente ETB, AMG y FQ y el antibiograma fenotipo en *M. tuberculosis* complex

N Montiel Quezel-Guerraz,<sup>1</sup> M Martínez-Lirola,<sup>2</sup>

P Bermudez,<sup>3</sup> M Ortega,<sup>4</sup> A Sanchez Porto,<sup>5</sup>

MC Dominguez,<sup>6</sup> A Peña Monje,<sup>7</sup> MT Cabezas.<sup>8</sup>

<sup>1</sup>Microbiología, Hospital Costa del Sol, Marbella,

<sup>2</sup>Microbiología, Hospital Torrecardenas, Almería,

<sup>3</sup>Microbiología, Hospital Regional Carlos Haya, Málaga,

<sup>4</sup>Microbiología, Hospital Virgen de la Victoria, Málaga,

<sup>5</sup>Microbiología, Hospital de La Línea, La Línea de la Concepción, <sup>6</sup>Microbiología, Hospital La Merced, Osuna,

<sup>7</sup>Microbiología, Hospital San Cecilio, Granada,

<sup>8</sup>Microbiología, Hospital de Poniente, El Ejido, Spain. e-mail: natalia@hcs.es

**Objetivos:** Correlacionar los resultados obtenidos de detección de mutaciones de resistencia de *M. tuberculosis* complex frente a Etambutol, Aminoglucósidos y Fluoroquinolonas mediante una técnica de biología molecular comercial, frente al estudio fenotípico detectadas mediante técnicas convencionales.

**Material y Métodos:** Hemos estudiado un total de 56 cepas identificadas como *M. tuberculosis* complex provenientes de 40 pacientes. Se estudiaron todas las cepas mediante el kit Genotype MTBDRsl (Hain Life-Science, Germany), que incluye la detección de genes de resistencia de Etambutol (ETB) embB, Fluoroquinolonas (FQ) gyrA y Aminoglucósidos (AMG) rrs; se siguieron las instrucciones del fabricante. Seguidamente, se realiza el estudio de sensibilidad frente a las siguientes drogas en medio líquido en el sistema automático BACTEC/MGIT 960 (Becton-Dickinson, USA): ETB [5.0 mg/ml]; Estreptomina STR [1.0 mg/ml]; Amikacina AK [1 µg/ml], Capreomicina CAP [2,5 µg/ml], Kanamicina KA [4 µg/ml], Ciprofloxacino CIP [1 µg/ml], Ofloxacino OF [2 µg/ml]), con un control de crecimiento. Se incubaba hasta que el control de crecimiento da positivo (index >400) dándose como resistente el tubo con antibiótico en el que se haya detectado crecimiento.

**Resultados:** Mediante Genotype MTBDRsl hemos detectado un total de 11 (19,6%) cepas con mutaciones, distribuidos de la siguiente forma: 3 (5,4%) con mutaciones aisladas en el gen embB (M306V); 2 (3,6%) con mutaciones aisladas en el gen gyrA (una D94H y otra D94G); 1 (1,8%) con mutaciones aisladas en el gen rrs (A1401G); 2 (3,6%) en el gen gyrA (D94A) y en el gen embB (M306V) y 2 (3,6%) en los genes gyrA (S91P), embB (M306V) y rrs (A1401G). Según el estudio de sensibilidad convencional hemos detectado las siguientes resistencias: 20 (35,7%) resistentes a estos antibióticos. Se detectan 8 (14,3%) resistencias aisladas a STR sin mutaciones genéticas asociadas; 8 (14,3%) a ETB, de las cuales, 6 (75%) se correlaciona con mutaciones en el gen embB (M306V); 5 (7,14%) a FQ, de las cuales, 4 (80%) se correlacionan con mutaciones en el gen gyrA (D94H, D94A, D94G y S91P); y 3 (5,4%) fueron resistentes a AMG, de los cuales, 2 (66,7%) tuvieron correlación con mutaciones en el gen rrs (A1401G).

**Discusión:** Existe una buena correlación entre las mutaciones de resistencia detectadas por Genotype MTBDRsl y las detectadas por el método tradicional. Algunas mutaciones de resistencia están todavía por introducir en estos sistemas comerciales y por investigar.

### PD-1043-01 Use of whole genome sequencing to further characterise an outbreak of extensively drug-resistant TB

B Mathema,<sup>1</sup> J Brust,<sup>2</sup> A Narechania,<sup>3</sup> D Verdugo,<sup>4</sup> NS Shah,<sup>5</sup> J Walker,<sup>6</sup> B Kreiswirth,<sup>4</sup> N Gandhi.<sup>7</sup>

<sup>1</sup>Department of Epidemiology, Columbia University, New York, NY, <sup>2</sup>Infectious Diseases, Albert Einstein College of Medicine, New York, NY, <sup>3</sup>Genomics, American Museum of Natural History, New York, NY, <sup>4</sup>TB Center, Public Health Research Institute, Newark, NJ, <sup>5</sup>TB Elimination, CDC, Atlanta, GA, <sup>6</sup>Genomics, Genomic Institute of Novartis Research Foundation, San Diego, CA, <sup>7</sup>Epidemiology, Emory University, Atlanta, GA, USA.  
e-mail: bm2055@cumc.columbia.edu

**Background:** Over the past two decades, numerous multidrug- and extensively drug-resistant tuberculosis (XDR TB) outbreaks have occurred worldwide, often among immunocompromised patients. In South Africa, a widespread drug-resistant TB epidemic, fueled by HIV co-infection, was uncovered in KwaZulu-Natal in 2005. Extensive molecular characterization of *M.tuberculosis* outbreak strains, including spoligotyping, IS6110-RFLP and sequencing of 10 drug resistance genes, revealed identical profiles highly suggestive of clonal spread. Interestingly, social network analysis indicated that the clonal outbreak was due to multiple generations of nosocomial transmission. Current genotyping methods that interrogate <1% of the genome were unable to further discriminate these highly clonal strains. Thus, we are using whole-genome sequencing (WGS) to examine the extent and nature of microvariation and genomic microclusters.

**Methods:** Using next generation techniques, we are generating paired-end WGS data on 50 XDR TB strains from a well-characterized nosocomial outbreak. Each strain is identical by spoligotyping, RFLP, and targeted sequencing of genes: *katG*, *inhA*, *rpoB*, *embB*, *pncA*, *gyrA*, *gidB*, *rrs*, *rpsL*, and *tlyA*. We are determining single nucleotide polymorphisms (SNPs) of all isolates compared to reference strain H37Rv using software programs BWA for short read alignment and SNP calling in SAMtools. We are evaluating both parsimony and maximum likelihood topologies resulting from the SNP matrices.

**Results:** Among the first 18 isolates completed, the average pairwise SNP difference was 11 (range 4–20). The majority of SNPs found were associated with cell wall and cell process (25%), intermediary metabolism and respiration (21%) and lipid metabolism (16%) among genes with assigned functional categories. SNPs were most abundant in Rv2048c (*pks12*) and Rv2931 (*ppsA*) that are involved in biosynthesis and translocation of surface-exposed lipids and have been implicated in antibiotic resistance. Matrices generated from the SNPs identified micro-clusters among 18 the genomes examined; additional genomes from this outbreak will likely produce topologies with robust statistical support.

**Conclusions:** Despite demonstrated clonality, we find evidence of microvariation within these outbreak strains. Estimates of average pairwise SNP differences are higher

than those previously reported, a possible effect of HIV co-infection. We anticipate that as we complete WGS of the remaining isolates discrete microclusters will emerge, which will have diagnostic utility for strain tracking in nosocomial and community settings. Further, these data, along with our epidemiologic analysis, may provide insight into patterns of *M.tb* microevolution in HIV co-infected populations.

### PD-1044-01 Epidemiology of multi-drug resistant *Mycobacterium tuberculosis* in South Africa: a molecular analysis of historical samples

N Maningi,<sup>1,2</sup> L Daum,<sup>3</sup> SA Worthy,<sup>3</sup> JD Rodriguez,<sup>3</sup> N Bapela,<sup>1</sup> G Fischer,<sup>3</sup> JP Chambers,<sup>4</sup> PB Fourie.<sup>1</sup> <sup>1</sup>Medical Microbiology, University of Pretoria, Pretoria, <sup>2</sup>Tuberculosis Research Laboratory, South African Medical Research Council, Pretoria, South Africa; <sup>3</sup>Molecular Biology Laboratory, Longhorn Vaccines and Diagnostics, San Antonio, TX, <sup>4</sup>Department of Biology, University of Texas at San Antonio, San Antonio, TX, USA. Fax: (+27)866883615. e-mail: bernard.fourie@up.ac.za

**Background:** Extensively drug-resistant tuberculosis (XDR-TB) was first specifically recorded in 2006 (MMWR March 24). The situation before this time is not known for strains resistant to the XDR-TB defining drugs rifampicin (R), isoniazid (H), the injectable agents kanamycin, amikacin, or capreomycin, and the indicator fluoroquinolones ofloxacin or moxifloxacin. The aim was to perform line probe assay and whole-genome sequencing for characterisation of known and novel mutations in genes associated with first- and second-line drug resistance (in 20-year old *Mycobacterium tuberculosis* (MTB) clinical isolates.

**Design/Methods:** MDR-TB isolates (phenotypic DST) cultured on Löwenstein-Jensen medium between 1993 and 1995 from the Western Cape and Gauteng Provinces in South Africa and stored at –20°C were re-processed for DNA-extraction and presented for line probe assay (Hain MTBplus and Hain MTBsl) and whole genome sequencing using the Illumina MiSeq platform.

**Results:** Of the 240 MDR-TB isolates, 171 (71.2%) were confirmed by Hain line probe assay as RH resistant. For the rest of the 240 isolates, 44 (18.3%) were mono-resistant to R, 5 (2.1%) were mono-resistant to H, and 20 (8.3%) showed no resistance to R or H. Of the 171 RH-resistant isolates by LPA, 41 samples were sequenced and all confirmed RH resistant. One isolate in the R mono-resistant group was found to be wildtype, all 5 of the H-resistant were confirmed by MiSeq, but only four of the 20 non-RH resistant group shown to be wildtype. This confirms that phenotypic DST performed in 1993 has misclassified a significant proportion of wildtype or mono-resistant strains as MDR-TB, but it also shows that LPA testing would misclassify strains in favour of wildtype. Two of the 240 MDR cultures had mutations on the *gyrA* and *rrs* genes, signifying XDR-TB status. A few other isolates were mono-resistant to quinolones, aminoglycoside or ethambutol, apart from INH and RIF. Mutation in the *rpoB* gene was most

frequent at codon 531, 526 and 516 (43.1%, 25.5% and 7.8% respectively), and in the *katG* gene were frequent at codon 315 (42.2%). We found 7 novel stop codons in the *katG* gene (evolution in *katG* resistance), and 2 mutations in the *inhA* gene (S100A and I200T). **Conclusion:** One isolate had mutations in *rpoB*, *katG*, *gyrA*, *pncA*, *rrs* and *rpsL*. This indicates that, as per the current definition, XDR-TB was rare, but probably already existed in South Africa in the early 1990s.

## 48. MOLECULAR DETECTION OF TB AND DRUG RESISTANCE - II

### PD-1045-01 Line probe assay GenoType MTBDRplus as an effective and rapid tool for the diagnosis of smear-negative tuberculosis in bronchoalveolar lavage fluid

M Irfan,<sup>1</sup> F Idrees,<sup>1</sup> K Jabeen,<sup>2</sup> R Hasan.<sup>2</sup> <sup>1</sup>Pulmonary Section, Department of Medicine, Aga Khan University, Karachi, <sup>2</sup>Pathology and Microbiology, Aga Khan University, Karachi, Pakistan. Fax: (+92) 213 4934294. e-mail: muhammad.irfan@aku.edu

**Background:** The Genotype Line probe assay (MTBDR Plus) has been validated in sputum for rapid diagnosis of tuberculosis (TB) and isoniazid and rifampicin resistance. Its utility in bronchoalveolar lavage (BAL) especially in smear negative cases is unclear.

**Objective:** To evaluate the accuracy of the MTBDR Plus in BAL in sputum scarce/smear negative patients.

**Methods:** Cross sectional study (Jan-Dec 2013) at Aga Khan University, Karachi Pakistan. Suspected pulmonary TB patients who underwent bronchoscopy were selected. Specimens on which both culture and MTBDR Plus was performed were analyzed. Sensitivity and specificity of MTBDR Plus with culture as reference method was determined.

**Results:** Of the 154 patients, 34 had culture-confirmed TB. MTBDR Plus was positive in 20/34 patients [Sensitivity 59% (95% CI: 41% to 75%) & Specificity 95% (95%CI: 89% to 98%)]. A significantly lower proportion was detected by smear compared with MTBDR Plus (29.4% versus 59%;  $p < 0.001$ ). All smear positive (Sm+) /culture positive (CS+) cases were MTBDR Plus positive. The sensitivity and specificity of MTBDR Plus in Sm+/CS+ cases was 100 % and 100% and in Sm-/CS+ cases was 42% and 95% respectively. 114 of 120 culture negative patients were also MTBDR Plus negative. Two cases of MDR TB were identified by MTBDR Plus.

**Conclusion:** MTBDR Plus detected TB cases more accurately and rapidly in BAL than smear with early detection of MDR TB. The use of MTBDR Plus in BAL for TB diagnosis will lead to early and appropriate treatment of such cases in our setting.

### PD-1046-01 Comparison of speedOligo test to Xpert MTB/RIF test for detection of tuberculosis in smear-negative HIV-infected patients

A Okeng,<sup>1</sup> E Kigozi,<sup>1</sup> S Walusimbi,<sup>1,2</sup> S Kyobe.<sup>1</sup>

<sup>1</sup>Microbiology, Makerere University, Kampala, Uganda;

<sup>2</sup>Public Health Sciences, Karolinska Institute, Kampala, Sweden. e-mail: simonwalusimbi@gmail.com

**Background:** Laboratory diagnosis of Tuberculosis (TB) traditionally relies on smear microscopy and culture. However, recent advances in technology have seen the introduction of molecular tests for diagnosis of TB. Molecular tests are more sensitive compared to microscopy and more rapid compared to culture. In addition, molecular tests are useful in speciation of mycobacterium and detection of drug resistant TB which are of increased clinical and public health relevance. We compared a new molecular test called SpeedOligo® DIRECT *Mycobacterium tuberculosis* test (SpeedOligo) to Xpert MTB/Rif test (Xpert) for detection of TB in smear-negative HIV-infected patients. SpeedOligo is a PCR based test, attached to a dipstick used for the qualitative detection of *Mycobacterium tuberculosis* (MTB) and Non-Tuberculosis Mycobacteria (NTM) in clinical samples. Xpert is an automated PCR test used for detection of TB and Rifampicin resistance in a one-off test giving results within three hours. The test can be performed on several types of clinical samples. Xpert was recommended by the World Health Organization as the initial diagnostic for HIV-associated TB since 2010.

**Design/Methods:** One hundred and nine (109) stored sediments obtained from previously processed smear-negative sputum using NALC/NAOH 2%, were tested with SpeedOligo. The SpeedOligo results were compared to the Xpert results which were not available until the final results of SpeedOligo were reported. The SpeedOligo test was performed as per the manufacturers' instructions. The test results of both SpeedOligo and Xpert were then compared to a combination of liquid (MGIT) and solid (L-J) culture results.



**Results:** Of the 109 samples, 79% (86/109) had complete results including those of culture. The sensitivity and specificity of SpeedOligo compared to Xpert were 64% (95% CI: 35%-87%) and 83% (95% CI: 73%-91%) respectively. We observed presence of background bands when the SpeedOligo strips were incubated for the



recommended 5 minutes which were misinterpreted as positive for MTB. Thus, a substantial proportion of tests 57% (12/21) which were positive on SpeedOligo were negative on Xpert and culture.

**Conclusion:** SpeedOligo had moderate sensitivity and high specificity for smear-negative TB when compared to Xpert. Visual interpretation of the SpeedOligo test resulted in a substantial proportion of false positive results which could limit its use for routine patient care

#### **PD-1047-01 The rapid phenotypic assay for simultaneously detection MTB susceptibility to drug combination by mycobacteriophage DNA analysis**

M Vladimirovsky,<sup>1</sup> N Smirnova,<sup>1</sup> Lubo Shipina,<sup>1</sup> K Blagodatskikh,<sup>2</sup> J Alekseev.<sup>2</sup> <sup>1</sup> Department of Laboratory Researchers, Research of Phthisiopulmonology Institute of the First Moscow State Medical University "I. M. Sechenov", Moscow, <sup>2</sup> Scientific Department, "Syntol" Ltd.Co, Moscow, Russian Federation. Fax: (+7) 495 681 5988. e-mail: mvladimirovskij@mail.ru

**Aim:** Development of a phenotypic method for the simultaneous determination of the sensitivity of MBT clinical isolates to combinations of several drugs

**Methods:** We have used eight clinical isolates of *M. tuberculosis* from clinical specimens obtained after the Bactec culture positive results. Cultivation of samples was provided in 1 ml volume Middlebrook media 7H9 with 10% OADC and 4mM CaCl<sub>2</sub> in 24-well plates with drugs at 37°C 48 hours followed by 24 hours incubation with mycobacteriophage D29. Phage was prepared by standard methods after *M. smegmatis* cultivation and counting phage plaques. 5·10<sup>4</sup> PFU of phage were added to each culture. Eight clinical isolates with drug sensitivity to 7 or 8 drugs were studied by known critical and after that subcritical concentrations (MIC) (mcg/ml): STR – 0,35, INH – 0,05, RIF – 0,1, EMB – 0,5, KAN – 0,5, CAP – 0,5, LFX – 0,25, AMK – 0,35. Results of drug susceptibility evaluation were provided by quantitative DNA phage detection with qPCR real-time calculation  $\Delta C_t$  ( $C_t$  drug -  $C_t$  control). 100  $\mu$ l of each MTB sample suspension after 48 hour drug-incubation was cultivated with Middlebrook 7H10 agar in Petri dishes. The drug susceptibility of clinical isolates to MIC drugs was evaluated not only to a single drug, but to combinations of 1-st and 2-nd lines drugs also.

**Results:** All eight clinical isolates showed susceptibility to above-mentioned drugs (besides streptomycin) by conventional Lowenstein-Jensen methods were studied with critical concentration drugs after short-time cultivation and revealed  $\Delta C_t > 2$  (from 2,3 to 6,4) obtained by quantitative DNA D29 phages detection.  $\Delta C_t$  DNA D29 for single MIC drugs ranged from 0.4 to 5.4 and allowed to determine the outcome of a combination of 2 or 3 drugs in this experiment. Summing  $\Delta C_t$  for 3 medicines simultaneously varied from 7.2 to 12. To obtain summing results of several preparations of antibacterial activity was necessary to meet a condition that the  $C_t$  of control test had to be not more than 20. Microbiological results of the culture on agar media after 48 hour

incubation with drug combinations correlated with  $\Delta C_t$  results of D29 DNA analysis.

**Conclusion:** In our study was shown the possibility of rapid detection of anti-TB drugs activity in a few combinations simultaneously to clinical isolates of *M. tuberculosis* by using technique with D29 mycobacteriophages.

#### **PD-1048-01 Role of loop-mediated isothermal amplification (LAMP) assay in rapid diagnosis of extrapulmonary tuberculosis**

A Win,<sup>1</sup> K Aye,<sup>1</sup> Win May,<sup>1</sup> Min Win,<sup>1</sup> Mu Shwe,<sup>1</sup> C Nakajima,<sup>2</sup> Y Suzuki.<sup>2</sup> <sup>1</sup>Department of Medical Research (Lower Myanmar), Research Institute, Yangon, Myanmar; <sup>2</sup>Division of Global Epidemiology, Hokkaido University Research Center for Zoonosis Control, Sapporo, Japan. Fax: (+951) 562061. e-mail: kotoe181@gmail.com

Tuberculosis (TB) is a major public health problem worldwide especially in developing countries. Myanmar is one of 22 high burden TB countries in the world. Extrapulmonary TB (ETB) is an important clinical problem because the radiological and clinical features are often atypical and diagnostic confusion may arise when sputum smears are negative. In Myanmar tuberculous meningitis (TBM) in children and tuberculous lymphadenitis (TB lymphadenitis) in general population are the most frequent causes of ETB. Their diagnoses are often difficult; so a reliable, simple, and rapid diagnostic test that can be performed in any standard laboratory could be helpful. Loop-mediated isothermal amplification (LAMP) is a new nucleic acid detection method that has been successfully implemented in the detection of *Mycobacterium tuberculosis* in clinical specimens. Therefore this study was aimed to determine the role of LAMP assay in diagnosis of ETB by finding out its comparative evaluation with PCR and HPE which were considered as gold standard in TBM and TB lymphadenitis, respectively. A total of 54 suspected cases of TBM with age range of 1 month to 12 years admitted at Yangon Children Hospital were included in the TBM study. CSF samples were tested Polymerase Chain Reaction (PCR) and LAMP for detection of *M. tuberculosis*. Twenty-nine out of the 54 (54%) suspected TBM patients were PCR positive and 25 out of 54 (46%) cases were PCR negative. Twenty-five out of 29 PCR positive cases and 4 out of 25 PCR negative cases were positive by LAMP assay. The LAMP method yielded a sensitivity of 86% and a specificity of 84%, compared to the PCR assay for TBM diagnosis. The positive and negative predictive values of LAMP were 86% and 84%, respectively. In the study of TB lymphadenitis, a total of 72 left over paraffin embedded lymph node samples from Pathology Department were investigated. Out of them, 55 (76%) were diagnosed as TB lymphadenitis and 17 (24%) were non TB lymphadenitis by HPE. LAMP diagnosed 57 (79%) and 15 (21%) as TB lymphadenitis and non TB lymphadenitis, respectively. The sensitivity of LAMP compared to HPE was 93% and the specificity was 65%. The positive and negative predictive values of LAMP were 89% and 73 %, respectively. As a result,

LAMP method is anticipated for the detection of *M. tuberculosis* from biological samples of ETB and is expected to become extensively apply especially in low-resource areas because of ease of application and cost effectiveness.

#### PD-1049-01 Construction of a three colour single-tube assay for resistance to first, second and third line antibiotics

M De Vos,<sup>1</sup> J Rice,<sup>2</sup> P Van Helden,<sup>1</sup> R M Warren,<sup>1</sup> W Wangh.<sup>2</sup> <sup>1</sup>Biomedical Sciences, Stellenbosch University, Cape Town, South Africa; <sup>2</sup>Biology, Brandeis University, Waltham, MA, USA. e-mail: margab@sun.ac.za

**Background:** Detection and treatment of XDR-TB requires rapid detailed analysis of the extent of resistance to first, second, and third line antibiotics. We are constructing such the requisite assay by combining components of other, independently tested LATE-PCR assays.

**Design/Methods:** A multiplexed single-tube LATE-PCR reaction has been constructed that simultaneously generates single-stranded DNA amplicons for the first line (rifampicin and isoniazid) and second line (fluoroquinolone, aminoglycoside/polypeptide and ethionamide) antibiotics. Gene targets for each class of antibiotics are analyzed at end-point in the same tube by hybridization to sets Lights-On/Lights-Off probes labeled in a three colors, one for each class. The reaction also contains an amplifiable and a non-amplifiable internal control to guarantee reliability and a proprietary reagent is included to ensure primer specificity throughout amplification.

**Results:** A large number of strains that harbor various combinations of alleles in the 1<sup>st</sup>-line (*inhA*, *katG*, *rpoB*); 2<sup>nd</sup> and 3<sup>rd</sup>line (*gyrA*, *gyrB*, *eis*, and *rrs1401*) gene targets are being analyzed using this assay in order to generate a library of fluorescent signatures that can distinguish all drug resistant mutations from H37Rv, a drug sensitive reference strain, as well as from each other. Each strain containing a variant sequence displays its own fluorescent signature in the appropriate color within the temperature range assigned for binding of the relevant probes. This reference library can then be used with appropriate software for comparison clinical samples and thereby determine detailed nature of drug resistance in that particular MDR-TB or XDR-TB patient.

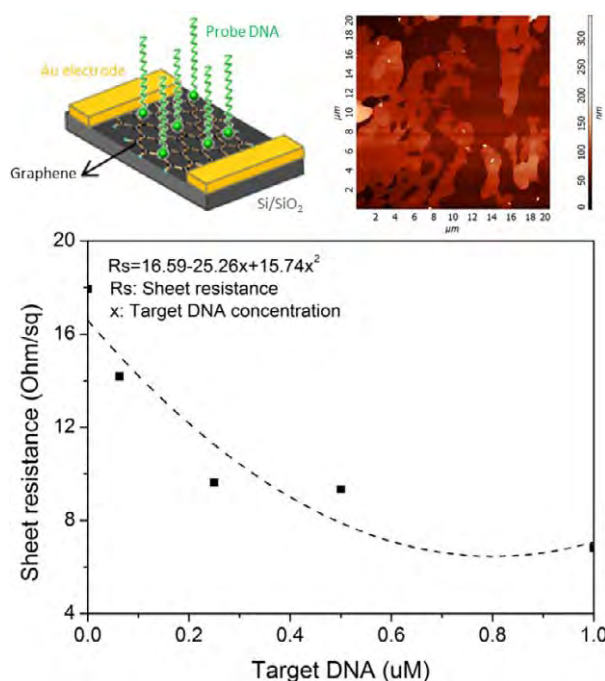
**Conclusion:** This assay offers the promise of a future kit that can be used in a fully automated system whose read-out will enable a health care provider to make a rapid, detailed diagnosis and thereby to immediately decide on an optimal, personalized course of treatment for each patient. Because the assay described here only uses three fluorescent colors, it could potentially be expand for analysis of the *tlyA* gene responsible for resistance to capreomycin in another color. Support by NIH Grant R01 A1099532, and Hain Lifescience.

#### PD-1050-01 Carbon nanotube and graphene based sensors for tuberculosis detection

F Rumiche,<sup>1</sup> G Lucero,<sup>1</sup> B Castaneda,<sup>2</sup> F Zvietcovich,<sup>2</sup> F Casado,<sup>2</sup> M Guzman.<sup>1</sup> <sup>1</sup>Grupo de Investigación en Nanomateriales, Pontificia Universidad Católica del Perú, Lima, <sup>2</sup>Laboratorio de Imágenes Médicas, Pontificia Universidad Católica del Perú, Lima, Peru. e-mail: frumiche@pucp.edu.pe

**Background:** Tuberculosis (TBC) affects about nine million people per year worldwide. Current methods used for the diagnosis of tuberculosis include radiology, sputum collection, microbiological culture, tuberculin test (TST), polymerase chain ration (PCR) and immunological assays. Every method exhibits particular advantages. However, they also have limitations in terms of sensitivity and specificity, cost, and the necessity of specialized personnel or infrastructure. Therefore, there is still an essential need to implement new methods of diagnosis highly reliable, fast and affordable. In this work, we propose and evaluate a nanostructured biosensor for diagnosis of tuberculosis.

**Design/Methods:** Thin film configuration sensors with an active area of 3x5 mm<sup>2</sup> were fabricated by functionalizing single wall carbon nanotubes (Sigma Aldrich CAS 308068-56-6, semiconductive: 98%) and graphene (Graphene Supermarket Monolayer Graphene) percolation networks with TBC complementary DNA strands (*Mycobacterium tuberculosis* H37Rv). Nanomaterials and fabricated nanostructures were characterized by optical microscopy, scanning and transmission electron microscopy, atomic force microscopy and Raman spectroscopy. The sensor electrical resistance variation (between baseline and after hybridization with target DNA, concentration range: 0.05-1 uM) was used as the sensing parameter.



**Results:** Single wall carbon nanotube based sensors exhibit a variation in the electrical resistance after hybridization with target DNA. However, no monotonic correlation between electrical resistance and TBC concentration was observed. A maximum sensitivity of detection, defined as the ratio between baseline resistance and post DNA hybridization resistance; of 68% was attained, for a target DNA concentration of 1 uM. Graphene based sensors also exhibit a variation in electrical resistance when exposed to TBC, moreover, sensitivity increases linearly with the square root of DNA target concentration, attaining a maximum value of 62% for a concentration of 1 uM.

**Conclusion:** We have successfully fabricated carbon nanotube and graphene based nanostructured sensors for TBC detection. Sensors are capable of producing a change in their electrical resistance when hybridized with DNA target. Particularly, graphene based sensors stand as a promissory alternative to implement functional devices for further experimentation.

#### PD-1051-01 Clinical validation of PrimeStore Molecular Transport Medium® for PCR-based detection of *Mycobacterium tuberculosis* in sputum samples

R Peters,<sup>1</sup> L Daum,<sup>2</sup> S Omar,<sup>3</sup> N Ismail,<sup>3</sup> G Fischer,<sup>2</sup> B Fourie.<sup>4</sup> <sup>1</sup>Anova Health Institute, Johannesburg, South Africa; <sup>2</sup>Longhorn Vaccines & Diagnostics, San Antonio, TX, USA; <sup>3</sup>TB Reference Laboratory, National Institute for Communicable Diseases, Sandringham, <sup>4</sup>Medical Microbiology, University of Pretoria, Pretoria, South Africa. e-mail: rph.peters@gmail.com

**Background:** PrimeStore Molecular Transport Medium® (PS-MTM) for collection and transport of sputum samples for molecular analysis of MTB has been claimed to preserve the integrity of mycobacterial DNA during transport at ambient temperatures. In this study, we compared results from sputum samples transported in PS-MTM with results from routine assays on the remaining sputum volumes.

**Design/Methods:** We present preliminary data on paired sputum specimens from 141 patients, one tested by MGIT and the other by Xpert. MGIT or Xpert positive samples (n=47) were matched to negatives (n=94) in a 1:2 ratio, and their stored associated PS-MTM aliquots sent to San Antonio by air at ambient temperatures for DNA extraction (PrimeXtract™) and real-time PCR (PrimeMix MTB®; IS6110 target).

**Results:** Concordance rate between Xpert and MGIT on the patient sample pairs was 92%, for PS-MTM with MGIT 87%, and 83% for PS-MTM with Xpert; this was not statistically different (Table 1). Compared to MGIT and Xpert, PS-MTM was positive in 20 additional cases and negative in 6. There was an indication of *M. tuberculosis* infection in 9 cases with isolated positive PS-MTM result as suggested by either concordant positive result for both PS-MTM samples (IS 6110) and/or positive PCR test for a second gene target (IS 1081) and/or positive Xpert test on an aliquot of sputum specimen used for MGIT. If these are included in a

composite standard with positive result for MGIT and/or Xpert, the detection rate for *M. tuberculosis* by PS-MTM (86–89%), MGIT (88%) and Xpert (89%) is similar.

**Conclusion:** This collection to detection system is a promising, and easy-to-use method for molecular detection of *M. tuberculosis*, allowing sputum samples from rural settings to be transported to central testing sites. Concordance of downstream molecular testing of PS-MTM samples with MGIT and Xpert MTB/Rif is good; rapid preservation of DNA in PS-MTM may have resulted in identification of cases that were undetected by routine methods due to sample degradation.

Table 1. Comparison of methods for detection of *Mycobacterium tuberculosis* in sputum samples

Comparison	Sputum sample	Concordant, positive	Dis-cordant, PS-MTM positive	Dis-cordant, PS-MTM negative	McNemar test for difference between tests
Xpert MTB/Rif and culture (MGIT)	Different samples	91.5%	n/a	n/a	Not significant
PS-MTM and culture (MGIT)	Same sample	86.7%	11	6	Not significant
PS-MTM and Xpert MTB/Rif	Same sample	80.3%	18	4	Not significant

#### PD-1052-01 GenoType® MTB-DRplus assay for molecular detection of multidrug-resistance in *M. tuberculosis* from slides and filter paper cards in Madagascar

MS Rabodoarivelo,<sup>1</sup> M Cnockaert,<sup>2</sup> JC Palomino,<sup>2</sup> P Vandamme,<sup>2</sup> V Rasolofo Razanamparany,<sup>1</sup> A Martin.<sup>2</sup> <sup>1</sup>Mycobacteriology, Institut Pasteur de Madagascar, Antananarivo, Madagascar; <sup>2</sup>Biochemistry and Microbiology, Laboratory of Microbiology, Gent, Belgium. e-mail: msylvianne@pasteur.mg

**Background:** Tuberculosis (TB) remains a global public health concern. Diagnosis of TB in many regions of the world, particularly in developing countries, remains based on sputum smear microscopic examination. The treatment of TB usually starts without the results of culture and drug susceptibility testing (DST) being known, due to the lack of other rapid and adequate tests and the need for trained staff, and specific equipment or infrastructure. In clinical practice, difficulties involved in the collection and shipment of samples have also been a major issue, and detection of drug resistance in low-resource countries is often hampered by the limitations of transport and storage of sputum samples from remote locations to the reference laboratory. The aim of this project was to evaluate a DNA-based method for timely detection of resistance to rifampicin (RMP) and isoniazid (INH) from DNA obtained from sample slides or filter cards, such as the FTA card system (Whatman International Ltd) and the GenoCard (Hain Lifescience, Nehren, Germany), used at



the reference TB laboratory of Antananarivo, Madagascar, where the incidence of TB is high.

**Design/Methods:** The feasibility of DNA extraction from these different supports and from sputum kept in ethanol for the subsequent detection of RMP and INH resistance using the commercial kit GenoType MTBDRplus (HAIN) was investigated. Sequencing method was considered as the reference method. For biosafety reasons, we assessed the viability of the bacilli in these stored samples.

**Results:** No viable bacteria were found from paper card inactivated by alcohol and from slide and ethanol systems. DNA extraction from the different systems was standardized by using Chelex solution. Resistance to RMP and INH from extracted DNA was readily detected by Genotype MTBDRplus and concordance of resistance profile was found between Genotype MTBDRplus and sequencing.

**Conclusion:** This may accelerate the detection of resistance and will have important impact in control of drug-resistant TB. The main achievements will be the simultaneous identification and genotypic detection of RMP and INH resistance from sputum slides, commercial card formats and alcohol-preserved sputum samples, collected in remote areas for safe shipping and long-term storage, while preserving the integrity of the DNA for PCR.

#### **PD-1053-01 Assessment of performance of the real time PCR in different biological samples used for diagnosis of extra-pulmonary tuberculosis**

F Fulco Santos,<sup>1</sup> L Lira,<sup>1</sup> A Peixoto,<sup>1</sup> LM Lapa Montenegro,<sup>1</sup> R Montenegro,<sup>1</sup> J Costa Lima,<sup>1</sup> G Guedes,<sup>1</sup> H Schindler.<sup>1</sup> <sup>1</sup>Imunology, Centro de Pesquisa Aggeu Magalhães, Recife, PE, Brazil.  
e-mail: fcfulco@hotmail.com

**Background:** Among all infectious diseases that afflict humans, tuberculosis (TB), caused by *Mycobacterium tuberculosis*, remains the most lethal. In Brazil, were reported in 2009, 10,164 new cases of extrapulmonary tuberculosis, and 605 in the State of Pernambuco. Control of the disease lies in an accurate diagnosis and a dynamic treatment to patients, interfering with the transmission chain.

**Design/Methods:** Control of the disease lies in an accurate diagnosis and a dynamic treatment to patients, interfering with the transmission chain. However, conventional diagnostic methods have limitations such as low sensitivity and time required. In order to determine the sensitivity and specificity of molecular techniques in the diagnosis of TB, we sought to evaluate the performance of Real-Time PCR in various samples of patients with suspected extrapulmonary TB treated in public hospitals in Pernambuco.

**Results:** We selected 57 patients of both sexes, included 1–89 years with clinical suspicion of extrapulmonary TB. The final diagnosis was established by the physician using criteria epidemiological, clinical and laboratory,

and subsequently compared to the results of qPCR. 146 biological samples were analyzed, including 49 blood, 46 urine, 27 biopsies, 21 other liquids. Of the 57 patients, 38 had a final diagnosis of extrapulmonary TB, with 28 qPCRs positive, with a sensitivity of 71.8% and specificity of 88%. Regarding the type of sample, the blood had a sensitivity of 55.9% and specificity of 80 %, urine 33.3% and 100%, biopsy 43.8% and 100% other liquids 28.6% and 100% respectively.

**Conclusion:** Taken together, blood and / or urine showed 62.9% sensitivity and 73.3% specificity, indicating that the higher the number of samples collected, the greater the likelihood of positive test. The qPCR in patients with extrapulmonary and paucibacillary is a fast, sensitive, and for the detection of *M. tuberculosis* in biological samples become a useful tool in the diagnosis, contributing to control the disease in these patients.

#### **PD-1054-01 Comparison of Longhorn PrimeSwab™ HydraFlock® and Copan FLOQSwabs™ for detection of *Mycobacterium tuberculosis* using real-time PCR and next-generation**

LT Daum,<sup>1,2</sup> SA Worthy,<sup>1</sup> JD Rodriguez,<sup>1</sup> M Karamchi,<sup>3</sup> JP Chambers,<sup>2</sup> ES Maliff,<sup>3</sup> TL Templet,<sup>3</sup> G Fischer.<sup>1</sup>

<sup>1</sup>Molecular Biology, Longhorn Vaccines & Diagnostics, San Antonio, TX, <sup>2</sup>Molecular Biology, University of Texas at San Antonio, San Antonio, TX, <sup>3</sup>Molecular Biology, Puritan Diagnostics, Guilford, ME, USA.

e-mail: longhorn-vandd@sbcglobal.net

**Background:** Robust specimen collection is critical for all molecular diagnostic applications. Sensitive real-time PCR detection and next-generation sequencing (NGS) rely on high quality nucleic acids where the swab contains consistent and sufficient material. PrimeStore Molecular Transport Medium® (MTM) is a collection and storage solution that safely inactivates bacteria and viruses, including *Mycobacterium tuberculosis* (MTB) while preserving DNA/RNA at elevated temperatures for prolonged periods.

**Specific Aim:** Carry out molecular detection by real-time PCR using two commercially available flocked swabs containing low and high MTB concentration, and subsequent NGS analysis.

**Methods:** For fluid absorption comparison, Longhorn PrimeSwab™ HydraFlock® (Puritan Diagnostics, Guilford, MA, USA) and Copan FLOQSwabs™ (Copan Diagnostics, Brescia, Italy) were placed in PrimeStore MTM® (Longhorn Vaccines, San Antonio, TX, USA) or nuclease-free water and retention volumes were determined by pre and post weight measurement. For molecular detection, swabs were swirled in MTB culture at low ( $2.7 \times 10^2$  CFU/mL) and high ( $2.7 \times 10^4$  CFU/mL) concentration and subsequently placed into PrimeStore® collection medium. MTB collected from swabs were subjected to nucleic acid extraction, real-time PCR (ABI 7500, LifeTech) and NGS (MiSeq, Illumina, San Diego, CA, USA).

**Results:** Using PrimeStore MTM® and nuclease-free water, PrimeSwab™ exhibited an average retention volume of 199 µl (SD=12) and 191 µl (SD=7) respectively, compared to 170 µl (SD=13) and 166 µl (SD=12) using Copan FLOQSwabs™. Real-time PCR cycle threshold (CT) values for low and high concentrations of MTB obtained by collection using PrimeSwab™ were 30.3 (SD=0.7) and 24.7 (SD=0.3), respectively, compared to 34.6 (SD=1.0) and 27.8 (SD=0.7) using Copan FLOQSwabs™. NGS of MTB from PrimeSwab™ revealed 443,562 total mapped reads with an average genomic coverage of 14.5X, compared to 310,234 reads and 9X coverage using Copan FLOQSwabs™.

**Discussion:** The Longhorn PrimeSwab™ HydraFlock® exhibited greater retention volume (~30 µl higher), equating to superior real-time PCR CT values and NGS metrics, compared to Copan FLOQSwabs™. There is significant need for safe and efficient transport of specimens especially in areas without consistent refrigeration and BSL-3. Thus, PrimeSwab™ and PrimeStore MTM® are important means for specimen collection/transport for molecular detection and NGS.

#### PD-1055-01 Association of *eis* and *rrs* gene mutations with phenotypic second-line injectable drug resistant patterns of *Mycobacterium tuberculosis*

L Malinga,<sup>1,2</sup> J Brand,<sup>1</sup> A Stoltz,<sup>2</sup> M Van Der Walt.<sup>1</sup>

<sup>1</sup>MRC TB Office of Research, South African Medical Research Council, Pretoria, <sup>2</sup>Internal Medicine, University Of Pretoria, Pretoria, South Africa. Fax: (+012)324 7922. e-mail: lesibana.malinga@mrc.ac.za

**Background:** Molecular drug susceptibility testing (DST) based on detection of mutations will improve rapid detection of second-line injectable drugs (SLID) resistance of Amikacin (AMK), Kanamycin (KAN) and Capreomycin (CAP). Resistant (R) profiles of SLID remain dependent on phenotypic DST despite advancement of rapid molecular technology. Possible cross and dual resistance phenomenon exists within SLID further complicating molecular diagnosis based on single nucleotide polymorphism (SNP). The study objective is to associate SNPs with phenotypic drug resistant cases of SLID.

**Design/Methods:** We examined 122 *Mycobacterium tuberculosis* isolates with phenotypic drug resistant profiles to AMK, KAN and CAP tested by MGIT 960 using WHO critical concentrations. Molecular DST was performed on MTBDRsl assay to determine molecular resistant markers within *rrs* gene associated with SLID. Sanger sequencing of *rrs* and *eis* genetic regions was performed to resolve discordance found between MGIT 960 and MTBDRsl.

**Results:** Of 122 isolates with MGIT results evaluated, 47 (38%) were cross resistant to AMK/KAN/CAP. The dual resistant cases were both 10 (8%) for AMK/KAN and AMK/CAP while 4 (2%) for KAN/CAP. Mono-resistant cases of KAN and CAP were 20 (16%) and 31 (25%) respectively. The MTBDRsl assay detected 22 (47%) and

1 (10%) cases of AMK/KAN/CAP and AMK/KAN respectively with A1401G mutation. Sequencing revealed 38 SNPs at *rrs* (G878A, G837T, G895T, A1219T, T1238A) and *eis* (C12T, G37A, C14T) regions and increased sensitivity of AMK/KAN/CAP R to 64%, AMK/KAN R to 70%, both KAN/CAP R and KAN R to 50%. A new G878A SNP was found in 20 (17%) of SLID cases.

**Conclusion:** DNA sequencing improved sensitivity of SLID resistant cases by 50–70%. The MTBDRsl assay has limited probes therefore unable to detect most SNPs associated with SLID resistance. The inclusion of more *rrs* and *eis* regions in future molecular assays will improve detection of SLID resistance. However more SNPs are needed to accurately detect SLID resistance and thus improve patient management.

## 49. FACTORS AFFECTING ACCESS AND HEALTH SEEKING BEHAVIOUR

### PD-1056-01 Assessment of knowledge and coping style in patients with tuberculosis

Q Dina,<sup>1</sup> G Abuouf.<sup>1</sup> <sup>1</sup> Pharmacy College, Kau, Jeddah, Saudi Arabia. e-mail: dinakq@hotmail.com

**Background and challenges to implementation:** Tuberculosis patients have a lot of problems to follow their regimen in the therapy. This study is to assess knowledge of patients with TB about their disease and its management, and to identify their coping style and reaction to the treatment.

**Intervention or response:** A cross sectional study were performed at hospitals and TB centre in Makah province. Data were collected through structured interview with T.B patients using the designed TB Questionnaire.

**Results and lessons learnt:** A total of 176 cases were recruited in the study. About 70% of them were lacking the knowledge about their own disease and its treatment. Patients with higher education level scored higher mean of their knowledge ( $P < 0.001$ ) than those with low level of education. Patient with resistant TB were found to have higher knowledge than those with non-resistance ( $P = 0.013$ ). Older patients showed lower score in their knowledge than those who's younger ( $P = 0.015$ ). Patients who were treated in hospital located in Jeddah showed higher total mean score of knowledge ( $P = 0.001$ ) than those treated in hospital located in Taif and Makkah. 120 (68.2%) of the patients reported that they were free from side effects; the most commonly reported side effects by patients were nausea, vomiting, cough, difficulty swallowing and buzz in ears.

**Conclusions and key recommendations:** The findings of the study showed the poor knowledge about causative microbe, signs and symptoms, transmission and prophylaxis of TB and its treatments. The need of more structured patients' education programs, which could be improved more through innovative methods in conveying such therapeutic information are warranted.

### PD-1057-01 Health-care seeking behaviour among coughers suspected of having tuberculosis: findings from a prevalence survey

M Senkoro,<sup>1,2</sup> S Gudmund Hinderaker,<sup>2</sup> S G Mfinanga,<sup>1</sup> N Range,<sup>1</sup> D Kamara,<sup>3</sup> S M Egwaga,<sup>3</sup> F Van Leth.<sup>4,5</sup>

<sup>1</sup>Muhimbili Medical Research Center, National Institute for Medical Research, Dar es Salaam, United Republic of Tanzania; <sup>2</sup>Centre for International Health, University of Bergen, Bergen, Norway; <sup>3</sup>Preventive Services, National Tuberculosis and Leprosy Programme, Dar es Salaam, United Republic of Tanzania; <sup>4</sup>Department of Global Health, Amsterdam Institute for Global Health and Development, Amsterdam; <sup>5</sup>KNCV Tuberculosis Foundation, KNCV Tuberculosis Foundation, The Hague, Netherlands.  
e-mail: senkorombazi@gmail.com

**Background:** Identification of Tuberculosis (TB) patients in Tanzania is done through passive case finding which depends on the TB suspect's health seeking behavior. This study was done with a general objective of assessing the healthcare seeking behavior of TB suspects.

**Design/Methods:** The study was done under a nationwide population based survey among the adult population. Participants were screened for TB using a symptom questionnaire and chest X-ray (CXR). Suspects with symptoms suggestive of TB were interviewed about their healthcare seeking behavior, socio-demographic and clinical factors. In this study we included those who had cough for at least 2 weeks and/or were coughing blood. Logistic regression analysis was used to assess associations between seeking care and socio-demographic and clinical factors.

**Results:** Of the 3388 TB suspects, 1053 (31.1%) had sought treatment for their symptoms. About 42% went to seek care at sites with TB diagnostic capacity; examination of sputum was done in 37.4% and CXR in 28.0% of them respectively. In sites with limited TB diagnostic capacity, referral for examination of sputum or CXR was done in less than 1%. Individuals being diagnosed with TB before (AOR 1.6, 95%CI 1.3-2.0), having other symptoms (AOR 1.4, 95%CI 1.2-1.6) and being from high socio-economic position (AOR 1.4, 95%CI 1.1-1.7) were more likely to seek treatment. Knowledge of TB was significantly associated with care seeking at sites with TB diagnostic capacity.

**Conclusion:** A third of the persons with cough symptoms indicative for TB had sought health care. Of these, about 42 % sought care in sites with TB diagnostic capacity but most of them were not offered TB-diagnostic procedures, precluding a timely diagnosis. The National Tuberculosis and Leprosy Programme is urged to explore engaging with health facilities outside the direct programme to improve TB case finding.

### PD-1058-01 Active communication campaign helps achieve increased awareness and early diagnosis of tuberculosis among brothel based female sex workers of Pune

O Bera,<sup>1</sup> B Pawar,<sup>2</sup> S Chadha,<sup>1</sup> R Deshmukh,<sup>3</sup> P Banuru Muralidhara,<sup>1</sup> A Jacob,<sup>1</sup> S Mohanty.<sup>1</sup> <sup>1</sup>Union South East Office, International Union Against Tuberculosis and Lung Disease, N. Delhi, <sup>2</sup>State Tuberculosis Control Society, ADHS, Pune, Maharashtra, <sup>3</sup>National AIDS Control Society, Office of WHO, N.Delhi, India.  
e-mail: oprakash@theunion.org

**Background and challenges to implementation:** Female sex workers (FSW) are usually transient, hard to reach group, often new migrants living in crowded conditions coming in contact with number of clients and associated TB-HIV co-infection amplifies the risk of spread of tuberculosis (TB). FSWs risk of acquiring HIV is reduced in recent years; however, the risk of getting TB infection has remained the same. The intervention study was designed with the objective of assessing awareness level of tuberculosis and impact of communication intervention among brothel based female sex workers of Pune, Maharashtra.

**Intervention or response:** At the onset, brothel based FSWs were mapped and baseline knowledge, attitude and practice (KAP) survey was done using questionnaire prepared in local language among randomly selected 341 brothel based FSW in May 2013. It was followed by interventions which included intensive three months door to door brothel campaign by trained NGO health staff using pictorial tool kits developed by project Axshya (Global fund round 9 Project) and interpersonally imparting knowledge on TB disease, diagnosis, treatment to 3000 FSW in Pune and was overall monitored and supervised by corporation health officials. An observatory period of nine months was maintained before the end line knowledge and practice assessment of new batch of randomly selected 341 sex workers was conducted in April 2014.

**Results and lessons learnt:** Of the 341 interviews in base line survey only 185 (54.3%) heard of TB as compared to 282 (82.7%) in end line survey. Significant ( $P<0.05$ ) increase of knowledge was observed in end line as compared to base line in variables such as cough of two week as major symptom (71%), sputum testing as method of diagnosis (69.7%), high chance of acquiring TB in HIV patients (72.4%), free treatment at all government health facilities (84.1%). Significant positive change of attitude regarding decreased stigma associated with TB (10.6%), increased sharing of TB Status (46%) and increased acceptance of TB treatment at Government and NGO health facility (57.5%). Practice of covering face while coughing or sneezing (58.7%) and HIV infected FSW to visit health facility even if cough of one day (47.2%) was significantly higher as compared to baseline study.

**Conclusions and key recommendations:** The above study demonstrates the importance of customized active awareness campaign for high risk populations. It also brings into focus the low level of TB awareness among



FSWs although they have high chances of acquiring TB due to poor living conditions, susceptibility due to co-infection with HIV and clientele. With the new vision of reaching the unreached in TB control, it is of imperative importance to tailor high impact awareness campaigns coupled with active screening in high risk populations.

**Table: Comparative analysis of baseline and End line KAP survey among Female Sex Workers in Pune, Maharashtra.**

Indicators	Baseline KAP Study (Total=341) N (%)	End line KAP Study (Total=341) N (%)	P Value
<b>Knowledge</b>			
Heard of TB	185(54.3)	282(82.7)	<.01
**Cough of two weeks as symptom of TB	125(36.6)	242(71)	
**TB spreads when a person having TB cough or sneezes	79(23)	243(71)	
**Sputum testing as method of diagnosis	69(20.2)	238(69.7)	
**HIV increases the chances of having TB	56(16.4)	247(72.4)	
** Knowledge of TB Contact examination	86(25.2)	212(62.1)	
**DOTS as TB treatment	34(10)	201(58.9)	
**TB treatment better in private health facility	156(45.7)	67(19.6)	
**TB Treatment free in nearest government health facility.	101(29.6)	287(84.1)	
** TB is curable	123(36.1)	261(76.5)	
<b>Attitude</b>			
**TB creates stigma	133(39)	36(10.6)	<.01
**TB Status sharing	11(3.2)	157(46)	
**TB treatment in Govt./ NGO Health facility	54(15.8)	196(57.5)	
<b>Practice</b>			
**Cover your face with cloth while coughing	23(6.7)	200(58.7)	<.01
**Cough of 2 weeks is a must to attend health clinics	88(25.8)	220(64.5)	
**HIV patient to attend health facility even if cough of one or more day.	23(6.7)	161(47.2)	

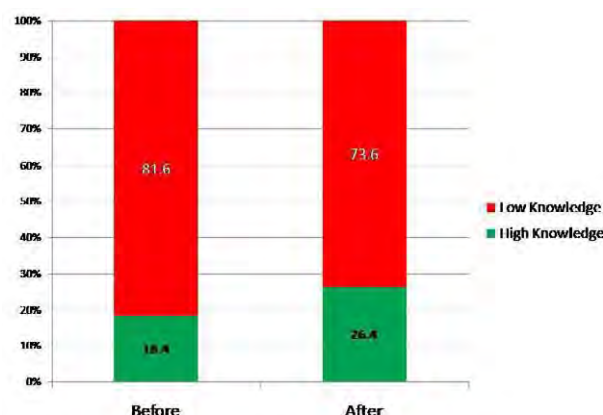
\*\* This questions are only for those "who have heard of TB"

## PD-1059-01 Potential of FM radio to deliver health message on tuberculosis for rural ethnic community in southern Shan State, Myanmar

S Saw,<sup>1</sup> ST Aung,<sup>2</sup> T Thida,<sup>3</sup> T Lwin,<sup>2</sup> Khin Su-hlaing,<sup>4</sup> Zaw Myint,<sup>2</sup> Khin Sandar-oo.<sup>1</sup> <sup>1</sup>Medical Statistics Division, Department of Medical Research (Lower Myanmar), Yangon, <sup>2</sup>National TB Programme, Department of Health, Naypyitaw, <sup>3</sup>Epidemiology Research Division, Department of Medical Research (Upper Myanmar), Pyin Oo Lwin, <sup>4</sup>Central Health Education Bureau, Department of Health, Naypyitaw, Myanmar. Fax: (+95) 1 251514. e-mail: ssaw.saw@gmail.com

**Background:** Advocacy, Communication and Social Mobilization (ACSM) is an important strategy in for controlling tuberculosis (TB) which is a major public health problem in Myanmar. Any ACSM intervention needs to be evidence-based for sustainable behavioral change. Previous study revealed that FM radio listening practice became popular and it could be an effective way of delivering health message especially for ethnic groups in rural areas. The study aims to identify effect of providing health messages on TB through FM radio in Myanmar.

**Design/Methods:** It was an intervention study (before and after design). Face-to-face interviews were conducted with 400 community members in 2 villages of Hopone Township, Southern Shan State, Myanmar before and after broadcasting health messages on TB through FM radio. Cherry FM radio broadcasted health messages on TB for twice a day for daily for two months. It broadcasted both in Myanmar and Pa-Oh languages. Four focus group discussions and 5 key informant interviews were conducted.



**Figure 1: Total knowledge scores before and after broadcasting health message on TB through FM radio**

**Results:** Significant increase in number of people has high knowledge score after broadcasting health messages on TB through FM radio (from 18.4% to 26.4%). There is an association between listening to FM radio and having high knowledge scores ( $p=0.001$ ). Initial action of treatment seeking when getting TB symptoms was also improved—33% in "Before intervention" to 70% in "After intervention" would seek treatment from public health centre. About 60% of respondents suggested FM

radio as an effective way of delivering health message and most respondents preferred story type of health message because it is easier to remember.

**Conclusion:** Using FM radio as one of the ACSM strategies is an effective way for delivering health messages. However it is necessary to consider further development of this intervention for longer duration and better programming according to preference of community.

#### **PD-1060-01 High and equitable coverage of civil society driven tuberculosis control project "Axshya" in India**

B Thapa,<sup>1</sup> A Das,<sup>1</sup> S Chadha.<sup>1</sup> <sup>1</sup>Tuberculosis, International Union Against Tuberculosis and Lung Disease, Delhi, India. e-mail: bthapa@theunion.org

**Background:** Project Axshya (meaning 'free of Tuberculosis') was launched in April 2010 as the civil society component of a five-year project funded by a Round 9 grant from the Global Fund to Fight AIDS, TB and Malaria (The Global Fund). The Government of India, The Union and World Vision India (WVI) are currently implementing the project activities in 374 districts across 23 states of India, reaching some 750 million people by 2015 with a network of 1200 NGOs and ~5000 community volunteers. The study examines the coverage and equity aspects of the civil society driven Tuberculosis (TB) control project Axshya in India.

**Design/Methods:** Data from the baseline (2011) and midline (2013) knowledge, attitude and practice survey (KAP) were used. Coverage refers to the percentage of general population 'who heard of TB', and TB patients who knew 'mode of transmission is by air' among various groups; age, gender, education (illiterate vs literate), settlement (rural vs urban), and ecological-development regions (North, South, East and West). Equity refers to similarities in coverage or reduced gaps of coverage among various subgroups of the general population and TB patients. Aggregated data from these two surveys were used and analyzed using descriptive statistics.

**Results:** The percentage coverage of the project among general population was higher (>80%) in 2013 in all groups; age, sex, education, settlement and ecological-development regions in comparison to 2011. The percentage coverage of the project among TB patients in various sub-groups ranged from 29%-70% in 2013 and was higher than the coverage in 2011 (19%-65%). The project was more equitable among general population, in 2013-coverage gap ranged from 3% to 11%-in comparison to 2011 (coverage gap ranged from 6 to 27%) among gender and ecological-development region, respectively. Similarly, the project was also equitable among TB patients in 2013.

**Conclusion:** The largest civil society driven project on TB care and control has high and equitable coverage which offers valuable lessons for India and elsewhere.

#### **PD-1061-01 Use of entertainment to raise awareness on tuberculosis**

N Aliyev.<sup>1</sup> <sup>1</sup>NA, Azerbaijan Health Communication Association, Baku, Azerbaijan. Fax: (+994) 50 377 19 82 (Cell). e-mail: jamila@ahca.az

**Background:** In Azerbaijan public remains insufficiently informed on transmission, ways of treatment and importance of treatment adherence of tuberculosis. Traditional methods, as print materials (brochure, booklets), articles in newspapers, TV shows with TB specialists do not prove to be desirably effective. Difficulties in obtaining free airing time on national TV is a constraint to use entertainment-education for public.

**Interventions:** We approached Azerbaijan's biggest and most popular movie theater to arrange demonstration of Public Service Announcements on tuberculosis symptoms, ways of transmission and importance of adherence during the movie sessions. 4,812 viewers were reached. 100 viewers were randomly interviewed after the sessions to reflect on information they received.

**Results:** As a result of the post-viewing interview the following data was obtained: -83% of viewers confirmed that they did not know that TB is a curable disease -89% confirmed that if them or their relatives or friends have symptoms similar to TB they will seek immediate care -94% stated that they will share information on TB symptoms, ways of transmission and dangers of non-adherence with their relatives or friends.

**Conclusions:** Use of entertainment facilities allowed reaching young audiences with low awareness level on TB. Exit-polls helped to evaluate immediate effect of demonstration of PSAs to the viewers.

#### **PD-1062-01 Opinion leaders perceptive on TB care and control: findings from a community-based survey of 30 districts in India**

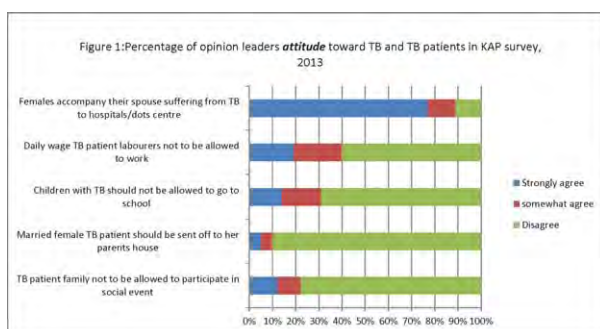
T Soni,<sup>1</sup> K Sagili,<sup>1</sup> A Jacob,<sup>1</sup> S Chadha.<sup>1</sup> <sup>1</sup>Public Health, International Union against Tuberculosis and Lung Diseases, New Delhi, India. e-mail: tanusoni.86@gmail.com

**Background:** Social Learning Theory hypothesizes that individuals such as opinion leaders who are perceived as credible, likeable and trustworthy are likely to be persuasive agents of behavioural change thus significantly affecting community's overall development. They mainly comprise of the elected representatives of a village, religious leaders, teachers or health functionaries like Auxiliary Nursing Midwives (ANM) or Anganwadi Workers (AWW). Being the primary functionaries at the grass root level, it is important that these people be equipped with correct knowledge about tuberculosis (TB) including care and control.

**Methodology:** A cross-sectional community-based "Knowledge, Attitude and Practice (KAP) survey about Tuberculosis was conducted in 2012-2013. Thirty districts of the 374 Project Axshya, a Global Fund supported project were selected randomly. Semi-structured questionnaire was used to interview a total of 611 opinion leaders.

**Results:** Of 611 respondents, 52% were male and 48% were female. Majority (79%) of the respondents were above age group of 36yrs and 30% with graduate degree. They were working as teachers, panchayat raj members, AWWs, village pradhans and religious leaders. On knowledge assessment, almost all opinion leaders heard of TB, its symptoms and they knew TB is curable. However, only 60% knew about DOTS. On interviewing about role played by them in their communities to address TB, 83% never took any initiative in creating awareness about TB or organised camps, workshops or any other activities. Even with the knowledge that TB is curable, it is observed that about 73% were not willing to share a meal with a person who had TB and 72% were not willing to get their sons or daughters married to someone they knew had TB. Though it is encouraging to observe that 75% will not isolate their family member having TB from the household, it also suggests that the remaining would still isolate their family members.

**Conclusion:** Opinion leaders could be an interface between community and TB service providers. Appropriate strategies need to be designed to involve opinion leaders effectively for TB care and control in developing countries like India where three-fourth of its population lives in rural areas. Local and national level leaders should be identified to promote the messages like “TB is curable” along with culturally appropriate social mobilization activities could be lead by the opinion leaders.



### PD-1063-01 Motivating TB care in Viet Nam by focusing on factors associated with TB care seeking behavior among people with TB symptoms

H Ngo,<sup>1</sup> M Gary,<sup>1</sup> J Neukom.<sup>1</sup> <sup>1</sup>Strategic Information, Population Services International, Hanoi, Viet Nam. e-mail: nh.ytcc@gmail.com

**Background:** Viet Nam is currently among the 12 highest TB burden countries in the world, with an incidence of 147/100,000 in 2012. PSI partnered with MOH to improve private clinic capacity to contribute to quality TB screening and referral services—using social franchising techniques. PSI designed evidence-based communications to address non-supply side factors associated with TB care including raising awareness of TB symptoms and promoting timely TB care. This paper describes results of a survey designed to identify practical

insights among a sample of individuals reporting TB symptoms in the last 6 months, to inform effective TB programming.

**Design/Methods:** In Dec 2013, 630 people who experienced long lasting cough more than 2 weeks in the last 6 months were recruited in 2 southern provinces: An Giang and Dong Thap. Cluster sampling was used to select 26,126 households from 70 communes in districts where PSI TB activities are implemented. Logistic regression models were used to identify factors associated with TB care seeking behaviors.

**Results:** Less than 3 out of 4 individuals with TB symptoms reported seeking care within 1 month of experiencing symptoms. Close to one-fifth (18%) of individuals with symptoms reported not seeking any care for their LLC. Main reasons for not seeking care for TB symptoms included low perceived severity of TB symptoms (51%) and concern regarding time/costs associated with seeking care (39%). Respondents who perceived themselves at risk of having TB were 2.35 times more likely to have sought TB care compared to those who did not suspect (95%CI = 1.506-3.667). Respondents who were able to identify at least 3 TB symptoms (unprompted) were 2.23 times more likely to have sought TB treatment compared to those unable to identify symptoms. (95%CI= 1.493-3.655) Individuals exposed to PSI's TB behavior change communication messages in the last 6 months were also 2 times more likely to have sought TB care (95%CI = 1.309-3.607.) Women and individuals with health insurance (an estimated 57% of respondents with TB symptoms) were also more likely to report seeking TB care.

**Conclusion:** Results from a 2013 survey highlight the importance of increasing exposure to BCC designed to raise awareness of TB symptoms and perceived risk of TB among individuals with TB symptoms. Future TB programs in Viet Nam should aim to reduce access barriers to care including time, distance and cost associated with seeking TB care.

### PD-1064-01 Behaviour change communications increases TB awareness and TB care seeking behavior among people with TB symptoms in Viet Nam

H Ngo,<sup>1</sup> Cuon Nguyen,<sup>2</sup> J Neukom.<sup>1</sup> <sup>1</sup>Strategic Information, Population Services International, Hanoi, Viet Nam, <sup>2</sup>Health Services, Population Services International, Hanoi, Viet Nam. e-mail: nh.ytcc@gmail.com

**Background:** Viet Nam has one of the highest tuberculosis burdens in the world. Despite achievements in public sector TB programming in recent years, gaps in access to and demand for TB screening, diagnosis and treatment services remain. To address these gaps, PSI implemented a program in 3 southern provinces with objectives: i) improve convenient access to TB care, by motivating franchised, Good Health, Great Life private clinics to screen and refer TB patients; ii) raise awareness regarding TB symptoms and risk perception by using multi-channel BCC. Key messages were disseminated



using channels accessible to communities at risk of TB. This paper reports on behavioral survey findings related to the effectiveness of TB BCC implemented under PSI's social franchising program.

**Design/Methods:** Two surveys were conducted among individuals reporting long lasting cough in past 6 months during Dec. 2012 (n=580) and Dec 2013 (n=630). Households were randomly selected using cluster sampling from communes in An Giang and Dong Thap. Descriptive analyses were used to explore changes in TB awareness and TB care seeking behaviors between the two surveys. Logistic regression models were used to identify associations between exposure to BCC and TB awareness and care seeking behavior.

**Results:** Awareness that a long lasting cough (LLC) is a key TB symptom increased from 52% to 64% ( $p<.05$ ) between 2012 and 2013. Self-perceived risk of TB more than doubled during the same period, from 22% to 47% ( $p<.05$ ). The percentage of respondents suspecting that their own symptoms may be TB also increased from 17% in 2012 to 31% in 2013 ( $p<.05$ ). Exposure to PSI BCC messages increased from 17% of individuals with LLC sampled in 2012 to 24% in 2013 ( $p<.05$ ). Associations were found between exposure to BCC and increased awareness of TB and TB symptoms. Respondents exposed to PSI's BCC in the past 6 months and able to correctly recall at least one key campaign message were almost twice as likely to be aware that LLC is a TB symptom (OR=1.8, CI95% = 1.157-3.286). Individuals exposed to PSI's BCC were twice as likely to report seeking TB care (95%CI = 1.309-3.607).

**Conclusion:** These results demonstrate significant changes in TB awareness and seeking behaviors among individuals with LLC in 2 provinces where PSI's social franchising and BCC activities were implemented. Data reveals positive correlation between BCC exposure and improved awareness and care seeking behavior following less than 12 months of BCC implementation using multiple channels accessible to individuals with TB symptoms. Future scale up of evidence-based, targeted BCC can further increase TB case detection in Viet Nam

#### **PD-1065-01 Impact of advocacy and social mobilisation on knowledge, attitude and practice on tuberculosis in Kenya**

H K Kipruto,<sup>1</sup> E Klinkenberg,<sup>2</sup> J Kioko,<sup>3</sup> J Onteri,<sup>3</sup> B Langat,<sup>3</sup> J Sitienei,<sup>3</sup> J Kangangi,<sup>1</sup> M Maina.<sup>4</sup> <sup>1</sup>TUB, WHO, Nairobi, Kenya; <sup>2</sup>TUB, KNCV, Hague, Netherlands; <sup>3</sup>Disease Prevention and Control, Ministry of Health, Nairobi; <sup>4</sup>OPH, USAID, Nairobi, Kenya. e-mail: kiprutoh@gmail.com

**Background and methods:** Although Kenya has made good progress in the fight against Tuberculosis, it continues to be a major public health problem. In 2007, Kenya reached the target for both TB case detection rate (70%) and treatment success rate (85%). Kenya has designed strategies aimed at mitigating the effects of TB and among them is advocacy and social mobilization whose ultimate aim is to increase the knowledge, attitude and practices (KAP) among the

population. In 2008 before implementing ACSM interventions, Kenya conducted a baseline KAP survey, followed by a second survey in 2013. Both surveys were cross-sectional involving school going children (primary and secondary), teachers, community members and leaders from randomly selected regions in Kenya. The second survey was powered to measure impact compared to baseline with a sample size of 2,306. All the 47 counties in the country were included in the sampling frame.

**Results:** Sixty percent of the 2,306 respondents were males and the mean age was 32 years with a standard deviation of 21.32. Among the respondents, knowledge that TB is an airborne disease was mentioned by 74%, cough of 2–3 weeks as suspicious of TB by 40%, awareness that TB services are free by 66% and 81% were able to identify where TB services are provided. This was similar with the baseline survey. The survey established that the respondents considered treatment of TB as a means of preventing and stopping transmission (67%) which is actually an important aim of TB control. The other reasons noted for treating TB were to achieve cure (43%) and to prevent death (29%). This was similar with the baseline survey. The policy of free TB treatment in Kenya was known to 66% of the respondents while 21% felt that TB treatment is not free and 11% did not know. Compared to 2008 findings (75%), there is a reduction in the level of awareness on free TB treatment. **Conclusion:** The study demonstrated that Knowledge on TB was adequate although more should be done. The respondents had knowledge that TB transmission is airborne and can be transmitted from one person to another. The respondents were able to identify the common signs and symptoms of TB including cough of 2–3 weeks. Overall the results do not show significant changes in knowledge, attitude and practice levels compared to the 2008 baseline study indicating the need to refocus messaging strategies in order to improve the knowledge on TB prevention among the population.

#### **PD-1066-01 Gender related barriers affecting health seeking behavior for tuberculosis treatment in Mozambique**

D Sacur,<sup>1</sup> N Kamp,<sup>2</sup> A Tiago,<sup>1</sup> S Machevo Chilundo,<sup>1</sup> E Oliveras,<sup>1</sup> I Manhiça.<sup>3</sup> <sup>1</sup>Mozambique, FHI 360, Maputo, Mozambique; <sup>2</sup>Regional Office, KNCV Tuberculosis Foundation, The Hague, Netherlands; <sup>3</sup>National Tuberculosis Program, Mozambique Ministry of Health, Maputo, Mozambique. e-mail: eoliveras@fhi360.org

**Background:** Despite effective methods of tuberculosis diagnosis and treatment, Mozambique ranks 19th among the 22 high tuberculosis (TB) burden nations. Globally, suboptimal health seeking behavior limits use of health services and is affected by sociocultural factors, including gender norms.

**Design/Methods:** This operations research study explored individual and sociocultural constraints to seeking TB care in order to inform the design of communication and advocacy strategies for TB control. The study was conducted in urban and rural sites (1 each) in 3 provinces

in northern, central and southern Mozambique that represented priority intervention areas in the National Strategy for TB Control 2008–2012 and reflected ethno-linguistic and cultural diversity. In-depth interviews (IDI) were conducted with 29 community health workers, 30 facility-based health workers, 36 community leaders, and 62 TB patients. They covered knowledge of TB transmission and treatment, care seeking, and barriers to care. Twenty-six Focus Group Discussions (FGD) were conducted with community members. Recordings of IDI and FGDs were transcribed verbatim and coded using codes derived a priori and from the data.

**Results:** While some reasons for failing to seek care were consistent for men and women, others differed. For example, long distances to health facilities were a major barrier noted by all participant types and was never linked to gender. However, female patients reported fear of social isolation as a barrier whereas men reported the costs associated with diagnosis and treatment as the main reasons for failing to seek care. Women's fears were supported in both the IDIs and FGDs; FGD participants noted cases in which women with TB had been abandoned and some female patients shared their experience of abandonment. No men shared similar experiences. Although providers did not discuss gender differences in care seeking, they reiterated the importance of stigma, noting that TB treatment is sometimes conflated with HIV treatment.

**Conclusion:** Stigma surrounding TB diagnosis and treatment is greater for women than for men in Mozambique and is a leading barrier to care seeking by women. While common barriers to TB care should be addressed, targeted efforts to gender specific barriers are needed to ensure equitable access to care. Further research looking more specifically at gender differences is needed to better understand both the issues involved and potential responses.

#### **PD-1067-01 How far the national media gives priority to tuberculosis control challenges as an important means of solution in TB high-burden country, India?**

S Nayak,<sup>1</sup> O Bera,<sup>1</sup> S Chadha,<sup>1</sup> R Dayal,<sup>2</sup> R Pathak,<sup>3</sup> A Buragohain,<sup>1</sup> A Das,<sup>1</sup> P Mishra.<sup>2</sup> <sup>1</sup>South-East Asia Office, International Union Against TB and Lung Diseases, New Delhi, <sup>2</sup>Health and Family Welfare, Govt. of Jharkhand, State Tuberculosis Cell, Ranchi, <sup>3</sup>Tuberculosis Control In India, WHO Country Office for India, New Delhi, India. Fax: (+91) 11 4605 4430. e-mail: snayak@theunion.org

**Background:** India accounts for 1/4<sup>th</sup> of the global TB burden with per annum estimation of 2.1 million cases and still 1/3<sup>rd</sup> of cases missing from the national notification system. The year 2013 experienced many operational issues. The programme has loaded with challenges of X/MDR TB, Pediatric TB, quality of care, notification from the private sector. There is an emergence need of penetrating the awareness to lowest level of the society for reaching the un-reached. Media is to play a major role in the community, programme and policy. This paper did an analysis of major national

electronic & print media in giving importance to issue related to TB.

**Design and Method:** 4 major national print dailies – The Hindu, Times of India (TOI), Hindustan Times (HT) and Indian Express Group (IEG) were selected for reviewing articles along with 2 key electronic media - NDTV and CNN-IBN. All news items of 4 national dailies were studied for 6 months (Oct'13-Mar'14) and 12 months (Apr'13-Mar'14) for both electronic media under 10 categories- (1)TB Epidemiology, events, NGO (2) Political/Admin commitment, quality care/DOTs (3) Drug/Equipment/Microscopy (4)TB and Comorbidities (5)X/MDR TB (6)Paed TB (7)Paed MDR TB (8)TB and Nutrition (9)TB & Nutrition (10)Notification and Pvt Sector.

**Results:** Six months news scanning from the web of 4 national dailies resulted in reporting of 239 news items (The Hindu – 114, TOI-78, HT-5, IEG-42) on TB. Quite significantly, 45% (108) of the total news items, published in March only, i.e. during WTD. Majority of the news - 39% items were in the category of TB epidemiology, events, case study & of NGOs. News on Political/Admin commitment is 13% followed by pediatric (MDR) TB 12.5% and X/MDR TB 12%. Other categories range from 2 to 7%. That of notification and pvt sector is 10%. 22% articles of TOI was based on political commitment and reviewing policies. One year scan of both electronic medias, found only 9 items on TB – 7 of NDTV and 2 of CNN-IBN covering on human interest story, pediatric TB, Drug issues and MDR TB.

**Conclusion:** The coverage of TB gets space in the media mostly during world TB Day. TB doesn't get adequate priority among other health issues in the mainstream media. The events of both GO get space towards publicity/awareness. Issues relating to political commitment and policy implications need much attention in the media. The media need to function as a watch dog on all the three key dimensions of TB – Policy, Programme and Patient.

#### **50. TREATMENT, MANAGEMENT AND DIAGNOSIS: A POTPOURRI OF TB AND HIV ISSUES**

##### **PD-1068-01 Factores de riesgo para rebote virológico en pacientes con coinfección TB-VIH**

R Martinez,<sup>1</sup> C Bueno,<sup>2</sup> C Jimenez,<sup>3</sup> A Valencia.<sup>1</sup>

<sup>1</sup> Enfermedades Infecciosas, Comfamiliar Risaralda, Pereira,

<sup>2</sup> Medico, Union HAART, Pereira, <sup>3</sup> Medico, Grupo VIHDA, Pereira, Colombia. e-mail: ricardoamartinezg@hotmail.com

**Background:** Al ser la tuberculosis la infección oportunista más frecuente en personas infectadas por el virus de la inmunodeficiencia humana, se hace necesario establecer factores de riesgo para rebote virológico en pacientes con supresión viral previa al tratamiento de la enfermedad tuberculosa, siendo objetivo del presente trabajo determinar factores asociados para esta

complicación diferentes a la pobre adherencia farmacológica

**Design/Methods:** Se realizó estudio descriptivo entre 87 pacientes atendidos en institución del occidente de Colombia, con diagnóstico de rebote virológico un año después de inicio de terapia antituberculosa, solo fueron incluidos pacientes con óptima adherencia

**Results:** Tiempo promedio de supresión viral previo a terapia antituberculosa 14 meses. 85% recibían inhibidor de proteasa (IP), 15% inhibidor no nucleosido de la transcriptasa inversa (INNTR), 10% inhibidor de integrasa. Como factores de riesgo para rebote virológico se señalan reemplazo de IP por INNTR OR 3.6 IC 1.2- 6.3, reemplazo de IP por inhibidor de integrasa OR 2.6 IC 1.03- 7.2 y reemplazo de IP por esquema triple de inhibidores nucleosidos (abacavir-lamivudina-zidovudina) OR 2.7 IC 1.4- 6-9, estos cambios fueron precipitados por no disponibilidad de rifabutina

**Conclusion:** Las interacciones medicamentosas entre IPs y rifampicina, hacen considerar el uso de la rifabutina como parte del esquema antituberculoso, sin embargo la no disponibilidad de esta última, obliga a cambios y construcción de esquemas no apropiados al pasar de fármacos con alta barrera genética como la aportada por un IP a medicamentos con una baja barrera como la asociada a INNTR e inhibidores de integrasa, incrementando así el riesgo de rebote virológico. Es pues necesario garantizar el suministro de rifabutina, considerándose como fármaco de primera línea en pacientes coinfectados TB/VIH que reciben IP

#### PD-1069-01 The cost of TB screening in Gauteng, South Africa

N Foster,<sup>1</sup> Y Hanifa,<sup>2</sup> A Grant,<sup>2</sup> V Chihota,<sup>3,4</sup> G Churchyard,<sup>2,3</sup> K Fielding,<sup>5</sup> E Sinanovic,<sup>1</sup> A Vassall.<sup>6</sup>

<sup>1</sup>Health Economics Unit, University of Cape Town, Cape Town, South Africa; <sup>2</sup>Clinical Research, London School of Hygiene and Tropical Medicine, London, UK; <sup>3</sup>Epidemiology, Aurum Institute, Johannesburg; <sup>4</sup>School of Public Health, University of Witwatersrand, Johannesburg, South Africa; <sup>5</sup>Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine, London; <sup>6</sup>Social and Mathematical Epidemiology, London School of Hygiene and Tropical Medicine, London, UK. e-mail: nicola.foster@uct.ac.za

**Background:** The WHO recommends that Persons Living With HIV/AIDS (PLWHA) should be screened for TB at every encounter with the health service in order to identify active TB infection. South Africa (SA) has a high burden of HIV and TB and implementing these WHO guidelines has important financial implications. There is limited data regarding the cost of TB screening in PLWHA in SA.

**Design/Methods:** An incremental cost analysis of adding TB screening to existing clinic services was conducted as part of the XPHACTOR study, comparing WHO recommendations and alternative screening approaches. The analysis was performed from a health service provider perspective in four clinics in SA. Screening costs included the time taken to symptom screen using a defined symptom survey, a brief HIV and TB history

taking and BMI assessment. A bottom-up costing methodology was used, which included observations of practice at each clinic. A total of 26 patients screened were observed at the four clinics between October 2012 and March 2014. Costs included the costs of human resources, furniture, equipment, consumables, training and building space. All costs are presented in 2013 USD (1 ZAR= 0.104 USD).

**Results:** Preliminary results indicate that the mean incremental cost per patient screened is \$2.76 (range: \$0.70-\$4.74). There was variation in the cost of screening between clinics and over time at the same clinic (Figure), primarily driven by how clinics organized the division of labour between professional nurses and lay health workers. The percentage of the cost per patient screened attributed to human resource costs was on average 84% (range: 66%-93%). The average cost per patient screened by a lay health worker was \$1.38 (range: \$0.70-\$2.74) compared to \$3.39 (range: \$2.13-\$4.74) if screened by a professional nurse.

**Conclusion:** Although the unit cost of screening is low, given that currently there are an estimated 5.26 million PLWHA in SA, who may visit health service several times per year, and the cost of screening at every encounter may prove substantial. Human resource cost was the largest contributor to the cost of TB screening and the WHO policy may thus have a wider impact on current human resource requirements. TB screening may therefore be more affordable if lay health workers are trained to conduct TB screening in PLWHA. The study will further investigate what the cost of screening is using different algorithms, as well as the downstream costs of diagnosis and treatment.



#### PD-1070-01 Why do presumptive TB cases refrain from HIV testing in Karnataka, India?

S Shastri,<sup>1</sup> NS Vishwanath,<sup>1</sup> S Managuli.<sup>1</sup> <sup>1</sup>Department of Health and Family Welfare Services, Lady Willingdon State TB Centre, Bangalore, India. e-mail: susha007@gmail.com

**Background** Tuberculosis (TB) still remains the most common opportunistic infection and cause of death among HIV-infected individuals. In India, for early HIV case finding, the Revised National TB Control Programme (RNTCP) and National AIDS Control Programme (NACP) has adopted provider-initiated HIV testing and counseling (PITC) for presumptive and diagnosed TB cases. This study is conducted to ascertain



the reasons for HIV testing not being done in presumptive tuberculosis patients undergoing sputum smear examination in the south Indian state of Karnataka.

**Methods** The data was collected from the 645 Designated Microscopy centres (DMC) in 31 districts of Karnataka during the month of January 2014. The TB laboratory register was the source of data for all the presumptive TB cases registered; cases were referred to integrated testing and counseling centre (ICTC) for HIV testing. The reasons for not having HIV results were ascertained by providers and patients.

**Results** A total of 41,326 presumptive TB cases were subjected for sputum examination. Among them 25,457(62%) were screened for HIV and information is available for 12347 (30%) patients who were not screened. The reason for not undergoing HIV screening was ascertained for 12189 (99%) patients; the main reasons were (a) 9662(78%) sputum samples were transported for TB diagnosis and HIV testing facility was not available at the transporting centre (b) 1553(12%) of cases refused HIV testing or testing was not done due to old age (c) 994(8%) of cases were not tested due to non-availability of testing kits or testing personnel.

**Conclusions** Under routine programmatic settings, four in ten individuals with presumptive TB were not screened for HIV. The main reasons for this gap are non availability of decentralized HIV testing facility, refusal of HIV testing or old age, non availability of testing kits and testing personnel. Adoption of point of care rapid HIV testing at primary health care level, increased resources and capacity building of the TB program staff in counseling skills will further strengthen the TB-HIV collaboration.

#### **PD-1071-01 Patterns of opportunistic infections occurring in people living with HIV in south-east Nigeria**

N Ekeke,<sup>1</sup> A Meka,<sup>1</sup> J Chukwu,<sup>1</sup> C Nwafor,<sup>1</sup> D. Oshi,<sup>1</sup> N Madichie,<sup>1</sup> C Ogbudebe.<sup>1</sup> <sup>1</sup>Medical Department, German Leprosy and Tuberculosis Relief Association, Enugu, Nigeria. e-mail: ekekengezi@gmail.com

**Background:** Nigeria is one of the countries in the sub-saharan African region with high prevalence of HIV. In 2010, a national HIV sentinel survey put the median HIV prevalence at 4.1%. Globally, opportunistic infections (OIs) are a leading cause of morbidity and mortality among people living with HIV. Empirical data on patterns of opportunistic infections among People Living with HIV (PLHIVs) are relevant for effective planning and implementation of HIV/AIDS care and treatment. Patterns of OIs prevalent among PLHIVs in south-west and south-south regions of Nigeria have been documented in 2008 by Ogunfowora et al<sup>1</sup> and Imade et al<sup>2</sup> respectively. Interestingly, the patterns vary between the two regions. No similar reports have been documented on the southeast region of the country. This study therefore, seeks to ascertain the pattern of OIs occurring in PLHIVs in the southeast region. It is hoped that the

results would contribute to quality care, treatment and support for PLHIVs in the region.

**Design/Methods:** One health facility offering comprehensive ART services was selected from each of the five states in southeast Nigeria using a multi-stage sampling technique. A 3-year (2010 – 2012) retrospective analysis of relevant data extracted from patients' records from the selected ART clinics was done to ascertain the pattern of OIs occurring among PLHIVs attending those clinics within the region. Data analysis was done using SPSS version 17.0.

**Results:** A total of 5377 PLHIVs were enrolled in the selected ART clinics over the period. About 66% were females. Approximately 7% were children (0–14 years) made up of 43% males and 57% females. Of the PLHIVs registered for care and treatment, 1566 (29%) developed various forms of OIs during treatment. More females (60%) developed OIs. Among all PLHIVs, Tuberculosis, occurring in 40% of the PLHIVs who developed OIs, was the most prevalent. Others included Oral thrush (21%), Upper respiratory tract infections (URTI) 17%, Vaginal Candidiasis 6%, Malaria 5%, Enteritis 4%, Herpes Zoster 3%, Fungal skin infections 2% and Kaposi Sarcoma, 2%. Among paediatric PLHIVs alone, OIs were TB (53%), URTI 17%, Oral thrush 15%, Enteritis 11% and Fungal skin infections, 4%.

**Conclusion:** The contributions of this study are two-fold. While completing the regional picture of pattern of OIs among PLHIVs in southern Nigeria, it provides a useful guide to clinicians and policy makers for efficient care and treatment of PLHIVs in the region.

#### **PD-1072-01 IPT in Indonesia: better late than never**

T N Dinihari,<sup>1</sup> J Tanumihardja,<sup>1</sup> N Sulaiman,<sup>2</sup> H Agustine,<sup>3</sup> Y Hartantri,<sup>4</sup> T Mahatmi Nisa,<sup>5</sup> R Palupy,<sup>6</sup> B Nababan.<sup>6</sup> <sup>1</sup>National TB Program, Ministry of Health, Jakarta, <sup>2</sup>National AIDS Program, Ministry of Health, Jakarta, <sup>3</sup>Pulmonology, Persahabatan Hospital, Jakarta, <sup>4</sup>Tropical Infection, Hassan Sadikin Hospital, Bandung, <sup>5</sup>HIV Unit, WHO, Jakarta, <sup>6</sup>Clinical Services Unit, Family Health International 360, Jakarta, Indonesia. Fax: (+62) 213 984 2972. e-mail: bnababan@fhi360.org

**Background:** Indonesia is one of TB and TB-HIV high burden countries. In 2011, around 42% of AIDS cases reported to National AIDS Program were also co-infected with TB. Despite WHO and UNAIDS recommendation on Isoniazid Preventive Therapy (IPT) for PLHIV in 1998, this activity was not included in the TB and HIV national program. Concern from clinicians on development of INH resistance was prominently affecting national policy. Genexpert was introduced in Indonesia in 2012 and installed initially at 6 centers. High sensitivity of Genexpert in diagnosing active TB seemed compelling for clinicians as well as national program in initiating a pilot project on IPT for PLHIV to assess the feasibility and management effectiveness of this activity to be done in Indonesia

**Intervention:** Series of coordination meeting for planning and preparation were conducted, involving both TB and

AIDS programs, partners and clinicians. Tools for assessment on the pilot sites were developed and 4 hospitals in two provinces were selected as the pilot sites. Technical guidelines, SOPs that include the use of Genexpert for PLHIV with TB symptoms, monitoring and evaluation tools were developed. Mentoring and evaluation meetings were part of the intervention to ensure the sites followed the procedures and to track progress. Challenges were identified and discussed ways to resolve. INH was planned to be provided to 200 PLHIV, daily for 6 months.

**Results:** Screenings were performed to 281 PLHIV, 216 (77%) were eligible for IPT, 11 PLHIV refused IPT. All together, 205 PLHIV were provided with IPT. By the end of the 6 months, 167 (81%) completed the 6 months regiment, 24 (12%) of them defaulted, 2 died because of AIDS related diseases (but not TB), 7 stopped INH due to side effects. One patient was diagnosed TB during the course of the regiment and identified as not adhere to daily dose of INH.

**Conclusions:** IPT in Indonesia is feasible, with high retention rate (81%), only 1 patient failed and developed TB during the course of IPT. Expansion plan was developed and now is being implemented in step-wise manner by NTP and NAP. Despite the late introduction, IPT is promising to decrease the burden of TB among PLHIV. However, surveillance and systematic monitoring of drug resistance needs to be ensured.

#### **PD-1073-01 Palm fruit juice mitigates the cytotoxic and genotoxic effects of AZT and isoniazid, key drugs in the treatment of HIV and tuberculosis**

A Osborne,<sup>1</sup> J.A. Sanchez,<sup>1</sup> W Wangh.<sup>1</sup> <sup>1</sup>Dept. of Biology, Brandeis University, Waltham, MA, USA.  
e-mail: wangh@brandeis.edu

**Background:** Millions of TB and HIV patients are treated with drugs that have toxic side effects. AZT, an inexpensive NRTI used in HAART, is associated with mitochondrial oxidative stress and DNA damage. Isoniazid (INH), a first line antibiotic used to treat or prevent tuberculosis, alters liver function in ~20% of patients and is fatal in 1%-2%. Toxic intermediates of INH in the liver deplete glutathione and oxygen radical scavenging enzymes. The resulting increase in free radicals can irreversibly damage mitochondria and mitochondrial DNA (mtDNA). We are investigating AZT and INH dependent mtDNA damage in cultured human liver cells, as well as whether palm fruit juice (PFJ), an extract rich in polyphenols from the fruit of the oil palm (*Elaeis guineensis*), mitigates such damage.

**Methods:** We tested effect of PFJ, at 25µg/ml of medium, on the level of mtDNA mutations caused by 7µM AZT in HepG2 cells cultured for 30 days. We also tested whether PFJ attenuates cell death caused by a higher dose of AZT (10–100µM). Additional cells were treated with 88µM INH for 30 days ±50µg/ml PFJ. Mutations were simultaneously measured in three mitochondrial gene

targets (HV2, CO2, and ND1) using a digital LATE-PCR Lights-On/Lights-Off probe assay.

**Results:** AZT for 30-days caused a 9-fold increase in mtDNA mutations. INH for 30-days caused a 17, 2.1, and 1.7-fold increase in mutations in HV2, CO2, and ND1, respectively. Co-treatment with PFJ decreased AZT-induced mutations by 35% in all three gene targets and INH-induced mutations by 100% in CO2 and ND1. Co-treatment with PFJ also decreased AZT dose-dependent cell death.

**Conclusions:** Our results with cultured hepatocytes suggest that patients on long term drug regimens containing AZT or INH, or both may be at risk for accumulating mtDNA mutations. Such damage might result in mitochondrial dysfunction and a gradual onset of mitochondrial-related diseases, including diabetes. The protective effects of PFJ on AZT and INH toxicity in cultured liver cells suggests a potential means of ameliorating such negative side effects of drugs in people. Our assay for drug-induced mtDNA mutations without sequencing is broadly applicable and could be used for early drug development or monitoring.

#### **PD-1074-01 Correlation of mycobacterial load with CD4 cell count in TB-HIV co-infected patients: a study based in a rural area of Swaziland**

G Obregon Boltan,<sup>1</sup> B Kerschberger,<sup>1</sup> A Antierens,<sup>1</sup> R Dela Tour.<sup>1</sup> <sup>1</sup>Operational Centre, Médecins Sans Frontières, Geneva, Switzerland.  
e-mail: flankan.damagon@gmail.com

**Background:** The World Health Organization states that sputum positivity decreases with atypical chest X-ray findings and lower CD4 counts. However, this evidence is scarcely described in the literature. We aimed to assess associations between the smear microscopy and the Xpert® grade and level of CD4 counts in sputum TB positive patients.

**Design/Methods:** Retrospective database analysis of 1,072 TB sputum samples which were routinely processed by fluorescent smear microscopy, Xpert®MTB/RIF and culture at 3 health facilities in the rural Shiselweni region (Swaziland), from August 2011 to December 2012. We examined the correlation of Mycobacterial load and CD4 cell count using the  $\chi^2$  test and Spearman correlation rank, and test for linear trends using Cochran-Armitage test.

**Results:** Of 1,078 TB cases, 604 (56.0%) had a known HIV status and of whom 431 (71.4%) were HIV-positive. The median CD4 count was 133 cells/µL (IQR: 65–279). The correlation between CD4 count and TB pulmonary form was weak in HIV co-infected patients ( $r=0.117$ ). High bacillary density (defined as > 10 AFB/field) was no significantly different between HIV-positive (29.6%) and negative (29.3%) patients. For HIV co-infected patients, higher grades of sputum smear positivity and Xpert®MTB/RIF degree medium and high were associated with higher CD4 count level of ≥500 cells/µL. In any case it was not possible to correlate the

sputum positivity decrease with lower CD4 count in HIV co-infected patients.

**Conclusion:** There was a very weak correlation between CD4+ count and TB form in HIV co-infected TB patients in rural Shiselweni, Swaziland. Therefore, the diagnosis of TB associated with HIV infection is more difficult, even when the CD4 count is  $> 500$  cells/ $\mu$ L.

#### PD-1075-01 Isoniazid preventive therapy among pre-ART patients in Malawi: a report on uptake and retention

Y Lo,<sup>1</sup> R Flick,<sup>1</sup> A Munthali,<sup>1</sup> K Simon,<sup>1,2</sup> A Dimba,<sup>3</sup> M Kim,<sup>1,2</sup> P Kazembe,<sup>1,2</sup> S Ahmed.<sup>1,2</sup> <sup>1</sup>Baylor College of Medicine- Abbott Fund Children's Clinical Center of Excellence, Baylor College of Medicine, Lilongwe, Malawi; <sup>2</sup>Baylor College of Medicine International Pediatric AIDS Initiative at Texas Children's Hospital, Baylor College of Medicine, Houston, TX, USA; <sup>3</sup>National Tuberculosis Control Programme, Malawi Ministry of Health, Lilongwe, Malawi. e-mail: yianlo712@gmail.com

**Background:** HIV impairs the host's ability to contain a TB infection; as a result, the risk of disease progression from latent to active TB is estimated to be 20 times greater in HIV-infected individuals than in immunocompetent individuals. To address this increased risk, the 2011 Malawi ART/PMTCT guidelines recommend provision of isoniazid preventive therapy (IPT) to patients enrolled in HIV care who have not yet initiated ART as both pre and post-exposure TB prophylaxis. Operational challenges have led to varying degrees of implementation. The objective of this report is to describe IPT utilization and patient outcomes since the rollout of the 2011 guidelines.

**Methods:** Data from 13 health centers were reviewed for rates of IPT initiation and completion, interruptions in IPT, and TB and ART outcomes. HIV-infected patients newly enrolled in HIV Care Clinics from April 2011 to September 2013 who had not yet initiated ART were included and followed up for a minimum of 30 days. The median length of follow-up was 153 days (IQR 91- 238).

**Results:** 3,038 records were reviewed, of which 437 (14.4%) were pediatric cases  $< 15$  years. A total of 1,029 (33.9%) patients began IPT. Among those who initiated IPT, 269 (26.1%) had experienced at least one treatment interruption  $\geq 2$  months, and 661 (64.2%) remained active on treatment until October 2013. The median duration of isoniazid received was 92 days (IQR 58–169) for patients who were active on IPT versus 56 days (IQR 29–89) for patients who had discontinued IPT ( $P < 0.0001$ ). Of the 368 who stopped IPT, 236 (64.1%) were LTFU, 3 (0.8%) transferred out, 1 (0.3%) experienced adverse side effects, 3 (0.8%) died and 125 (34.0%) discontinued IPT according to guidelines due to initiation of ART. Among the patients who started ART, 3 (2.4%) were LTFU, 2 (1.6%) died and zero patients were confirmed for active TB.

**Conclusion:** IPT is underutilized as a TB prevention strategy and is challenged by high rates of LTFU and interruptions due to isoniazid stock-outs. However, our observations of only one event of adverse side effects, no

cases of active TB and a low mortality rate among IPT recipients provide support for continued efforts to improve utilization and training for IPT in HIV care.

#### PD-1076-01 Predictive value of C-reactive protein in the diagnosis of tuberculosis immune reconstitution inflammatory syndrome

W O Worodria,<sup>1,2,3</sup> A Kiragga,<sup>1,3</sup> D Mazapkwé,<sup>1</sup> A Muhofa,<sup>1</sup> R Ssegonga,<sup>1</sup> J Katusiime,<sup>4</sup> Y Manabe,<sup>1,5</sup> R Colebunders.<sup>6</sup> <sup>1</sup>Research Department, Infectious Disease Institute, Kampala, <sup>2</sup>Department of Medicine, Mulago Hospital, Kampala, <sup>3</sup>Department of Medicine, Makerere College of Health Sciences, Kampala, <sup>4</sup>Clinical Services, Mulago-Mbarara Joint AIDS Programme, Kampala, Uganda; <sup>5</sup>Department of Medicine, John Hopkins and Bloomberg Institute, Baltimore, MD, USA; <sup>6</sup>Department of Clinical Sciences, Institute of Tropical Medicine, Antwerp, Belgium. e-mail: worodria@yahoo.com

**Background:** Paradoxical tuberculosis associated immune reconstitution inflammatory syndrome (TB-IRIS) occurs among patients living with HIV/AIDS (PLWHA) having tuberculosis (TB) with advanced CD4 depletion. The current recommendation to start ART 2 weeks after TB treatment among patients with CD4  $< 50$  cells/ $\mu$ L is associated with increased risk of TB-IRIS. Currently there are no validated tests for TB-IRIS. We hypothesized that CRP could predict TB-IRIS.

**Design/Methods:** ART naïve HIV-infected adults with TB and CD4 counts  $< 100$  cells/ $\mu$ L were started ART 2 weeks after TB diagnosis, and followed up at 2, 4, 12 weeks. Serum CRP was measured at baseline and each follow up time. Kaplan-Meier survival estimates were used to obtain cumulative probability of TB-IRIS and a Cox Proportional Hazards model was used to investigate whether time-updated CRP is a predictor of TB-IRIS.

**Results:** Of 189 participants enrolled majority were male 100(53%), aged 32 years (IQR:28–39) and median CD4 count 25 cells/ $\mu$ L (11–48). 108(57.1%) had pulmonary TB. 171 patients were initiated on ART, of these 24(14.0%) developed TB-IRIS a median 28days (IQR:13–69) after ART initiation. CRP (mg/L) at ART initiation, week 2 and 4 were 8.4 (IQR:4.7–22.7), 12.2(IQR:5.9–34.1) and 12.8 (IQR:6.0–48.9), respectively. The cumulative probability of TB-IRIS at months 1, 2 and 3 following ART initiation was 8.3%, 10.4% and 16.5%. Patients with CRP  $> 10$ mg/L were more likely to develop TB-IRIS (HR 5.98(95%CI: 21.3–16.62),  $p < 0.001$ ).

**Conclusion:** CRP is an important biomarker for diagnosis of TB-IRIS. Further investigation into whether CRP could be used for decision making in preventive or therapeutic interventions on TB-IRIS.



### PD-1077-01 Comparison of different screening methods on tuberculosis case finding in HIV positive population

Z Xu,<sup>1</sup> Y Tan,<sup>1</sup> L Bai.<sup>1</sup> <sup>1</sup>TB Control Department, Hunan TB Control Institution, Changsha, China.  
e-mail: evan.xu21@gmail.com

**Background:** To detect the prevalence of tuberculosis (TB) in HIV positive population in Zhuhui district and Yanfeng district of Hunan province, China, and compare the detection rate of liquid culture, chest X-ray examination and sputum smear examination in people who live with HIV (PLHIV).

**Design/Methods:** Zhuhui district and Yanfeng district are high HIV epidemic areas in China, the HIV prevalence reached 107/100,000 and 154/100,000 respectively. The study objects are those PLHIV who were diagnosed as HIV positive before June 30, 2012 and could be followed and traced in the two districts. All research objects were screened through liquid culture (BACTEC™ MGIT™ 960 operating system), chest X-ray examination, sputum smear examination. In addition, mycobacterial species identification was conducted in all liquid culture positive cases.

**Results:** Total 205 PLHIV received TB screening, 19 HIV positive patients were diagnosed with TB, among which eight were diagnosed through chest X-ray examination (3.9%), two through sputum smear examination and 10 through liquid culture (4.8%). Only one patient was both sputum smear positive and liquid culture positive. All eight X-ray positive cases were neither sputum smear positive nor liquid culture positive. However, there was significant statistical difference among the three screening methods for TB case finding ( $P=0.009$ ). Furthermore, four patients were diagnosed with non-tuberculous mycobacteria (NTM) infection through liquid culture. The rates of TB/HIV and NTM/HIV co-infection were 9.26% (19/205) and 1.95% (4/205) respectively.

**Conclusion:** There was high TB prevalence (9.26%) in HIV positive population in Zhuhui district and Yanfeng district. Comparing with chest X-ray examination and sputum smear examination, liquid culture can significantly increase TB case finding and it help to identify NTM infection in PLHIV. In areas with high HIV/TB prevalence, liquid culture could be an effective method for TB screening.

### PD-1078-01 Timing is everything: the value of ART, CPT AND HIV testing date variables in TB surveillance systems

E Mitchell,<sup>1</sup> S Gacheri,<sup>2</sup> J K Sitienei,<sup>2</sup> B Langat,<sup>2</sup> H K Kipruto.<sup>3</sup> <sup>1</sup>Knowledge Research & Policy, KNCV TB Foundation, The Hague, Netherlands; <sup>2</sup>Division of Leprosy Tuberculosis and Lung Disease, Ministry of Health, Nairobi, <sup>3</sup>Tuberculosis, World Health Organization, Nairobi, Kenya.  
Fax: (+31) 70 358 4004. e-mail: mitchelle@kncvtb.nl

**Background and challenges to implementation:** Delay in HIV testing and ARV and CPT initiation results in

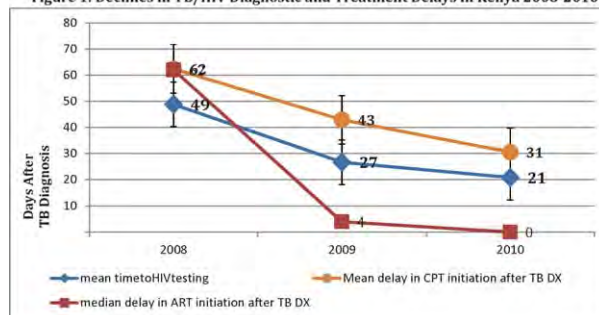
morbidity and mortality among TB patients. The WHO 2013 Revised Case Definitions and Reporting Forms guidance recommends dropping the date variables for start of CPT and ARV from TB surveillance systems. The value of the start date(s) is unknown and its use in policy making and program management was unclear. We sought to explore if measurement of time intervals (delays) offered insights on program performance.

**Intervention or response:** We analyzed electronic case-based surveillance data from 4 provinces of Kenya from 2008–2010 ( $n=2269$ ), to calculate provision of testing and treatment over time as well as timeliness of services. We compared the mean and median time from TB diagnosis to HIV testing and CPT and ART initiation.

**Results and lessons learnt:** Testing for HIV increased steadily and the provision of CPT and ART to TB/HIV patients increased four-fold during the period, but the demand for CPT and ART in newly diagnosed HIV+ TB patients outpaced the supply. Treatment success in TB/HIV patients appeared to stagnate. However, a closer look at the time variables told a different story. Between 2008 and 2010 time from TB diagnosis to HIV testing declined by 53%, and time from TB diagnosis to initiation of CPT and ART declined by 50% and 16% respectively (Figure 2). The national TB program cut the time to HIV testing and CPT provision in half, and virtually eliminated the delay to ART initiation. The difference in TB/HIV patient mortality was substantial: 7% for ART recipients vs. 15% without ART, 10% for CPT recipients vs. 19% without CPT. As expected the combined use of ART and CPT had the largest protective effect (OR 0.29; 95% CI 0.16–0.52). ART initiation and TB/HIV Treatment outcomes in the TB/HIV patient cohort can be influenced by many factors outside NTP control and hence should not be the only two measures of TB program performance. Programs can scale up HIV testing, CPT, and ART, without seeing an immediate reflection in coverage or TB/HIV patient outcomes. Process variables also have a role to play in capturing program performance.

**Conclusions and key recommendations:** The date variables for HIV testing, CPT and ART initiation in TB recording and reporting systems provide complementary information for monitoring of the effectiveness of TB service delivery and should not be eliminated from the national TB recording and reporting systems.

Figure 1: Declines in TB/HIV Diagnostic and Treatment Delays in Kenya 2008–2010



### PD-1079-01 Performance characteristics of facility-based Ziehl-Neelsen sputum-smear microscopy for the diagnosis of tuberculosis among people living with HIV

J Cavanaugh,<sup>1</sup> S Modi,<sup>2</sup> A Okumu,<sup>3</sup> H Alexander,<sup>2</sup> S Musau,<sup>3</sup> K McCarthy,<sup>1</sup> B Burmen,<sup>3</sup> K Cain,<sup>2,3</sup> <sup>1</sup>Division of Tuberculosis Elimination, Centers for Disease Control and Prevention (CDC), Atlanta, GA, <sup>2</sup>Division of Global HIV/AIDS, CDC, Atlanta, GA, USA, <sup>3</sup>KEMRI/CDC Research and Public Health Collaboration, Kisumu, Kenya.  
e-mail: smodi@cdc.gov

**Background:** Due to low technical requirements, Ziehl-Neelsen (ZN) microscopy is the principal diagnostic test for persons with presumed tuberculosis (TB). However, the performance characteristics of ZN microscopy for TB diagnosis among persons living with HIV (PLHIV) at decentralized healthcare laboratories have not been well described in Kenya.

**Design/Methods:** We collected three sputum specimens from PLHIV at 15 HIV care facilities in Nyanza Province. All specimens had ZN microscopy at the facilities; two specimens from each patient had ZN microscopy, Xpert MTB/RIF, and liquid culture at KEMRI/CDC Reference Laboratory. Specimens with *Mycobacterium tuberculosis* complex (MTBC) identified by at least one culture or Xpert MTB/RIF (Xpert) were considered laboratory-confirmed; specimens with negative results on all cultures or Xpert tests were considered MTBC-negative. **Results:** Of 2071 collected specimens, 1965 had valid results for facility-based microscopy and Xpert or culture; 163 of which were laboratory-confirmed with MTBC. The sensitivity, specificity, negative and positive predictive value of facility-based ZN microscopy were, respectively, 18.4%, 98.9% 93.1%, and 60%. By comparison, of 1440 specimens with valid results for reference laboratory microscopy and Xpert or culture, 133 were laboratory-confirmed; sensitivity, specificity, negative and positive predictive value were 39.2%, 100%, 95.1%, and 100%.

**Conclusion:** Field-based ZN microscopy has half the sensitivity of reference laboratory microscopy. The low positive predictive value suggests that a substantial proportion of specimens positive by ZN microscopy do not have MTBC. Reference laboratory microscopy performed considerably better, suggesting issues with technique and training. Efforts should be made to improve the quality of field-based microscopy.

### 51. THE GAMUT OF TRAINING: FROM PATIENTS TO PROFESSIONALS

#### PD-1080-01 Capacity building on PMDT for eastern Africa countries: center of excellence (CoE) on PMDT in Rwanda 2010–2013

F Birungi,<sup>1</sup> Y Habimana-mucyo,<sup>2</sup> V Ombeka,<sup>3</sup> I Leimane.<sup>4</sup>

<sup>1</sup>Biostatistics and Epidemiology, University of Rwanda, College of Medicine and Health Sciences, School of Public Health, Kigali, <sup>2</sup>MDR TB, NTP Rwanda, Kigali, Rwanda;

<sup>3</sup>Africa Regional Office, KNCV, Kenya, Nairobi, Kenya;

<sup>4</sup>Tuberculosis, KNCV, The Netherlands, The Hague, Netherlands. e-mail: fbirungi@nursph.org

**Background:** Since 2005, Rwanda has been implementing diagnosis and treatment of DR TB, integrating TB/HIV services and boosted a treatment success rate over 87%. The Centre of Excellence (CoE) on training on programmatic management of DR TB (PMDT) for East Africa was established in Kigali, Rwanda in mid-2010 with funding from USAID East Africa through TB CAP project of USAID implemented by Royal Netherlands Tuberculosis Foundation (KNCV) as a lead partner.

**Intervention or response:** CoE supports many different activities such as training courses, workshops, experience exchange visits, study tours and fora for knowledge management that are the most effective when they are interconnected. Since 2010 CoE has been implemented training/ learning events: PMDT, Laboratory, TB-IC, TB/HIV, Study tours to Rwanda NTP. The main target populations were program managers, TB doctors, PHC doctors, laboratory specialists.

**Results and lessons learnt:** As Public Health and TB management face new challenges every year, CoE updates training curricula on yearly basis to conform to global and regional developments. For example PMDT course curriculum has been updated over the last four years based on the latest policies in TB diagnostics, treatment, new drugs, reporting system etc. Field visit had been part of PMDT training to develop certain skills of participants. To strengthen team of CoE facilitators and standardize overall approach trainings of trainers (ToT) for regional and national teams have been delivered in 2010 and 2011, training evaluation has been standardized since 2011, follow-up evaluation was introduced in 2012, field visit for gap analysis initiated in 2013. Team of CoE has gradually taken over tasks and responsibilities from international stakeholders and is fully accountable for course development and implementation. Their participation and facilitation during the PMDT theoretical and practical classes increased from 50% in 2011 to more than 80% in 2013.

**Conclusion:** Most eastern Africa countries are now implementing PMDT. The CoE has had important role in building capacity of staff in these countries. However, these efforts should be complemented with regional fora for sharing experiences including ensuring cross countries supervision and monitoring visits.

**PD-1081-01 Trainings for nurses and paramedical personnel in MRT-TB management**

D Ruzanau,<sup>1</sup> A. Radionova,<sup>2</sup> S. Volf,<sup>3</sup> P. Krivonos,<sup>4</sup> A. Budritskiy,<sup>5</sup> A. Zalutskaya,<sup>6</sup> A. Nikolenko,<sup>6</sup> V.S. Korzh Zinkevich.<sup>7</sup> <sup>1</sup>Department of TB, Gomel State Medical University, Gomel, <sup>2</sup>GMG, UNDP/GFATM Project in the Republic of Belarus, Minsk, <sup>3</sup>Grodno State Medical University, Grodno, <sup>4</sup>Belorussian State Medical University, Minsk, <sup>5</sup>Vitebsk State Medical University, Vitebsk, <sup>6</sup>TB Lab., Republican Scientific and Practical Centre of TB and Pulmonology, Minsk, <sup>7</sup>Office of the European Expertise and Communications, Minsk, Belarus. Fax: (+103) 75232749831. e-mail: druzanoff@mail.ru

In many countries of the former Soviet Union, the international standards of diagnosis, treatment and infection control (IC) of tuberculosis (TB) have been only recently introduced. Thus, in Belarus the DOTS strategy has been used for the last 5 years, which not only required the introduction of new approaches and guidelines, but also new methods of training as most medical specialists had outdated knowledge, low competence inadequate to the epidemic situation (the ratio of MDR TB among new cases and among previously treated is 34.6% and 76.6 %, respectively). Furthermore, the current education system was aimed only at doctors and did not include nurses and paramedical personnel. To explore the results of training of nurses and paramedical staff in TB and other hospitals managing MDR TB in Belarus. The effectiveness of training was assessed by pre-training, post-training and postponed (3 months later) questioning, as well as targeted surveillance. The effectiveness of traditional seminars (lectures) and active trainings on various aspects of diagnosis, treatment, support and IC of MDR TB was compared. The trainings for nurses and paramedical personnel have been held since 2012, traditional DOTS lectures - since 2009. The trainings were given in 6 regions of Belarus on the topics: "Supervised treatment for MDR TB", "Forming of adherence in MDR TB patients", "IC TB", "Microscopy in TB detection", "Detection of MDR TB", "HIV/TB", "TB detection in exposed groups of population", "MDR TB in penitentiary system", "Social support for MDR TB patients", "Pharmaceutical management". Besides nurses of TB and non-TB hospitals, prison staff also participated in the trainings, as well as volunteers of the Belarusian Red Cross and paramedical staff of TB hospitals. The trainings were given by the national team of 7 coaches who had undergone training in international educational centers. The trainings were much more efficient than traditional lectures. 3 months later from 55.7 to 92.0 % of the participants put their knowledge and skills into practice. The criteria to assess the effectiveness of the training were developed. 10 modules of the training courses for nurses and paramedical staff were proposed. The trainings aimed at development of competencies (knowledge and skills) and behavior change is the most effective with the introduction of modern TB programs.

**PD-1082-01 Assessment of knowledge on tuberculosis management practices among medical interns and post-graduates in medical colleges of the Tamilnadu, India**

HR Shivaramakrishna,<sup>1</sup> S Anjum,<sup>1</sup> D Ranganathan,<sup>2</sup> R Sridar,<sup>3</sup> J Arivoli.<sup>4</sup> <sup>1</sup>India Country Office, World Health Organization, New Delhi, <sup>2</sup>TBCD, Madras Medical College, Chennai, <sup>3</sup>TBCD, Stanley Medical College, Chennai, <sup>4</sup>TB, State TB Officer, Chennai, India. Fax: (+91). e-mail: shivaramkrishnah@rntcp.org

**Background:** Tuberculosis (TB) continues to be one of the most important global public health threats. The disease is rapidly developing which is resistant to multi drugs. TB knowledge among doctors is recognised as important tool for TB control in India, which has one of the highest TB prevalence in the world. This study aims to study the awareness about Tuberculosis diagnosis and management among the interns and Post Graduates of various Medical Colleges in Tamilnadu State of India.

**Design/Methods:** The survey was conducted among 682 interns and 212 post graduate students of 7 of 21 Government Medical colleges of the Tamilnadu State from February to March 2014. Colleges were selected by simple random sampling technique. The authors distributed pre-tested questionnaire which were completed under supervision without allowance for discussions. The questionnaire was given to every participant, who answered the questions anonymously and the answers were kept confidential. The questionnaire contained a set of multiple choice questions that assessed knowledge of TB, methods of diagnosis and management practices.

**Results:** Current incidence of tuberculosis was correctly answered by 14%, ZN staining for AFB was identified as the best diagnostic procedure/technique for PTB by 68%. The number of sputum samples to be collected under Directly Observed Therapy of Short Course (DOTS) was answered correctly by 82%, Serological tests was considered the best procedure by 18%, dosage of anti-tubercular drugs under DOTS was answered correctly by 61%, type of patients for category II was answered correctly by 70%. Side effects of anti-tubercular drugs was correctly answered by 56%. Only 36% recognized that streptomycin should not be used in pregnancy, only 47 % could state correctly the definition of MDR-TB and only 8% new the definition of XDR-TB. Only 28% state correctly the diagnostic facilities of MDR and only 41% new the correct treatment of MDRTB.

**Conclusion:** This study shows that the knowledge among the interns and the post graduates is inadequate despite DOTS being a regular part of the Health system. There is urgent need to revamp and reform undergraduate medical education and change in medical curriculum with need to institute practical training at DOTS centres in the curriculum of medical students in India.



# **PD-1083-01 How family-based counseling/education can impact the health of patients with tuberculosis in Armenia, 2013**

N Truzyan,<sup>1</sup> V Petrosyan,<sup>1</sup> T Harutyunyan,<sup>1</sup> B Crape.<sup>1</sup>

<sup>1</sup>School of Public Health, American University of Armenia, Yerevan, Armenia. Fax: (+374) 10512566.

e-mail: tnune@aua.am

**Background:** Non-adherence to TB treatment is the main cause of MDR development. Approximately 43% of previously-treated TB cases in Armenia become MDR-TB. This pilot intervention was designed to improve treatment adherence, diminish stigma of TB, and inform TB healthcare professionals about the effectiveness of brief family-based counseling/education (FBCE) with the psychological component leading to successful TB treatment outcomes.

**Design/Methods:** FBCE was conducted in three regions of Armenia, using two teams of professional psychologists and TB nurses. Regions were selected considering TB rates and lack of training programs. Overall, 136 regular TB patients and their family members participated in 90-minutes interactive counseling sessions conducted for each TB patient and family in their homes. To evaluate FBCE effectiveness, we used two approaches: 1) baseline/follow-up surveys and 2) compared treatment outcomes of TB patients participated in FBCE with the national statistics for TB patients of same regions a year prior to intervention.

**Results:** The intervention substantially improved knowledge of TB patients and family members about TB, including modes of TB transmission, common signs of TB, TB prevention, proper TB treatment, and consequences of not following the treatment plan. The mean knowledge score improved for both TB patients (from 19.2 to 21.6,  $p < 0.001$ ) and their family members (from 18.0 to 21.7,  $p < 0.001$ ), alleviating fear and anxiety related to the disease. FBCE reduced stigma of TB disease among patients and their families. The percent of participants that thought TB was not negatively impacting their family relationships increased from 60% to 71% with a notable improvement in interpersonal relationships within these families and improved support for TB patients. TB patients who participated in the intervention had significantly better rates of successful treatment outcomes than those reported in the national statistics (96% vs. 73%), lower default/failure rates (4% vs. 22%), and lower death rates (0% vs. 5%) (Fisher's exact test,  $p = 0.0004$ ).

**Conclusion:** Appropriately designed household-based educational and psychological support interventions can substantially reduce rates of MDR TB and TB mortality by improving family support and adherence of TB patients to treatment. This intervention can be effectively applied in resource poor countries and in settings where Directly Observed Therapy is ineffective or inadequate.

# **PD-1084-01 Training and involving district TB officers as soft skills trainers to overcome communication gaps between TB patients and care-providers**

P Bhattacharya,<sup>1</sup> V Lal,<sup>1</sup> V Bal,<sup>2</sup> B Samuel.<sup>3</sup> <sup>1</sup>Public Health-TB control, German Leprosy & TB Relief Association (GLRA-India), Kolkata, <sup>2</sup>Soft Skills, Enlightenindia, Pune, <sup>3</sup>Public Health - TB control, World Vision India, New Delhi, India. e-mail: drbhattacharya014@gmail.com

**Background & challenges to implementation:** INDIA leads the High Burden Countries with 1/4<sup>th</sup> of the global TB incident cases, along with 1/5<sup>th</sup> of global multi-drug resistance (MDR)-TB burden. India also contributes to 31% share of total 'missed TB cases' globally. Poor communication between care providers and TB patients was attributed to as one of the main factors for poor treatment adherence amongst TB cases. German Leprosy & TB Relief Association (GLRA India), as part of Project Axshya funded by Global Fund, strategically planned to train and involve District TB Officers (DTO) as soft-skill trainers to build communication skills of the health staffs working with Revised National TB Control Program (RNTCP). The intervention was done between June 2011 and December 2013 in 8 districts comprising of 1.83 million populations with 38 TB units and 183 designated microscopy centres (DMC).

**Intervention or response:** Two module based state-level training-of-trainers' (ToT) workshops on soft-skills in context to TB control for all DTOs in West Bengal were organised jointly with the state TB cell (6/2011 & 9/2013) hiring soft skills consultants. These trained DTOs were involved in training of 1053 government health staffs (doctors, paramedics, DOT Providers) in the 8-intervention districts (Each training session of 2 days, with around 25 participants).

**Evaluation questionnaire for government health workers associated with RNTCP trained in soft skills by trained District TB Officers under Project Axshya in West Bengal, India (n=63)**

Scale-4 : High, or significant positive change Scale-1 : Low, or no change				
	Scale-4	Scale-3	Scale-2	Scale-1
1. How much the training supported you to become active listener and encourages your patients to discuss problems freely?	21	37	5	0
2. Rate your achievement in communication skills while communicating with your patients following your workshop?	44	13	5	1
3. As a result of the training, how would you rate your attitude towards your patients and others around you?	27	21	11	4
4. Have you noticed any positive changes in the behaviour of patients and others around you after the workshop?	31	16	12	4
5. Indicate the amount of effort made to improve relations with patients and colleagues?	28	25	10	0
6. Do you feel you are increasingly approached by TB patients or their family members asking for help after your training?	16	24	16	7
7. How would you rate the change in attitude of your friends and family members towards you?	6	34	17	6
8. Do you feel you are better equipped now for empathy building and dealing with feelings of your patients?	41	15	6	1
9. How do you feel the training has contributed to team building at your work-place?	22	29	7	5
10. Do you feel any change in confidence level in resolving conflicts after your soft-skills training?	16	22	13	12

**Results & lessons learnt:** Results were analysed through structured interviews and quarterly RNTCP indicators:

1. Interview of TB patients (n=325) attending DMC and DOT centres run by soft skills trained staffs (T1), as well, those run by untrained staffs (U1). 62% of interviewed patients acknowledged staffs more supportive in T1 than before in contrast to 18% in U1.
2. 69% of interviewed soft-skills trained staffs (n=63) reported significant gain in communication skills at work place.
3. RNTCP indicators of districts with higher soft-skills trainings were proportionate to reduction in defaulted TB cases.

**Conclusions and key recommendation:** DTOs as RNTCP program managers are more aware of the gaps in TB control. West Bengal experience by GLRA India was unique in demonstrating proven effectiveness of soft-skills training through trainers from within the program in addressing challenges of communication between care providers and TB patients. This intervention needs to be replicated in all areas &/or countries with similar challenges in rapid pace.

#### **PD-1085-01 Organising of "patient health education sessions" for tuberculosis patients**

I Felker,<sup>1</sup> T Petrenko,<sup>2</sup> O Filippova.<sup>3</sup> <sup>1</sup>Endoscopy department, Novosibirsk Tuberculosis Research Institute, Novosibirsk, <sup>2</sup>Department of Science, Novosibirsk Tuberculosis Research Institute, Novosibirsk, <sup>3</sup>Organizational and methodological department, Novosibirsk Tuberculosis Research Institute, Novosibirsk, Russian Federation. e-mail: felkeririna@sibmail.com

**Background and challenges to implementation:** Currently one of perspective integrated technologies of prophylactic and curative care is "Patient health education sessions". The goals of "Patient health education sessions" are increasing of motivation and improving patient compliance, also it helps to formation of partnerships with the doctor during the treatment course and mutually beneficial cooperation.

**Intervention or response:** Purpose of our study was investigation possibility to organize "Patient health education sessions" for TB patients which will be based in Novosibirsk TB Research Institute (NTRI). In February, 2014 we conducted a survey which was attended by 130 TB patients and 49 nurses.

**Results and lessons learnt:** Most of the nurses (83.7%) consider it necessary to establish school for patients in tuberculosis hospital. At the same time in the school should be involved different specialists - nurses, doctors, psychologists, lawyer, an epidemiologist, narcologist. Especially psychological help is needed (88% of nurses). Form of classes can be as a group (28 persons (68.3%)) and individual (24.4%). According to of health care workers' opinion (93.2%) duration of sessions should be not more than 30 minutes, 1 time per month (70%). Analysis of the survey results in patients showed that 93% are willing and ready to receive additional knowledge. More than half of the patients (67 people - 55.4% of respondents) noted the need to work with a

psychologist. The majority of patients requiring psychological help were patients suffering from TB less than one year (58%).

**Conclusions and key recommendations:** After analyzing all the data, since March, 2014 "Patient health education sessions" was organized based on NTRI. We made decision to hold classes ones a week for 30–45 minutes. To monitor the effectiveness of this school we plan to conduct re-survey of patients every 2 months. Thus, the organizing of the "Patient health education sessions" for TB patients turned popular and necessary initiative. We sincerely hope for the positive results of our work

#### **PD-1086-01 Effectiveness of training health care workers on TB-HIV management to improve TB treatment outcomes in Swaziland**

N Ndwandwe,<sup>1</sup> L Dlamini Mdluli,<sup>2</sup> C Mlambo,<sup>1</sup> M Calnan,<sup>1</sup> S Haumba,<sup>1</sup> J Ongole.<sup>1</sup> <sup>1</sup>USAID ASSIST, University Research Co.,LLC, Mbabane, <sup>2</sup>TB, National Tuberculosis Programme, Manzini, Swaziland. Fax: (+268) 2404 7199. e-mail: nompumelelon@urc-sa.com

**Background and challenges to implementation:** In Swaziland, a country with HIV prevalence estimated at 26% and TB incidence at 1340/100,000 and TB/HIV co-infection rate at 80%, the education of health care workers on TB/HIV management is essential in reducing the burden of TB in the population and especially in people living with HIV (PLHIV).

**Intervention or response:** A comprehensive training curriculum was developed to promote TB services and improve the management of TB patients and was piloted in 20 health facilities in the Hhohho region. The curriculum targets in-service nurses working in health facilities. Training modules include; epidemiology and control of TB; transmission and pathogenesis of TB; Intensified case finding; laboratory diagnosis of TB; clinical diagnosis of TB; TB case definitions; childhood TB; TB treatment; monitoring TB treatment; collaborative TB and HIV activities; IPT; Patient support and DOT; IPC; basic facts of MDR-TB; MDR-TB suspicion and diagnosis; MDR-TB treatment; monitoring MDR-TB treatment; TB supply chain management and monitoring and evaluation. Training effectiveness and knowledge gain was assessed by correlating pre and post-training results of HCWs and through participatory observations at the time of on-site clinical mentoring and supervisory visits.

**Results and lessons learnt:** Pre-training assessment identified gaps in basic knowledge on Clinical diagnosis of TB, Childhood TB, Monitoring TB treatment, IPT, IPC, MDR-TB suspicion and diagnosis and MDR-TB treatment. Mean test results increased from 38.8% pre-training to 74.6% post-training. Important issues regarding Clinical diagnosis of TB, Childhood TB, MDR-TB suspicion and diagnosis, MDR-TB treatment and Childhood TB remained poorly understood post-training. On-site clinical mentoring was used as an opportunity to address the gaps identified during the training, promote staff motivation, participatory problem solving

and continuing education. Training was also used as an opportunity to improve patient-centred care and HCWs' communication skills. The training has resulted in improved treatment success rates among Pulmonary TB cases from a baseline of 71% in April-June 2013 to 84% in January-March 2014.

**Conclusions and key recommendations:** In-service trainings on TB management coupled with clinical mentoring and supervisory visits improve the knowledge base, motivation of HCWs and in-turn promotes the delivery of services for TB patients. .

### PD-1087-01 Improvement in patient self-efficacy and recognition of high-quality sputum specimens following animated instructional video in Karachi, Pakistan

R Forse,<sup>1</sup> R Hashmi,<sup>1</sup> A Codlin,<sup>1</sup> N Iqbal,<sup>2</sup> A Habib,<sup>2</sup> A Khan,<sup>1</sup> T Seimon.<sup>1</sup> <sup>1</sup>TBXpert PPM Program, Interactive Research & Development, Karachi, <sup>2</sup>Health Informatics, Interactive Health Solutions, Karachi, Pakistan.  
e-mail: rachel.forse@irdresearch.org

**Background and challenges to implementation** Simple verbal instructions can decrease the submission of salivary specimens, increase the return of morning specimens and significantly improve smear positivity rates. However, healthcare workers (HWs) in low-income settings often do not have adequate time to provide sputum instructions to all suspected TB patients. We developed an animated instructional video which is designed to systematically convey steps to producing a high-quality sputum specimen with minimal input from HWs.

**Methods** The instructional video was embedded inside an Android app, allowing patients to self-administer a pre- and post-test to measure changes in self-efficacy and knowledge. The app was designed for a low-literacy setting and includes voiceovers which read all text to the patient in colloquial Urdu. A short video demonstration at the beginning of the app teaches patients how to interact with the tablet. Answer choices were designed as simple colored shapes so that patients would only need to identify either color or shape to know which icon indicates their response. Suspected TB patients at the diagnostic facility of an ACF program in Karachi viewed the animated instructions and took the app's tests.

**Results** The video was evaluated among 80 patients found to be symptomatic of TB who were asked to produce a sputum specimen. Each viewed the instructional video and completed the pre- and post-tests. In the pre-test, 40% of patients believed they could differentiate between sputum and saliva specimens. Self-efficacy increased to 93% in the post-test and was found to be statistically significant ( $p < 0.0001$ ). Patients were then asked to identify an image of a sputum specimen of sufficient volume from a series of 4 images, which included a sputum specimen of insufficient volume, saliva, urine and sputum of sufficient volume. In the pre-test, 60% identified the correct image. This significantly increased to 90% in the post-test ( $p < 0.0001$ ).

**Conclusion** We have shown significant improvement in the self-efficacy and ability of suspected TB patients in identifying images of sputum specimens which are acceptable for testing after viewing an animated instructional video. Further work is required to quantify the impact of the instructional video on patient yields, HW workload, and costs compared with simple verbal instructions.

	Pre	Post	Percent Change	p-value
Do you think you can tell the difference between sputum and saliva samples?				
Yes	32 (40%)	74 (93%)	+131%	
No/Don't Know	48 (60%)	6 (7%)	-88%	$p < 0.0001$
Tap the picture that you think shows a good sample of sputum to submit for TB testing.				
Image of sputum specimen of sufficient volume	48 (60%)	72 (90%)	+50%	
Images of insufficient volume of sputum, saliva, or urine	32 (40%)	8 (10%)	-75%	$p < 0.0001$

### PD-1088-01 Building capacity of physicians/ medical and health professionals on clinical, management of drug-resistant TB in India

A Trivedi,<sup>1</sup> B Thapa,<sup>1</sup> S Prasad,<sup>2</sup> K Sagili.<sup>1</sup> <sup>1</sup>Tuberculosis, USEA The Union Union, New Delhi, <sup>2</sup>CSR, Lilly MDR TB Partnership, New Delhi, India. e-mail: atrivedi@theunion.org

**Background:** Multidrug-resistant TB (MDR-TB) has become significant public health problem and an obstacle to effective TB control. India has the highest number of MDR cases globally. PMDT services have been initiated in India (2007-08) and scaled up across the country by March 2013. The National Tuberculosis Control Programme is rapidly but systematically scaling up the MDR services across the country to address the challenge of MDRTB. The treatment outcomes are ~48% with high rates of death and loss to follow up. While the programme conducts Programmatic Management of DR-TB (PMDT) training programmes regularly, one of the felt needs is developing and updating the knowledge and skills of clinicians managing MDR cases. Initiative taken to build capacity of Health professionals on clinical and operational management of Drug-Resistant TB in India at national and also at state level under the implementing project funded by Lilly foundation.

**Intervention:** Intensive training of health professionals is conducted for five days (50 hours) with an interactive methodology. The training course gives a special emphasis on the clinical, diagnostic and therapeutic issues related to treatment of MDR-TB. The course includes lectures, interactive sessions, field visits to DR-

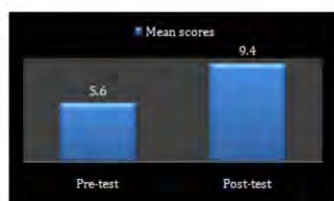


TB centres, MDR-TB ward and National TB Reference Laboratory (NITRD). Two courses were conducted at national level at NITRD New Delhi and two at state level at Tamilnadu and Kerala. 111 physicians/medical and health professionals have been trained so far.

**Results:** The courses were evaluated by pre- and post-tests using a set of 15 questions. The pre-tests indicated a knowledge gap in diagnostics and treatment. These were also areas where maximal gain in knowledge was observed after the trainings. Most of the test scores were obtained in the higher score interval (11–15) after the training. The mean score increased from 5.6 (pre-test) to 9.4 (post-test). This showed the knowledge of the participants was enhanced after the training. Trained participants of the course are being used as facilitators for similar courses being conducted.

**Conclusion:** Comprehensive courses on clinical management of PMDT have been conducted to build capacity among clinicians to manage MDR-TB and creating a pool of trainers across the country for dissemination of the knowledge to clinicians at the state and district level. There is expansion of the training through wider network amongst Public Health Professionals.

The participant wise mean score for pre-test was 5.6 which improved to 9.4, an increase of 68%.



#### PD-1089-01 Knowledge, attitude and practice of tuberculosis management among fresh graduate doctors in Indonesia

R A Ahmad,<sup>1</sup> LA Chandra,<sup>1</sup> N Wilasto.<sup>1</sup> <sup>1</sup>Center for Tropical Medicine, Faculty of Medicine, Universitas Gadjah Mada, Yogyakarta, Indonesia. Fax: (+62) 274 547 147. e-mail: risandono.ahmad@gmail.com

**Background:** Medical doctors are the frontline providers in TB case management. The Indonesia NTP had regularly provided in-service TB trainings for health providers. However, doctors turnover are high, as the NTP cannot influence human resource policy of local governments. To avoid this situation the NTP in collaboration with the DG of higher education had developed guideline to integrate TB management and control into medical curriculum in 2006. Currently, 22 medical schools across Indonesia reported to have implemented this guideline. This survey evaluated the implementation of the initiative.

**Design/Methods:** An online survey, which was developed using LimeSurvey® application, was conducted. Of the 22 medical schools invited, 19 provided lists of contact addresses of newly graduated doctors in 2011–2012. All names were invited to fill the online questionnaire. The

questionnaire consisted of questions regarding TB knowledge, i.e. TB cause, transmission, diagnosis and case management; attitude toward TB control program and their reported TB case management practice.

**Results:** A total of 1986 doctors were invited, with 431 (21.70%) completed the survey questionnaire. Most respondents (82.6%) reported that they managed TB cases last year, of which 51% reported to manage pediatric TB and 53% managed MDR-TB. Approximately 50% of respondents reported to prescribe first line anti-TB drugs for new TB patients, while few respondents (< 4%) reported to prescribe second-line anti-TB drugs. Most of Respondents (>70%) gave correct answer on TB cause, transmission, sign and diagnosis. However only 64% correctly answer the regimen for new TB case, 33.4% of respondents reported ever heard about ISTC and only less than 40% correctly answer question regarding drug management and patient education. Most of respondents (>90%) agreed that TB patients should be treated and reported according to the DOTS standard and that all doctors should be involved in TB control program.

**Conclusion:** The TB pre-service training potentially reduces the NTP needs for in-service trainings. Most doctors have adequate knowledge on TB epidemiology and diagnosis but not TB treatment. Additional topics on pediatric TB and MDR TB should become a priority in medical school as many fresh graduate doctors reported to manage these cases.

#### 52. TB CASE FINDING: IF YOU LOOK FOR IT, YOU WILL FIND IT

##### PD-1090-01 Will centralised community screening or home-based visit result in high participation rate of TB screening among general population?

TA Nguyen,<sup>1</sup> G Marks,<sup>1</sup> G J Fox,<sup>1</sup> V N Nguyen,<sup>2</sup> P T B Nguyen,<sup>1</sup> P N Tran,<sup>1</sup> K H Tran,<sup>3</sup> S V Nguyen.<sup>3</sup>

<sup>1</sup>Research, Woolcock Institute of Medical Research, Ha Noi,

<sup>2</sup>Management, Viet Nam National Lung Hospital, Ha Noi,

<sup>3</sup>Tuberculosis, Center for Social Disease Prevention, Ca Mau, Viet Nam. e-mail: thuanh.nguyen@sydney.edu.au

**Background:** Viet Nam has a high prevalence of tuberculosis (TB). However, less than two thirds of the 180,000 new cases each year are diagnosed. Active case finding may have a role in improving case detection. This study was to assess the relative effectiveness of (i) centralized community screening and (ii) home-based screening in maximizing the participation rate in TB screening among the general population living in a rural area in Viet Nam.

**Design/Methods:** A cross-sectional survey was conducted in two rural villages in Ca Mau Province. Each village was divided into two areas based on geographic characteristics. Screening was conducted in both villages with areas assigned to either centralized community screening or home-based screening. Study participants were those

aged 15 and above, who were usual residents of the village and capable of providing informed consent. Information on the screening activities was delivered to the community via invitation letters delivered to each household by village leaders and by messages over loud speakers. In the study areas where centralized community screening was applied, houses of village leaders and community health stations were used to conduct the screening. In the study areas where home-based visits were implemented, the research team consisted of two members who went to each household. During the screening, people were asked about their symptoms of TB and asked to produce a spontaneous sputum specimen.

**Results:** Of 2,034 people living in study areas, 1,625 met the eligibility criteria including 1,050 in the home-based screening areas and 575 in the centralized screening areas. The screening participation rate was 76% in the home-based visit area and 31% in the centralized community screening area (OR=7.1, 95%CI: 5.7–9.0). Centralized community screening method was more likely, in comparison with household visit, to attract people who reported current respiratory disease (11.8% and 7.0%, respectively) or who had experienced TB treatment in the past (3.9% and 0.5%, respectively). People who participated in two screening methods did not differ in gender, education, or current symptoms of daily cough or daily sputum.

**Conclusion:** TB screening applying centralized community screening is less attractive to people who do not suspect that they may have TB. TB screening at household, with adequate information provided to households prior to implementing activities should be applied to increase the screening participation rate.

#### PD-1091-01 TB case finding using mobile team in two selected peri-urban townships of Yangon region

TMM Khaing,<sup>1</sup> K Naing,<sup>2</sup> T Lwin.<sup>3</sup> <sup>1</sup>National TB Programme, Yangon Regional TB Center, Yangon, <sup>2</sup>Yangon Regional TB Center, Northern District TB Team (Yangon Region), Yangon, <sup>3</sup>Department of Health, Disease Control, Nay Pyi Taw, Myanmar. Fax: (+95)67–421201. e-mail: mywaddy@gmail.com

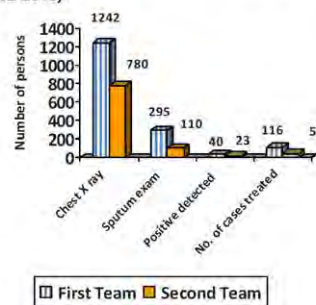
**Background and challenges to implementation:** WHO Global TB Report (2012) showed that reduction in TB prevalence and mortality was prominent but a slow reduction in TB incidence. The gap remained persistent so that active case finding activities should be promoted especially in Yangon Region.

**Intervention or response:** The government sector strengthened TB case finding activities by using mobile team in two peri-urban townships in Yangon Region. The objectives of this study are (1) To increase TB case finding by conducting active case finding activities and (2) To compare the output of mobile team TB screening activities (1st & 2nd time) in the same townships. The community was informed about mobile team activities during pre-visit. Township Medical Officers with their Basic Health Staff (BHS) played an important role in informing community. Health talks were provided by respective

BHS. The community became motivated to participate in TB screening. The persons with presumptive TB identified have been undergone with Chest X-ray screening. If abnormalities were detected, sputum microscopy was followed. The persons who diagnosed TB were treated with anti-TB drugs at Township Health Department.

**Results and lessons learnt:** From September 2012 to August 2013, two townships were covered by mobile team TB screening activities for 2 times. Total (2,022) individuals were screened by Chest X ray and 405 were examined by sputum AFB microscopy. 169 TB patients including 63 smear positive were detected. Radiological examination rate was 0.3%. Smear examination was done in 20%. Smear positivity rate was 15.6%. The proportion of smear positive pulmonary TB cases and treated TB cases obtained by mobile team were 9.2% (63/682) and 10.2% (169/1655) respectively. Mobile team activities contributed 15% of annual targeted presumptive TB, 5% of annual sputum examined, 2.5% of annual smear positive cases and 2.7% of annual treated TB cases in the region. The comparison between two mobile team activities showed the number of sputum examined, positive cases detected and treated cases were lower in the second than in the first time.

Graph: Comparison between mobile team activities in Yangon Region (2012-2013)



**Conclusions and key recommendations:** The mobile team TB screening contributed to increase the number of annual presumptive TB and sputum examined. This activity should be practiced in peri-urban townships biannually since it could cut TB transmission and can lead to reduction of TB prevalence and incidence in high TB prevalence areas like Yangon Region.

#### PD-1092-01 Effectiveness of active-case detection using mobile team in selected township in Myanmar

S Thein,<sup>1</sup> GK Nu,<sup>2</sup> H Nishiyama,<sup>3</sup> N Yamada,<sup>4</sup> K Okada,<sup>5</sup> T Lwin.<sup>6</sup> <sup>1</sup>National TB Programme, Upper Myanmar TB Center, Mandalay, <sup>2</sup>Japan International Cooperation Agency, Major Infectious Disease Control Project, Yangon, Myanmar; <sup>3</sup>Japan Anti-TB Association, Research Institute of Tuberculosis, Tokyo, <sup>4</sup>Japan Anti-TB Association, Research Institute of Tuberculosis, Tokyo, <sup>5</sup>Japan Anti-TB Association, Research Institute of Tuberculosis, Tokyo, Japan; <sup>6</sup>Department of Health, Disease Control, Nay Pyi Taw, Myanmar. Fax: (+95) 67–421201. e-mail: mywaddy@gmail.com

**Background and challenges to implementation:** Proposed post 2015 global TB strategy aims decline rate of TB

incidence to 10% per year. Only with passive case detection (PCD), such decline rate may not be achieved. Ngazun Township is geographically low migrated area with 137,000 population. Active case detection (ACD) by mobile team has been widely implemented since 2011. The objective is to examine how notification of TB cases has changed in Ngazun Township after widely implementing ACD.

**Intervention or response:** Between 2011 and 2013, ACD by mobile teams were frequently and thoroughly conducted by local basic health staffs with strong leadership of a township medical officer under guidance of NTP. They included health talk, medical care, drug provision if necessary and sputum collection/ transportation. For presumptive TB, sputum smear examinations were performed. For negative smear, chest x-ray (CXR) was taken at the township health centre. All services were provided free of charge. Mobile team activities were conducted, for example, by township team 30 times and Rural Health Centre team 12 times even just in 2013. The activities were motivated at regular quarterly TB evaluation meeting and the output was recorded and monitored by NTP and JICA. The JICA Project trained 32 community volunteers to detect more TB cases early by community awareness, referral of presumptive TB and sputum collection/transportation to laboratories.

**Results and lessons learnt:** The number of presumptive TB increased from 110 in 2010 (before intervention) to 884 in 2011, 834 in 2012 and 880 in 2013 (after intervention). Accordingly, the total number of new smear-positive TB (NSP) notified was 50 in 2010, 103 in 2011, 94 in 2012 and 50 in 2013, while the total number of all forms of TB notified was 121 in 2010, 169 in 2011, 186 in 2012 and 193 in 2013. The contribution rate of NSP detected by mobile team was average 38% in 3 years. The treatment success rate of NSP in 2013 maintained satisfactory with 96% (90/94).

**Conclusions and key recommendations:** Widely implemented ACD may lead to both detection of undiagnosed TB cases and early diagnosis of smear-negative TB in the community. Although careful monitoring and evaluation of notified TB cases are required, thorough ACD in a short period may be effective in accelerating the decline in TB prevalence and incidence.

**Ngazun Township Case Notification Data (2010–2013)**

Year	NS+	All TB Cases	CNR (all TB) per 100,000 population	<15 out of All TB (%)	No. of Presumptive TB
2010	50	121	89	22%	110
2011	103	169	123	17%	884
2012	94	186	138	19%	834
2013	50	193	143	30%	880

#### **PD-1093-01 The role of community health workers (Sun Primary Health - SPH providers) in TB control programme in Ayarwaddy Region, Myanmar**

P Swe,<sup>1</sup> S Zarni,<sup>1</sup> O Myint.<sup>1</sup> <sup>1</sup>Program Management Division, Population Services International/Myanmar, Yangon, Myanmar. Fax: (+95)1 527 668. e-mail: ppswe@psimyanmar.org

**Background** Tuberculosis (TB) is a major public health problem in Myanmar. According to the National TB prevalence survey (2010), the smear positive TB prevalence in 15 years and above was 216.1/100,000 in rural areas where around 70% of total population of Myanmar is living. Using a public-private mix approach, PSI/Myanmar implemented in 2004 a DOTS program through its franchised network (Sun Quality Health, SQH) of private clinics. The majority of the franchised clinics are located in urban and peri-urban areas. In 2008, the second network of community health workers (Sun Primary Health, SPH) was developed to deliver health care services in rural areas.

**Intervention** The SPH network comprised of community health workers in the Ayarwaddy region was started in 2008. As of 2013, a total of 229 SPH providers were trained to lead TB active case findings (ACF). SPH providers provide basic knowledge about TB, screen for TB based on symptoms, and trace TB contact persons for screening. Symptomatic individuals are referred to the nearest SQH clinic for TB diagnosis and treatment. SPH providers collect sputum and transport them to the laboratory, inform patients of lab results and collect drugs for TB patients where transportation is difficult. SPH also supervises DOTS for TB patients who are on treatment. PSI/Myanmar provides transportation fees for TB patients and small performance based incentives for SPH providers.

**Results** In 2013, 161 out of 229 trained SPH providers participated in the network; 52% actively participated in ACF activities. It has been challenging to ensure activities take place, as transportation is difficult and there are inadequate diagnostic facilities. However, SPH in the Ayarwaddy region has helped increase TB case notification in local SQH clinics by an average of 10% each year. From 2009 to 2013, 908 TB patients living in project areas were identified by SPH providers and received treatment at SQH clinics. The treatment success rate was higher for TB patients referred and supervised by SPH providers than patients who sought TB care on their own and did not have SPH as supervisors (89% vs 84% for new smear positive patients).

**Conclusions** Community involvement in TB early case detection and treatment through SPH has proved to work, and it is crucial for people to ensure TB control efforts in rural areas. Community health workers in rural areas are able to screen TB, refer symptomatic clients to treatment and provide support supervision during the DOTS treatment.



Treatment outcome of TB patients referred by SPH in 2012

Outcome	TB patients identified & supervised by SPH		TB patients not supervised by SPH	
	NSS(+)	All Cases	NSS(+)	All Cases
Cured	72%	2%	66%	66%
Completed	17%	93%	18%	22%
Defaulted	3%	3%	7%	5%
Failed	2%	1%	4%	2%
Transferred Out	1%	1%	2%	2%
Died	5%	1%	3%	3%

### PD-1094-01 Innovative approaches for increased case finding: the role of house-to-house in TB case finding

O Onazi,<sup>1</sup> M Gidado,<sup>2</sup> M Onoh,<sup>3</sup> J Yisa,<sup>4</sup> Josh Obasanya,<sup>5</sup> R Eneogu,<sup>5</sup> J Kuye,<sup>5</sup> S Gande.<sup>1</sup> <sup>1</sup>M&E, KNCV/TB CARE I, Abuja, <sup>2</sup>Program, KNCV/TB CARE I, Abuja, <sup>3</sup>Program, The Leprosy Mission Nigeria, Abuja, <sup>4</sup>Program, Niger state TB and Leprosy Control Program, Abuja, <sup>5</sup>Program, National TB and Leprosy Control Program, Abuja, Nigeria.  
e-mail: jonazi@kncvnigeria.org

**Background and challenges to implementation:** Community engagement using active case finding approach can assist in detecting cases and curtailing transmission and infectivity of TB bacilli. Nigeria over the years has however been unable to attain the global target of 70% case notification rate suggesting the need for more proactive approaches to TB case finding. Additionally, recent findings from the TB prevalence survey in Nigeria in 2012 revealed that 75% of previously undetected cases found during the survey were sputum smear-positive indicating that many cases go unreported and undetected in the community. The intervention was aimed at actively finding TB cases in the community

**Intervention or response:** Three Local Government Areas (LGAs) with low TB case notification rates were selected. Through advocacy to the district head, community mapping and identification of community volunteers and Ward Development Committee (WDC) members were selected and trained to suspect TB. A house-to-house screening of community members was carried out using symptomatic TB screening tools. All smear positive TB patients detected were notified and placed on treatment.

**Results and lessons learnt:** In all, a total of 2,921 community members were screened over a period of 3 quarters July 2013–March 2014. Of persons screened, 763 (26%) were found to be presumptive TB cases and using AFB microscopy 114 (15%) were found to be smear positive. Data from the LGA indicated a yield of additional 67 (26%) over the baseline data (257). Of these, One (1) was presumptive DR-TB case, 3 sputum smear negative cases were diagnosed by medical officers, one (1) of which was extra pulmonary TB cases were found.

**Conclusions and key recommendations:** Though there are debates about the yield of house to house screening however there are important lessons learned. The most important benefit is the information shared and

increased awareness about TB in communities which is often left behind after the screening exercise might have been completed there by ensuring that the community is better informed. The present study indicates that ICF in communities contribute to improvements in case finding.

### PD-1095-01 Taking TB screening, treatment and care to the unreached miners' settlements in Oyo State, Nigeria

O Lawal,<sup>1</sup> O Oladimeji,<sup>2,3</sup> O Eltayeb,<sup>4</sup> O Daniel,<sup>5</sup> A Iyiola,<sup>1</sup> A Awe,<sup>5</sup> J O Obasanya,<sup>6</sup> T Odusote.<sup>7</sup>

<sup>1</sup>Tuberculosis, Oyo State Ministry of Health, Ibadan, Nigeria; <sup>2</sup>Research, Liverpool School of Tropical Medicine, Liverpool, UK; <sup>3</sup>Tuberculosis Research Unit, Zankli Medical Center, Abuja, <sup>4</sup>Tuberculosis, Damien Foundation Belgium, Ibadan, <sup>5</sup>TUB, World Health Organisation, Abuja, <sup>6</sup>Tuberculosis, Federal Ministry of Health, Abuja, <sup>7</sup>TB-HIV, United States Agency for International Development, Abuja, Nigeria.  
e-mail: droladfb@gmail.com

**Background:** Oyo State is one of the six states in the south west of Nigeria with a population of approximately 6.6 million. There are unreached and neglected twelve-mining settlements within the pockets of five LGAs in the state. These mining communities constitute estimated ten-percent of immigrant population from neighbouring countries (Gambia, Senegal, Liberia and Guinea) involved with buying and selling of precious mineral stones. The objective of this study was to reflect how the program has strategically improved access to TB screening, Treatment and care among the unreached mining communities.

**Design/Methods:** Ten mining communities were identified through the Ministry of Commerce and Mining. Twenty-four community volunteers from the mining workers were trained on conduction of TB awareness among the inhabitants. Training was also conducted on TB screening, collection and transportation of sputum to nearest microscopic centre/s. House to house screening and suspect screening were conducted with weekly sputum collection at designated points. The TB patients were also linked to DOTS provider in the locality.

**Results:** Between April to September 2013, a total of 6 TBLs, 24 Community-Volunteers and 36 General health Workers were trained on the case finding activities. Sputum were collected from 2500 TB suspects and smear positive TB with a total notification of 222 for all forms of TB. 8% and 12% were HIV rates in TB patients and suspects respectively. All detected co-infected patients were placed on CPT and 6 placed on ART. There were 63% male are among the notified TB cases while 65% of the co-infected are female.

**Conclusion:** Engaging other ministries and extending awareness about the risk of TB to unreached mining communities. Improving access with regular awareness on sign and symptoms of TB in these communities can result in significant achievements in TB control.

### PD-1096-01 Experience of BRAC in patient centered care: enhance the accessibility and intensify the TB interventions

S Islam,<sup>1</sup> M Akramul Islam,<sup>1</sup> S Munim,<sup>1</sup> S Alam,<sup>1</sup> R Amzad,<sup>1</sup> M.M. Rahman.<sup>2</sup> <sup>1</sup>HNPP, BRAC, Dhaka, <sup>2</sup>TB, NTP, Dhaka, Bangladesh. e-mail: shayla.dhaka@gmail.com

**Background and challenges to implementation:** TB is a major public health concern in Bangladesh. BRAC, a development organization initiated community based tuberculosis control program in 1984 in one sub-district. This model was gradually expanded since 1994 in collaboration with National Tuberculosis Control Program (NTP) and currently covering two-third of the country. TB control interventions intensified throughout the country to increase notification of all types of TB cases and improve treatment outcomes. Community involvement and assessing the needs and expectations of TB patients is essential for universal access to TB care. **Intervention or response:** BRAC expanded peripheral laboratory facilities with solar system in very remote areas to increase the identification of smear positive TB cases. Outreach sputum collection centers are conducted to improve access to diagnosis. BRAC's frontline health worker known as Shasthya Sebika (SS) plays an important role in implementing community based DOT. They disseminate TB messages in the community during household visits and refer TB symptomatic for sputum examination at NTP designated laboratories. People with persistent TB symptoms and negative smear results are referred to higher level health facilities for X-ray, FNAC and biopsy. Treatment for all TB patients is initiated by graduate medical doctors and daily DOT is ensured by SS.

**Results and lessons learnt:** From January 2012 to December 2013, 9,324 additional outreach sputum collection centers were held and referral linkage established with 4,967 additional private medical practitioners. A total of 8 peripheral laboratories with solar system were expanded to cover hard to reach areas. Service intensification resulted improved case notifications from 93,646 in 2011 and 1,04,984 in 2012, and 1,24,906 in 2013 maintaining treatment success rate over 93%. Case notification in hard to reach areas also increased from 70/100000 population in 2011 to 99 in 2011 and 120 in 2013.

**Conclusions and key recommendations:** Patient centered approach by involving community people showed better result in TB control. This approach could increase early case detection and maintain high cure rate. DOTS expansion by involving community health workers is found to be effective as they are well respected by the community.

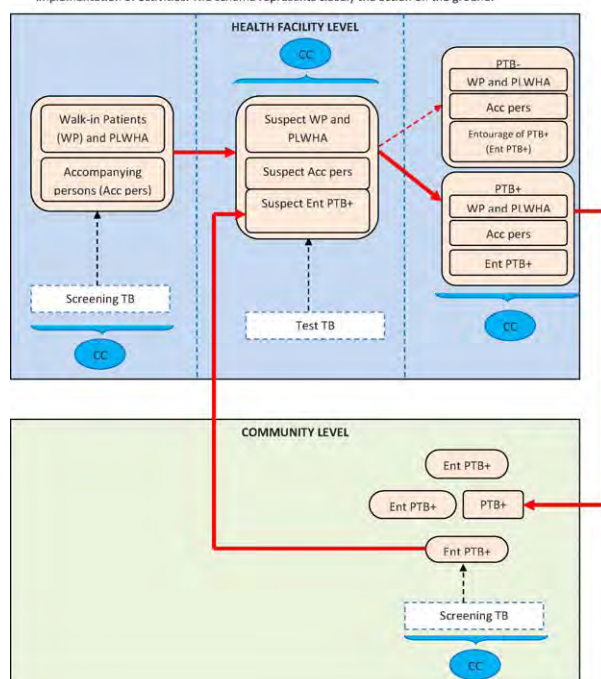
### PD-1097-01 Improvement of TB detection rate: what is implemented by TB Reach in Côte D'Ivoire?

Y Agbassi,<sup>1</sup> S Touré.<sup>1</sup> <sup>1</sup>Project management, ACONDA-VS-CI, Abidjan, Côte D'Ivoire. e-mail: ayjpatrick@gmail.com

**Background:** Of the 24222 tuberculosis (TB) cases detected in 2012 in Cote d'Ivoire(CI), 14660 new cases were smear-positive pulmonary TB (SS+) cases. It is therefore very important to roll back this form of TB in CI. This triggered the implementation of a TB Reach project whose objective is to increase the number of TB cases (SS+) detected within the general population and HIV patients (HIV+) in Abidjan and in the western part of CI.

Conceptual framework of the activities of community counselors on the ground

Within the project conducted with TB Reach in Côte d'Ivoire, the CC act at health facility and community level. At the facility level, they are engaged in screening Walk-in Patients and population living with HIV/AIDS (PLWHA). But also, they deliver the screening form to accompanying persons (Acc Pers) of these aforementioned patients. Thereafter, they administer the TB screening sheet to at least 10 people in the environment of patients diagnosed PTB+ (Env PTB+). In the diagram below; the signs CC1, CC2, CC3 and CC4 in blue color represent the different points where the CC act in the implementation of activities. The scheme represents closely the action on the ground.



**Methods:** Overall, the activities consist in screening systematically walk-in patients (WP) and HIV+ in health centers; seeking actively TB cases in the environment of all SS+; organizing community monitoring. Specifically, 36 community counselors (CC) and 34 health workers have been trained to fill a TB screening form. On the sites, CC organize communication training sessions to encourage behavioral change. CC administer the form to WP and HIV+ and health workers are more inclined to screen patients for TB. In addition, CC deliver the screening form to the accompanying persons. After screening, CC and health workers refer suspect patients for TB testing. CC also conduct home-based visits to administer the screening form to at least 10 persons in the environment of each SS+ case. Subsequently, they refer

suspect patients to health centers for TB testing. They also stay in touch with the suspect persons in the community. Funds are provided to allow indigent patients from the community visiting health centers for TB testing. Coaching, monitoring and evaluation missions are organized jointly by an Ivorian NGO (ACON-DA) and the national tuberculosis program (NTP) on intervention sites to coordinate activities. These interventions aim at increasing the SS+ and TB all forms detection rate respectively from 3560 (baseline) to 4210 SS+ (650 additional cases (AC)) and from 6142 to 7070 all forms (928 AC) by screening 516362 persons. **Key results:** After 53% of case-finding time elapsed, 220424/516362 (43%) persons have been screened among the general population and the HIV+. 3158/4210 SS+ were detected (258/650 AC= 40%) and 5303/7070 all forms were detected (523/928 AC = 56%)

**Conclusion:** In CI, the treatment is initiated for all cases from the detection day. Thanks to this project, the increased detection of TB patients allows a better orientation of their treatment. The faster SS+ detection helps reduce the delay in the TB treatment. The intervention is likely to be extended on other intervention sites thanks to the convincing results to date.

#### **PD-1098-01 Community interventions: can facilitation mechanisms make a difference in improving case detection? A case study from Maharashtra in India**

D Lekharu,<sup>1</sup> A Kapoor,<sup>1</sup> A Pathak,<sup>1</sup> B Entoor Ramachandran,<sup>2</sup> S Chadha.<sup>2</sup> <sup>1</sup>Programs, Population Services International, New Delhi, <sup>2</sup>PMU, The Union South East Asia office, New Delhi, India. e-mail: daisy@psi.org.in

**Background and challenges to implementation:** Project Axshya is implemented by Population Services International (PSI) in ten districts of Maharashtra state and Kolhapur Municipal Corporation (MC) is one of them. The Corporation area has been struggling with improving TB case detection. PSI has engaged community volunteers and trained them to adopt several facilitation mechanisms to improve the TB case detection in the area among the marginalised and vulnerable population.

**Intervention or response:** In Kolhapur MC PSI is focusing on four DMCs, of which D.Y Patil Hospital, Firangai Hospital are ones where the program is being implemented. The brigade of community volunteers who are the front line workers conduct active case finding through door to door visits. They conduct community awareness sessions and identify chest symptomatics with cough for 'two weeks or more' for sputum test at the nearest Designated Microscopy Center (DMC) in the government health facility. They also facilitate sputum collection and transport from the community households, private provider clinics, hospitals and ART centers.

**Results and lessons learnt:** The active case finding along with the sputum collection and transport facilitation

mechanism have made a remarkable change in the TB case detection rates in the two DMCs. The contribution of PSI in D Y Hospital DMC ranges from 29 percent to 50 percent from Oct'13 to March'14 and in Firangai Hospital DMC varies from 40 percent to 80 percent respectively.

**Conclusions and key recommendations:** Well developed strategies and implementation approaches can bring results through community strengthening efforts through identification of a cadre of community volunteers and recommended for conducting capacity building activities and built-in facilitation mechanisms.

#### **PD-1099-01 Role of community TB-officers for screening and improve TB case finding in the community**

R Pe,<sup>1</sup> K Choun,<sup>1</sup> S Thai,<sup>1</sup> N Lorent,<sup>1,2</sup> J Van Griensven.<sup>1,2</sup> <sup>1</sup>Infectious Diseases, Sihanouk Hospital Center of HOPE, Phnom Penh, Cambodia; <sup>2</sup>Clinical Sciences, Institute of Tropical of Medicine, Antwerp, Belgium. Fax: (+855)23 882 614. e-mail: kimchengchoun@sihosp.org

**Background:** Community based participation in active case finding (ACF) programs has been supported by the WHO and the Cambodian national TB program. Communities DOTS implementation is believed to contribute to improve service accessibility for those living far from health facilities, early case detection and treatment, increase cure rates, reduce defaulter and death. We evaluate the role of communities staff & village health-volunteers for improve TB case finding in the community.

**Design/Methods:** A community-based ACF project was implemented in poor urban villages in Phnom Penh in three operational health district (ODs) in Phnom Penh, Cambodia since February 2012 until 31 December 2013. A house-to-house TB-symptom screening strategy was implemented by community TB-officers and village health-volunteers. TB diagnosis was made by smear microscopic and X-pert. We perform X-pert for all patients that had previous TB treatment, confirmed or suspected HIV-infection and smear negative return. All positive results were sent immediately to community staff by SMS, patients diagnosed with TB were referred to existing public TB treatment facilities. TB community's staffs can support travelling cost for poorest patient to health center for control sputum smear.

**Results:** Over the two years period, a total of 351 TB cases were diagnosed. Of these, 1172 (33.4%) were diagnosed by the communities-based ACF program. This included 2055 smear -positive pulmonary TB cases, of which 1070 (52.1%) diagnosed by the community-based ACF program. We observe that from 2010 to 2013 number of all TB case finding increase from 1451 cases, 1480 cases, 1894 cases, 1616 cases respectively and active case finding for all form TB cases 531 cases (28%) in 2012 and 641 cases (39%) in 2013. If we compare 2 years before implementation the project from 2010 to 2011 and 2 years after implementation the project (2012-2013), they observe that all form TB diag-



nosed 2931 (2010–2011) and all form TB diagnose after implementation the project 3510 (2012–2013) with increase 20%. Among all form TB diagnosed from ACF, they observe that PTB smear positive have 1072 (91%).

**Conclusion:** One third of all TB cases and half of all smear-positive pulmonary TB cases were identified by the communities-based ACF program, suggesting this approach is effective. The impact on overall TB case detection and associated delays remains to be defined.

	year	NTP		ACF	
		all form TB	PTB (+)	all form TB by ACF	PTB (+) by ACF
Before implementation the project	2010	1451	572		
	2011	1480	738		
After implementation the project	2012	1894	1072	531	484
	2013	1616	953	641	586
		2931	1310	0	0
				2012	91.14877589
				2013	91.41965679
		3510	2025	1172	1070
		all form	PTB (+)	all form ACF	PTB (+) ACF
				1172	1070

#### PD-1100-01 Door to door TB screening contributes to case detection and enhances TB prevention in the Neslon Mandela Bay District (NMB), Eastern Cape, South Africa

B Mpini,<sup>1</sup> L Canzibe,<sup>2</sup> T Dayimani.<sup>3</sup> <sup>1</sup>Health, Mfesane, Port Elizabeth, <sup>2</sup>Health, University Research Corporation, Port Elizabeth, <sup>3</sup>Health, University Research Corporation, Pretoria, South Africa. Fax: (+27) 41 5822929. e-mail: buyiswa@mfesane.org.za

**Background and challenges to implementation:** The high burden of TB in South Africa continues to be a challenge as latest statistics identifies TB as number one killer. Prevention efforts become imperative in the fight against any epidemic. To contribute to prevention of TB in NMB District, a District seen as one of those with a high TB crisis Mfesane in partnership with USAID TB Programme implemented a door to door screening strategy to contribute to intensive TB detection in the community.

**Intervention or response:** Mfesane a Not-for-Profit Organization sub-grantee of the USAID TB Programme SA employed Community Health Care Workers (CHCWs) in the NMB District. After the CHCWs were trained in basic TB information and DOTs by the USAID TB Programme staff they embarked on door to door TB screening of households in Sub District C in NMB. After the screening, TB suspects identified using a TB symptomatic screening tool were referred to Mfesane mobile clinic for sputum collection and testing. The Mfesane Mobile clinic conducted community outreach campaigns to the communities where door to door screening was done thus providing easy access to TB suspects as they did not have to walk distances to facilities for sputum collection.

**Results and lessons learnt:** In the period June 2013 to March 2014 Mfesane CHCWs screened 6720 people through door to door strategy. Of this number 964 were identified as TB suspects and were referred to Mfesane Mobile clinic for sputum collection and testing. This contributed to increased community TB case detection in NMB thus contributing to TB prevention.

**Conclusions and key recommendations:** Door to door TB screening contributes to TB prevention by increasing TB case detection in the community. Community Outreach collection of sputum and testing through a mobile clinic enhances number of TB suspects presenting themselves for TB testing as it provides for easy access to the people. The use of CHCWs in TB prevention strategies is a cost effective strategy that yields good results for the community participation in the fight against the TB crisis. Door to door screening increase number of people screened in the community as it is done in the privacy of the household thus avoiding the challenge of having to go to the facility to be screened.

#### 53. CASE FINDING/LTBI: ADULTS AND CHILDREN

##### PD-1101-01 Evaluation of routine contact investigation in Ethiopia: a missed opportunity in preventing childhood TB

D Assefa Lemma,<sup>1</sup> G Yosef,<sup>2</sup> E Klinkenberg.<sup>3,4</sup> <sup>1</sup>OR and M & E, KNCV Tuberculosis Foundation TB CARE I, Addis Ababa, <sup>2</sup>TB, Addis Ababa City Administration Health Office, MoH, Addis Ababa, Ethiopia; <sup>3</sup>Research, KNCV Tuberculosis Foundation, The Hague, <sup>4</sup>Department of Global Health, Amsterdam Institute for Global Health and Development, Amsterdam, Netherlands. e-mail: dawita8246@gmail.com

**Background:** One of the key actions outlined in the 2013 global roadmap to address childhood TB is for countries to implement child contact investigation and provide preventive treatment. We identified that there is limited information on the status and factors influencing implementation of child contact screening and management in Ethiopia.

**Design/Methods:** Structured questionnaires were administered to smear positive TB patients living with children ≤ 5 years in their household and care providers in TB, HIV and child health clinics of primary health care setting in Addis Ababa. The outcome measures were self reported household child contact screening and management, practice and perspective of care providers validated using records and TB/HIV register. Double data entry and univariate analysis done using EpiData 3.1 software.

**Results:** From 27 health centres visited in Addis Ababa, 688 registered smear positive TB patients were approached of whom 203 (29.5%) reported to have household contacts of 5 years and below. Health care workers had requested 48 (23.6%) to bring their child for TB screening and 45 (93.8%) had complied with the request. A total of 230 children were living in a household with a smear positive PTB patient and 152

(66.1%) of these children were not screened for TB. Among the 78 (33.9%) children screened, 2 had TB, 76 screened negative and only 3 (3.8%) were put on IPT. None of the HCW interviewed said to routinely record and report figures on contact screening and IPT provision.

**Conclusion:** Implementation of child household contact screening was found to be sub-optimal and there is an important opportunity lost in preventing TB among children under 5 years of age. This could be partly attributed to lack of monitoring tools and untrained staff at key entry points such as child health and HIV clinics.

#### PD-1102-01 Occurrence of diseases in contact investigation tuberculosis and efficient of preventive treatment

B Kisa,<sup>1</sup> N Sarimurat,<sup>1</sup> S Koyman,<sup>2</sup> S Sayici,<sup>1</sup> S Kotan,<sup>1</sup> A Babalik,<sup>3</sup> Zeki Kilicaslan.<sup>4</sup> <sup>1</sup>TB, TB Dispensary, Istanbul, <sup>2</sup>TB, Public Health, Istanbul, <sup>3</sup>Pulmonary, Sureyyapasa Hospital, Istanbul, <sup>4</sup>Pulmonary, Istanbul University, Istanbul, Turkey. Fax: (+90) 2122450911. e-mail: aylinbabalik@gmail.com

Aim of this study was detection rate of disease and efficient preventive treatment in contact investigation in pulmonary tuberculosis. In this study, located in Istanbul 2005–2009, in four of our dispensary, contact tracing of patients with pulmonary tuberculosis were evaluated retrospectively. In this period, there were 7453 contacts in 1909 pulmonary tuberculosis patients, 6114 of 7453 were tested at least once and had an average 2.9-year follow-up. This follow-up process in all close contacts, detection rate of disease in contacts was 2.46 % (184/7453). Detection rate of disease in contacts of smear-positive cases was 3.05% (163/5335), while detection rate of disease in smear negative cases was 0.99% (21/2118). Under 16 years old, Detection rate of TST positive in contacts of smear positive cases was 33.3% (376/1126), in contacts of smear negative cases was 19.50% (71/364). Under 16 years old, detection rate of disease in smear positive cases was 2.31% (32/1384), detection of diseases in smear negative cases was 0.55% (3/536). Detection rate of disease in 16–35 years old contacts of smear positive cases was 4.34% (96/2207), in upper 35 years old was 2.06% (36/1744). Detection rate of disease in under 16 years old treated contacts of smear positive cases was 0.65% (6/912), untreated contacts of smear positive cases was 1.98% (9/455). These rates were in 16–35 years old contacts 0% (0/330) vs 2.94% (54/1832), in upper 36 years old contacts 0% (0/215) vs 0.98% (15/1522). As a result of contacts of smear-positive patients are at high risk of being infected and becoming disease. Preventive treatment of contacts both in children as well, including especially between the ages of 15–35, are also effective in adults.

#### PD-1103-01 Household contact investigation of patients with multidrug-resistant tuberculosis in Tbilisi, Georgia

T Chakhaia,<sup>1</sup> M Magee,<sup>2</sup> R Kempker,<sup>2</sup> M Gegia,<sup>1</sup> L Goginashvili,<sup>3</sup> L Tsakadze,<sup>4</sup> N Dzidzikashvili,<sup>4</sup> H Blumberg.<sup>2</sup> <sup>1</sup>USAID Georgia TB Prevention Project, University Research Co., LLC, Tbilisi, Georgia; <sup>2</sup>School of Medicine, Emory University, Atlanta, GA, USA; <sup>3</sup>Ambulatory, National Center for Tuberculosis and Lung Diseases, Tbilisi, <sup>4</sup>MDR-TB, National Center for Tuberculosis and Lung Diseases, Tbilisi, Georgia. e-mail: tschakhaia@gmail.com

**Background:** Household contacts of patients with multidrug and extensively drug-resistant tuberculosis (M/XDR-TB) are at high risk for TB. WHO recommends conducting contact investigations to screen close contacts for TB, but this is not routinely done in low and middle income countries. We sought to determine rates of active TB and latent TB infection (LTBI) among household contacts of M/XDR-TB patients in Georgia, a high-burden MDR-TB country.

**Design/Methods:** A prospective cohort study was conducted among index cases with active pulmonary M/XDR-TB registered at the National Center for TB in Tbilisi, Georgia from August 2012–November 2013. Household contacts were brought in by their index cases or a home visit was performed. Contacts not diagnosed with active TB during baseline investigation were offered a tuberculin skin test (TST). Contacts with positive TST and without active TB at the time of contact investigation were defined as LTBI. Contacts were evaluated for active TB disease every 6 months after baseline investigation. Incident TB cases in contacts were defined as the development of active TB disease during follow-up (>60 days after baseline investigation).

**Results:** 401 household contacts of 118 index M/XDR-TB cases were enrolled. Among all contacts, 7 (1.8%) were found to have active TB, including 4 at baseline and 3 who developed active TB disease during follow-up (incident rate 895.7 per 100,000 person years). These 7 cases included 5 pulmonary (3 MDR) and 2 extrapulmonary TB cases. Among 129 contacts who received a TST, 59.7% (CI 50.7%–68.2%) had LTBI. Contacts with LTBI were older (median age 39 vs. 34 years,  $p < 0.05$ ) and more likely to sleep in the same room as the index patient (38% vs. 23%,  $p < 0.05$ ) than contacts without LTBI. The index patients of contacts with LTBI were more likely to be married (65% vs. 42%,  $p < 0.05$ ) and have TB symptoms with duration  $\geq 1$  month before treatment (86% vs. 67%,  $p < 0.05$ ). In multivariable analysis, exposure to an index TB case that had TB symptoms with duration  $\geq 1$  month before treatment was significantly associated with LTBI (aOR 3.4 95% CI 1.1–10.0).

**Conclusion:** The burden of active TB disease and LTBI was high among contacts of active M/XDR-TB cases. Prolonged symptoms in M/XDR-TB index cases prior to TB diagnosis were associated with increased risk of LTBI among contacts. Improving public awareness of common TB symptoms may decrease delays in diagnosis and prevent household transmission of TB.

### PD-1104-01 Settlement risk of LTBI activation in employees of large TB hospital

M Zorina,<sup>1</sup> I Felker,<sup>2</sup> P Filimonov,<sup>3</sup> T Petrenko.<sup>4</sup>

<sup>1</sup>Epidemiology, Novosibirsk Tuberculosis Research Institute, Novosibirsk, <sup>2</sup>Endoscopy department, Novosibirsk Tuberculosis Research Institute, Novosibirsk, <sup>3</sup>Laboratory and experimental sector, Novosibirsk Tuberculosis Research Institute, Novosibirsk, <sup>4</sup>Department of Science, Novosibirsk Tuberculosis Research Institute, Novosibirsk, Russian Federation. e-mail: felkeririna@sibmail.com

**Background:** Latent TB infection (LTBI) is reservoir tuberculosis (TB) and all efforts against TB will be not sufficiently effective without control on LTBI. The incidence rate among health care TB workers is 2 times higher than TB incidence in the population. According to the results of QuantiFERON-TB test LTBI is identified in 30–50% of TB hospital staff. Currently there are no known influencing factors and data of LTBI activation in personnel of TB clinic.

**Design/Methods:** 180 employees of Novosibirsk TB-research institute have been tested using the QuantiFERON-TB test. A positive test results were detected in 55 (30.5%) cases. 45 persons agreed to provide the results of chest CT (previous 6 months) were included in the study. We calculated the risk of LTBI activation, using the Online TST/IGRA Interpreter (<http://www.tstin3d.com>) in 45 employees.

**Results:** Risk of active TB during nearest 2 years more than 60% was detected in 62% cases. We examined the association between risk of TB activation and age, professional affiliation, work experience, different medico-biological and social risk factors in staff with LTBI. The main and the single significant risk factor for TB activation in our study was fibrosis and calcinates on chest X-ray (OR 21.4; 95% CI 5.2–88.2). The association between risk of TB activation and income, occupation, living conditions, work experience and age was not found.

**Conclusion:** In our study, the major risk factor of LTBI activation was abnormal chest X-ray (the presence of fibrosis and calcinates in the lungs), which we assume is the result of many factors: its own immune system activity, duration and intensity of MTB exposure and other factors.

### PD-1105-01 The effectiveness of isoniazid preventive therapy in adolescent and adult TB contacts: a population study

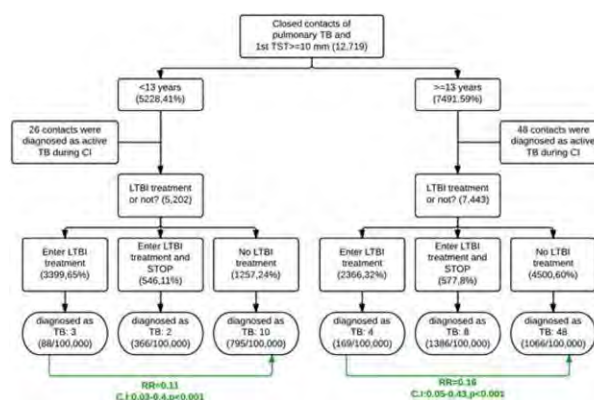
P-C Chan,<sup>1</sup> YH Huang,<sup>1</sup> M-J Lu,<sup>1</sup> P-H Lee,<sup>1</sup> CB Hsu,<sup>1</sup> K-F Wang,<sup>1</sup> C-H Chen.<sup>1</sup> <sup>1</sup>Division of HIV/AIDS and TB, Centers for Disease Control, Taiwan, Taipei City, Taiwan. e-mail: pcanita.tw@cdc.gov.tw

**Purpose:** The latent TB infection (LTBI) program among contacts in Taiwan targeted child contacts aged <13 years before 2012. However, there were still some pilot projects provided IPT to LTBI contacts aged ≥13 years. The study was to evaluate the effectiveness of isoniazid preventive therapy (IPT) provided to adolescent and adult TB contacts aged ≥13 years with LTBI country-

wide in Taiwan since year 2008. Materials and methods: TB contacts aged ≥13 years received tuberculin skin test (TST) for contact investigation between April, 2008 and Dec, 2011 were enrolled. LTBI was defined as TST ≥10 mm in non-HIV contacts in Taiwan. Subsequently developing of TB diseases was monitored and analyzed by stratification of receiving IPT or not. The data were obtained from the National Surveillance Network of Communicable Disease (NSNCD), Centers for Disease Control, Taiwan by Mar. 31, 2013.

**Results:** A total of 7491 contacts exposed to contagious pulmonary TB index cases were tested positive for LTBI (Figure). Forty-eight of them were diagnosed as active TB diseases within 90 days after TB diagnosis of the index cases, which reflected TB rate of 641/100,000 person. Among the 7443 LTBI contacts who did not have active disease during the contact investigation, 2943 contacts (40%) started IPT. Among those who started IPT, 2366 (80%) completed treatment and 4 developed TB afterwards (169/100,000 person). Among those who started IPT without completion of it, 8 were found to have active TB (1386/100,000 person). Overall, TB rate of 1066/100,000 was observed among those who did not start IPT, provided the estimated effectiveness of 84% from completion of IPT (RR: 0.16 [95% CI: 0.05-0.43]) to prevent active TB.

**Conclusions:** The effectiveness of IPT in adolescent and adult TB contacts was 84% with positive TST using 10 mm as the cutoff point. However, 8 cases of breakthrough disease were observed in the pilot program before launch of national LTBI program. For further expansion of LTBI program to adolescent and young adult contacts, training program for LTBI physicians providing both advocacy of LTBI diagnosis and eligibility for IPT treatment should be mandatory.





### PD-1106-01 Predictive value of interferon- $\gamma$ release assays and tuberculin skin testing in children contacts of tuberculosis cases

M N Altet Gomez,<sup>1</sup> J Dominguez,<sup>2</sup> MA Jiménez,<sup>1</sup> MA De Souza-Galvao,<sup>1</sup> C Mila,<sup>1</sup> I Latorre,<sup>2</sup> & Orcau Palau,<sup>3</sup> JA Caylà.<sup>3</sup> <sup>1</sup>Unidad de Tuberculosis Vall d'Hebrón-Drassanes, Hospital Universitario Vall d'Hebrón, Barcelona, <sup>2</sup>Servei de Microbiologia, Institut d'Investigació Germans Trias i Pujol, Badalona, <sup>3</sup>Agència Salut Pública de Barcelona, Agència Salut Pública de Barcelona, Barcelona, Spain. e-mail: jadomb@gmail.com

**Objectives:** There is little data on the Positive Predictive Value (P.P.V) and the Likelihood Ratio positive (L.R.+) of IFN- $\gamma$  in the development of TB in children. The objective of this study is to investigate the risk of developing TB after recent infection in contacts followed up. TB infection was diagnosed by using QuantiFERON-GIT and Tuberculin Skin Test (T.S.T).

**Patients and methods:** 457 contacts (<15 years old) of TB cases, were studied in the unit TB Vall d'Hebron-Drassanes of Barcelona: there were 272 TST  $\geq$  5mm and 172 QFN.GIT  $\geq$  0.35 IU/ml. Contact tracing was done following National Guidelines. There were 299 contacts with bacillary cases, having a follow-up of 48 months.

**Results:** There were 32 cases of TB diagnosed during contact tracing (between 1–12 weeks after index case was diagnosed), which were excluded from the follow-up. 299 contacts of smear-positive index cases developed 7 TB cases during follow-up: all with T.S.T  $\geq$  5mm and QFN.GIT  $\geq$  0.35 IU/ml. The table shows the incidence rate (I.R) / 1000 persons.year during follow-up according to initial results of T.S.T/ QFN.GIT and the treatment provided. Children that didn't accept LTBI treatment have a high TB incidence: the P.P.V is higher with QFN.GIT that with T.S.T. The likelihood (L.R+) that a child with TB infection develops TB if not treated is 13 times greater if QFN.GIT was positive and 1.5 times greater if it was the T.S.T. A child with good compliance to the LTBI treatment developed TB during treatment.

Test		N	TB cases	T.I/ 1000 p.a	P.P.V.	L. R. (+)
All Contacts with follow-up	Total	299	7	5.85		
	QFN.GIT(+)	121	7	14,5	6 (2–10)	2.6
	QFN.GIT(-)	178	0	0		
	TST $\geq$ 5mm	180	7	9,7	4 (1–7)	1.7
Contacts Don't treated	TST < 5mm	119	0	0		
	Total	72	6	20.8		
	QFN.GIT(+)	11	6	136.4	55 (25–84)	13.2
	QFN.GIT(-)	61	0	0		
	TST $\geq$ 5mm	49	6	30.6	12 (3–21)	1.53
	TST < 5mm	23	0	0		

**Conclusions:** this results show that QFN.GIT is a good biomarker of TB infection and of the TB development prediction. The LTBI treatment and their enforcement are a priority as a tool for the TB control. The study was funded using a grant from the FIS (08/1738)

### PD-1107-01 An evaluation of chest X-ray in the context of community-based screening of child tuberculosis contacts

R Triasih,<sup>1,2</sup> C Robertson,<sup>3</sup> T D Duke,<sup>2</sup> S M Graham.<sup>2</sup>

<sup>1</sup>Pediatric, Dr. Sardjito Hospital/Faculty of Medicine, Universitas Gadjah Mada, Yogyakarta, Indonesia; <sup>2</sup>Centre for International Child Health, The University of Melbourne Department of Paediatrics and Murdoch Childrens Research Institute, Royal Children's Hospital, Melbourne, VIC, <sup>3</sup>Respiratory Medicine, Royal Children's Hospital, Melbourne, VIC, Australia. Fax: (+62) 274 583 745. e-mail: rina\_triasih@yahoo.com

**Background:** Chest X-ray (CXR) is the commonest investigation used to diagnose tuberculosis (TB) in children. There are very few published data on CXR findings of children in the context of community-based contact screening, which may identify children with less severe disease than hospital-based studies. We aimed to describe the quality and findings of CXRs of child TB contacts; and to evaluate inter-reviewer agreement.

**Design/Methods:** We screened children that had close contact with a pulmonary TB case in Yogyakarta, Indonesia. All eligible children had a CXR in antero-posterior and lateral views. The CXRs were interpreted independently by four reviewers (two radiologists and two paediatricians). No clinical information was provided to the reviewers.

**Results:** A total of 530 CXRs of 265 child contacts were reviewed. The majority (??%) of the CXRs was reported as moderate to good quality. The agreement on CXR quality among four reviewers for AP view was slight to fair (weighted kappa: 0.16 to 0.35), and was moderate for lateral view (weighted kappa: 0.32 to 0.53). The majority (65% to 77%) of the CXRs was reported as normal by all reviewers with fair to moderate agreement. Hilar lymphadenopathy (6 – 16%) and parenchymal infiltrate (8–21%) were the commonest CXR abnormalities. Inter-reviewer agreement in identifying hilar lymphadenopathy was poor (kappa: 0.03 to 0.25).

**Conclusion:** Most child contacts investigated at the time of initial screening had a normal CXR. Hilar lymphadenopathy was the most frequent CXR abnormality, but inter-observer agreement was very poor.

### PD-1108-01 Screening of latent tuberculosis infection among recently arrived immigrants: usefulness of tuberculin skin test and QFT-GIT

A Sánchez-Montalvá,<sup>1,2</sup> F Salvador,<sup>1,2</sup> T Tortola,<sup>2,3</sup> M Yuste,<sup>4</sup> B Treviño,<sup>2,5</sup> N Serre,<sup>2,5</sup> D Pou,<sup>2,5</sup> I Molina.<sup>1,2</sup>

<sup>1</sup>Infection Disease, Vall d'Hebron Teaching Hospital, Barcelona, <sup>2</sup>International Health, PROSICS Barcelona (International Health Program of the Catalan Health Institute), Barcelona, <sup>3</sup>Microbiology Department, Vall d'Hebron Teaching Hospital, Barcelona, <sup>4</sup>CAP Trinitat Vella, Institut Català de la Salut. SAP Muntanya, Barcelona, <sup>5</sup>Infectious Disease, Vall d'Hebron Teaching Hospital-Drassanes, Barcelona, Spain. e-mail: adsanche@vhebron.net

**Background:** Tuberculosis (TB) is an important issue in the international health agenda. Latent Tuberculosis

Infection (LTI) treatment has shown to be an effective approach to accomplish TB control in TB low-burden countries. Despite having shown promising results in specific group of patients, interferon-gamma release assays (such as QuantiFERON®-Gold in tube) usefulness is unknown in recently arrived immigrants. The aim of this study is to describe the results of TST and QTF-GIT assay in recently arrived immigrants.

**Methods:** We present a cross-sectional study between November 2012 and December 2013, conducted in PROSICS Barcelona venues (International Health Program of the Catalan Health Institute) and primary health care centers of the north area of Barcelona (SAP Muntanya). Immigrants from high TB burden countries, between 18 and 35 years old, with less than 3 years in low TB countries, were selected. After signing informed consent a thorax x-ray, blood test, TST and QTF-GIT were performed. HIV patients were excluded, as well as patients who received treatment for active TB at any moment or had recent contact with a TB patient. Patients with LTI, defined as TST and QTF-GIT positives were treated with a 3-months course of isoniazid and rifampicin. Patients with other combination of results are being closely followed up.

**Results:** Overall, 175 patients were included. Geographical origin of patients were as follows: 41.7% of patients came from Africa, 30.3% came from Latin America, 25.1% came from Asia (mainly from Pakistan), and 2.9% of patients came from Eastern Europe. Mean age was 24 years (SD 4.96), 59.4% were men, and mean length of stay in the country was 13.4 (SD 9.96) months. TST was positive in 38.8% of patients, while QTF-GIT was positive in 23.9% of patients. Concordance of the test was 80.9%. In 17.1% of the patients TST results was positive while QTF-GIT was negative. Only 3 patients show QTF-GIT positivity while TST was negative, despite booster was performed. Patients with bigger TST size were more likely to have a more positive QTF-GIT result. Africa region has the biggest rate of LTI (37.5%) according to our definition.

**Conclusion:** QTF-GIT and TST shows great concordance, however 17.1% of patients show positive TST with a negative QTF-GIT result. TST may overestimate LTI rates due to BCG vaccine and exposure to atypical mycobacterias. QTF-GIT may be used alone for LTI screening in recently arrived immigrant.

#### PD-1109-01 Enhanced case detection following household contact tracing for childhood tuberculosis in The Gambia

U Egere,<sup>1</sup> T Togun,<sup>1</sup> A Sillah,<sup>1</sup> B Ahadzie,<sup>1</sup> N Heinrich,<sup>2</sup> B Kampmann.<sup>1,3</sup> <sup>1</sup>Vaccinology (Childhood TB Research Group), Medical Research Council Unit, Banjul, Gambia; <sup>2</sup>Paediatrics, Centre for International Health, University of Munich, Munich, Germany; <sup>3</sup>Paediatrics (Academic), Imperial College London, London, UK. e-mail: uegere@mrc.gm

**Background:** Although the WHO recommends contact tracing for children exposed to smear positive TB in their households, this practice is rarely implemented in high burden settings, primarily due to resource constraints.

We set up contact tracing among child contacts of adult smear positive TB cases to investigate the potential yield and its challenges in the greater Banjul Area of The Gambia where approximately 80% of all TB cases in the country are diagnosed.

**Design/Methods:** Child contacts aged <15 years in households of adults with smear positive tuberculosis were screened for TB using basic symptom screening questionnaire and tuberculin skin testing (TST) in the community, with subsequent clinical examination and investigation of all symptomatic and/or TST positive (induration  $\geq 10$ mm) contacts in a dedicated childhood TB clinic at the MRC Unit in The Gambia. TB disease was diagnosed according to the 2013 revised case definition proposed by the WHO comprising bacteriologically confirmed and clinically diagnosed TB. All contacts under 5 years without TB disease were offered Isoniazid prophylaxis for 6 months.

**Results:** Between February 2012 and March 2014, 2903 child contacts of 381 adult smear positive TB cases were screened in the community. The median (IQR) age was 6 (3 – 10) yrs. Of these, 731 children required further investigation at the childhood TB clinic; 431 (65%) were asymptomatic but had positive TST results and 318 (43.5%) had symptoms suggestive of tuberculosis. 53/731 (7.2%) were diagnosed with TB disease, of which 19 were bacteriologically confirmed and 34 were clinically diagnosed. This amounted to a prevalence of 1825/100,000 in child contact population. The overall notification for childhood TB in the national register increased from 4.3% in 2011 to 6.9% in 2013. Of the under 5 year old child contacts, 625 were started on Isoniazid prophylaxis of which 358 of 457 (78.3%) completed 6 months of prophylaxis. Prophylaxis is still ongoing in 168 and 99/625 (15.8%) children dropped out to date.

**Conclusion:** Contact tracing and screening of TB exposed children increased the yield of childhood TB in this West African setting. There was a high uptake of INH prophylaxis with good adherence. The cost effectiveness of these interventions needs to be assessed in this setting.

#### PD-1110-01 The iAdhere Study: reasons patients declined or accepted study participation

K Chapman,<sup>1,2</sup> A Borisov,<sup>1</sup> M Engle,<sup>3</sup> R Belknap,<sup>4</sup> S Goldberg,<sup>1</sup> D Wing,<sup>5</sup> J Mangan.<sup>1</sup> <sup>1</sup>Division of Tuberculosis Elimination, Centers for Disease Control and Prevention, Atlanta, GA, <sup>2</sup>Research Collaboration, CDC Foundation, Atlanta, GA, <sup>3</sup>Division of Infectious Diseases, University of Texas Health Science Center at San Antonio, San Antonio, TX, <sup>4</sup>Denver Metro TB Program, Denver Public Health Department, Denver, CO, <sup>5</sup>Regional Academic Health Center, Clinical Research Unit, University of Texas Health Science Center, Harlingen, TX, USA. e-mail: icx3@cdc.gov

**Background:** The Centers for Disease Control and Prevention's Tuberculosis (TB) Trials Consortium is concluding iAdhere (Study 33), an open label, international multicenter, randomized clinical trial. The study

compares adherence between directly observed and self-administered therapy of 3-months (12 doses) of weekly rifapentine and isoniazid (3HP) for latent TB infection (LTBI) ([www.clinicaltrials.gov/show/NCT01582711](http://www.clinicaltrials.gov/show/NCT01582711)). Understanding reasons for decline and motivations for participation can help strengthen recruitment and retention in clinical trials and might help to understand the degree to which study results are generalizable.

**Methods:** iAdhere's target enrollment is 1,000 adults with LTBI, eligible for treatment with 3HP. All persons declining enrollment were asked to provide reasons. Following a study amendment, study participants were asked to report motivations for enrolling. Through standardized data collection forms, reasons for declining or accepting participation were collected prospectively. Descriptive statistical analysis was conducted.

**Results:** 2,013 candidates were screened for participation. 980 (49%) were enrolled and 1027 (51%) were not enrolled due to: 1) failure to meet eligibility criteria [215 (21%)], 2) site decision [274 (27%)], or 3) candidate choice [538 (52%)]. Of the 538 who declined (81% screened at U.S. sites, 51% male, 80% foreign-born), 462 (86%) provided at least one reason for decline for 655 total reasons. The top 5 reasons for not enrolling were: standard therapy preferred (13% of all reasons), not interested in study medication (11%), not interested in LTBI therapy (10%), DOT is inconvenient (9%), and concerns over pill burden (8%). Of 980 enrolled participants, 169 (89% screened at U.S. sites, 38% male, 63% foreign-born) provided 410 reasons motivating their enrollment. The top 5 reasons for enrolling were: access to shorter regimens (23% of all reasons), avoidance of progressing to TB disease (17%), improving one's health (6%), once-weekly dosing (5%), and helping others with the same diagnosis (3%). Enrolling because of incentives was reported by one participant.

**Conclusions:** Concerns about established versus research treatment and lack of interest in LTBI therapy were common reasons for not participating. Improving one's health, avoiding progression to TB disease, and faster treatment were cited as reasons for enrolling. Future efforts could explore whether addressing these issues would increase enrollment.

## PD-1111-01 Comparison between tuberculin skin test and interferon gamma release assay (IGRA) results in children: a household contact study in Vitória, Brazil

P Rodrigues,<sup>1,2</sup> R Peres,<sup>1,2</sup> F Silva,<sup>1,2</sup> J Ellner,<sup>3</sup> E Jones-López,<sup>3,4</sup> R Dietze,<sup>1,2</sup> R Ribeiro-Rodrigues,<sup>1,2</sup> A E Miranda.<sup>2</sup> <sup>1</sup>Núcleo de Doenças Infecciosas (NDI), Universidade Federal do Espírito Santo (UFES), Vitória, ES, <sup>2</sup>Programa de Pós-Graduação em Doenças infecciosas (PPGDI), Universidade Federal do Espírito Santo (UFES), Vitória, ES, Brazil; <sup>3</sup>Medicine, Section of Infectious Diseases, Boston Medical Center and Boston University School of Medicine, Boston, MA, <sup>4</sup>Medicine, Division of Infectious Diseases, New Jersey Medical School, Rutgers University, Newark, NJ, USA. Fax: (+55) 27-33357206. e-mail: pmarques@ndi.ufes.br

**Background:** Children with latent tuberculosis (TB) infection (LTBI) have an increased risk of progression to disease compared to adults. However, the diagnosis of LTBI in children is challenging because of false-positive tuberculin skin test (TST) results (BCG vaccination and environmental mycobacteria) and uncertainty of IGRA results in this age group. The objective of our study was to compare the performance of TST and IGRA in children aged 3 months to 14 years.

**Patients and Methods:** This study is part of a household contact study conducted in Vitória, Brazil from 2008 to 2013. Index TB cases were sputum smear ( $\geq 2+$ ) and culture-positive. We collected demographic and clinical data and measured LTBI with TST and Quantiferon-Gold-In-Tube. Children were categorized into two age groups: 0–4 and 5–14 years old. A TST  $\geq 10$ mm was considered positive. We calculated Kappa concordance and chi-squared test.

**Results:** 273 children were enrolled. The mean age for children in the  $<5$  age group was 2 years (range 0.3–4 years), and 9 years (5–14 years) in the  $\geq 5$  age group. Both age groups were comparable regarding gender and BCG vaccination scar. BCG did not influence TST nor IGRA results ( $X^2$   $p=0.483$  and  $p=0.405$ ). Agreement between TST and IGRA in children  $<5$  years old was higher (94,12%  $k = 0.883$ ; 95% CI: 0.754 – 1.0), compared to children  $\geq 5$  years old (86,04%,  $k = 0.715$ ; 95% CI: 0.622 – 0.808).

**Conclusions:** In this household contact study from an intermediate prevalence country, agreement between TST and IGRA results was higher in children  $<5$  than in older children. Although routine dual testing with both TST and IGRA is not currently recommended, results from both tests may aid in the diagnosis of LTBI in children.

iAdhere Participant Characteristics\*

	TOTAL SCREENED		ENROLLED				NOT ENROLLED					
			TOTAL		Motivations Form Completed <sup>†</sup>		TOTAL <sup>‡§</sup>		By Patient Choice <sup>**</sup>			
	n	Col%	n	Row%	Col%	n	Row%	Col %	n	Row%		
2007	980	(49)				169	(17)	1027	(51)	538	(52)	
SEX												
Female	967	(48)	473	(49)	(48)	104	(22)	494	(51)	(48)	264	(53)
Male	1,040	(52)	507	(49)	(52)	65	(13)	533	(51)	(52)	274	(51)
BIRTH PLACE												
Foreign Born	1,553	(77)	727	(47)	(74)	107	(15)	826	(53)	(80)	428	(52)
USA	454	(23)	253	(56)	(26)	62	(25)	201	(44)	(20)	110	(55)
SCREEN COUNTRY												
NON US	418	(21)	227	(54)	(23)	18	(8)	191	(46)	(19)	104	(54)
US	1,589	(79)	753	(47)	(77)	151	(20)	836	(52)	(81)	434	(52)
AGE GROUP												
2–17 yrs.	4	()				7		4	(100)	()		
18–34 yrs.	866	(43)	440	(51)	(45)	70	(16)	426	(49)	(41)	205	(48)
35–64 yrs.	1,052	(52)	511	(49)	(52)	94	(18)	541	(51)	(53)	298	(55)
≥65 yrs.	85	(4)	29	(34)	(3)	5	(17)	56	(66)	(5)	35	(63)

\*Preliminary data before 15 April 2014

<sup>†</sup>Enrolled patients who completed the motivation for enrollment survey

<sup>‡</sup>Row % indicates percentage of total screened

<sup>§</sup>Others not enrolled: ineligible ( $n=215$ , 21%) & not enrolled by site choice ( $n=274$ , 27%)

<sup>\*\*</sup>Row % indicates those not enrolled by patient choice compared to others not enrolled



### PD-1112-01 Identification, evaluation and monitoring of children under five years old household tuberculosis contact in 30 municipalities of Chocó, Colombia

J M Hernández,<sup>1,2</sup> H Andrade,<sup>3</sup> L Murillo,<sup>4</sup> L Velasquez,<sup>3</sup> M Mejía,<sup>1</sup> A Gomez,<sup>1</sup> J Robledo.<sup>1,2</sup> <sup>1</sup>Antioquia, Corporación para Investigaciones Biológicas, Medellín, <sup>2</sup>Antioquia, Universidad Pontificia Bolivariana, Medellín, <sup>3</sup>Chocó, IPS Erchichijay, Quibdó, <sup>4</sup>Chocó, Dirección Seccional de Salud del Chocó, Quibdó, Colombia. Fax: (+574)4415514. e-mail: jrobledo@cib.org.co

**Background:** the systematic study of household contacts of TB patients is one of the more effective activities to identify new TB cases. In these contacts it is recommended to treat those with latent tuberculosis with isoniazide to decrease the risk to develop an active form of the disease. These measures are particularly important in children under 5 years since they have an increase risk to develop the disease after being infected.

**Design/Methods:** we randomly selected 159 adult tuberculosis cases reported in 30 municipalities of Choco, Colombia and analyzed the records of the tuberculosis control program related to activities of diagnosis and treatment for latent and active disease in children under five years old household tuberculosis contact. A descriptive analysis of the different variables and a multivariate analysis were performed to determine the association of being diagnosed and treated for latent and active tuberculosis.

**Results:** 103 children were identified as household tuberculosis contact of 159 adult pulmonary tuberculosis patients. Only 61 (59.2%) of them had clinical and or microbiological evaluation. Signs and symptoms were assessed in 63.3% of children; tuberculin was performed in 25.2%; in 22.2% of children a Chest X-rays was performed, AFB examination was done in 14.5% and cultures in 1.9% of patients. Thirteen (21.3%) cases were diagnosed with latent TB and 8 (13.1%) with active TB. Tuberculin administration was associated with treatment for latent TB (OR: 11.4 CI:2.18–60.04), and the evaluation of lymphadenopathy was associated with the treatment for active TB (OR: 9.04 CI:1.7–46.7).

**Conclusion:** the study of children under five years old household tuberculosis contact shows weaknesses in the department of Chocó (Colombia). The program should strengthen its capacity to register and study the all household contacts of patients with pulmonary tuberculosis under 5 years, due to the high prevalence of the disease that is found in this age group.

### 54. TB IN THE ELDERLY: EFFECTS AND OUTCOME

#### PD-1113-01 Missed opportunities in treating elderly contacts with latent TB infection at the Singapore TB Control Unit

A Chua,<sup>1</sup> K M Kyi Win,<sup>1</sup> J Cutter,<sup>2</sup> C Chee,<sup>1</sup> Y T Tang.<sup>1</sup>

<sup>1</sup>TB Control Unit, Tan Tock Seng Hospital, Singapore,

<sup>2</sup>Communicable Diseases Division, Ministry of Health, Singapore. Fax: (+65) 63567391.

e-mail: angeline\_pg\_chua@ttsh.com.sg

**Background:** Risk-benefit considerations may lead to withholding treatment for latent TB infection (LTBI) in the elderly and result in missed opportunities to prevent active TB. We looked at the impact of INH-induced hepatitis and compared the outcome of 2 groups of elderly contacts.

**Methods:** We report the experience of Singapore's National TB Programme in screening and treating LTBI in elderly contacts (ie  $\geq 65$  years of age) from 2006 to 2011. Household and workplace contacts were screened with the tuberculin skin test; those in congregate settings (eg nursing homes, prisons) were screened with the QuantiFERON-Gold In-tube assay. Contacts on LTBI treatment were monitored 4 to 6 weekly. Liver function tests were performed at baseline, 1 and 4 months of treatment and when symptoms were reported. Treatment regimen was INH for 6 months in household contacts and for 9 months in institutionalized contacts. Contacts were matched with the National TB Notification Registry as at 31 December 2013

**Results:** Elderly contacts comprised 8% of all contacts screened from 2006 to 2011; 52.3% were aged 65–74 years ("young-old") and 47.7%  $\geq 75$  years ("old-old"). Of the "old-old", active TB was found in 23(1.4%) and LTBI was diagnosed in 360/1637(22%); treatment was not started in 162(43.2%) due to high baseline ALT/AST and in 60(37%) due to age/medical conditions (vs 7.5% in the young-old); 56(34.6%) refused LTBI treatment. Of those treated, completion rate was 64.8%; prematurely stopped in 9.8% due to raised ALT/AST. 5.6% died during LTBI treatment from causes unrelated to INH-induced hepatitis. As of 31<sup>st</sup> December 2013, 12/1614(0.7%) contacts  $\geq 75$  years (vs 0.3% contacts 65–74 years) had developed active TB; 8/1093(0.7%) had tested negative for LTBI and were not considered for treatment; 4/360(1.1%) had tested positive for LTBI but 2 were not started on LTBI treatment because of age, 1 defaulted and 1 refused treatment giving an active TB rate of 3%(4/133) in these contacts who were not started/did not complete treatment. None who completed treatment developed disease

**Conclusion:** Awareness of INH toxicity risk, careful monitoring and low threshold for stopping INH can avoid serious complications. Completion of LTBI treatment resulted in reduction of active TB risk. The relative risk of 2.2 for active TB between the  $\geq 75$  and 65–74 groups was partly contributed by withholding LTBI treatment in the "old-old". From 2014, we started using 4 months RIF for institutionalised elderly with LTBI

### PD-1114-01 Determinants of death before start of and during tuberculosis treatment among elderly patients: a population-based follow-up study in Taipei, Taiwan

Y Yen,<sup>1</sup> YS Lin.<sup>2</sup> <sup>1</sup>Section of Infectious Diseases, Taipei City Hospital, Taipei, <sup>2</sup>Department of Pharmacy, Taipei Veteran General Hospital, Taipei, Taiwan.  
e-mail: dam37@tpech.gov.tw

**Background:** People with weakened immunity because of age or comorbidities comprised the fastest-growing portion of tuberculosis (TB). In spite of the increasing longevity worldwide, surveys focusing specifically on geriatric TB are scarce. We conducted a population-based study to identify prognostic factors of mortality before and during TB treatment among geriatrics.

**Methods:** We provided a population-based follow-up study of patients aged 65 and above with pulmonary TB in an Asian city with aging population. A total of 2,546 patients were enrolled, including 743 (29.2%) cases of 85 years old or beyond. Study subjects were categorized by treatment outcomes: treatment success, death prior to TB treatment or death during TB treatment. Demographics and laboratory findings were compared between the three groups.

**Results:** After controlling for potential confounders, age was the leading determinant of mortality. Adjusted odds ratios (AOR) of death during treatment were 1.87 (aged 75–84) and 3.40 (aged 85 and above) while comparing with patients aged 65 to 74. AORs of death prior to treatment were 2.64 and 5.04. Other prognostic factors were comorbidities, positive findings of pleural effusion on chest X-ray and lower educational level. Subjects with negative results of acid-fast smear had higher rates of death prior to treatment. In the contrast, those with cavity on chest X-ray had lower mortality during treatment.

**Conclusion:** To reduce mortality among geriatric TB patients, it is important for clinicians to keep high awareness of TB and to provide intervention earlier, particularly for the suspects with extremely old age, more comorbidities and lower educational level.

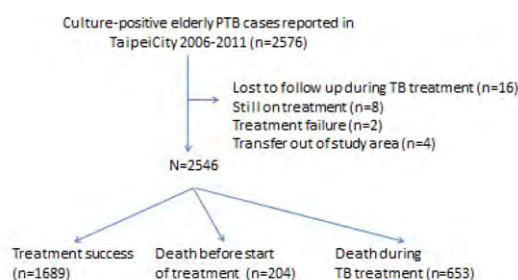


Figure Titles:

Figure 1. Study population. PTB=pulmonary tuberculosis.

### PD-1115-01 Age is a key determinant for indeterminate QuantiFERON-TB Gold assay results

M Tebruegge,<sup>1,2,3,4</sup> P Elkington,<sup>1,5</sup> B Marshall,<sup>1,5</sup> S Patel,<sup>5</sup> S Faust,<sup>2,4,5</sup> H de Graaf,<sup>4</sup> P Sukhantar,<sup>4</sup> H Schuster.<sup>5,6</sup>

<sup>1</sup>Department of Paediatrics, Academic Unit of Clinical & Experimental Sciences, Faculty of Medicine, University of Southampton, Southampton, <sup>2</sup>Institute for Life Sciences / University of Southampton, Southampton, UK; <sup>3</sup>Department of Paediatrics, The University of Melbourne, Melbourne, VIC, Australia; <sup>4</sup>NIHR Wellcome Trust Clinical Research Facility / University Hospital Southampton, Southampton, <sup>5</sup>University Hospital Southampton / NHS Foundation Trust, Southampton, <sup>6</sup>Public Health England Microbiology Services, Southampton, UK. Fax: (+44) 23 8079 5023.  
e-mail: m.tebruegge@soton.ac.uk

**Background:** Indeterminate interferon-gamma release assay (IGRA) results cause a clinical management dilemma, as they convey no information regarding the TB infection status of the patient. Although previous publications suggest that indeterminate results are more common in children, the currently available data regarding the influence of age on the performance of IGRA remain limited.

**Design/Methods:** Analysis of data from 3263 QuantiFERON-TB Gold In-Tube (QFT-GIT) assays performed over a three-year-period (2011–2013) at a regional reference laboratory in England. For data analysis patients were grouped as follows: children (<18 years), adults (18–64 years), and elderly (>65 years). Mann-Whitney U and chi-square tests were used for the analysis of continuous and categorical data, respectively.

**Results:** The majority (n=114; 95.8%) of indeterminate results were due to insufficient interferon-gamma production in the positive control sample; few were due to high interferon-gamma concentrations in the nil control sample (n=5; 4.2%). Indeterminate QFT-GIT results were significantly more common in children (9.1% of 263 tests performed in this age group) and the elderly (7.5% of 378), compared with adults (2.6% of 2622; both comparisons: p<0.0001). In children there was a positive correlation between age and interferon-gamma concentrations in the positive control sample (Spearman's correlation coefficient r=0.1444; p=0.0194), while in adults and the elderly a significant inverse relationship was observed (r=-0.1203; p<0.0001). Among children and elderly patients with indeterminate results, 36.4% and 27.3% were immunocompromised (ie immunodeficient or receiving immunosuppressant medication), respectively.

**Conclusions:** Indeterminate QFT-GIT results are significantly more common in both children and the elderly compared with adults. Only a minority of children and elderly patients with indeterminate results were immunocompromised, indicating that age is a key determinant for the performance of QFT-GIT assays. A significant trend for individuals at both ends of the age spectrum to generate less interferon-gamma in the positive control sample was observed, likely reflecting immune-maturation and immunosenescence. Consequently, use of age-specific cut-offs for positive control samples or use of a

control stimulant that produces consistent responses across all age groups may reduce the unacceptably high rate of indeterminate results in children and the elderly.

### PD-1116-01 Factors associated with tuberculosis mortality among patients younger than 50 years in Taiwan, 2010–2011

P-H Lee,<sup>1</sup> Y-A Lin,<sup>1</sup> P-C Chan,<sup>1</sup> P-W Chu,<sup>1</sup> CB Hsu,<sup>1</sup> K-F Wang,<sup>1</sup> C-H Chen,<sup>1</sup> T-H Wen.<sup>2</sup> <sup>1</sup>HIV/AIDS and TB, Centers for Disease Control, Taipei, <sup>2</sup>Department of Geography, National Taiwan University, Taipei, Taiwan. e-mail: leepinhui@cdc.gov.tw

**Background** Tuberculosis (TB) remains the leading causes of death among notifiable diseases in Taiwan. Investigating factors associated with mortality among young TB patients would help to improve delayed diagnosis, to timely initiate anti-TB treatment and to avoid unfavorable outcomes.

**Methods** We conducted the nation-wide retrospective nested case-control study from the study cohort of 5,269 new TB patients with age  $\leq 50$  years reported to the TB registry during 2010–2011. Case was defined as all-cause of death before or during anti-TB treatment. For each case, one control was selected from the study cohort matching by age ( $\pm 1$  year) and sex with the case-control ratio of 1:1. Demographic and clinical information was collected by medical chart review. We used conditional logistic regression model to calculate the odds ratio (OR) and 95% confidence interval (CI) for the associated factors with TB mortality after adjusting potential confounders of body weight, bacteriological status, presentation of chest X-ray at TB diagnosis, and underlying diseases of HIV, malignancy, cirrhosis, end-stage renal disease, and long-term use of immunosuppressive agents.

Table 1. Factors associated with mortality during anti-tuberculosis treatment among patients with age  $\leq 50$  years (n=512)\*

Table 1. Factors associated with mortality among patients with TB, by age group	Case, (%)	Control, (%)	Univariable analysis		Multivariable analysis	
			OR (95%CI)	p-value	aOR (95%CI)	p-value
<b>Weight at TB diagnosis*</b>						
<50 kg	89 (34.8)	43 (16.8)	Reference	-	Reference	-
50-69 kg	118 (46.1)	157 (61.3)	0.37 (0.23-0.60)	<0.001	0.43 (0.22-0.96)	0.017
≥70 kg	25 (9.8)	56 (21.9)	0.20 (0.10-0.39)	<0.001	0.17 (0.06-0.48)	0.001
<b>Bacteriological finding</b>						
Sputum + and culture +	118 (46.1)	106 (41.4)	1.57 (0.99-2.50)	0.066	1.28 (0.62-2.64)	0.510
Sputum – and culture +	94 (36.7)	87 (34.0)	1.51 (0.94-2.42)	0.086	0.75 (0.35-1.60)	0.462
Culture –	44 (17.2)	63 (24.6)	Reference	-	Reference	-
Any resistance to 1 <sup>st</sup> line anti-TB drugs	37 (14.5)	33 (12.9)	1.14 (0.69-1.87)	0.612	1.06 (0.48-2.37)	0.882
Cavitation on chest X-ray	71 (27.7)	70 (27.3)	1.02 (0.69-1.50)	0.922	0.73 (0.36-1.50)	0.389
Bilateral pulmonary lesions	148 (57.8)	96 (36.2)	2.45 (1.70-3.54)	<0.001	2.41 (1.33-4.37)	0.004
HIV	26 (10.2)	5 (2.0)	5.20 (2.00-13.64)	0.001	5.74 (1.58-20.90)	0.008
Malignancy	73 (28.5)	17 (6.6)	5.31 (2.93-9.60)	<0.001	10.65 (4.22-26.83)	<0.001
Cirrhosis	56 (21.9)	15 (5.9)	5.55 (2.73-11.29)	<0.001	12.08 (4.16-35.06)	<0.001
End-stage renal disease	93 (36.3)	84 (32.6)	1.41 (0.82-2.43)	0.219	0.99 (0.35-2.29)	0.905
Long-term use of immunosuppressive agents	19 (7.4)	2 (0.8)	9.00 (2.09-39.79)	0.003	39.51 (5.96-261.89)	<0.001

\* Statistic method: conditional logistic regression

<sup>†</sup> Missing value of weight records among 24 cases (9.4%)

**Results** We identified 273 (5.2%) mortality cases in the TB cohort with age  $\leq 50$  years. After excluding 17 cases with unavailable information through chart review, only 67 (26%) of 256 cases died directly related to TB, but 46 (18%) of cases died before initiating anti-TB treatment. The mean age of cases was 42.1 ( $\pm 7.4$ ) years and the majority was male (77%). The analysis of 256 case-control pairs (n=512) revealed that comorbid with cirrhosis (aOR=12.08, 95% CI: 4.16, 35.06), malignancy (aOR=10.65, 95% CI: 4.22, 26.83), HIV (aOR=5.74, 95% CI: 1.58, 20.90), long-term use of immunosuppressive agents (aOR=39.51, 95% CI: 5.96,

261.89), and bilateral pulmonary lesions (aOR=2.41, 95% CI: 1.33, 4.37) were significantly associated with mortality before and during anti-TB treatment (table 1). **Conclusions** Comorbid diseases, instead of the direct TB-related cause, were associated with mortality before and during anti-TB treatment among TB patients with  $\leq 50$  years in Taiwan. Clinicians should be aware of the potential impact of nosocomial transmission and further investigation for diagnosis delay is needed.

### PD-1117-01 Is lower body weight at initiation of treatment more lethal for TB patients?

P Bhat,<sup>1</sup> B Naik,<sup>1</sup> P Nayak,<sup>1</sup> B Basti,<sup>2</sup> M D Suryakanth,<sup>3</sup> P Malik,<sup>1</sup> A Sreenivas.<sup>1</sup> <sup>1</sup>TB Control, World Health Organisation, Country office for India, New Delhi, <sup>2</sup>Community Medicine, VMKV Medical College, Salem, Tamil Nadu, <sup>3</sup>TB Control, State TB Cell, Bangalore, India. e-mail: bhatp@tbcindia.nic.in

**Background:** India accounts to one fifth of the global TB burden. It is implementing all the components of STOP TB strategy and the WHO guidelines for TB control under the Revised National TB Control programme (RNTCP) since 1997. Karnataka (population 63 million) is a southern State in India implementing RNTCP with overall annual case notification of  $\sim 103$  per 100,000 population and success rate of  $\sim 83\%$  for new smear positive cases. While the services provided under DOTS in the State is satisfactory, the reason for not achieving the national average success rate of 86% is unknown. There were field observations that the adverse outcomes were more common among patients with lower body weight at initiation of treatment. Neither STOP TB nor RNTCP have any strategy to monitor TB treatment based on body weight of the patients. We studied the outcomes of TB patients registered for treatment in 2012, in two districts of Karnataka with the specific objective to examine if there was any change in treatment outcomes with different weight bands.

**Design/Methods:** In this cross sectional study, we reviewed treatment cards of all adult TB patients weighing more than 30 kgs, registered for treatment in the year 2012 from two districts (Gadag and Uttara Kannada) of Karnataka covering  $\sim 2.6$  million populations.

**Results:** Of the 2147 adult patients (with initial body weight more than 30 kgs) enrolled for treatment, the mean body weight was 43 kgs (IQR 38–48 kgs), with p5 at 32 kgs and p95 at 58 kgs. Outcome “died” was highest among patients weighing between 30–39.9 kgs across all the types of TB (Chi square=13.82, df=2,  $P<0.001$ ); failure was also highest in this weight band among retreatment cases (Chi square=6.72 df=2,  $P<0.05$ ) (Table 1).

**Conclusion:** Lower body weight at initiation of treatment is associated with higher risk of death across all types of TB and with failure among retreatment cases. While further study is indicated to explore the reasons for these findings, clearly, National TB Programmes should have strategies to monitor treatment based on initial body weight.



**Table 1. Outcomes of TB patients registered for treatment based on their body weight at initiation of treatment in Gadag and Uttara Kannada, Karnataka, India, 2012.**

Treatment Outcome by Type of TB Cases	30–39.9 kgs N (%)	40–49.9 kgs N (%)	50 kgs and above N (%)	Total N (%)
<b>New Cases</b>				
Cured Treatment	312 (53.8)	417 (52.9)	140 (40.2)	869 (50.6)
Completed	170 (29.3)	255 (32.4)	168 (48.3)	593 (34.6)
Defaulted	41 (7.1)	54 (6.9)	19 (5.5)	114 (6.6)
Died	*50 (8.6)	42 (5.3)	18 (5.2)	110 (6.4)
Failed Treatment	6 (1.0)	17 (2.2)	3 (0.9)	26 (1.5)
Transferred out	1 (0.2)	3 (0.4)	0 (0.0)	4 (0.2)
Total	580 (100)	788 (100)	348 (100)	1716
<b>Previously Treated Cases</b>				
Cured Treatment	49 (34.5)	96 (44.7)	27 (39.1)	172 (40.4)
Completed	30 (21.1)	55 (25.6)	22 (31.9)	107 (25.1)
Defaulted	20 (14.1)	30 (14.0)	10 (14.5)	60 (14.1)
Died	20 (14.1)	16 (7.4)	3 (4.3)	39 (9.2)
Failed Treatment	*21 (14.8)	17 (7.9)	6 (8.7)	44 (10.3)
Transferred out	1 (0.7)	1 (0.5)	0 (0.0)	2 (0.5)
Shifted to Cat IV	1 (0.7)	0 (0.0)	1 (1.4)	2 (0.5)
Total	142 (100)	215 (100)	69 (100)	426

\* Chi square=7.17 df=2. P<0.05 significant, ^ Chi square=8.95 df=2. P<0.05 significant, \$ Chi square=6.72 df=2. P<0.05 significant

### PD-1118-01 Impact of advanced age on the delay and outcome of anti-tuberculous treatment: a national cohort study in Taiwan

C-H Lee,<sup>1</sup> HC Lin,<sup>1</sup> P-Y Lin,<sup>1</sup> CW Suk,<sup>1</sup> K-J Bai,<sup>1,2</sup> J-H Chang,<sup>1,2</sup> J-Y Wang,<sup>3</sup> M-C Yu.<sup>1,2</sup> <sup>1</sup>Department of Pulmonary Medicine, Taipei Medical University - Wanfang Hospital, Taipei, <sup>2</sup>School of Respiratory Therapy, Taipei Medical University, College of Medicine, Taipei, <sup>3</sup>Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan. e-mail: chlee.tw@gmail.com

**Background:** Studies reporting the treatment outcome of tuberculosis (TB) in advanced age ( $\geq 65$ ) are currently lacking. Among them, the clinical presentation of TB are myriad and atypical, causing delay in diagnosis and disease transmission. The high risk of adverse events further discourages empiric use of anti-TB treatment. This national cohort study investigated the treatment outcome and prognostic factors of TB patients in advanced age, with a special emphasis on the delay of anti-TB treatment.

**Methods:** Between 2004 and 2009, adult ( $\geq 20$  years) TB patients were identified from the National Health Insurance Research Database of Taiwan. Outcome status, including complete treatment, death, failure, and default, was noted at one year after anti-TB treatment. Delay in treatment referred to the period between the earliest visit with clues of TB within previous six months and the commencement of anti-TB treatment. Factors associated with mortality and delay in anti-TB treatment were analyzed using multivariate logistic and linear regression analyses, respectively.

**Results:** A total of 81569 adult TB patients with a male-female ratio of 2.2 were identified. Among them, 14089 (17.3%) were  $\geq 80$  in age, and 27100 (33.2%) between 65 and 80. Within one year after anti-TB treatment, the completion rate was 57.2% in patients  $>80$ , 69.9% in patients between 65 and 80, and 79.1% in patients  $<65$ . The mortality rate was 34.7%, 18.7%, and 6.6%, respectively. Patients with a fatal outcome had a longer delay in anti-TB treatment ( $77.9 \pm 63.7$  vs.  $55.3 \pm 57.8$  days,  $p < 0.001$ ). Independent risk factors for mortality included older age, presence of systemic co-morbidities, low income, and longer delay in anti-TB treatment. Independent predictors for longer delay in anti-TB treatment included older age, presence of systemic co-morbidity, and low income, whereas male sex and performing *Mycobacterium tuberculosis* – nucleic acid amplification test (MTB-NAAT) were associated with shorter delay in anti-TB treatment.

**Conclusion:** Advance age was associated with a poorer treatment outcome and longer delay in anti-TB treatment. Rapid diagnostic tests for TB can prevent treatment delay and should be integrated in the diagnostic algorithm for TB, especially in patients with advanced age.

### PD-1119-01 Tuberculosis burden among the Thai elderly during 2003–2009

P Hunchangsith.<sup>1</sup> <sup>1</sup>Mahidol University, Institute for Population and Social Research, Salaya, Nakhon Prathom, Thailand. Fax: (+66) 2441 9333. e-mail: pojjana.hun@mahidol.ac.th

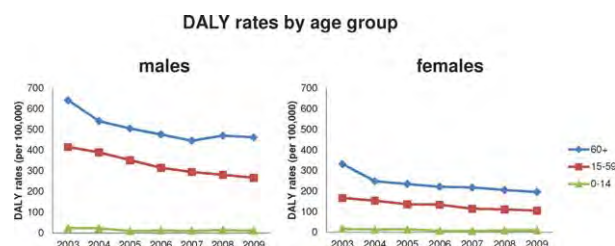
**Background:** Thailand was one out of 22 high-burden countries for tuberculosis (TB) globally in 2012. TB is one of the most frequent infectious diseases among the elderly worldwide. Furthermore, the proportion of elderly people is growing around the world. In Thailand, TB remains a major cause of premature mortality and morbidity among the elderly. This paper estimates burden of disease due to TB among the Thai elderly and explores its trend during 2003–2009.

**Design/Methods:** This study follows a standard global burden of disease estimation technique to calculate TB disease burden in disability-adjusted life years (DALYs). The DALYs combine a measure for premature death in years of life lost and a measure of morbidity in years lost due to disability.

**Results:** TB DALYs rates in total and for every age group (60+, 15–59, and 0–14) decreased in both men and women during the study period. TB had the highest DALYs rate in the elderly Thai population, decreased from 472 per 100,000 in 2003 (males: 642, females: 332) to 316 per 100,000 in 2009 (males: 463, females: 196), or equivalent to the average rates of change of 5% in males and 8% in females. It is to be noted that the rates of change from 2003 to 2004 were 16% in males and 25% in females, which were noticeably larger than the rates from other period. In addition, years lost due to premature mortality contributed around 90% to the DALYs for both men and women during the period

observed, and steadily declined from 92% in 2003 to 86% in 2009.

**Conclusion:** TB DALYs rates per 100,000 population among the Thai elderly gradually decreased from 2003 to 2009. The large decline of DALYs rate from 2003 to 2004 might be due to the results of directly observed treatment, short course program to control TB in Thailand that successfully covered all districts from 2002.



#### PD-1120-01 The impact of very old age on the treatment of tuberculosis: an experience in one referral hospital in Taiwan

HC Lin,<sup>1</sup> K-J Bai,<sup>1</sup> M-C Yu.<sup>1</sup> <sup>1</sup>Department of Internal Medicine, Wan-Fang Hospital, Taipei Medical University, Taipei, Taiwan. e-mail: jiun21@ms79.hinet.net

**Background:** As prolonged life expectancy in general population in Taiwan, we will face more old-age tuberculosis (TB) patients, especially very old-age patients more than eighty years old. This study was to evaluate the diagnosis and treatment of these patients.

**Methods:** A retrospective study was performed to evaluate the treatment outcome of tuberculosis patients between January 2008 and December 2012 at Taipei Medical University-Wan Fang Hospital. Characteristics of these patients including demographic data, cause of visiting hospital, comorbidities, microbiologic evidence, previous TB history, extra-pulmonary involvement, and adverse effects of treatment were evaluated. Difference among three age-groups was compared: young-age group (<65 years old), old-age group ( $\geq 65$  years old, <80 years old), and very old-age group ( $\geq 80$  years old).

**Results:** Six hundred and twenty-one TB patients were diagnosed by microbiologic (73.7%), pathologic (20.9%), and clinical diagnosis (4.2%) during the period. Their mean age was  $59 \pm 23.3$  years old with male to female ratio of 1.9. There were 331 patients (53.3%) in young-age group, 121 patients (19.5%) in old-age group, and 169 (27.2%) patients in very old-age group. Compared with young-age patients, most of very old-age patients (92.9%) had TB-associated symptoms when visiting hospital while only 68.9% in young-age group ( $p < 0.05$ ). Besides, there were more microbiologic evidence (86.4%) and comorbidities (95.9%) noticed. Compared with old-aged patients, there were significantly more patients (43.3%) having discontinuing one or more anti-TB drugs during treatment period due to adverse effects ( $p < 0.05$ ). Three most common causes of discontinuing drug in very old-age group were hepatitis

(32.9%), decreased vision acuity (29.3%), and dermatitis (13.4%). Among these very old-age patients developing hepatitis, pyrazinamide was most common to induce hepatitis (63%). All-cause mortality was also higher in this very old-age group (30.8%).

**Conclusion:** The impact of very-old age on the treatment of tuberculosis is critical. More adverse effects of anti-TB treatment leading to discontinuing drug were experienced in this group. The patient-centered program with closely monitoring of adverse effects for early detection and treatment should be emphasized.

#### PD-1121-01 Pulmonary tuberculosis: clinical and therapeutic particularities in elderly compared to young

H Blibech,<sup>1</sup> H Racil,<sup>1</sup> A Ayari,<sup>1</sup> S Bacha,<sup>1</sup> S Cheikh Rouhou,<sup>1</sup> N Chaouech,<sup>1</sup> A Chabbou.<sup>1</sup> <sup>1</sup>Tunis El Manar University. FMT. Abderrahmen Mami Hospital., Laboratoire de recherche Etude et prévention des maladies liées au tabac, Ariana, Tunisia. e-mail: han-no@hotmail.fr

Tuberculosis (Tb) is still endemic in our country; it represents an important worldwide health problem. The aim of this study is to identify clinical, radiologic, microbiologic and the prognostic particularities of confirmed pulmonary tuberculosis (PTb) in elderly compared to young. We performed a comparative retrospective study of 39 elderly (aged over than 65 years) and 61 young patients (aged less than 35 years), hospitalized in our department between 2005 and 2013. The mean age is 26 in young patients and 73 in old patients. Comorbidities are prevalent in old patients with a high frequency of hypertension, diabetes mellitus, heart diseases and COPD. However, imprisonment seems to be a predisposing factor in young. Fever, weight loss and anorexia are more frequent in young. Respiratory symptoms are similar in both groups; however dyspnea is more frequent in older (43% vs 11%). The main radiological abnormalities are infiltrates and cavitations in both groups. Bilateral involvement is more common in elderly (61% vs 50%), however cavitations are more observed in young (59% vs 30%). There are no significant differences between the two groups regarding positivity of sputum smear microscopy. Extra pulmonary locations are more frequent in elderly (20% vs 4%). The diagnosis is delayed to a maximum of 90 days in elderly vs 60 days in young. Smear negativity is longer in elderly (61 days vs 34 days). Side effects of Tb drugs are more frequent in elderly. Tb-related mortality is observed only in elderly (12%). Clinical particularities in elderly explain low suspicion of the disease and the delay of diagnosis and treatment.

## 55. TB SPATIAL EPIDEMIOLOGY IN HIGH-BURDEN SETTINGS

### PD-1122-01 Effectiveness of community contacts screening in addition to household contact screening to limit TB transmission in community

R K Fatima,<sup>1</sup> E Qadeer,<sup>1</sup> M Ul Haq,<sup>1</sup> Yaqo Aashifa.<sup>1</sup>

<sup>1</sup>Research, National TB Control Program, Islamabad, Pakistan. Fax: (+92) 51 8438 081.

e-mail: drrazia\_fatima@yahoo.com

**Background:** Pakistan ranks sixth globally among the 22 high TB burden countries with 64% of case detection rate and contributes 43% of the disease towards the eastern-Mediterranean region of World Health Organization (WHO). There is a need to enhance TB case finding to meet MDG targets.

**Design/Methods:** Active case finding through contact screening using GIS software in 3 cities in Punjab Province i.e. Lahore, Faisalabad and Rawalpindi and the Capital Territory utilizing all SS+ notified cases as index cases registered at BMU's. project funded through TB Reach wave 3 is focusing on contact screening is being carried out within household and a diameter of 100m around each index case using GIS Technology and therefore strengthen current contact screening strategy adopted by NTP. Household contacts, i.e. those normally resident or sharing the same airspace, are verbally screened initially, following by a widening circle screening of close community contacts. The coordinates of the household are entered into a GIS database via a mobile phone link. There are 50 field officers trained for this project. All the TB presumptive found from the screening are subject to smear microscopy; those found positive are registered. However, those found negative are subject to Gene Xpert. Gene Xpert positive cases with or without rifampicin resistance are also registered for treatment at the respective sites. TB presumptive aged less than 15 years identified are referred to child TB managing sites for diagnosis and treatment and is followed up.

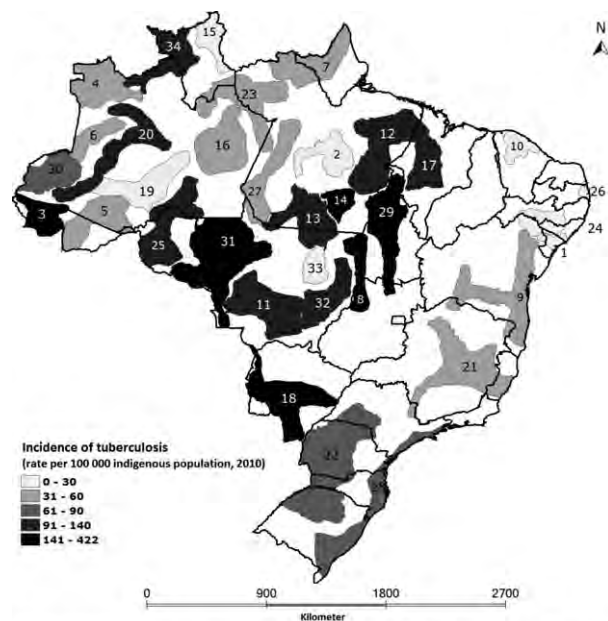
**Results:** From 1st July 2013 to 26<sup>th</sup> February 2014, total of 141,897 individuals were screened, among them 21,620 are household and 120,299 are community based, total suspects found are 2,906 (household=811, community=2095), in which smear positive cases are 264 (community=196, Household=68), gen expert positive cases are 65, MDR cases are 08, child referred are 578 and total registered cases are 331.

**Conclusion:** Contact screening among community is proved to be effective in addition to household screening for early case detection and to limit spread of disease.

### PD-1123-01 Spatial distribution of tuberculosis amongst indigenous population, Brazil, 2010

T Magalhães,<sup>1</sup> A De Paula Lobo,<sup>1</sup> D Chaves Kühleis,<sup>1</sup> M Jacobs,<sup>1</sup> V Camargo Da Costa,<sup>1</sup> D Barreira.<sup>1</sup> <sup>1</sup>National Tuberculosis Control Program, Brazilian Ministry of Health, Brasília, DF, Brazil. e-mail: tatiana.magalhaes@saude.gov.br

**Background:** Spatial analysis in healthcare is an important tool to the decision making process. It also shows etnoepidemiological diversity. In Brazil, indigenous population represents 0.4% of the population and 1.1% of all notified tuberculosis cases. Primary health-care services are of the central government responsibility through the Ministry of Health coordination. To perform healthcare actions in indigenous areas, there are 34 special healthcare indigenous districts (SHID) that work in partnership with States and municipalities. The aim of this study was to map tuberculosis incidence rate in indigenous population according SHID in 2010.



**Figure 1:** Spatial distribution of tuberculosis amongst special healthcare indigenous districts (SHID). 1)Alagoas e Sergipe; 2)Altamira; 3)Alto Rio Juruá; 4)Alto Rio Negro; 5)Alto Rio Purus; 6)Alto Rio Solimões; 7)Amapá e Norte do Pará; 8)Araguaia; 9)Bahia; 10)Ceará; 11)Culabá; 12)Guamá-Tocantins; 13)Kalapó do Mato Grosso; 14)Kalapó do Pará; 15)Leste de Roraima; 16)Manaus; 17)Maranhão; 18)Mato Grosso do Sul; 19)Médio Rio Purus; 20)Médio Rio Solimões e Afluentes; 21)Minas Gerais e Espírito Santo; 22)Interior Sul; 23)Parintins; 24)Pernambuco; 25)Porto Velho; 26)Putinguara; 27)Rio Tapajós; 28)Itoral Sul; 29)Tocantins; 30)Vale do Javari; 31)Vitória; 32)Xavantina; 33)Kikiga; 34)Yanomami.

**Design/Methods:** It was conducted an ecological study considering SHID as the unit measure and new tuberculosis cases notified in 2010. Tuberculosis data were obtained from the Brazilian National Surveillance System (BNSS) and demographic data of the 34 SHID were retrieved from the Indigenous Healthcare Information System (IHIS). Data included: year of diagnosis (2010), type of case entry (new or not available), clinical endpoint (cure, abandon, TB-related death, other causes of death, MDR-TB and ignore/blank fields, and residency. Data were analysed on a Excell spreadsheet and mapping results tabulated on Terra View® software.

**Results:** In 2010 a total of 469 tuberculosis cases were notified in the indigenous population, distributed in 32 of the 34 SHID; 29% (135) cases came from Mato Grosso do Sul State. Incidence rate was 76.9/100.000



cases, ranging from 4.2/100.000 (SHID Pernambuco) to 421.7/100.000 (SHID Araguaia). In 14 (41%) SHID, incidence rate was over 91/100.000 cases (figure 1).

**Conclusion:**

**Results** show the importance of actions to tuberculosis control focused on indigenous population. There is also a need to prioritize areas with a higher risk to sickening. Using a spatial analysis methodology allowed us to identify differences in tuberculosis distribution, showing SHID with high incidence rates.

**PD-1124-01 Validation of an online mapping methodology to locate village of residence of tuberculosis patients in Mombasa**

R Deya,<sup>1,2</sup> M Dunbar,<sup>3</sup> J Wakefield,<sup>4</sup> S Graham,<sup>2,5,6</sup> R S McClelland.<sup>2,5,6</sup> <sup>1</sup>UNITID, University of Nairobi, Nairobi, Kenya; <sup>2</sup>Epidemiology, University of Washington, Seattle, WA, <sup>3</sup>CSDE, University of Washington, Seattle, WA, <sup>4</sup>Biostatistics, Statistics, University of Washington, Seattle, WA, <sup>5</sup>Medicine, University of Washington, Seattle, WA, <sup>6</sup>Global Health, University of Washington, Seattle, WA, USA. e-mail: ruthdeya@uw.edu

**Background:** In Kenya, the TB-HIV epidemic has led to increasing morbidity and mortality especially in urban areas. National tuberculosis programs need to identify high burden communities and employ aggressive prevention measures like intensive case finding and contact tracing in order to interrupt ongoing transmission. We evaluated the accuracy of an online mapping method to locate TB patients' village of residence using addresses provided in TB registers in Mombasa, Kenya.

**Methods:** To validate the spatial accuracy of a health-worker-based online mapping procedure based on Google Maps, we compared whether latitude-longitude point locations of TB patients matched those collected using a Global Positioning System (GPS) device during a home visit. Patient, clinic, and village-level characteristics associated with correct location in village of residence were evaluated using logistic regression.

**Results:** Between July 2012 and July 2013, 246 participants were mapped using both methods. The online method located 140 cases (56.9%) in the correct village of residence, 80 (32.5%) and 26 (10.5%) were incorrectly allocated to neighboring and non-neighboring villages, respectively. Mean (SD) error distance between the two methods was 225.2m ( $\pm 296.2$ ) for all cases, 106.5m ( $\pm 92.5$ ) and 382m ( $\pm 386.9$ ) for those correctly and incorrectly located, respectively. Type of clinic, clinic-caseload, village status, and density were significantly associated with being correctly mapped in bivariate analysis. In multivariate analyses, medium clinic caseloads (201 – 400 versus 0 – 200 cases per year; adjusted OR 2.75 95% CI 1.37 – 5.53;  $p$  0.004); moderate number of households per village (1,001 – 2,000 versus 0 – 1,000 households; aOR 0.42 95% CI 0.21 – 0.85;  $p$  0.016); high village density ( $>30,000$  versus 0 – 15,000 per km<sup>2</sup>; aOR 0.43 95% CI 0.19 – 0.94;  $p$  0.035) and attending municipal clinics (aOR 0.45 95% CI 0.20 – 0.99;  $p$  0.048) were significantly associated with correct village location.

**Conclusion:** This online mapping tool correctly allocated almost 60% of TB cases while majority of misclassifications were located in neighboring villages. New mapping tools such as online Google Maps could be improved and employed in surveillance of TB for timely diagnosis, follow-up and treatment. Tuberculosis programs in dense urban areas with high caseload clinics may benefit from improving the quality of addresses entered in TB registers in order to effectively implement prevention activities.

**PD-1125-01 Spatial analysis of deaths distribution by tuberculosis as an associated and primary cause, Ribeirão Preto (SP) Brazil**

M Yamamura,<sup>1</sup> M Santos Neto,<sup>1</sup> MP Popolin,<sup>1</sup> MCC Garcia,<sup>1</sup> ACV Ramos,<sup>1</sup> J Crispim,<sup>1</sup> I Fronteira,<sup>2</sup> RA Arcêncio.<sup>1</sup> <sup>1</sup>Maternal-Infant Nursing and Public Health, Ribeirão Preto School of Nursing, University of São Paulo, Ribeirão Preto, SP, Brazil; <sup>2</sup>International Public Health and Biostatistic, Institute of Hygiene and Tropical Medicine of the University Nova of Lisboa., Lisboa, Portugal. e-mail: mellinayamamura@yahoo.com.br

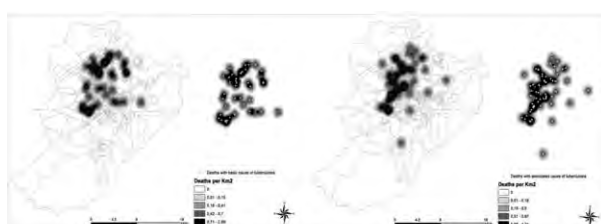
**Background:** Researches on deaths by tuberculosis (TB) are being promoted because they are considered an evaluating instrument of the health systems conditions. It was possible to characterize the clinical and epidemiological profile of deaths with associated and basic causes by TB, and identify the geographic areas that are vulnerable to these events.

**Design/Methods:** Partially ecologic study conducted in Ribeirão Preto/São Paulo, in Brazil. It was possible to consider all deaths by TB recorded in the Mortality Information System (MIS), in the period 2006–2012, which obtained the associated and basic cause to the CID 10 from A15.0 to A19.9. In the bivariate analysis performed in the Statistica software, it was possible to adopt the dependent variable of the basic cause by TB (yes or no), and the chi-square test of proportions with the probability of type I error of 5%. In the estimation of the vulnerable areas for deaths due to TB, it was developed the geocoding through the use of Terra View software and the Kernel density estimation technique for analysis.

**Results:** Were reported 114 deaths, 50 of them as a basic cause and 64 as an associated cause. The minimum age was 27 and the maximum age was 91 years, with a mean of 52 years. The pulmonary clinic form was the most frequent in both situations. Most of the deaths occurred with males (73.60%), caucasian (62.28%), unmarried (44.74%), and the place of death occurrence was in the hospital (81, 58%). The age ( $p = 0.008$ ) and death declaration filling ( $p = 0.003$ ) were statistically significant, in the bivariate analysis. It was possible to find out that mortality as the primary cause of TB occurred in people aged over 52 years old, and the Death Registration System (DVS) performed the death confirmation. The deaths with associated cause were related to younger people, and the confirmation happened through other means and not by the DVS. In the Figure 1, it is possible to observe that the location of deaths with a basic cause has a greater tendency for density, in the northern area,

and they are represented by darker shades. In the deaths with associated cause the density appears to be homogeneous.

**Conclusion:** The recognition of the epidemiological-clinical profile and the visualization of cases distribution heterogeneity may assist in the planning of health actions in order to respond to the needs and specificities of each area. Furthermore, the deaths with associated cause by TB could be related to the pair TB/HIV.



*terium tuberculosis* (Mtb). Though a number of recent studies suggested that tuberculosis (TB) cases often clustered in some hot regions, the transmission mechanism of Mtb in China has not been clearly understood. The objective of this study was to describe the spatial distribution of clustered tuberculosis cases, and to investigate the mechanism of recent transmission of Mtb in Shanghai, China.

**Design/Methods:** We enrolled all sputum culture positive TB cases during January 2006 to December 2009 in Songjiang District, Shanghai. Demographic and clinical information was collected. 7-loci mycobacterial interspersed repetitive unit-variable number of tandem repeat (MIRU-VNTR) method was used to genotype strains of Mtb. Logistic regression was performed to identify the factors associated with clustering. Handheld Global Positioning System (GPS) was used to collect the positional information on tuberculosis cases' living address. Kernel density estimation was used to estimate the spatial risk value. Contour lines were displayed to designated relatively high-density areas of cluster cases and unique cases respectively.

**Results:** During the study period, 532 smear culture positive pulmonary TB cases were detected. Among those, 524 (98.5%) cases with complete information were included. Totally, 151 cluster strains were identified, dividing into 53 clusters. The sizes of clusters varied from 2 to 10. The cluster rate was 28.82%. Logistic regression showed that multi-drug resistance (MDR) was an independent risk factor of clustering (adjusted OR=2.668; 95% CI: 1.348 to 5.283). Compared with cluster cases, the density of unique cases was significantly higher in the northeast corner of Songjiang District (Region I); while the density of the cluster cases was significantly higher near the west boundary (Region II). Chi-square test showed that the proportion of resident cases was significantly larger in Region II ( $\chi^2=27.3586$ ,  $p<0.0001$ ).

**Conclusion:** A considerable recent transmission of Mtb occurred in the study setting, especially in Region II. MDR-TB was more likely to be clustered. Our findings highlight the need to develop and implement specific tuberculosis control strategies, such as more exhaustive case finding, rapid diagnosis and treatment among some certain subgroups and certain regions.

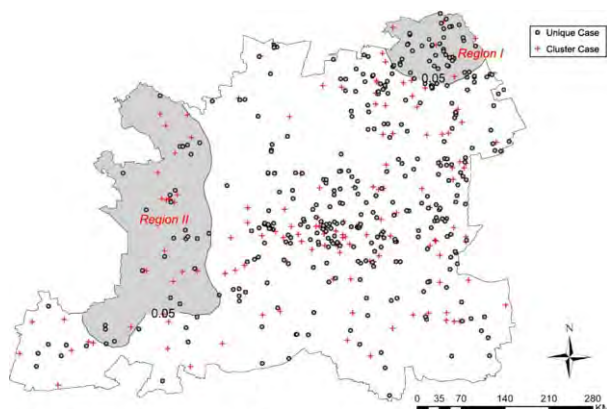


Figure 1. Spatial distribution of tuberculosis cases in Songjiang District, Shanghai, China. Cluster cases and unique cases are displayed respectively. In Region I, the density of unique cases was significantly higher, while in Region II, the density of cluster cases was significantly higher.

### PD-1128-01 TB map, a useful tool for outreach treatment follow up, contact tracing and local programmatic investigation: experience from Cimahi city, west Java

F Manan,<sup>1</sup> I Tochija,<sup>1</sup> R Arifin Panigoro,<sup>1</sup> M Reksoprodjo,<sup>1</sup> H Diatmo.<sup>1</sup> <sup>1</sup>National Board, Indonesian Association Against Tuberculosis, Jakarta, Indonesia. Fax: (+621)7397494. e-mail: henry.ppti@gmail.com

**Background:** Contact tracing and investigation is difficult to implement in Indonesia due lack of outreach staff from Primary Health Center. In Cimahi City, West Java; District Health Office, in collaboration with Indonesian Association Against TB (PPTI), trained outreach volunteers to follow up TB cases in community (village and cluster levels) to prevent default. The map tool was used for adherence purpose, contact tracing and local TB situation investigation.

**Intervention:** The DHO and PPTI used the existing administrative clusters as catchment area for each outreach volunteer to follow up TB patients and for family members contact tracing. The volunteers asked whether family members (including children) had TB symptoms, and transferred them for TB investigation. The active TB cases were map according to their addresses.

**Result:** A total of 35 outreach volunteers in Leuwigajah village were trained in 2010. The map tool was introduced to the volunteers. The outreach volunteers and supervisors used the maps and patient's list to follow up for adherence. PPTI also used these maps for contact tracing.

Leuwigajah village	2011	2012	2013
Suspects	121	139	173
Notified cases	21	41	39
SS+	9	13	15
SS-	9	19	15
Childhood TB (percent of all cases)	3 (14%)	9 (22%)	9 (23%)
Defaulter	0	0	0

Each year around 50 family members were traced and investigated for TB. We also found that the proportions of childhood TB in 2012 and 2013 were high. PPTI had brought these findings to discuss with DHO to investigate whether it was over diagnosis or more hidden cases of adult TB patients close to childhood TB cases.

**Conclusion:** Geographic map of TB patients at cluster level is useful to outreach volunteers for treatment follow up and contact tracing. The TB map is also useful to program management team to interpret local situation for further investigation.



### PD-1129-01 Análisis espacial de casos de tuberculosis en Juazeiro Do Norte/ CE/ Brasil, 2001–2012

T Figueiredo,<sup>1</sup> TC Silva,<sup>1</sup> M.L. Pinto,<sup>1</sup> LCF Gomes,<sup>2</sup> EL Silvo,<sup>3</sup> E Silva,<sup>3</sup> M Bertolozzi,<sup>4</sup> ML Pinto,<sup>5</sup> TB Freire.<sup>5</sup>

<sup>1</sup>Programa de Pós Graduação em Saúde Pública, Universidade Estadual da Paraíba, Campina Grande, PB, <sup>2</sup>Programa de Pós Graduação em Geografia Física, Universidade Federal do Ceará, Fortaleza, Ceará, <sup>3</sup>Estatística, Universidade Estadual da Paraíba, Campina Grande, PB, <sup>4</sup>Saúde Coletiva - Escola de Enfermagem da USP, Universidade de São Paulo, São Paulo, SP, <sup>5</sup>Departamento de Enfermagem, Universidade Estadual da Paraíba, Campina Grande, PB, Brazil. e-mail: taniaribeiro\_2@hotmail.com

**Objetivo:** identificar el patrón espacial de nuevos casos de tuberculosis en el municipio de Juazeiro do Norte/ CE/ Brasil, durante el período de 2001 a 2012.

**Método:** este es un estudio con diseño híbrido, ecológico y tendencia temporal. Los nuevos casos notificados con todas las formas clínicas de la tuberculosis se incluyeron como sujetos de la investigación. Trazó el perfil demográfico de socio, hizo análisis espacial de los casos de tuberculosis mediante la técnica Kernel y el método de agrupación de vecino más cercano con la simulación. Utilizamos el software SIG, ArcGis 10 y SPRING.

**Resultado:** de los 914 casos nuevos de tuberculosis, se puede observar un predominio de hombres, de edades comprendidas entre 20 y 39 años, baja escolaridad, forma clínica pulmonar, sanación porcentaje de 79,1% y abandono de 5,3%. En cuanto a la distribución espacial, mapas de puntos fueron obtenidos en los casos de tuberculosis que fue utilizada como una estrategia de visualización espacial de la enfermedad. Así que si podría tener un análisis más preciso de la agregación espacial de los casos, se construyó un mapa con la intensidad Kernel. Por lo tanto, detectó que durante el período comprendido entre 2001 y 2006, se puede identificar una distribución homogénea de los casos, que se concentran en la región central del mapa, sin embargo, la zona con mayor densidad de casos se encuentra en la parte de la región sur. Mientras que en el período comprendido entre 2007 y 2012, se puede ver en el mapa de la distribución espacial de su mayor concentración en la región central, con un enfoque en la región sur y en algunos casos en la región periférica del mapa. Según el análisis vecino más cercano con la simulación, los casos de tuberculosis detectados tienen una distribución no aleatoria, mostrando una correlación espacial.

**Conclusión:** fue posible concluir que la presente investigación se hace relevante, en que puede contribuir al fortalecimiento del control de la enfermedad y proporciona información que optimiza las actividades tales como: búsqueda activa, educación para la salud, notificación de casos nuevos y supervisar el tratamiento, realizado por profesionales de atención primaria de la salud.

### PD-1130-01 Spatial analysis and active case finding in Guarulhos Municipality, Sao Paulo, Brazil

ESM Rodrigues Pires,<sup>1</sup> N Matsuda De Lima,<sup>1</sup> V Souza Pinto,<sup>2</sup> D Arakaki Sanchez.<sup>3</sup> <sup>1</sup>Epidemiology and Public Health Dept, Guarulhos Health Secretary, Guarulhos, SP, <sup>2</sup>TB Division/ TB Control Program, Sao Paulo State Health Secretary, Sao Paulo, SP, <sup>3</sup>TB Dept, Panamerican Health Organization, Brasilia, DF, Brazil. Fax: (+55) 11 30668294. e-mail: valdirsp@gmail.com

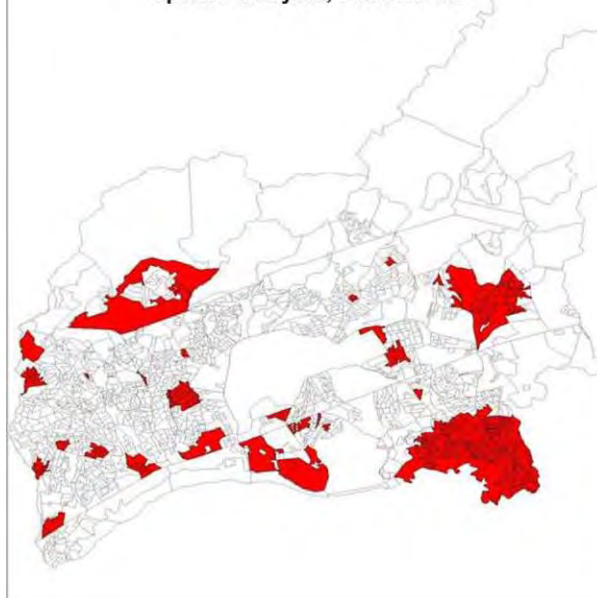
**Background and challenges to implementation:** Even with effective treatment and good cure rates tuberculosis (TB) remains as major health problem worldwide. In different socioeconomic times the growth of cities, agglomeration of urban centers and more recently with the emergence of AIDS endless researches do not exhaust the new contours TB is acquiring every time. Early diagnosis and proper treatment are essential to control TB. The mapping of endemic areas of Guarulhos municipality was elected due to be the second most populated municipality in the State of Sao Paulo, with 1.221.979 inhabitants.

**Intervention or response:** The aim of this study is to identify the spatial distribution of TB new cases in Guarulhos, from 2006 to 2013 and providing maps of the areas to TB active case finding.

**Results and lessons learnt:** Spatial statistical analysis were performed to verify the TB spatial distribution pattern through the census (Figure 1). In the period were reported 3,237 new cases. It was observed that groups at high risk of becoming ill by TB can be a useful tool for the development of a surveillance system based on territorial, identifying priority population groups, as well to break the transmission chain necessary to early diagnosis.

**Conclusion:** The active case finding should be prioritized for health services and were identified 358 census tracts at high risk for TB– those areas are under responsibility of 13 primary healthcare facilities (UBS).

**Figure 1 – Maps of TB clusters with purely spatial analysis, 2006-2013.**



## 56. TB RELAPSES, RECURRENCE AND RETREATMENT

### PD-1131-01 Evaluation of recurrent tuberculous lymphadenitis

S M M Kamal,<sup>1</sup> Md Mainnul Hasan Chowdhury,<sup>2</sup> MS Hossain,<sup>1</sup> MA Jalil Chowdhury,<sup>2</sup> T Islam Khan,<sup>3</sup> AKM Younus Jamal,<sup>4</sup> A Van Deun,<sup>5</sup> R Hasan.<sup>6</sup> <sup>1</sup>National Tuberculosis Reference Laboratory, National Institute of Diseases of the Chest and Hospital(NIDCH), Dhaka, <sup>2</sup>Medicine, Bongabondhu Sheikh Mujib Medical University(BSMMU), Dhaka, <sup>3</sup>Medicine, National Institute of Diseases of the Chest and Hospital(NIDCH), Dhaka, <sup>4</sup>Pathology and Microbiology, National Institute of the Diseases of the Chest and Hospital(NIDCH), Dhaka, Bangladesh; <sup>5</sup>Mycobacteriology, Institute of Tropical Medicine(ITM), Antwerp, Belgium; <sup>6</sup>Director, National Institute of Diseases of the Chest and Hospital(NIDCH), Dhaka, Bangladesh. e-mail: ntrlnidchbd@yahoo.com

**Setting:** National Tuberculosis Reference Laboratory (NTRL) & Bangabandhu Sheikh Mujib Medical University (BSMMU), Bangladesh.

**Background:** Recurrence after treatment is not uncommon with tuberculous lymphadenitis, and may be due to paradoxical immune response, non-TB mycobacteria, failure/relapse due to drug resistant tuberculosis or misdiagnosis.

**Objective:** To document the causes of recurrent or refractory tuberculosis lymphadenitis in Bangladesh and to develop a management algorithm.

**Materials and Methods:** successive patients with enlarging lymph nodes during or after starting anti-tuberculosis treatment were investigated clinically and previous treatment records were analyzed. Specimens were collected by fine needle aspiration or biopsy for cyto/histopathology and bacteriologic investigations at NTRL (smear and culture for mycobacteria, Xpert MTB/RIF. Follow-up of all patients was done at 2 weeks, 2 months and 6 months after surgical clearance or anti-tuberculosis treatment.

**Result:** Thirty-five patients (13 males and 22 females) with mean age 26 years (standard deviation =12) were investigated. Altogether 29 tuberculosis cases were diagnosed by cyto/histopathology, three lymphoma, one sarcoidosis, one reactive lymphadenitis and one pyogenic abscess. Among the 29 TB cases, 23 were Xpert MTB/RIF positive, three with rifampicin resistance. One rifampicin resistant case was confirmed by culture, the remaining 28 were culture negative. One case was positive by microscopy. After six months follow-up, among culture negative cases (n=28) no difference was observed between patients continuing tuberculosis or not ( $Z=0.47$ ,  $P>0.5$ ). Local surgical clearance resulted in rapid healing without continuation of tuberculosis treatment.

**Conclusion and recommendation:** In Bangladesh recurrent tuberculous lymphadenitis is mostly culture negative and due to paradoxical immune reaction. Surgery without continuation of tuberculosis drugs is the preferred treatment.

### PD-1132-01 Risk factors for recurrent tuberculosis of all cured cases in Israel, 1999–2011

Z Mor,<sup>1,2</sup> V Zhdanov,<sup>2,3</sup> N Bilenko.<sup>3,4</sup> <sup>1</sup>Tuberculosis and AIDS, Ministry of Health, Jerusalem, <sup>2</sup>Ramla Department of Health, Ministry of Health, Ramla, <sup>3</sup>School of Public Health, Ben Gurion University in the Negev, Beer Sheva, <sup>4</sup>Ashkelon Department of Health, Ministry of Health, Ashkelon, Israel. Fax: (+972)36836632. e-mail: turkiz1@netvision.net.il

**Background:** Recurrent tuberculosis (TB) is one of the factors hampering eradication efforts, and be related to the quality of the National TB program. This study aims to assess the incidence of recurrent-TB in Israel and identify the associated risk factors in order to support eradication efforts.

**Methods:** This study included two components of all Israeli TB cases from 1999 and 2011: (a) a retrospective cohort study comparing those recurred to those who did not in the Cox regression model, generating hazard ratio (HR) and 95% confidence interval (CI); (b) a matched case-control component to perform in-depth analysis to identify demographic and behavioral variables associated with recurrent-TB in the logistic regression, generating odds ratio (OR) and 95% CI.

**Results:** During the 11-years of follow-up of all 3515 Israeli citizens who were cured of TB, comprising of 23,805 person-year, 37 cases (1.05%) recurred (1.5 recurrent-TB per 1000 person-years). Factors which were independently associated with a greater risk of recurrent-TB included being a male (HR 3.2, 95% CI 1.4–7.4), co-infection with HIV (HR 3.9, 95% CI 1.5–10.4), having positive sputum culture (OR 2.7, 95% CI 1.1–6.9) and avoiding more than 25% of the directly observed therapy meetings (OR 3.2, 95% CI 1.1–10.27).

**Conclusion:** TB recurrence was identified in ~1% of cure cases. The low incidence in Israel suggests satisfactory performance of the National TB Program. It is recommended that males, HIV-infected patients and those with positive sputum culture or do not adhere to anti-TB treatment should be followed-up after treatment completion to prevent recurrent-TB.

### PD-1133-01 High relapse rate of Category I smear-positive cases

V Rolan,<sup>1</sup> R Mehra.<sup>1</sup> <sup>1</sup> Health, Chest Clinic Gulabi Bagh, North DMC, New Delhi, India. e-mail: rk\_mehra@yahoo.com

**Background:** Analysis of large number of CAT I Pos cases when followed up after Cure has found to have High self reporting Relapse Rate thereby posing challenge to the Service Providers and the community. The confidence of the community is also affected.

**Design/Methods:** CAT I regimen - 2HRZE thrice weekly as IP followed by 4HR thrice weekly as CP is given to New Cases. CAT II regimen - 2SHRZE thrice weekly + 1HRZE thrice weekly as IP followed by 5HRE thrice weekly as CP is given to Re-treatment Cases (Relapse, Failure, Default etc.) Cat I sm pos cases regd from 1994 to 2012 in Gulabi Bagh District (Popln 10 L) were meticulously followed up. Self reporting relapses out of

these cured cases were put on CAT II and were also followed up. The Treatment Outcome in both situations was statistically analysed.

**Results:** Big cohort included 9224 CAT I Pos cases regd from 1994 to 2012 (Nineteen yrs.). Avg Cure Rate was 87% (8005 out of 9224). Till 31.12.2013, AS MANY AS 689 relapses were reported out of the cured cases (8.6%). On analysing the time of relapse over complete three years follow up, out of 497 relapse cases reported within three years of cure in cases regd from 1994 to 2009, AS MANY AS 241 ( 48.5%) were reported AS EARLY AS within Six months of cure. The Success Rate of these relapse cases when put on CAT II, however, was fairly acceptable (78%). Therefore, it was observed as follows:- 1. HIGH self reporting Relapse Rate (8.6%). 2. EARLY reporting - most relapses reported WITHIN SIX MONTHS of cure (48.5%). 3. SIGNIFICANT Success Rate (78%) of Relapse Cases.

**Conclusion:** These results indicate that there is fair possibility of ENDOGENOUS RE-ACTIVATION of disease rather than EXOGENOUS RE-INFECTION in these Relapse Cases. This may be the result of inability to create complete bacteriological eradication in these cured cases after successful treatment as per the RNTCP guidelines. The authors submit key recommendations as under :- 1. Re-appraisal of the initial CAT I regimen w.r.t. its Regularity / Duration. 2. Provision of regular radiological assessment during the course of treatment. 3. Provision of timely follow-up of CAT I cases once Cured with a view to identifying the relapse cases at the earliest so that the infection spread in the community is controlled after putting these cases in CAT II promptly. 4. Genotyping Study and Research of the AFB strain during initial infection to analyse the reason of relapse and modifying TB Control measures in the community accordingly.

#### PD-1134-01 Tuberculosis retreatment in northern Portugal

P Cecilia,<sup>1</sup> E Silva,<sup>2</sup> O Oliveira,<sup>3</sup> A Correia,<sup>4</sup> A Carvalho,<sup>5,6</sup> R Duarte.<sup>5,6</sup> <sup>1</sup>Pneumology, Hospital de Braga, Braga, Portugal, <sup>2</sup>Pneumology, Hospital de Viseu, Viseu, <sup>3</sup>Clinical Epidemiology, Predictive Medicine and Public Health of the University of Porto Medical School, Porto, <sup>4</sup>Public Health, Regional North Health Administration, Porto, <sup>5</sup>Pneumology, Centro Hospitalar de Vila Nova de Gaia/Espinho, Gaia, <sup>6</sup>Chest Disease Centre, Chest Disease Centre of Vila Nova de Gaia, Gaia, Portugal. e-mail: ceciliafpacheco@gmail.com

**Introduction:** Current treatment for tuberculosis (TB) has proven efficacy. Disease relapse, treatment after default or treatment failure requires retreatment, usually with more drugs, during a longer period of time and with an increased probability of side effects. Objective: To assess risk factors and outcome for retreatment TB patients.

**Methods:** Case control study. Cases: All retreatment TB cases reported in 2012 in Northern Portugal; Controls: New cases that were registered during the same period. Cases and controls were selected from the national database, which integrates the data from the mandatory

registration of TB. For each case we randomly selected 2 controls in the data base. Clinical records of patients were analysed. Risk factors included were sex, age, HIV infection, diabetes mellitus, immunosuppression, drug resistance, pulmonary versus extra-pulmonary TB, unemployment, drug abuse and alcoholism. The World Health Organization (WHO) standart definition was used for treatment outcome (treatment success, died, failure, default and transferred out). The association between explanatory variables and retreatment was evaluated by logistic regression models. The crude and adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were determined.

**Results:** We analyzed 57 cases and 118 controls. Of the 57 retreatment cases identified, 46 (81%) have been successfully treated in the past. Male sex (adjusted OR: 3.31, 95% CI: 1.48-7.38,  $p=0.003$ ), HIV-positive status (adjusted OR: 4.34, 95% CI: 1.54-12.24,  $p=0.006$ ) and age over 40 (adjusted OR: 2.75, 95% CI: 1.23-6.14,  $p=0.013$ ) were independent risk factors identified for retreatment. The number of cases of pulmonary TB was higher in the group of retreatment (96.5% vs. 84.7%,  $p=0.04$ ). There were no differences when compared factors as diabetes mellitus, immunosuppression, drug resistance, unemployment, intravenous drug abuse and alcoholism. The treatment success rate was lower among patients who had received prior TB treatment than in patients who were never treated for TB (80,7% vs 92,4%,  $p=0.04$ ). In retreatment group 6 patients (10,5%) died while 7 patients (5,9%) died among the new cases, although this was not a statistically significant difference ( $p=0.36$ ).

**Conclusion:** Male sex, HIV-positive status and age over 40 were risk factors identified in retreatment patients. Retreatment patients had a higher number of cases of pulmonary TB and a lower treatment success rate.

#### PD-1135-01 A new operational definition of intermittent adherence to tuberculosis treatment is associated with high recurrence risk

M Tovar,<sup>1,2</sup> T Wingfield,<sup>2</sup> R Montoya,<sup>2</sup> N Becerra,<sup>2</sup> B Valiente,<sup>2</sup> E Ramos,<sup>1</sup> T Valencia,<sup>1</sup> C Evans.<sup>1,3</sup> <sup>1</sup>IFHAD: Innovation For Health And Development, LID 218 Universidad Peruana Cayetano Heredia, Lima, <sup>2</sup>IPSYD: Innovacion Por la Salud Y el Desarrollo, Asociacion Benefica PRISMA, Lima, Peru; <sup>3</sup>IFHAD, Infectious Diseases & Immunity, Wellcome Trust Imperial College Centre for Global Health Research, London, UK. e-mail: marco.tovar@upch.pe

**Background:** Intermittent adherence to tuberculosis (TB) treatment is associated with adverse clinical outcome. Post-treatment follow-up data to detect TB recurrence are rarely available for assessment of adverse clinical outcome. No consensus exists concerning an operational definition of intermittent adherence. We created an operational definition of intermittent adherence and examined its association with risk of TB recurrence.

**Design/Methods:** From January 2002 through June 2011, consecutive TB patients diagnosed by the national TB program (NTP) were enrolled in Ventanilla. Inter-



mittent adherence was defined as missing more than 12 doses during the intensive phase or more than two doses during the maintenance phase. We included all first episode of TB that had TB drug susceptibility test (DST) that was susceptible to isoniazid and rifampicin by the Microscopic-Observation Drug-Susceptibility (MODS) technique. Time-to-event analysis was used to test for hazard ratios (HR) with 95% confidence intervals (CI) for intermittent adherence predicting TB recurrence. Population attributable fraction (PAF) was calculated.

**Results:** 4255 patients were enrolled, of whom 86% (3191) met inclusion criteria. 89% (2833) of these eligible patients were cured and 1151 of them had a DST result that was susceptible for 90% (1033) patients. 4.4% (45/1033) had a TB recurrence. There were 3 intermittent adherence groups: 'adherent' (384 patients, 37%) had no evidence of intermittent-adherence throughout treatment; 'late intermittency' (585 patients, 57%) had intermittent-adherence only during the maintenance phase; and 'early intermittency' (64 patients, 6.2%) had intermittent adherence during the intensive phase. Patients with early or late intermittency were more likely than adherent patients to have TB recurrence (late intermittency, HR=2.0 (CI=1.2–3.3); early intermittency HR=2.2 (CI=1.0–4.6)). There was a trend for more recurrences to be attributed to late-intermittency (PAF=42%, CI=0–67) than early intermittency (PAF=30%, CI=0–53).

**Conclusion:** Intermittent adherence during the maintenance phase was the most frequent form of intermittent therapy during TB treatment. While non-adherence during either treatment phase was associated with high risk of subsequent TB recurrence, our results imply that non-adherence during the maintenance phase may be responsible for at least as many TB recurrences as during intensive phase.

#### **PD-1136-01 Factors associated with failure to smear convert by Month 2 among Category 1 TB patients in Karachi, Pakistan**

K D'souza,<sup>1</sup> A Malik,<sup>1</sup> A Zaidi,<sup>1</sup> M Jaswal,<sup>2</sup> S Butt,<sup>2</sup> S Mahroz,<sup>2</sup> S Khowaja,<sup>1</sup> A Codlin.<sup>1</sup> <sup>1</sup>International Health, Interactive Research and Development, Karachi, <sup>2</sup>TB Control, The Indus Hospital, Karachi, Pakistan.  
e-mail: kimberly.dsouza@irdresearch.org

**Background:** Failure to smear convert at Month 2 of anti-TB treatment is associated with adverse treatment outcomes. The identification of risk factors which can predict non-conversion could help program teams focus finite resources to prevent loss of follow up and treatment failure in high burden settings.

**Methods:** Data, including baseline demographics, clinical records and smear microscopy results, were abstracted from electronic medical records for all smear-positive Category 1 patients registered at the Indus Hospital TB Program in Karachi, Pakistan, between 2007 and 2013. Only smear-positive patients with a second month sputum result were included in the study. For patients with smear microscopy results at both Month 2 and 3 of

treatment, only Month 2 results were abstracted. Pediatric patients (<15 years of age) were excluded from the analysis. A multivariate logistic regression model was built and odds ratios for association between sputum smear non-conversion at Month 2 and baseline demographics and medical characteristics of the patients were calculated. Gender and weight did not have a significant effect and were excluded from the final regression model.

**Results:** The smear results for 1,980 patients were analyzed. The adjusted OR for age group <35 years compared to 35–54 years and ≥55 years were 1.32 (95% CI: 1.00–1.72) and 1.42 (95% CI: 1.00–2.00), respectively. The odds of non-conversion increased significantly as the baseline sputum grade increased (reference: 1–9 AFB) with ORs for 1+, 2+ and 3+ grades being 1.99 (95% CI: 1.06–3.73), 3.91 (95% CI: 2.09–7.31) and 6.68 (95% CI: 3.64–12.28), respectively.

**Conclusion:** For this population, age greater than 35 years and high baseline sputum smear result have a significant impact on sputum smear microscopy non-conversion at Month 2 of treatment. This information can be used to provide additional social support and stricter follow up to at risk patients in order to prevent loss of follow up and treatment failure.

#### **PD-1137-01 Detection of Chest X-ray abnormalities and tuberculosis using computer-aided detection vs interpretation by radiologists and a clinical officer**

A Khan,<sup>1</sup> A Zaidi,<sup>1</sup> R Philipsen,<sup>2</sup> S Khowaja,<sup>1</sup> B Van Ginneken,<sup>2</sup> A Khan,<sup>1</sup> T Dossul.<sup>1</sup> <sup>1</sup>International Health, Interactive Research and Development, Karachi, Pakistan; <sup>2</sup>Nijmegen Medical Centre, Radboud University, Nijmegen, Netherlands. Fax: (+92)2134327696.  
e-mail: anum.najeem@irdresearch.org

**Background:** There is renewed interest in chest radiography (CXR) as a screening tool for tuberculosis in high burden countries. Limited availability of skilled personnel in low-resource settings is a major barrier to its wider-scale adoption. Computer-aided detection (CAD) has been shown to be effective in supporting TB diagnostic algorithms in African settings; however, limited real-world applications of such systems have been evaluated. This study compares automated readings of a CAD system for CXR abnormalities with the interpretations of radiologists and a clinical officer.

**Design/Methods:** Suspects for lung diseases were identified through active screening in the private sector at Family-Practitioner clinics. These suspects were referred to the lung health diagnosis and screening center for CXR from three low-income towns of Karachi, Pakistan. CXRs were analyzed using CAD4TB v3.07 (Diagnostic Image Analysis Group, Nijmegen, The Netherlands), a system designed for TB diagnosis that computes an abnormality score (0–100) on the basis of shape, symmetry and texture of the lung fields. CXRs were reviewed by two radiologists and a clinical officer who were masked to the CAD4TB score and patient disease status. Interobserver Agreement (Cohen's Kappa)

between CAD4TB and each radiologist and clinical officer for CXR abnormality was analyzed at various cut-points of CAD4TB.

**Results:** CXRs from 186 suspects were included in the study for analysis. A CAD4TB score of 80 maximized agreement between CAD4TB and each reviewer (Radiologist 1: Kappa 0.62, Radiologist 2: 0.54, Clinical Officer: 0.60). Mean sensitivity and specificity for CXR abnormality of CAD4TB compared to the reviewers was 78% and 79% respectively. A high proportion of non-TB CXR abnormalities as reported by the reviewers were also classified as abnormal by CAD4TB at a cut-point of 80 (Radiologist 1: 88.2%, Radiologist 2: 71.9%, Clinical Officer 60%). Agreement between CAD4TB and each reviewer subsequently increased after including only TB CXR abnormalities (Radiologist 1: Kappa 0.63, Radiologist 2: 0.67, Clinical Officer: 0.71).

**Conclusion:** CAD4TB has the potential as a screening tool for TB in high burden countries. Detection of non-TB abnormalities by CAD4TB may lead to challenges in interpretation of results in programmatic settings. Use of additional data relevant to local disease epidemiology such as patient demographics as well as symptom screening may improve accuracy of CAD4TB when utilized in TB control programs.

#### **PD-1138-01 Situation analysis of sputum smear-negative and culture-positive tuberculosis cases from Cambodian prevalence survey 2011 for further reduction of TB**

S Hirao,<sup>1</sup> K Okada,<sup>1</sup> N Yamada,<sup>1</sup> S Saint,<sup>2</sup> S Peou,<sup>2</sup> T E Mao.<sup>2</sup> <sup>1</sup>Centre for International Cooperation and Global TB Information, The Research Institute of Tuberculosis (RIT) Japan Anti-Tuberculosis Association (JATA), Kiyose, Tokyo, Japan; <sup>2</sup>National Center for Tuberculosis and Leprosy Control (CENAT), Ministry of Health, Phnom Penh, Cambodia. Fax: (+81) 42-492-4600. e-mail: hiraojapan@hotmail.com

**Background:** In Cambodia, repeat national prevalence surveys were conducted in 2002 and 2011. Both survey revealed that the prevalence rate of smear-negative, culture-positive (S-C+) tuberculosis (TB), which are at higher risk of progression to smear-positive (S+), was twice higher than that of S+ TB. The objective of the study was to examine the situation of S-C+ TB cases from Cambodian prevalence survey 2011.

**Methods:** We categorized chest X-ray (CXR) films of the participants with sputum S-C+ from the survey as follows; lesion side (right, left or both), cavity (exist or not) and lesion expansion (class 1: less than 1/3 of unilateral lung field, class 2: 1/3 to whole unilateral lung field or class 3: more than whole unilateral lung field) were measured.

**Results:** Excluding 7 cases without films and 5 cases with normal CXR, 203 cases were assessed. Of those, 95 cases (46.8%) had only right side, 40 cases (19.7%) had only left side and 68 cases (33.5%) had both sides in terms of lesion side. Fourteen cases (6.9%) had cavitary lesion and 189 cases (93.1%) did not show any cavities. The numbers of cases which were classed to be 1, 2 and 3

were 145 (71.4%), 55 (27.1%) and 3 (1.5%), respectively.

**Conclusions and recommendations:** If S-C+ TB cases are defined as an earlier stage of S+ TB cases, 203 cases may progress to S+ TB cases in near future. Furthermore, as the cases with cavitary lesion on CXR are more likely to be smear positive, 14 cases might be spread TB bacilli. If bilateral lesion and class 2 and 3 lesion expansion were interpreted as advanced stage of pulmonary TB disease, these cases which were 68 (33%) cases as bilateral and total 58 cases as class 2 and 3 lesion expansion may have a higher risk of progression to S+ TB cases in a shorter period of time. To accelerate the current annual decline rate in TB incidence (only 2%), we may need to diagnose more TB cases with S-C+ before the disease progression. To achieve this, sputum culture test and/or nucleic acid amplification test such as Xpert MTB/RIF and LAMP are required.

#### **PD-1139-01 Recurrence of TB among cured NSP TB patients over one year follow-up and role in amplification of resistance**

M Toshniwal,<sup>1</sup> S Soni,<sup>2</sup> K Rade,<sup>1</sup> P Malik,<sup>1</sup> M Pawar,<sup>3</sup> A Sreenivas.<sup>1</sup> <sup>1</sup>Tuberculosis, WHO Country Office India, New Delhi, <sup>2</sup>TB, City TB Office Amravati Municipal Corporation, Amravati, <sup>3</sup>Tuberculosis, State TB Office, Pune, India. e-mail: toshniwalmanoj@hotmail.com

**Background:** India's Revised National TB Control Program (RNTCP) uses sputum smear microscopy as primary diagnostic tool as well as for follow-up to monitor progress on treatment till the end of treatment to declare cure for pulmonary Tuberculosis (PTB) cases. Treatment is provided with thrice weekly intermittent regimen under direct observation for 6–7 months in new smear positive (NSP) PTB. At present there is no protocol being implemented for long term follow-up of cured PTB patients after treatment completion. We evaluated what proportion of NSP TB patients cured under RNTCP had a repeat episode of PTB within 1–2 years of treatment completion and amplification of drug resistance.

**Method:** Study was conducted in 1.1 million population in two districts of Maharashtra, India. All the cured NSP PTB patients in TB registry of Oct 2011 to Mar 2012 were visited to identify repeat episode of TB. Diagnosis of patients were re-confirmed from medical records by supervisor & drug susceptibility testing (DST) results were also studied.

**Results:** In the cohort of 156 NSP TB cases, 131 were declared as cured. Of these 120 (92%) were visited & 29 (24%) had recurrent TB. Recurrence of TB is 27% in males and 20% in females. The recurrence rate was 18228 cases per lakh Person-year follow-up, 82 times higher than the estimated TB incidence of the general population. TB recurrence took average 4.6 months, with likelihood of TB recurrence at the 3<sup>rd</sup>, 6<sup>th</sup> & 12<sup>th</sup> month of follow-up was 10%, 17% & 24% respectively. Patients with recurrent TB took an average of 19 days more than the non-recurrence group indicating missed doses during treatment. Out of the 29 recurrent TB cases,

results for DST results were available for 26 (90%) patients and 3 (12%) were reported to be R-resistance.

**Conclusion:** The rate of TB recurrence is high and most episode occur within the first year. Policy of long term follow-up of cured PTB patients for two years as recommended in Standards for TB Care in India needs to be adopted and program may augment its capacity to ensure it. Patients missing doses and males are at higher risk of recurrence. Higher rate of recurrent TB within a year advises to replace policy of use of Smear microscopy with culture to declare the patient as cure. Evaluation of treatment regimen and its implementation is also required in view of the results of this study. Further studies are required in larger population with genotyping to determine to differentiate reinfection and relapse.

**Table:**

Recurrence of TB among cured NSP TB patients over one year follow-up & role in amplification of resistance

	Particulars	Males	Females	Total
1	Number of NSP registered	102	54	156
2	Number (%) of NSP reported cured among registered	85 (83%)	46 (85%)	131 (84%)
3	Number of eligible cured patients to be visited	84	45	131
4	Number of eligible cured patients actually visited	79 (93%)	41 (89%)	120 (92%)
5	Number (%) who reported repeat episode of TB among visited	21 (27%)	8 (20%)	29 (24%)
6	Number of reported repeat episode of TB on RNTCP treatment	19	8	27
7	Number of reported repeat episode of TB who are on non-RNTCP treatment	2	0	2
8	Number for whom Drug Susceptible Testing results available	19	7	26
	Line Probe Assay – R resistance	1	0	1
	CBNAAT (GeneXpert) – R-resistance	2	0	2
9	Number (%) of Patients who are Rifampicin resistant among tested	3 (16%)	0	3 (12%)

#### PD-1140-01 Recurrent tuberculosis, relapse or reinfection after successful treatment: a retrospective cohort study

I Berggren,<sup>1</sup> M Pergert,<sup>1</sup> A Pennhag,<sup>2</sup> I Zedenius.<sup>1</sup> <sup>1</sup>Dep of Communicable Disease Control and Prevention, Stockholm County Council, Stockholm, <sup>2</sup>Dep of Microbiology, Public Health Agency of Sweden, Stockholm, Sweden. Fax: (+46) 8315767. e-mail: ingela.berggren@sl.se

**Setting** Patients with repeated episodes of treated tuberculosis within Stockholm County, Sweden 1998–2013.

**Objectives** To identify among successfully treated culture-positive tuberculosis cases the relationship between types of recurrence, i.e. endogenous or exogenous reinfection in a low-endemic environment.

**Methods** Retrospective analysis of molecular patterns (RFLP/Spoligotyping and/or MIRU-VNTR/Spoligotyping) from all culture-positive cases reported in the National TB register (SmiNET) for more than one episode of tuberculosis. Relapse was inferred when patterns from the same individual were identical, and reinfection if paired samples differed in the molecular typing.

**Results** A total of 2896 cases with an index episode of tuberculosis were reported. A subsequent recurrent episode was recorded for 74 and a third episode for 5 patients. 40 were culture positive in all episodes with molecular typing available in 32. Of the 32 recurrent tuberculosis episodes with molecular typing available, 28

were relapse cases and 4 were due to reinfection. Median time to relapse was 21 months (9–117 months) and to reinfection 46 months (24–139 months). Age and sex distribution did not differ between the two groups. All re-infected and 2/3 of relapsing patients were born in high endemic countries.

**Conclusion** Recurrence of tuberculosis in treated patients is a rare event in our setting. Relapse is dominating and only very few re-infections are seen. Increased travelling and migration from high endemic areas has increased the number of index episodes but has not generated a high level of re-infection.

#### PD-1141-01 Reinfection and relapse among new smear-positive tuberculosis patients in Lima, Peru

L Otero,<sup>1,2</sup> F Barletta,<sup>3</sup> L Rigouts,<sup>3</sup> C Seas,<sup>1</sup> E Gotuzzo,<sup>1</sup> P Van Der Stuyft.<sup>2</sup> <sup>1</sup>Instituto de Medicina Tropical Alexander von Humboldt, Universidad Peruana Cayetano Heredia, Lima, Peru; <sup>2</sup>Department of Public Health, Institute of Tropical Medicine, Antwerp, <sup>3</sup>Department of Biomedical Sciences, Institute of Tropical Medicine, Antwerp, Belgium. e-mail: larissaotero@gmail.com

**Background:** Routine tuberculosis (TB) program indicators collapse all recurrent TB episodes in “relapse” cases. Understanding the contributions of reinfections and relapses to recurrent TB is important to evaluate TB control activities. A large proportion of reinfection among recurrent episodes of tuberculosis suggests ongoing transmission in the community.

**Methods:** We enrolled new smear-positive TB patients in 33 health facilities of a district in North Lima from March 2010 until December 2012. Patients were followed up for two years after treatment completion. TB records were reviewed weekly to ascertain a recurrent episode among participants. To elicit cases that might have been diagnosed in other health facilities (in the private or social security system or in other districts) household visits were conducted at month 12 and at month 24 after treatment completion. A sputum sample at diagnosis of the first episode and two samples from the recurrent episode were cultured in Löwenstein-Jensen and fingerprinted with spoligotyping to determine phylogenetic lineages. When the same lineage was found, DNA was further analysed by mycobacterial interspersed repetitive unit-variable number tandem repeat 15-loci typing (MIRU15).

**Results:** Of the 1295 patients enrolled, 984 (75.9%) completed first line TB treatment and were followed up for a recurrent episode. Thirty eight (3.9%) patients had a recurrent episode within two years of treatment completion. Seventeen patients were excluded from the analysis (4 were culture negative, 13 were culture positive but with no molecular data). Among the 21 with molecular data available for both episodes, 9 (43%) had the same strain and were thus probably relapses, and 12 (57%) had a different strain (8 had different lineages, 4 same lineages different MIRU15) and were reinfection episodes. The median (IQR) time between treatment completion and relapse was 3.7 months (interquartile



range (IQR) 2.7–17.9), and 7.5 months (IQR, 4.8–11.3) between treatment completion and diagnosis of a recurrent episode due to reinfection.

**Conclusions:** The high proportion of reinfections suggests ongoing transmission in the community. Strengthening case detection at the health facilities and prompt start of treatment is urgent in order to reduce transmission.

## 57. TB CONTROL

### PD-1142-01 Monitoreo continuo de cohortes para mejora de resultados del tratamiento de casos de tuberculosis en el periodo 2000–2012 en México

M A Garcia,<sup>1</sup> Iour Martinez,<sup>1</sup> Mart Castellanos.<sup>1</sup>

<sup>1</sup> Tuberculosis, Secretaria de Salud, Mexico DF, Mexico. Fax: (+55) 26146433. e-mail: novimarta@hotmail.com

**Objetivo:** Demostrar mejores resultados mediante monitoreo continuo de las cohortes del tratamiento anti tuberculosis.

**Antecedentes:** Con base en pobres resultados de tratamiento antituberculosis registrados en México en el periodo 2000–2009, se programó la evaluación trimestral de cohortes de tratamiento, para la toma de decisiones ante el cumplimiento de los Objetivos del Desarrollo del Milenio.

**Método:** Se realizó análisis prospectivo nacional del éxito terapéutico en casos nuevos pulmonares Bk+ (TBP Bk+), desglosadas por estado, institución y sexo, casos con coinfección TB/Sida y comorbilidad TB/DM; casos en municipios indígenas y casos en prisiones.

**Resultados:** Incremento significativo del éxito terapéutico nacional, al pasar de 70.7% en el 2000 a 87.1% en 2012. Con un rango de éxito entre estados que van de 72.7 en Baja California hasta 100% en Tlaxcala; Según institución, el IMSS con 89.1 vs 86.4% para la Secretaría de Salud; mujeres y hombres con 90.7 y 84.9% respectivamente; los casos de municipios indígenas alcanzan un 86.9% en éxito terapéutico y los casos en prisiones 49.4%. Los casos con comorbilidad TB/DM alcanzan 85.5% contra 57.1% para TB/VIH.

**Conclusiones:** El seguimiento trimestral de casos de tuberculosis ingresados a tratamiento, permite identificar áreas de oportunidad para la toma de decisiones y actuar en consecuencia para el mejoramiento de resultados del tratamiento con lo que se alcanzó la meta establecida para 2015 de los ODM de éxito terapéutico.

### PD-1143-01 Actuación de la enfermería en el control de la tuberculosis en la Comunidad de Rocinha, Rio de Janeiro, Brasil

V Santos,<sup>1</sup> F Assumpção De Souza,<sup>1</sup> F Scarparo Cunha.<sup>1</sup>

<sup>1</sup> Postgrado en Enfermería - Másters, Universidad Federal del Estado del Rio de Janeiro, Rio de Janeiro, RJ, Brazil. e-mail: vivianabreu85@gmail.com

**Background:** La investigación busca entender las percepciones de los enfermeros sobre sus acciones en el

tratamiento de observación directa de la tuberculosis en la comunidad de Rocinha, en Río de Janeiro (RJ) - Brasil. Rocinha presenta la mayor tasa de incidencia en RJ, reflejando la presencia de enormes desigualdades sociales en medio de uno de los barrios más ricos de la ciudad.

**Métodos:** Estudio cualitativo apoyado por el método de análisis del discurso de la sede francesa, comprendiendo cómo un objeto simbólico tiene sentido para el analista, poniendo en tela de juicio la interpretación. Se entrevistó a 11 enfermeros de las clínicas familiares ubicadas en la Comunidad de Rocinha. Se utilizó el software Atlas.ti 6.0 como una herramienta para el almacenamiento y organización de las entrevistas transcritas. Los resultados surgieron de recortes relacionados con el lenguaje y las condiciones de producción. Por lo tanto, la formación del corpus a través de la construcción discursiva que cumplieron con los criterios derivados de los principios teóricos del análisis del discurso, teniendo en cuenta los objetivos del análisis, y que han permitido su comprensión.

**Resultados:** Los enfermeros están vinculados a la realización de procedimientos, tales como la toma de medicinas o asignar la actividad a los agentes de salud para que se adhieran al control de la tuberculosis. Esto ocurre de una manera jerárquica en relación con los requisitos de un modelo de gestión existente. El estudio destaca la falta de relaciones dialógicas entre los profesionales que intervienen en el control de la tuberculosis. Otro dato significativo es el comportamiento condicionado por las estructuras dominantes de los enfermeros. Esto se opone a la decisión del paciente de elegir su forma de tratamiento. Excluye a las expectativas, intereses y valores de los individuos en interacción.

**Conclusión:** El flujo vertical y jerárquico representado por enfermeros impide cambios efectivos en el control de la tuberculosis en Rocinha. Revela una especie de práctica autoritaria por parte de estos profesionales. Hay una inflexibilidad en las relaciones de aquellos que cuidan y los que son cuidados, lo que compromete la capacidad de resolver problemas, incluso estrictamente clínicos. Este estudio propone la necesidad de invertir más en la educación como medio para la transferencia de conocimientos entre los profesionales que participan del programa de tuberculosis en la comunidad de Rocinha.

### PD-1144-01 Tratamiento empírico antituberculoso en pacientes con sida y fiebre de origen desconocido

R Martinez,<sup>1</sup> A Valencia,<sup>1</sup> C Bueno,<sup>2</sup> C Jimenez.<sup>3</sup>

<sup>1</sup> Medico, Comfamiliar Risaralda, Pereira, <sup>2</sup> Medico, Union HAART, Pereira, Colombia, <sup>3</sup> Medico, Grupo VIHDA, Pereira, Colombia. e-mail: ricardoamartinezg@hotmail.com

**Background:** La fiebre de origen desconocido en el paciente inmunocomprometido por VIH plantea problemas no solo relacionados con la ausencia de diagnóstico sino también con la aproximación terapéutica en el enfermo que por su condición presenta deterioro progresivo y elevada mortalidad. En el presente estudio

se plantea el beneficio de de la terapia empírica antituberculosa en estas condiciones

**Design/Methods:** Se realizó estudio de cohortes en 78 pacientes ( 39 por cada cohorte) con vih y fiebre de origen no establecido a pesar de estudios de extensión protocolarios que incluyeron imágenes, pruebas serológicas ,moleculares y cultivos, se considero cohorte expuesta la que recibió terapia empírica antituberculosa

**Results:** El recuento promedio de CD4 fue de 117 .La respuesta clínica favorable en la cohorte expuesta fue evidente en 52.7% de pacientes. El tiempo promedio de mejoría sintomática fue 17 días. La disminución en el valor de proteína c reactiva precedió 6 días a la respuesta clínica en 80% de los casos. Tras 2 meses de terapia antituberculosa existía absoluto control de síntomas y de marcadores serológicos en los pacientes con respuesta inicial favorable. En pacientes que no presentaron modificación sintomática o de marcadores serológicos de inflamación tras 1 mes de terapia antituberculosa, esta fue retirada. La terapia empírica fue factor protector con OR 0.62 IC 0.09 – 7.2 p 0.042 considerando a la muerte como desenlace final

**Conclusion:** Teniendo en cuenta que la tuberculosis es la enfermedad oportunista más frecuente en pacientes con vih y la principal causa de mortalidad , se plantea el potencial beneficio de terapia empírica, no solo como prueba diagnóstica sino también con fin terapéutico, siendo pertinente abandonar esta conducta si no existe respuesta posterior a 30 días de terapia

#### **PD-1145-01 Abogacía a nivel local como instrumento fundamental en la atención centrada en la persona con tuberculosis resistente en el sureste Mexicano**

J De La Cruz,<sup>1</sup> N Enriquez Rios,<sup>1</sup> Mart Castellanos.<sup>1</sup>

<sup>1</sup>Tuberculosis, Secretaria de Salud Mexico, Tapachula, Mexico. e-mail: jcdela125@hotmail.com

**Objetivos:** Evaluar el impacto de las acciones de abogacía a nivel local, como estrategia de fortalecimiento al DOTS para asegurar la adherencia al tratamiento en TB-MFR.

**Métodos.** Se aplicó un cuestionario estructurado al personal que trataron casos con tuberculosis farmacoresistente en Chiapas de la cohorte de casos de 2010. Los datos se analizaron con el programa IBM SPSS statistics, en términos de distribución y frecuencia de las variables estudiadas.

**Resultados.** Se estudiaron a 17 casos con tuberculosis farmacoresistente confirmados por cultivo y pruebas de farmacoresistencia: la media de edad fue de 51.65. Según género 70.6% hombre, 29.4% mujer. Clasificación final: 82.4% curados y 17.6% defunción. Gestión de fármacos para manejo de reacciones adversas para el 100% de los casos. Persona que realiza la gestión: 52.9 % programa jurisdiccional de tuberculosis, 23.5% médico tratante, 17.6% enfermería y 5.9% trabajo social. Lugares de gestión de fármacos: 52.9% jurisdicción sanitaria, 35.3% particulares, 5.9% hospitales, y 5.9% empresas departamentales. Gestión de Apoyo

alimentario en un: 64.7% de los casos. Persona que realizó la gestión: 45% enfermería, 27.3% trabajo social y 27.3% programa jurisdiccional. Lugar de la gestión: 95% banco de alimentos. Gestión para realización de estudios de laboratorio se realizó en un 100 % y se realizó la gestión en: 52.9% hospitales de segundo nivel, un 29.4% en hospitales de tercer nivel y laboratorios particulares en un 5.9%. Gestión de estudios de gabinete, en: 88 % de los casos. Lugar de gestión: 64.6% hospitales de segundo nivel, el 23.1 % en empresas particulares y 5.7% hospitales de tercer nivel. Gestión de audiometría gestión en: 100% de los casos. Quién realizo la gestión: 82.2% programa jurisdiccional, 11.8% trabajo social y 5.9% enfermería. Lugar donde se gestión: 76.5% hospital 3° nivel y 23.5 % consultorios particulares. Gestión para transporte a unidad de salud de forma gratuita. Cobertura: 41.2% de los casos. Gestión para valoración psiquiátrica. Cobertura: 88.2% de los casos. Gestión para apoyo económico. Cobertura: 23.5% en una sola ocasión. Otras gestiones: El 52.5% se le proporcionó atención domiciliaria.

**Conclusión:** Abogacía local con diversos aliados, como estrategia para garantizar la atención centrada en la persona; eleva tasa de curación en tuberculosis farmacoresistente fortaleciendo al DOTS.

#### **PD-1146-01 Encuesta de conocimientos, actitudes y prácticas sobre TB en el personal de salud de las redes públicas de servicios de salud, 2012**

Y Tavez Villaman,<sup>1</sup> R Orlando,<sup>2</sup> E Lebron Mendez,<sup>1</sup>

B Marcelino,<sup>3</sup> L Lerebours,<sup>4</sup> J Medina,<sup>1</sup> Y Alcantara,<sup>2</sup>

K Romero.<sup>3</sup> <sup>1</sup>Unidad Ejecutora de Proyectos Fondo Mundial,

Ministerio de Salud Publica, Distrito Nacional, <sup>2</sup>CONAPOFA,

Ministerio de Salud Publica, Distrito Nacional, <sup>3</sup>Programa

Nacional de Control de la Tuberculosis, Ministerio de Salud

Publica, Distrito Nacional, <sup>4</sup>Sub Direccion, Clinica Familiar

Complejo Micaeliano, La Romana, Dominican Republic.

e-mail: belkys\_tb@yahoo.es

La encuesta de conocimientos, actitudes y practicas sobre TB en el personal de salud de las redes públicas de servicios de salud tuvo como objetivo obtener información sobre los conocimientos, actitudes y practicas sobre TB del personal de salud de las redes públicas de servicios de salud con representatividad nacional, discriminando entre los centros de salud de primer nivel y especializado, entre médicos, enfermeras, bioanalistas, promotores y de servicios responsables de la atención. Se entrevistaron 1,164 trabajadores de la salud en centros del ministerio de salud pública donde el 42% son de enfermería, un 41% médicos y el restante 17 %, bioanalistas. De forma global, el 80,4% son mujeres y el promedio de edad en general es de 41,6 años ( $\pm$ DE: 10,5 años). Un total de 964 encuestados (487 enfermeras y 477 médicos) se les aplicó preguntas sobre conocimientos y prevención de TB y de estos el 42,2% (414) dijo haberse capacitado en TB. De estos el 79,6% respondió que están de acuerdo con que la TB es una enfermedad infecciosa ocasionada por el *Mycobacterium tuberculosis*, el 72.\*% estuvo en desacuerdo que la fiebre

y la dificultad para respirar son los síntomas más importantes, el 74% está en desacuerdo con que la radiografía de tórax es el mejor método de diagnóstico para TB. De 200 bioanalistas encuestadas en el 56% opina que en los centros donde laboran ofrecen servicio de bacteriología exclusivamente para baciloscopia. Un 64.2 de ellas opina que el tiempo entre la recepción de muestra y entrega de resultados es de dos a tres días, un 23% en un día. De 477 médicos encuestados, el 78,5% refiere que ha tratado pacientes con TB, un 54,7% ha atendido casos de TB no confirmados por baciloscopia y el 84,7% refiere haber atendido casos infectados con VIH. Sobre los conocimientos de TB de los promotores, el 90,5% respondió que es una enfermedad causada por el bacilo de Koch, un 8,1% dice que es por un virus. El 93,2% responde que se transmite por el aire y un 5,4% dice que por alimentos y agua. El 91,9% contesta que la TB se contagia de una persona a otra cuando esta tose o estornuda y un 5,4% por comer directamente de un enfermo. Si bien existen un nivel aceptable de conocimientos, actitudes y prácticas sobre la tuberculosis en los recursos humanos entrevistados, aún queda por seguir trabajando para lograr criterios más uniformes y que sean transmitidos adecuadamente a los usuarios y a la comunidad.

**PD-1147-01 Transferencia de políticas relacionadas al tratamiento directamente observado para el control de la tuberculosis en João Pessoa-Paraíba-Brasil**

L Sá,<sup>1</sup> RCC Oliveira,<sup>1</sup> DCB Dias,<sup>1</sup>  
KDO Karinne Dantas De Oliveira Adário,<sup>2</sup>  
PFP Pedro Fredemir Palha,<sup>3</sup> Jord Nogueira,<sup>1</sup>  
EMNA Edna Marília Nóbrega Fonseca De Ara,<sup>1</sup>  
JVST Janaina Von Sohsten Trigueiro.<sup>1</sup> <sup>1</sup>Programa de Pós-Graduação em Enfermagem, Universidade Federal da Paraíba, João Pessoa, PB, <sup>2</sup>Gestão do Trabalho e Educação em Saúde, Secretaria de Saúde do Município de João Pessoa, João Pessoa, PB, <sup>3</sup>Escola de Enfermagem de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, SP, Brazil. Fax: (+55) 3216 7216. e-mail: sa.lenilde@gmail.com

**Background:** La Transferencia de políticas comprende un proceso que cuenta con participación y involucramiento de gestores profesionales de salud para desarrollar y evaluar la transferencia de determinada política, principalmente, con conocimiento y acciones innovadoras relativas a modificaciones en asistencia de los servicios de Atención Primaria de Salud. El estudio objetivó investigar el discurso que Gestores de Salud presentan al transferir políticas para la ejecución del Tratamiento Directamente Observado (TDO) junto a Unidades de Salud de Familia en João Pessoa-Paraíba-Brasil.

**Design/Methods:** Estudio exploratorio, de abordaje cualitativo, realizado con 20 (veinte) trabajadores de salud actuando como gestores del control de la tuberculosis en João Pessoa. El material empírico se colectó de mayo a junio de 2013 por medio de entrevista semidirigida. En la organización del corpus se utilizó software Atlas.ti versión 6.0, mediante creación de una Unidad Hermenéutica que permite codificar declaraciones de

entrevistados según sus categorías de análisis previamente definidas por el investigador. Tras la codificación por el software, el corpus discursivo se analizó basado al referencial teórico-analítico del Análisis de Discurso de línea francesa. Al estudio lo aprobó el Comité de Ética en Pesquisa de la Universidad Federal de Paraíba bajo protocolo n° 0301/2012.

**Results:** Se evidenció fragilidades en la conducción y organización de acciones relacionados a los componentes de la estrategia Directly Observed Treatment-short course (DOTS). En el discurso de los gestores se reveló desconocimiento sobre el TDO y silenciamientos referente al repase de las directrices que nortean la implementación del TDO y sobre la descentralización de las acciones de control para la periferia del sistema. Estas evidencias fragilizarían las acciones referidas al control de la enfermedad y al cuidado del enfermo.

**PD-1148-01 El Discurso de enfermeros de la Atención Primaria de Salud relacionada al Tratamiento Directamente Observado en João Pessoa, Paraíba - Brasil**

L Sá,<sup>1</sup> S L E Andrade,<sup>1</sup> PGO Diniz Pin,<sup>1</sup> LM Alcantara,<sup>1</sup>  
S De Santana Abreu,<sup>1</sup> R Figueiredo Ramalho,<sup>1</sup>  
TC Scatena Villa,<sup>2</sup> AJR Barreto.<sup>1</sup> <sup>1</sup>Programa de Pós-Graduação em Enfermagem, Universidade Federal da Paraíba, João Pessoa, PB, <sup>2</sup>Departamento de Enfermagem Materno- Infantil e Saúde Pública, Escola de Enfermagem de Ribeirão Preto/EERP/USP, Ribeirão Preto, SP, Brazil. Fax: (+55) 3216 7216. e-mail: sa.lenilde@gmail.com

**Background:** La tuberculosis (TB) es la segunda causa principal de muerte por enfermedades infecciosas. Para el control de la enfermedad fue propuesta la estrategia Directly Observed Treatment Short Course (DOTS), siendo el Tratamiento Directamente Observado (TDO) su elemento clave. En el municipio de João Pessoa, Paraíba-Brasil, apenas 31,2% de los enfermos de TB fueron tratados por el TDO en 2011. El enfermero es un importante profesional de salud involucrado con la realización de esa modalidad de tratamiento. Este estudio, teniendo como referencial teórico-analítico el Análisis de Discurso, tuvo como objetivo analizar el discurso de los enfermeros de los servicios de la Atención Primaria de Salud relacionada al tratamiento directamente observado de la tuberculosis.

**Design/Methods:** Estudio cualitativo, del cual participaron 13 (trece) enfermeras. Para obtención de las informaciones se utilizó la técnica de la entrevista semidirigida. La recolección de informaciones fue realizada los meses de agosto a octubre de 2012.

**Results:** El análisis del discurso de las enfermeras revela que estas profesionales se destacan en la ejecución del tratamiento de la TB e interpretaciones sugieren fragilidades en la operación del TDO, principalmente relacionadas a la falta de involucramiento de otros profesionales del equipo de salud. Apuntan que algunos profesionales no valorizan ese tipo de tratamiento, otros se muestran inseguros en su ejecución. Importante observar que el prejuicio fue relacionado al profesional de salud y no a la comunidad, lo que puede reflejar en una oferta de



cuidado no pautada en la integralidad, además de concurrir para la centralización de acciones y sobrecarga de trabajo de las enfermeras.

**Conclusion:** Las fragilidades en la operación del TDO, bien como dificultades para adhesión a esa modalidad terapéutica por los profesionales, pueden justificar su bajo porcentaje en el municipio estudiado. Los resultados apuntan para la necesidad de discusión del problema entre la academia y la gestión en salud del municipio. Se sugiere que el Programa de Control de la Tuberculosis local desarrolle procesos de capacitación innovadores en función de un discurso profesional menos afectado por el prejuicio y más afectado al cuidado, de modo que pueda responsabilizarse por un control de la TB más efectivo mediante la ampliación del tratamiento por el TDO.

#### **PD-1150-01 Comportamiento epidemiológico de la TBP en la Región de la Frontera Norte de México y los determinantes sociales. 1990–2012. Retos y desafíos**

Y Dávila,<sup>1</sup> M A García,<sup>1</sup> Mart Castellanos.<sup>1</sup> <sup>1</sup>PNT, Secretaría de Salud, México, DF, Mexico.  
e-mail: gpejazz@gmail.com

**Objetivo:** Identificar y analizar el comportamiento epidemiológico de la TBP, en los estados de la Frontera Norte de México, respecto a la media nacional y en consideración de los determinantes sociales.

**Antecedentes:** La región fronteriza norte consta de 6 estados: Baja California, Sonora, Chihuahua, Coahuila, Nuevo León y Tamaulipas; estos reportan una carga de enfermedad promedio superior a la media nacional tanto para las tasas de incidencia, como para las de mortalidad; cerca de la tercera parte de la incidencia nacional se ubica en esos estados. También es posible encontrar Determinantes Sociales como causas que determinan las inequidades en salud y la mayor predisposición a adquirir y enfermar por TBP. Algunos factores han sido: pobreza, estigma, discriminación, exclusión, bajo nivel educativo, poca conocimiento de la presencia de enfermedad, limitado acceso geográfico a los servicios de salud, sistema de salud y mecanismos de aseguramiento de la salud debilitados, así como la situación de migración, el uso y acceso a drogas, privación de la libertad y el reciente incremento de la violencia.

**Intervención:** Se están buscando estrategias de colaboración que impulsen la detección, diagnóstico, tratamiento oportuno y que consideren a los Determinantes Sociales de Salud como punto de partida para el análisis y seguimiento, sobre todo con otras instancias.

**Resultados:** Las tasas de incidencia por TBP en esa región han tenido un incremento de 43 puntos porcentuales, comparado con la media nacional que ha sido de 36.7 puntos del año 1990 al 2013. La mortalidad ha disminuido de  $7.8 \times 100,000$  habitantes en 1990 a 3.5 en el 2011, comparado con  $6.5 \times 100,000$  a 1.9 para la media nacional. En el análisis de seguimiento de las cohortes de tratamiento de los últimos cinco años se identifica una mejoría, el porcentaje de curación ha pasado de 85.3% en el año 2008 a 87.1% en el año 2012 a nivel nacional y

de 81.0 a 82.2%, para el mismo periodo, en la región. Estos cambios reflejan que los determinantes sociales deberán ser considerados en el diseño de estrategias de atención en esta área.

**Conclusiones:** Las características socioculturales, económicas y políticas que se generan por los factores geográficos y la estrecha relación con la primera potencia económica mundial han creado condiciones particulares, respecto al resto del país que deben ser considerados y abordados de manera específica, a fin de fortalecer las actividades de prevención y control de la TBP en esta región.

#### **PD-1151-01 Éxito del TAES mediante apoyo alimentario recolectado en la estrategia de participación social TBTONES de municipios de Chilpancingo, Guerrero, México**

V Leyva,<sup>1</sup> G Sosa,<sup>1</sup> R E Huicochea.<sup>1</sup> <sup>1</sup>Tuberculosis, Servicios de Salud del Estado de Guerrero, Chilpancingo, Guerrero, Mexico. Fax: (+52) 55 261 46 438.  
e-mail: arceliaavena@yahoo.com.mx

**Objetivo:** Apoyar la adherencia al tratamiento antituberculosis (TAES), mediante la colecta de alimentos en municipios de la región centro del Estado de Guerrero, México.

**Justificación:** La presencia de TB en municipios de la región centro afecta a personas de alta vulnerabilidad social, en promedio anual se registran 114 casos de TB, de los cuales 21.7% están asociados a Diabetes Mellitus, 25.7% a la Desnutrición 25.7%, 6.0% al alcoholismo y el 2.7% al VIH/SIDA, lo que hace necesario realizar la colecta de alimentos, para coadyuvar al éxito del TAES en la región.

**Metodología:** La colecta de alimentos no perecederos formó parte de las actividades de la Red TAES de Enfermería, en la conmemoración anual del Día mundial de lucha contra la TB. Se integraron grupos de trabajo en localidades sede "TBTONES", distribuyendo invitaciones al sector público/privado y población en general, a través de perifoneo; se recolectaron recursos en especie y económicos, los cuales fueron proporcionados cada mes a pacientes seleccionados en tratamiento antituberculosis.

**Resultados:** Del 2011 al 2013, se realizaron 51 TBTONES, recabándose 22 toneladas de alimentos no perecederos, \$34,874.00 (para pasajes), elaboración de promocionales 1,221 (oficios, recados, perifoneos), se identificaron 19 casos nuevos de TBP y 227 enfermos fueron beneficiados con estos apoyos, de los cuales el 99.5% curaron y 0.5 % falleció durante el tratamiento.

**Conclusiones:** La estrategia TBTON de participación comunitaria logró la sensibilización participativa de la población en apoyo a los afectados por TB, disminuyendo el riesgo de morir y la transmisión del *Mycobacterium tuberculosis* en la comunidad.

**PD-1152-01 Prevalencia de sintomáticos respiratorios, perfil epidemiológico y control de tuberculosis en unidades de primer nivel, Veracruz, México**

EE Ferreira-Guerrero,<sup>1</sup> A Hernández,<sup>2</sup>  
LD Ferreyra-reyes,<sup>1</sup> G Delgado-Sánchez,<sup>1</sup>  
R. Montero-Campos,<sup>1</sup> S. Canizales-Quintero,<sup>1</sup>  
L Cruz-Hervet,<sup>1</sup> L García.<sup>1</sup> <sup>1</sup>Research Center for Infectious Diseases, National Institute of Public Health, Cuernavaca, Morelos, <sup>2</sup>Epidemiological Surveillance Unit, National Institute of Respiratory Diseases, Mexico, Mexico.  
e-mail: cielo2219@gmail.com

**Background:** La tuberculosis (TB) es curable, la OMS calcula que se han salvado 22 millones de vidas con las estrategias DOTS y Alto a la Tuberculosis, sin embargo se requiere mayor detección de sintomáticos respiratorios (SR) y curación de TB, en algunos países el reto de comorbilidades como la Diabetes y el VIH/SIDA complican el éxito del tratamiento. En México la TB y las enfermedades respiratorias crónicas (asma y EPOC) son con frecuencia no diagnosticadas. Es común la prescripción inadecuada y el uso excesivo de antibióticos. **Objetivo:** Determinar la prevalencia de sintomáticos respiratorios, los factores asociados y el impacto en su atención en el nivel de atención primaria, en el marco de la OMS "Enfoque práctico sobre la salud pulmonar".

**Design/Methods:** De marzo a agosto de 2013 se realizó un estudio observacional en cuatro unidades de atención primaria en Orizaba, Veracruz, México. Se aplicó cuestionario estandarizado a toda persona mayor de 15 años de edad que acudió a consulta, antes y después de su atención. Se firmó consentimiento informado. Se recopiló información sociodemográfica, clínica y epidemiológica. Seguimiento al mes investigando diagnóstico médico, pruebas, manejo terapéutico y evolución. Análisis en Stata versión 12.

**Results:** Entrevistamos 3245 adultos; después de la consulta 356 (11.0%) recibió diagnóstico de enfermedad respiratoria. 595 (18.3%) presentaban tos con flema por más de dos semanas (SR); 26 pacientes (4.4%) fueron identificados por los trabajadores de la salud como SR, solo 13 pacientes (56.5%) con TB y tratamiento, 9 (39.1%) no se concluyó estudio de BAAR y sin tratamiento, el resto con mejoría. La proporción de diabetes en SR fue alta (38.5%) comparada con el total de pacientes (15.3%). Los principales factores identificados fueron: acudir a consulta SIN cita médica (OR=1.23, IC95%:1.02-1.5, p=0.02), edad de 65 a 74 años (OR=1.6, IC95%:1.09-2.34, p=0.01), haber presentado tuberculosis (OR= 3.21, IC95%:1.72-3.88, p<0.0001).

**Conclusion:** La detección de SR es baja en el nivel de atención primaria, incluso en quienes acuden por cualquier otro motivo a la consulta. Urgente reforzar estrategias integrales e innovadoras en el personal de salud que mejoren la calidad de la atención del SR y coadyuvar en el logro de metas para el control de la tuberculosis. **Financiación:** FOSSIS SALUD-2010-1-

140645. Este estudio refleja la posición de los investigadores y no la del INSP.

**PD-1153-01 Grupos de Ayuda Mutua en tuberculosis, mediante talleres de adherencia al TAES, en el municipio de Iguala, Guerrero México**

V Leyva,<sup>1</sup> R E Huicochea,<sup>1</sup> A Dorantes.<sup>1</sup> <sup>1</sup>Tuberculosis, Servicios de Salud del Estado de Guerrero, Chilpancingo, Guerrero, Mexico. Fax: (+52) 55 261 46 438.  
e-mail: arceliaavena@yahoo.com.mx

**Objetivo:** Fortalecer los conocimientos sobre Tuberculosis en las personas afectadas, mediante la vinculación con la familia y personal de salud, para coadyuvar a la adherencia del TAES, en el municipio de Iguala, Guerrero.

**Justificación:** El municipio de Iguala aporta el 49% de la morbilidad, de la Jurisdicción Sanitaria Norte del Estado, promedio anual 29 casos, con presencia de 2 casos de TBFR, tratados por medio privado y uno por contacto, por lo que se implementan talleres de adherencia al TAES, para sensibilizar a las personas afectadas, con interacción de familia y personal de salud, compartiendo información sobre la enfermedad, sentimientos y necesidades desde la perspectiva de los enfermos y personal involucrado, testimonios de ex enfermos, a fin de lograr el éxito de tratamiento y disminuir los riesgos (TBMFR).

**Metodología:** Previo impartición de talleres de adherencia, se seleccionaron enfermos de TB con BK negativa en fase inicial de TAES, con Red de apoyo familiar, mediante oficio de invitación al personal de salud; con horario de 10:00 a 13:30 hrs, en sesión plenaria ¿Cómo me siento ahora? los enfermos y familiares clarifican información sobre la TB, tratamiento (Mitos y Realidades), expresando de manera expositiva y lluvia de ideas, sus temores, ideas, percepciones y la importancia de apoyar y fomentar la corresponsabilidad con el personal de salud, la importancia de conocer ¿Qué es la TB y el tratamiento?, revisión de la carta de derechos y responsabilidades de los enfermos, ¿Cómo hacer un lado el estigma y la discriminación? a través de dinámicas de autoestima y como parte del proceso de sensibilización testimonios de ex enfermos de TB.

**Resultados:** Se impartieron tres talleres, de octubre 2011 al 2013, asistiendo 42 enfermos de TB, con familiares y enfermeras responsables del TAES; el rango edad de 17 a 81 años, con mayor frecuencia mujeres (59.5%) y 40.5 hombres, la curación fue del 88%, abandono y fracaso respectivamente el 2.5%, y el 7.1%, continua en tratamiento, 42 despenas otorgadas por el DIF municipal, refrigerio aportado por IMSS, ISSSTE y el Programa de TB.

**Conclusiones:** La estrategia demostró utilidad para el empoderamiento de las personas afectadas por TB y su vinculación en el proceso del tratamiento con la familia y el personal de salud identificando la idiosincrasia de los enfermos de TB, que confluye en la elevación de la

autoestima y de la corresponsabilidad para lograr el éxito del tratamiento.

## 58. MDR-/XDR-TB MANAGEMENT: NEW APPROACHES

### PD-1154-01 Robot-assisted lobectomy for destructive pulmonary tuberculosis: first experience

P Yablonsky,<sup>1</sup> G Kudriashov,<sup>1</sup> A Avetisyan,<sup>1</sup> I Vasilyev,<sup>1</sup> S Nuraliev,<sup>1</sup> O Sokolova.<sup>1</sup> <sup>1</sup>Thoracic Surgery, St. - Petersburg State Research Institute of Phthisiopulmonology, St. - Petersburg, Russian Federation. Fax: (+7) 812-579-25-73. e-mail: dr.kudriashov.gg@yandex.com

**Objectives:** Robot-assisted lobectomy is currently effective for treating early stage lung cancer (Xiaojing Zhao, 2010). The role of this method for treating patients with pulmonary tuberculosis is unclear.

**Aim:** to determine the effectiveness and safety of performing robot-assisted lobectomy in cases of pulmonary tuberculosis

**Methods:** Eight patients (36+6years old), five men and three women, were underwent lobectomy using da Vinci Si Surgical System (Intuitive Surgical) from June to December 2013. Indications for lobectomy (ERM, Vol. 61, 2013): failure of adequate long-time anti-TB chemotherapy according to DST of MTB (more than 6 month's), tuberculous lung destruction located within the boundaries of a single lobe, TB-positive sputum. Contraindications for robot-assisted lobectomy: previous pleural effusion or lung resection on the side of the planned operation.

**Results:** All patients successfully underwent robot-assisted lobectomy. Four chest wall incisions (10–15 mm), including one port for camera, two instrumental ports and one assistant port (in 10th intercostal space). No ribs retraction were done. Mean operative time was 130–300 min. and mean intraoperative blood loss was 50–300 ml. There were no perioperative complications, additional incisions and conversion to a thoracotomy. Postoperative course of chemotherapy according to DST of MTB. In early postoperative period rate of conversion of sputum smears for acid-fast bacilli was 100%.

**Conclusions:** Robot-assisted lobectomy is feasible in cases of pulmonary tuberculosis with good effectiveness and acceptable complication rate.

### PD-1155-01 Culture monitoring of MDR-TB treatment for diagnosis XDR-TB in Bangladesh

MS Hossain,<sup>1</sup> S M M Kamal,<sup>1</sup> Dr. Wahiduzzaman Akanda,<sup>2</sup> A Van Deun,<sup>3</sup> MA Husain,<sup>4</sup> S Sultana,<sup>5</sup> M Rahman,<sup>6</sup> Mr. Arif Rahman.<sup>7</sup> <sup>1</sup>National Tuberculosis Reference Laboratory, National Institution of Diseases of the Chest and Hospital (NIDCH), Dhaka, <sup>2</sup>Respiratory Medicine, NIDCH, Dhaka, <sup>3</sup>Mycobacteriology, Institute of Tropical Medicine, Antwerp, Belgium, <sup>4</sup>Director, MBDC and Line Director TB-Leprosy, National Tuberculosis Control Program, Dhaka, <sup>5</sup>National Professional Officer, World Health Organization, Dhaka, <sup>6</sup>TB CARE II, University Research Corporation, Dhaka, <sup>7</sup>Research Associate, Bangladesh Unnayan Porishad, Dhaka, Bangladesh. e-mail: bd.shamim1983@gmail.com

**Setting:** National Tuberculosis Reference Laboratory (NTRL), National Institute of Diseases of the Chest and Hospital (NIDCH).

**Background:** NTRL, NIDCH is the main laboratory responsible for the diagnosis and follow-up of drug-resistant tuberculosis in Bangladesh. Non-conversion of follow-up cultures from the 4th month of treatment for multi-drug resistant tuberculosis (MDR-TB) onwards could be due to extensively drug-resistant tuberculosis (XDR-TB) or other mycobacteria (NTM).

**Objective:** To detect XDR-TB among non-converting MDR-TB patients.

**Methods:** One follow-up sputum specimen was submitted from enrolled MDR-TB patients, monthly in intensive and quarterly in continuation phase. Culture and drug-susceptibility testing (DST) was performed on Löwenstein-Jensen media following standard methods. Cultures showing growth of over 20 colonies from the 4th month onwards were determined as tuberculosis complex or NTM. If confirmed tuberculosis, 2<sup>nd</sup>-line DST was performed with kanamycin and ofloxacin, initially at the supra-national laboratory in Antwerp, Belgium and after certification for 2<sup>nd</sup> line DST at NTRL.

**Results:** Since 2010, among 1140 MDR-TB patients on treatment, 152 (13.3%) had cultures corresponding to the selection criteria. Four were NTM, 148 (97.4%) were tuberculosis complex and 2<sup>nd</sup> line DST was done. Only 142 (96%) yielded interpretable results, of which 108 (76%) were susceptible to both kanamycin and ofloxacin, 24 (16.9%) showed resistance to ofloxacin only (pre-XDR), and ten (7%) to both kanamycin and ofloxacin (XDR-TB).

**Conclusion:** In Bangladesh, non-conversion during MDR-TB treatment is in almost one quarter of cases explained by pre-XDR or XDR. Replacing ofloxacin by a more potent fluoroquinolone should be considered.



### PD-1156-01 How much do family members of MDR-TB patients understand about Tuberculosis treatment?

S Gadala,<sup>1</sup> M Arulanantham,<sup>1</sup> Tomi Thomas,<sup>1</sup> P Banuru Muralidhara.<sup>2</sup> <sup>1</sup>Project Axshya, Catholic Health Association of India, Hyderabad, <sup>2</sup>Project Axshya, Union Against Tuberculosis & Lung Diseases, New Delhi, India. Fax: (+91) 40-27811982. e-mail: srinivasa-rao@chai-india.org

**Background:** MDR-TB is growing concern for India in recent days. This could be mainly contributed due to irrational perception pattern adopted by healthcare providers starting from unqualified or less-than-fully-qualified to specialists including pulmonologist. With increase in number of MDR-TB cases, community engagement strategies were piloted under Project Axshya focusing on counseling families of MDR-TB patients. The process was adopted with an aim to involve family members, create awareness about treatment process, adverse reactions, and to restrain from defaulting.

**Method:** The pilot was conducted in Salem district of Tamil Nadu, India. From the total sample of 75 families, 50 family members of the MDR-TB patients in Salem district were randomly selected and interviewed with a structured question.

**Result:** Family members interviewed (96%) were unaware about type of TB treatment and other treatment details. In addition members (48%) were apprehensive about the patient who took treatment for cough rather than TB per se. 64% reported to have stopped treatment (duration lasting from 1 to 7 days) for personal reasons. More than 80% of affected patients belong to families of low income and 52% of TB patients were unable to work leading to catastrophic burden.

**Conclusion:** Family member's awareness levels are low for MDR-TB treatment. Treatment success by programme is aimed only at cure rate, irrespective of socio-economic burden caused due to MDR-TB. More community awareness programmes like Project Axshya are needed to create awareness about TB and MDR-TB.

### PD-1157-01 Patients after surgery for pulmonary TB in the intensive care unit: factors associated with the duration of stay

A Yatsenko,<sup>1</sup> O Soloviev,<sup>1</sup> T Petrenko,<sup>1</sup> P Filimonov,<sup>1</sup> I Tyutlina.<sup>1</sup> <sup>1</sup>Science, Novosibirsk Tuberculosis Research Institute, Novosibirsk, Russian Federation. Fax: (+738)32037825. e-mail: andryat@yandex.ru

**Objective:** To analyze the preoperative hemostatic disorders in patients with pulmonary tuberculosis and to assess their relationship with the duration of stay of patients in the intensive care unit.

**Materials and Methods :** Design - a cohort of 31 patients with pulmonary tuberculosis, from 21 to 61 years old, successively admitted for surgical treatment, without critical problems hemostasis. The following types of surgeries were performed: lung resection, pneumonectomy, osteoplastic thoracoplasty. Blood loss was  $402 \pm 81$  ml and the minimum - 50 ml, maximum - 2050 ml.

Multiple linear regression was applied to assess the relationship between exposure and outcomes.

**Results:** Factors, which effected the length of stay of the patients in intensive care were analyzed: admission diagnosis for the surgical department, the presence of bacterial positivity, cavitation, the phase of tuberculous process, MDR/XDR, length of tuberculosis diseases, bronchoscopy data, the number of segments of the lung affected by TB, hemostasis data, the volume of blood loss, duration of surgery and anesthesia, amount of an exudate in the first three days. The application of multivariate analysis (multiple linear regression) revealed that the patient stay in the ICU is directly related to the duration of surgery and baseline of soluble fibrin monomer complex (SFMC).

**Conclusion:** Our data showed that the predictors of length of stay of patients, which underwent surgery for pulmonary tuberculosis, in the department of anesthesiology and intensive care, were SFMC and duration of surgery.

### PD-1158-01 Characterisation of extensively drug-resistant (XDR) and totally drug-resistant (TDR) *Mycobacterium tuberculosis* strains in Pakistan

Z Hasan,<sup>1</sup> Asho Ali,<sup>1</sup> Sana Jafri,<sup>1</sup> K Jabeen,<sup>1</sup> R Inayat,<sup>1</sup> R Hasan.<sup>1</sup> <sup>1</sup>Pathology and Microbiology, The Aga Khan University, Karachi, Pakistan. Fax: (+92) 2149 34294. e-mail: zahra.hasan@aku.edu

**Background:** Pakistan has a tuberculosis (TB) incidence rate of 231/ 100,000 annually. Multi-drug resistant tuberculosis (MDR-TB), strains resistant to rifampicin and isoniazid is approximately 5 % of all TB cases. In addition, extensively drug-resistant tuberculosis (XDR-TB), defined as MDR-TB resistant to fluoroquinolone and also aminoglycoside is reported. XDR-TB is demonstrated previously to be 4.5% of MDR-TB in Pakistan. In addition, there are strains which are resistant to all first and second line anti-tuberculous drugs tested, or totally drug resistant (TDR) TB. Here we have used spoligotyping and 15 loci-MIRU typing to characterize XDR isolates in order to characterize relationships between XDR and TDR strains.

**Design/Methods:** Antimicrobial susceptibility was determined by agar proportion method and compared with the wild type *Mycobacterium tuberculosis* H37Rv. Resistance to first line and second line anti-tuberculous agents was determined. Seventy-three strains were identified as XDR TB strains at the Aga Khan University Hospital Clinical Laboratory during the period 2006–2011. These strains were characterized by Spoligotyping was performed using standard method. Variability in MIRU loci was determined by PCR based 15-loci VNTR typing analysis.

**Results:** Of the 73 XDR-TB strains tested studied, 3 (4%) were found to be totally-drug resistant (TDR) to first and second line agents. Spoligotyping of the isolates revealed that XDR strains comprised Central Asian Strain family (58.3%), Beijing (8.3%), T clade (6.6%), U clade

(3.3%), East African lineage (1.6%) and Unique isolates (20%). Of the TDR-TB isolates identified, there was one each from CAS1-Delhi, Beijing and T1 lineages. Standard 15 loci MIRU-VNTR typing was performed on all 73 strains. MIRU-VNTR analysis did not show any clusters between strains.

**Conclusion:** This is the first report of TDR-TB strains from Pakistan. MDR and XDR TB rates continue to increase due to drug resistance in *M. tuberculosis* isolates in Pakistan. This work further highlights the imperative need to improve diagnosis and treatment programs to avoid incidence and spread of difficult to treat strains.

#### **PD-1159-01 First case of XDR-TB cured after 10 years of illness with regimen based on Group 5 drugs and bedaquiline in a programmatic approach in Peru**

D Vargas,<sup>1</sup> A Mendoza,<sup>2</sup> J Cabrera,<sup>2</sup> A Alarcon.<sup>2</sup>

<sup>1</sup>Neumología, Hospital Nacional Hipólito Unanue, Lima,

<sup>2</sup>Lima, Estrategia Sanitaria Nacional de Prevención y Control de Tuberculosis, Lima, Peru.

e-mail: mendozalberto@hotmail.com

**Background:** Peru has implemented the programmatic management of XDR-TB patients based on Group 5 drugs, surgery and central venous catheters (Type Port).

**Objective:** To report the first case of XDR-TB to be discharged as cured with a regimen based on Group 5 drugs and bedaquiline by the Ministry of Health of Peru.

**Methods:** Case report

**Results:** A 41 year old female from Lima, a physician, was diagnosed with pulmonary TB in April 2002 while she was a medical student. Her first DST in this episode corresponded to XDR-TB, only susceptible to cycloserine and p-amino salicylic acid (PAS). The patient was discharged as having failed to respond to five antituberculosis regimens, including first-line drugs and fluoroquinolones, injectable (second-line), ethionamide, cycloserine and PAS. She underwent surgery twice: right lobectomy and left segmentectomy. During treatment, she conceived a child clinically healthy. In 2010 she was discharged as an "incurable" case with culture (+++). In April 2012 she began a regimen with: linezolid, imipenem/amx-clavulanate, thioridazine, moxifloxacin, pyrazinamide, capreomycin, cycloserine and PAS (this drug was suspended at the third month). Between 3 and 9 months she received bedaquiline (changed to levofloxacin and temporarily suspended thioridazine for the risk of QT prolongation). Imipenem was stopped at 12 months through a central Port Catheter and complete two years of treatment with linezolid, thioridazine, amx-clavulanate, levofloxacin and cycloserine. Among the adverse drug reactions (ADRs) she had was an episode of pulmonary embolism, severe nausea and vomiting associated to PAS. Then reacting to bedaquiline, she had linezolid anemia, fainting by disautonías, hypokalemia, hypomagnesemia and bilateral mild hearing loss. The adverse reactions required the permanent cessation of only PAS. Her weight had increased 2 kg during treatment, but the clinical and bacteriological courses

were favorable, resulting in a negative sputum culture after the second month and remaining that way throughout the treatment, despite having until the 11th month an intermittent smear that was scanty or (+). After that, the monthly smear and culture were always negative. Radiographically has not shown significant changes with bilateral sequelae images.

**Conclusions:** With a regimen based on the Group 5 treatment, thioridazine and bedaquiline has been possible to cure a XDR-TB patient with a 10 year long history of the disease.

#### **PD-1160-01 Cost-effectiveness analysis of LPA-based algorithm for detection of multidrug-resistant tuberculosis in Arkhangelsk Region, Russian Federation**

E Bogdanova,<sup>1</sup> E V Gospodarevskaya,<sup>2</sup> G Balantsev,<sup>1</sup>

P Eliseev,<sup>3</sup> A Maryandyshev,<sup>3</sup> E Nikishova,<sup>3</sup> A Detjen,<sup>4</sup>

S Squire.<sup>5</sup> <sup>1</sup>Management department, Northern Arctic

Federal University, Arkhangelsk, Russian Federation; <sup>2</sup>Deakin University, Deakin University, Melbourne, ACT, Australia;

<sup>3</sup>Phthiopulmonology department, Northern State Medical University, Arkhangelsk, Russian Federation; <sup>4</sup>The

International Union Against Tuberculosis And Lung Disease, International Union Against Tuberculosis And Lung Disease, New York, NY, USA; <sup>5</sup>Liverpool School of Tropical Medicine, Liverpool School of Tropical Medicine, Liverpool, UK.

e-mail: limenda@mail.ru

**Background:** The Line Probe Assay (LPA) is recommended by WHO as a rapid diagnostic tool to define drug susceptibility of *M. tuberculosis*. Its clinical and cost effectiveness in Russia remains uncertain. In 2011–2013, under the USAID-funded TREAT TB initiative, Northern State Medical University in collaboration with The International Union Against Tuberculosis And Lung Disease and Liverpool School of Tropical Medicine conducted a clinical trial on Policy Relevant Outcomes from Validating Evidence on Impact of LPA in Arkhangelsk region.

**Objectives:** To assess the cost-effectiveness of LPA for diagnosis and treatment of MDR-TB in Arkhangelsk region, and estimate the savings associated with the speedier LPA diagnostic for the state health care system and the patients.

**Design/Methods:** Costs and outcomes of 24 months of LPA-based diagnosis and treatment algorithm for 72 SS<sup>+</sup> and 60 SS<sup>-</sup> patients were compared with old algorithm for 67 SS<sup>-</sup> patients diagnosed with LJ and 96 SS<sup>+</sup> with BacT/Alert or LJ. Cost-effectiveness analysis included the costs to the health system (microscopy and drug susceptibility test, hospitalization, medications) and patient costs (travel cost, lost productivity, supplementary medicine and food) collected at the baseline and two subsequent interviews using the questionnaire.

**Results:** LPA-based algorithm corresponded to the speedier assignment of the correct treatment: by mean value of 50.1 days for LPA vs BacT/Alert liquid culture (SS<sup>+</sup>), by 132.3 days for LPA vs LJ (SS<sup>+</sup>), by 60.7 for LPA+Bactec MGIT vs LJ (SS<sup>-</sup>) and by 40 days for LPA+LJ vs LJ (SS<sup>-</sup>). The speedier diagnosis resulted in

the earlier discharge of SS+ patients from hospital, who then faced higher daily travel expenditures to collect drugs from a medical facility. The overall health system savings on diagnosis and treatment were per SS+ patient: \$2101 per SS+ patient (LPA vs BacT/Alert liquid culture) and \$4459 per SS+ patient (LPA vs LJ); per SS- patient: \$1711 (LPA+Bactec MGIT vs LJ) and \$1217 (LPA+LJ vs LJ). One-way sensitivity analyses of the key parameters and probabilistic sensitivity analysis were conducted.

**Conclusion:** Clinically superior LPA-based algorithm is associated with cost reduction to Russian Health Care system and to patients. A targeted subsidy/home treatment may provide an incentive for MDR-TB patients to stay in treatment and lessen the burden of disease.

### PD-1161-01 Does diagnostic technology and travel distance reduces delays in treatment initiation of MDR-TB patients in India?

M Toshniwal,<sup>1</sup> Jaya Toshniwal,<sup>2</sup> D Deshmukh,<sup>3</sup> P Malik,<sup>1</sup> V Sahasrabhojaney,<sup>4</sup> S Soni,<sup>5</sup> S P Patil,<sup>6</sup> A Sreenivas.<sup>1</sup>

<sup>1</sup>Tuberculosis, WHO Country Office, India, New Delhi, <sup>2</sup>DRTB Centre, Government Medical College, Akola, <sup>3</sup>TB, G G Rath TB Hospital, Amravati, <sup>4</sup>Medicine, Government Medical College, Akola, <sup>5</sup>Tuberculosis, City TB Office Amravati Corporation, Amravati, <sup>6</sup>Tuberculosis, State TB Office, Pune, India. e-mail: toshniwalmano@hotmai.com

**Background:** Highest MDRTB burden country has rapidly scaled up PMDT services across India. It was started in Akola Division, Maharashtra India in 2009 with linked to Intermediate Reference Laboratory (IRL) at Nagpur (~300 km from districts) for diagnosis & treatment initiation. Samples of presumptive MDRTB used to be transported to lab. MDRTB patients get admitted for 7–30 days at DRTB Centre for evaluation & treatment initiation. Long distances posing difficulties created the need for regional/district level facilities for improving patient access.

**Intervention:** Decentralization of treatment initiation services from to Akola (~150 km) in 2010 to District level in 2012 was done with involvement medical college for clinical expertise. PPP model with Government TB hospital & private medical college started in 2012. Diagnostic technology used was Solid(LJ) in 2009, LPA from 2010 & GeneXpert from mid-2012-13 (2 district). Retrospective data analysis done for 4 districts (4.83 million pop). Treatment delay (TD) defined as time taken to initiate treatment after diagnosis. All the patients registered in DRTB register from 2009 to March 2014 with complete information available were included in analysis. Information on date of diagnosis, treatment initiation, diagnostic technology used, travel distance was considered for their impact on TD.

**Results:** Average treatment delay was same of 51 days in 188 (68%) males & 88 females (32%) MDRTB patients. Patients diagnosed with LJ were 44(16%), LPA-157(58%) & CBNAAT-71(26%) with average TD of 132, 44 & 17 days respectively. TD of 142 days in 2009 reduced to 26 days in 2014 with program maturation. TD reduced from 156 to 34 days with reduction in

average distance of DRTB Centre from >200 km to <50 km. Annual patients of 23 in 2010 increased to 90 in 2013 in same population.

**Conclusions/key recommendations:** Decentralized rapid molecular diagnostic test & treatment initiation services at district level improves faster diagnosis & quick treatment initiation of MDRTB patients. Placement of the rapid molecular diagnostic tests at district level as envisaged in National Strategic Plan should be fast-track. District level infrastructure development & partnerships with available Private/NGO/Corporate health facilities can definitely help in decentralizing the treatment services at district level. PPP model DRTB Centre needs inclusion in NGO/PP Scheme for sustainability. Decentralization of both the services has synergy effect.

Table: Treatment delays in MDRTB patients in relation to diagnostic technology & distance of DRTB Centre

		Average Treatment delays in days	No. of patients	%	
Diagnostic Technology:	Solid	132	44	16%	
	LPA	44	157	58%	
	CBNAAT	17	71	26%	
Year wise:	2009	142	11	4%	
	2010	129	23	8%	
	2011	77	62	23%	
	2012	31	76	28%	
	2013	23	90	33%	
	2014 (Jan-Mar)	26	10	4%	
Distance from DRTB Centre:	>200 km	156	12	4%	
	151-200 km	86	35	13%	
	101-150 km	83	21	8%	
	51-100 km	47	34	13%	
	upto 50 km	34	170	63%	
Gender:	Male	51	184	68%	
	Female	51	88	32%	
Treatment delays in days based on Diagnostic technology & Distance of DRTB Centre		Average Distance in Km to reach DRTB Centre			
Diagnostic Technology:		0-50	51-100	151-200	>200
	SOLID	107	105	147	160
	LPA	36	30	74	111
	CBNAAT	14	68	25	0

### PD-1162-01 Review of the Indonesia programmatic management of drug-resistant tuberculosis, 2009–2014

S Laksono,<sup>1</sup> DE Mustikawati,<sup>2</sup> T N Dinihari,<sup>2</sup> E Lukitosari,<sup>2</sup> M Akhtar.<sup>1</sup> <sup>1</sup>TUB, WHO CO Indonesia, Jakarta, <sup>2</sup>NTP, MOH Indonesia, Jakarta, Indonesia. e-mail: wawan\_tbc@yahoo.co.id

**Background:** With multi drug resistance (MDR) estimated at 1.9% among new and 12% among re-treatment notified tuberculosis cases Indonesia is expected to have 6,800 MDR TB cases annually and considered among the high burden countries. Programmatic Management of Drug-Resistant Tuberculosis (PMDT) started in mid-2009. National TB Programme follows ambulatory treatment policy with standardized treatment regimen. **Methods:** Review of the PMDT supervisory visit report, quarterly and annual report and national guidelines. E-TB manager system is fully implemented in all sites to provide real time data on PMDT. Outcomes were defined according to the standard internationally recommended definitions.

**Results:** By March 2014 fifteen provinces have 17 PMDT treatment referral centers and more than 700 treatment



satellites. Eight quality assured laboratories are providing culture and drug susceptibility testing services and 26 geneXpert machines are in place to boost the labs capacity. A total of 2,835 cases were diagnosed with confirmed drug resistance, among these 1,892 (67%) were registered for treatment. Enrolment of patient increased 100%, diagnosing 1,074 drug resistant TB cases and enrolling 819 for treatment which is more than the total number of cases put on treatment during previous four years. The full ambulatory and rapid decentralization treatment policy were introduced so that patients can receive services from any PMDT implementing site regardless whether they belong to any part of the country. The current challenges in case finding are only third of retreatment cases and 0.03% of new cases examined for DR TB, and among confirmed cases only 75% enrolled. Treatment result among 414 cases registered for treatment during 2009 and 2011 period the treatment success rate is over 72% in the first two year and drastically decrease to 58% when the program was expanded in 2011.

**Conclusion:** Diagnostic capacity is pre-requisite for PMDT expansion and it should followed by strengthen network for presumptive case referral to diagnostic centers. High initial default is the next challenges. Cure rates (72%) among first two cohort completing treatment is at par with international standards however it was decrease caused by high lost to follow up rate. Initial and during treatment default rates are high; limited programme access, and socio economic support are some of the key limiting factors. Collaboration with community and CSOs are the way forward.

#### PD-1163-01 Antiretroviral therapy in patients diagnosed with rifampicin resistance in an observational study, South Africa

Y Voss De Lima,<sup>1</sup> L Scott,<sup>2</sup> P Da Silva,<sup>3</sup> M Patel,<sup>4</sup> C Hayes,<sup>5</sup> W Stevens,<sup>6</sup> T Wojno,<sup>7</sup> A Van Rie.<sup>4</sup> <sup>1</sup>Clinical HIV Research Unit, The University of the Witwatersrand, Johannesburg, , <sup>2</sup>Molecular Medicine and Haematology, University of the Witwatersrand, Johannesburg, , <sup>3</sup>Mycobacteriology (TB) Referral laboratory, National Health Laboratory Services, Johannesburg, South Africa; <sup>4</sup>Epidemiology, The University of North Carolina, Chapel Hill, NC, USA; <sup>5</sup>TB laboratory, National Health Laboratory Services, Port Elizabeth, <sup>6</sup>National Priority Programme, National Health Laboratory Services, Johannesburg, <sup>7</sup>Microbiology, National Health Laboratory Services, Bloemfontein, South Africa.  
e-mail: yara.vossdelima@gmail.com

**Background:** The South African national antiretroviral treatment (ART) guidelines state that all drug resistant tuberculosis (TB) cases irrespective of CD4 count are eligible to start ART. The effects and uptake of ART in patients with drug resistant TB in a routine health care setting are still being established.

**Methods:** In an observational study (EXIT-RIF), a cohort of 542 patients diagnosed with multi-drug resistant TB, 264 (48.7%) by LPA/DST and 278 (51.3%) by Gene Xpert, were enrolled across 3 Provinces in South Africa (Eastern Cape, Free State and Gauteng). Patients enrolled

were diagnosed with rifampicin resistance (RR) TB between January 2012 to March 2013 and followed up for 12 months. We examined clinical characteristics and outcomes among HIV-infected patients in the cohort. All patients were treated in the public sector by routine clinic and hospital staff.

**Results:** Overall, 499 (92.1%) of the 542 patients in the cohort knew their HIV status. Of these, the majority (n=412, 82.6%) were HIV-infected. One quarter (n=104, 25.2%) of these patients died prior to study enrolment. Of the patients who were alive at study enrolment, 237 (76.9%) patients patient reported being on ART: 131 (55.3%) initiated ART before MDR diagnosis, 93 (39.2%) after MDR diagnosis, 2 (0.8%) at the same time as MDR diagnosis, and ART start date was unknown for 11 (4.6%). Among those on ART prior to MDR diagnosis, median time on ART was 18.5 months (IQR: 6.8–45.8). At baseline, median CD4 was 140 cells/mm<sup>3</sup> (IQR: 51–280), median viral load was 4.96 log<sub>10</sub> copies/mL (IQR: 3.54–5.80), and 47 (11.4%) patients had an undetectable viral load. At 12 months, among those with known HIV status, mortality was higher among HIV-infected patients compared to those without HIV-infection (36.2% v. 14.9%, p=0.0001). Median time to ART among those who were ART naïve at MDR diagnosis was 31 days (IQR: 20–73) from first sputum collection and did not differ between study arms. ART uptake after MDR diagnosis was similar between patients diagnosed by Gene Xpert and LPA/DST (46.2% v. 53.8%, p=0.82). Mortality among HIV-infected patients on ART was lower at 12 months than those not on ART, but did not reach statistical significance (18.6% v. 28.6%, p=0.26).

**Conclusions:** The methods used for diagnosis of RR did not have an effect in the uptake or timing of ART amongst the pre-ART patients. Adherence and delivery of treatment needs be investigated further as reduction in mortality was not significant.

#### PD-1164-01 Video observed therapy: a qualitative study of MDR-TB patient perspectives

J Hall,<sup>1</sup> P Windish,<sup>1</sup> Y Appleby,<sup>1</sup> A Story,<sup>1</sup> S Hemming,<sup>2</sup> L Possas.<sup>2</sup> <sup>1</sup>Find&Treat, University College London (UCL) Hospitals, London, <sup>2</sup>NIHR TB Reach Study, UCL, University College London, London, UK. Fax: (+020)3 447 9938.  
e-mail: joehall@nhs.net

**Background:** Video Observed Therapy (VOT) using internet and mobile technologies is potentially an efficient and cost-effective alternative to Directly Observed Therapy (DOT) for monitoring tuberculosis treatment adherence. For multi-drug resistant (MDR) TB patients, clinic based or community based DOT is often impractical due to complicated dosing schedules. Since 2008 Find&Treat have been using VOT to support treatment adherence. This study aimed to provide insight into the attitudes and perspectives of MDR TB patients supervised using VOT to inform future development of

this intervention including assessing suitability for VOT and providing practical training.

**Methods:** A series of semi-structured interviews were conducted with 10 MDR TB patients resident in London who received VOT between October 2013 and March 2014. The interviews were conducted in the patients own homes or informal settings such as café's and recorded. Interviews were transcribed verbatim and comments organized into themes for analysis covering practical and technical issues, impact on daily life, emotional response including feelings around surveillance, privacy and security.

**Results:** The interviews provided powerful insights into patients' experiences of using and attitudes towards VOT. The relationship between viewer and viewee was explored as were the ways in which VOT often helped to regularise and provide structure around tablet-taking. Several practical issues around the use of internet technologies were highlighted which could help to improve training and support and inform the design of future technological applications. Overall patients reported very high levels of satisfaction with the service. A typical response: I was getting tired of DOT. I thought I'd be freer to continue with my life. All that time and effort you've saved me. I didn't need much convincing. With the DOT I felt like you had a disease & a kind of stigma. For that reason they are monitoring you. It felt like being a criminal.

**Conclusion:** This is the first qualitative study to explore the application of VOT to the treatment of MDR TB. The study found evidence that VOT is practical and highly acceptable to patients provided they receive effective training and on-going support. Qualitative investigation of patients' experiences is essential to inform the future design and implementation of this promising intervention.

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## 59. MDR-TB: EPIDEMIOLOGY

### PD-1165-01 First national survey of anti-tuberculosis drug resistance in Azerbaijan

I Akhundova,<sup>1</sup> N. Alianova,<sup>1</sup> M Seyfaddinova,<sup>1</sup> E Mammedbekov,<sup>1</sup> N Aliyeva.<sup>2</sup> <sup>1</sup>Scientific Research Institute of Lung Disease, Ministry of Health of Azerbaijan, Baku, <sup>2</sup>Project Implementation Unit, Ministry of Health of Azerbaijan, Baku, Azerbaijan. Fax: (+994) 12421575. e-mail: akhundova.irada@gmail.com

**Background and challenges to implementation:** Specific objectives of the survey were to determine among new and previously treated pulmonary TB cases in the general population (excluding the penitentiary setting):- i) anti-TB drug resistance patterns, ii) anti-TB drug resistance patterns between different categories of previously treated cases, and iii) socio-demographic and clinical characteristics associated with anti-TB drug resistance patterns.

**Intervention or response:** Started on 28 October 2012 the survey was completed by 30 April 2013. All patients in the country aged 15 years or more suspected of pulmonary TB submitted at least two sputum specimens. Patients with long-lasting TB disease (i.e. failure after any kind of anti-TB treatment on two or more occasions), who provided sputum specimens later than 5 days after starting TB treatment or who had extra-pulmonary TB were excluded from the survey.

**Results and lessons learnt:** There were 789 bacteriologically confirmed pulmonary TB cases included in the survey, of whom 549 were new patients and 240 were previously treated. Among all new and previously treated cases, 231 (42%) and 146 (61%) were resistant to any anti-TB drug, and 72 (13, 1%) and 66 (27,5%) had MDR-TB respectively. Amongst the cases of MDR-TB 9 (12,7%) of new and 9 (13,6%) of previously treated TB cases had XDR-TB.

**Conclusions and key recommendations:** The survey of anti-tuberculosis drug resistance confirmed the hypothesis on serious decrease of drug resistance since the Baku anti-TB drugs resistance survey conducted in 2006–2007 (22,3% of new cases and 56,3 of retreated cases). However, Azerbaijan remains a high MDR-TB burden country with several important risk factors contributing to this epidemic of drug-resistance.

### PD-1166-01 The particularity of *M. tuberculosis* strains circulating in the penitentiary system of Kazakhstan

A Ibrayeva,<sup>1</sup> A Alenova,<sup>2</sup> U Kozhamkulov,<sup>1</sup> D Raimbek,<sup>1</sup> E Zholdybayeva,<sup>1</sup> T Abildaev.<sup>3</sup> <sup>1</sup>Research Center, National Center for Biotechnology, Astana, <sup>2</sup>Immunology Department, National Center for TB problems, Almaty, <sup>3</sup>Managing Director, National Center for TB problems, Almaty, Kazakhstan. e-mail: arike.alenova@mail.ru

**Background:** The incidence of tuberculosis (TB) in 2012 among prison population in Kazakhstan was 1073 per 100,000 people, the incidence of TB in civilian system was 81.7 per 100,000 people. A high level of multi-drug resistant (MDR) types of tuberculosis is being observed in the prisons. That is why it is extremely important to study the genetic variability and profile of antibiotics resistance of *M.tuberculosis* strains circulating in prison system as compared with civilian sector of Kazakhstan.

**Methods:** 60 *M.tuberculosis* isolates collected from patients in Kazakhstan prisons and 125 in civilian sector were used for study through DNA sequencing (ABI 3730 Genetics Analyzer) and MIRU-VNTR (Mycobacterium Interspersed Repetitive Unit - Variable Number Tandem Repeat) analysis.

**Results:** We found that the numbers of TB strains with unique genotypes isolated from civilian patients were 50.4%, and the same unique genotypes isolated from the prison patients were 31.7%. This finding is statistically significant ( $\chi^2 = 4.42$ ,  $p = 0.035$ ) and may reflect low genetic diversity of *M.tuberculosis* strains isolated from prison patients. All clusters belonged to members of the W-Beijing family and are associated with MDR, which was confirmed by the DNA sequencing. The frequency of

mutations in rpoB531 and katG315 genes of *M. tuberculosis* strains in the civil and penitentiary system is the same as in the gene rpoB531 (82.4% vs. 88.3%) with replacement of serine to leucine (TCG → TTG) and katG315 (98.4% vs. 100%) when substituting histidine on leucine (CAC → CTC) respectively. The MIRU-VNTR analysis was carried out on 24 MIRU-VNTR loci. Based on the information received from VNTR-analysis a phylogenetic tree was constructed using the web-source [www.miru-vntrplus.org](http://www.miru-vntrplus.org).

**Conclusion:** The obtained study results should be used to improve and fine-tune the strategy of the epidemiological control and TB treatment in the penitentiary system of Kazakhstan.

### PD-1167-01 Quality of life of patients with MDR-TB and effectiveness of its treatment

D Ruzanau,<sup>1</sup> M. Uranova,<sup>1</sup> A. Khailiaukin,<sup>2</sup> I. Buynevich,<sup>1</sup> A. Demidova.<sup>3</sup> <sup>1</sup>TB and Pulmonology, Gomel State Medical University, Gomel, <sup>2</sup>Office expertise, Gomel Regional Clinical Hospital, Gomel, <sup>3</sup>MDR-TB, Gomel Regional Clinical Hospital, Gomel, Belarus. Fax: (+103)75232749831. e-mail: druzanoff@mail.ru

Diagnosis of TB and its long-term treatment “changes life and attitude to it forever” (Erich M. Remarque, 1936), and is a serious trial for economic and social status of a patient, and cannot but affect their quality of life (QL). The aim of the research is to study QL of MDR TB patients and its effect on the treatment effectiveness. In the Republic of Belarus, according to the data of 2013 supervision, MDR TB prevalence is 34.6% new cases and 76.6 % recurrent cases, which is the highest rate in the world. The key indicators for MDR TB treatment stay low (only 49.2% patients were successfully treated among the 2011 cohorts). The QL was studied in all MDR TB patients (206 patients) in Gomel region of Belarus (1.52 million people) in 2011. The nonspecific questionnaire “SF-36” was used for the study over the first two weeks after chemotherapy. To compare, the results of the QL study were analyzed in 40 practically healthy persons (HP). At the second stage (24 months later), the group of MDR TB patients were subdivided using retrospective stratification method: A-patients with effective chemotherapy regimen (cure, treatment completed N=98) and B-patients in isolation from treatment (N=32). All the 36 items of the questionnaire were grouped into eight scales, the indicators of each scale varied between 0 and 100 conventional units (CU). The results are shown in the following table:

QL scale	MDR TB patients		HP N = 40
	Subgroup A with N = 98	Subgroup B with N = 32	
GH	52.3 ± 6.02	69 ± 5.71	66.7 ± 6.3
PE	81.2 ± 4.3	80.6 ± 4.8	91.5 ± 3.1
RP	50.3 ± 4.97	51.3 ± 5.6	85.2 ± 5.3
RE	65.4 ± 3.06	54.2 ± 2.95	70.2 ± 5.45
SF	41.3 ± 4.97	63.6 ± 4.38	69.4 ± 3.91
BP	88.4 ± 5.28	83.75 ± 6.32	90.8 ± 6.56
VT	65.8 ± 5.61	65.7 ± 3.41	69.2 ± 4.25
MH	62.7 ± 3.27	58.25 ± 6.4	68.6 ± 3.22

All patients in their dynamics must be tested by SF-36 to ensure timely assistance and correction. MDR TB leads to a decrease of all QL parameters of patients except their physical functioning and the intensity of pain, which means that the patients' psychological state is significantly worse than physical one. Moreover, the results proved that patients with poor adherence do not realize seriousness of their illness (high evaluation of their health state) and do not limit their social contacts. The whole long-term chemotherapy in MDR TB patients must be accompanied by psychological support which takes into consideration the QL results by the scales.

### PD-1168-01 Prevalence of multi-drug resistant tuberculosis among suspects of different categories in Uttar Pradesh

A Jain,<sup>1</sup> U Singh,<sup>1</sup> PK Singh,<sup>1</sup> P Dixit,<sup>1</sup> G Chooramani.<sup>1</sup>

<sup>1</sup>Microbiology, King George's Medical University, Lucknow, India. e-mail: amita602002@yahoo.com

**Background:** India ranks second in harboring maximum number of multi drug resistant tuberculosis (MDR-TB) cases. The nation and state-wise precise prevalence estimate of MDR TB among different categories of suspect population, though not available, could be very useful for rationale design or upgrading the strategy for effective control of MDR-TB. Uttar Pradesh (UP), a large and most populous state of country remains one of most challenging state for TB control programmes. Here we sought to present our observations on prevalence of MDR cases (defined herein as resistant to rifampicin) in various categories of suspects/patients of UP during July, 2012 to March, 2014 under revised national TB control programme (RNTCP).

**Design/Methods:** A total of 3544 TB suspects were tested for MDR-TB using line probe assay kit (Hain Life-sciences GmbH, Germany) at Intermediate Reference Laboratory (IRL), KGMU, Lucknow. Of the total 3544TB suspects, 1453 were under 'Category A' (includes cases of treatment failure, smear positive at four month onwards of treatment and contact of known MDR-TB) and 2091 were under 'Category B' (in addition to 'Category A' it includes smear positive previously treated cases at diagnosis and any follow-up smear positive case). The suspects of 'Category A' were from 32 districts of UP whereas the 'Category B' suspects belong to two districts (Lucknow and Kanpur) of UP.

**Results:** Based on test results, 47.5 and 26.4% prevalence of MDR TB were observed in suspects belonging to 'Category A' and 'B', respectively. Among the total MDR TB cases under 'Category A', there were 46.5 and 47.9% MDR-TB cases of treatment failure and cases of smear positive at 4<sup>th</sup> month of treatment, respectively. A very high prevalence (58.9%) of MDR-TB was detected in contacts of known MDR patients however the number of tested suspects was comparably low. In 'Category B', the proportion of MDR-TB in smear positive previously treated cases and any follow-up smear positive case were 28.2 and 19.2%, respectively.



**Conclusion:** Overall data showed high prevalence of MDR-TB in suspects of both categories and its sub-categories. More comprehensive information from different states / regions of country is required to have better insight on epidemiological dynamics of MDR-TB in India.

**PD-1169-01 Perceptions, behaviour and experience of patients and practitioners in Karakalpakstan on the use of tuberculosis medication: a qualitative study**

B Stringer,<sup>1</sup> K Lowton,<sup>2</sup> P Du Cros,<sup>1</sup> E Hasker,<sup>3</sup> D Ulmasova,<sup>4</sup> NN Parpieva,<sup>5</sup> N Sergeeva,<sup>1</sup> M Tillyashaykhov.<sup>5</sup> <sup>1</sup>Programmes Unit, Médecins Sans Frontières, London, <sup>2</sup>Social Science Health and Medicine, Kings College London, London, UK; <sup>3</sup>Epidemiology, Institute of Tropical Medicine, Antwerp, Belgium; <sup>4</sup>Tuberculosis, Ministry of Health, Tashkent, <sup>5</sup>Republican Specialized Scientific and Practical Medical Center of Phtisiology and Pulmonology, Ministry of Health, Tashkent, Uzbekistan. e-mail: beverley.stringer@london.msf.org

**Aim:** Médecins Sans Frontières (MSF) and the Ministry of Health (MoH) run a decentralised multidrug-resistant tuberculosis (MDR-TB) programme in Karakalpakstan, Uzbekistan. Uzbekistan has some of the highest reported rates of MDR-TB in the world, affecting 23% of new and 62% of retreatment TB cases. In order to formulate policy for effective practice, the national Research Institute and the Chief Ministry of Health TB doctor wanted to understand the extent to which patient and practitioner beliefs, behaviours and knowledge of TB medication use illuminated inadequate drug regulation. We aimed to understand patients' and prescribers' attitudes to TB drug prescription, TB drug prescription practices and the problems of TB drug regulation in this high-burden MDR-TB context.

**Methods:** The study was conducted in the MoH/MSF programme in 2012 in three administrative districts of Karakalpakstan. Participants (12 patient, 12 practitioner) were recruited purposively by snowball method. Using a flexible participatory technique, data were gathered using field notes and in-depth interviews guided by topic-led questions, and analysed thematically by open coding, drawing on grounded theory principles with participant validation of responses and attention to deviant cases. The MSF and Uzbekistan ERBs granted Ethics approval.

**Findings:** Two main themes emerged: risk, shame and stigma; and positive influences on treatment. Patients reported misuse of TB drugs to be most likely at the initial stage of illness and treatment. Motivated by shame, they hid their condition by resorting to drug treatment options outside the TB programme. It was perceived that there was a failure to promote health information through the health system and that incorrect information was passed through lay networks leading to wrong diagnoses and inappropriate therapies. Patient access to free quality drugs once in the TB programme, perceived to give good results, was an overwhelming feature for all participants. Communication, trust and support were important elements in enhancing care and control.

**Conclusion:** Effective case finding and community education strategies should be included in programming to diminish the problem of shame and desire for patients to seek treatment elsewhere. The study reinforces the need for political engagement with the public and private sector and a decentralised treatment approach as equally important for effective regulation of TB drugs.

**PD-1170-01 Trends of the prevalence of new patients amongst MDR-TB notified cases, Peru 2009–2013**

J Cabrera,<sup>1</sup> CA Mendoza,<sup>1</sup> J Camara,<sup>1</sup> C Figueroa,<sup>1</sup> D Chavarri,<sup>1</sup> R Espinoza,<sup>1</sup> J Diaz,<sup>1</sup> A Alarcón.<sup>1</sup> <sup>1</sup>National Tuberculosis Program, Ministry of Health, Lima, Peru. Fax: (+511) 4293155. e-mail: jolcriver@hotmail.com

**Background:** Every year, Lima and Callao regions report 80% of MDR-TB cases in Peru. Two small studies have shown a high prevalence of MDR-TB amongst new patients without traditional risk factors for drug resistant-TB in these regions.

**Objective:** To determine the trend of the prevalence of new patients amongst MDR-TB reported cases between 2009 and 2013 in Lima and Callao.

**Methods:** The electronic files for the confirmed MDR-TB patients reported to the Peruvian National TB Program from Lima and Callao regions during the first half of each year, 2009 to 2013, were reviewed. A new MDR-TB case was defined if he or she did not receive any anti-TB regimen at all, or having received it fewer than 30 days from the date of sampling for drug susceptibility test.

**Results:** There were 2367 MDR-TB cases identified (482 in 2009, 403 in 2010, 464 in 2011, 495 in 2012 and 523 in 2013). The average age was 31, remaining the same over those 5 years, and 66% were male. Regarding the history of previous anti-TB treatment, a significant progressive increase in the proportion of new cases among MDR-TB was observed: 40% in 2009, 52% in 2010, 55% in 2011, 60% in 2012, and 67% in 2013 ( $P < 0.0001$ ).

**Conclusions:** A sustained increase of the prevalence of new cases with MDR-TB was evidenced in Lima and Callao regions. This highlights the active transmission of this type of resistant-bacteria in these urban setting among young people in Peru. These results support the recently approved policy in Peru, regarding universal access to MDR-TB diagnosis, through rapid tests, regardless of conventional risk factors.

**PD-1171-01 Implications of revised methods for estimating the global burden of multidrug-resistant tuberculosis**

S Nourzad,<sup>1</sup> H Jenkins,<sup>2</sup> C Mitnick.<sup>2,3,4</sup> <sup>1</sup>Global Health and Social Medicine, University of Amsterdam, Amsterdam, Netherlands; <sup>2</sup>Division of Global Health Equity, Brigham and Women's Hospital, Boston, MA, <sup>3</sup>Global Health and Social Medicine, Harvard Medical School, Boston, MA, <sup>4</sup>PIH, Partners in Health, Boston, MA, USA. e-mail: Susan\_Nourzad@hms.harvard.edu

**Background:** Estimates of the global burden of multidrug-resistant tuberculosis (MDR-TB) vary widely; the

true extent of the burden globally remains unknown. Variability in estimates is partially due to changes in methods used to estimate the prevalence of MDR-TB. These changes, however, have implications for estimates of progress toward universal access to resources needed to treat all affected patients. In this study we compare estimates derived from two different methods and illustrate the impact the chosen method can have on perceived coverage of diagnostic and treatment services for MDR-TB worldwide.

**Methods:** We analyzed data reported to WHO by 217 countries/territories and compared the global and regional estimates of the burden of MDR-TB in notified TB cases to estimates of the burden among incident TB cases. We also compared treatment coverage using the two estimation methods. Countries with reported notification, estimated incidence, and estimated percent MDR among notified cases for year 2012 (or 2011) were included.

**Results:** The global number of MDR-TB patients, when calculation is based on notified TB cases, 300,000 (95% confidence interval (CI): 220,000 – 380,000). That figure is 422,161 (95% CI: 387,636 – 458,026) when calculation is based on incident cases, reflecting a difference of 41%. The differences between the estimates range from 6% to 121% by WHO region. Treatment was available to 26% of notified MDR-TB cases and only 18% of incident cases in 2012.

**Conclusion:** The global burden of MDR-TB is higher when calculated based on TB incidence. Consequently, the per cent of MDR-TB patients who receive treatment is lower than previously estimated. This leads to continued transmission and mortality due to untreated, or inadequately treated, MDR-TB. These findings underscore the need to improve case detection and to base funding and other resource requirements on MDR-TB burden calculated among incident, rather than among notified, TB cases.

#### PD-1172-01 The role of private health facilities in managing drug-resistant TB patients in an urban setting: experiences from Kampala, Uganda

E Kizito,<sup>1</sup> S Mwanja,<sup>2</sup> D Birabwa-Male,<sup>2</sup> C Aguti,<sup>1</sup> F Mugabe,<sup>3</sup> M Ruhweza,<sup>1</sup> E Birabwa,<sup>4</sup> S Balcha,<sup>4</sup> <sup>1</sup>Track Tuberculosis Activity Project (TRACK TB), Management Sciences for Health (MSH), Kampala, <sup>2</sup>Mulago National Referral Hospital, Kampala, <sup>3</sup>Ministry of Health, National Tuberculosis and Leprosy Programme, Kampala, <sup>4</sup>United States Agency for International Development (USAID), Kampala, Uganda. e-mail: ekizito@msh.org

**Background and challenges to implementation:** At the beginning of 2013, over 100 drug resistant TB (DR TB) cases had been notified and were awaiting treatment in Kampala, Uganda. Unfortunately, Mulago the National Referral Hospital is the only DR-TB treatment initiation site in Kampala, with just 39 patient beds. Therefore, it was not possible to admit all 100 DR-TB patients at Mulago. To address this, the hospital staff began to implement the NTP's adopted mixed model of MDR-TB

patient care that includes a period of hospitalization, then a period of ambulatory care. Mulago partnered with private, community-based health units that could provide its DR-TB patients with post-hospitalization ambulatory care and treatment.

**Intervention** With support from the PEPFAR- and USAID-funded TRACK TB project, Mulago Hospital's MDR-TB team developed partnerships with several follow-up health units (FUUs) that were near the patients' homes. Mulago staff then trained health workers at the FUUs in drug supply management and storage, infection control, and overall DR-TB patient management using standardized tools. They also provided the units with DR-TB drugs and mentored the units' staff on a monthly basis. Each unit received clinical supplies like gloves, syringes, respirators, and face masks. The training, mentorship and provision of supplies enabled the staff at the FUUs to conduct daily direct observed therapy (DOT) for DR-TB patients, contact tracing, and health education. Each FUU signed a commitment letter indicating that they would provide DOT for all DR-TB patients in their care.

**Results** After these interventions, 70 out of 90 active DR-TB patients currently on treatment (78%) were receiving DOT at the FUUs. NTLF and partners conducted a cohort review to assess patient outcomes after six months of treatment. The review showed that, among 24 patients enrolled in April-June 2013, 20 were still on treatment (83%). Of those on treatment, 18 (90%) were receiving DOT from private health units. Of the 22 DR-TB patients that were being managed in private units, 16 (73%) had converted to culture negative and 4 (18%) had died

**Conclusions** Private health units are able to provide DOT to the majority of the MDR-TB patients in Kampala. A cohort review shows that, after six months, the majority of the patients receiving DOT from private health units are still on treatment and have converted to culture negative. The NTP should sustain and expand these interventions in Kampala.

Facility	Patients on treatment			Patients not on treatment		
	20/24 (83%)			4/24 (17%)		
	Culture negative	Culture positive	Culture unknown	Lost to follow-up	Died	Not evaluated
Public	1	0	1	0	0	0
Private	16	0	2	4	0	0

### PD-1173-01 Magnitude of MDR-TB resistance in Kinshasa, DR Congo

G Bakaswa,<sup>1</sup> Jan Verhaegen,<sup>2</sup> M Ieven,<sup>3</sup> V D Armand,<sup>3</sup> M Kaswa-kayomo,<sup>1</sup> JJ Muyembe,<sup>4</sup> S Bisuta Fueza,<sup>1</sup> M Boelaert.<sup>3</sup> <sup>1</sup>Programme national de lutte contre la TB, Ministère de la Santé Publique, Kinshasa, Democratic Republic of Congo; <sup>2</sup>Mycobactériologie, KU Leuven, Leuven, Belgium; <sup>3</sup>Mycobactériologie, Institut de Médecine Tropicale, Anvers, Belgium; <sup>4</sup>Mycobactériologie, Institut de Recherche Biomédicale, Kinshasa, Democratic Republic of Congo. e-mail: kmutala@yahoo.fr

**Background:** The Democratic Republic of Congo (DRC) is classified among the 27 countries with a high burden of MDR-TB, but the actual data on the magnitude and the distribution of MDR-TB in DRC are scanty as a result of the scarce laboratory infrastructure and some logistical limitations. Conventional methods for diagnosing MDR-TB such as mycobacterial culture and drug susceptibility testing (DST) are slow and cumbersome requiring at least 2 months for MDR case detection. In 2010, the National Public Health Laboratory of DRC-the Institut National de Recherche Biomédicale (INRB)-in Kinshasa and National Tuberculosis Program (NTP) did start the implementation of the GenoType® MTBDRplus assay for rapid detection of MDR in Kinshasa. The aims of the study were to implement rapid molecular testing for MDR TB case under field conditions and to determine the magnitude of MDR TB in Kinshasa, DR Congo.

**Methods:** GenoType® MTBDRplus assay was performed directly on sputum specimens collected among a prospective cohort of MDR TB suspects in Kinshasa from March 2011 to March 2013.

**Results:** Of 587 consecutive individual MDR-TB suspects who did submit their sputum at TB clinics during the study period, a total of 211 MDR-TB (36%), 28 (5%) RMP and 40 (7%) INH mono-resistant results were obtained from DNA extracts tested with MTBDRplus. Overall, 1% (6/ 587) yielded an invalid test due to absence of the control band.

**Conclusion:** The challenges posed by MDR-TB in Kinshasa seriously jeopardize the progress made in recent years to control TB in DR Congo. Urgent call for providing NTP with accurate rapid diagnostic tools and appropriate drugs supplying system is relevant to control the spread of MDR TB cases in the central Africa.

### 60. MDR-TB: SPECIAL LOCATIONS

#### PD-1174-01 Using community-based care to achieve low defaulter rates among multidrug-resistant tuberculosis (MDR-TB) patients of Cambodia

S Khann,<sup>1</sup> T E Mao,<sup>2</sup> K Tan,<sup>2</sup> Y Rajendra.<sup>1</sup> <sup>1</sup>STOP TB, World Health Organization, Phnom Penh, <sup>2</sup>National Center for Tuberculosis and Leprosy Control, Ministry of Health, Phnom Penh, Cambodia. e-mail: khann.sokhan@yahoo.com

**Background:** MDR-TB is fast-worsening challenge globally, partly due to the poor treatment outcomes. The treatment duration is long with many drug side effects.

**Objective:** Evaluate community based care model of MDR-TB treatment in Cambodia.

**Method:** A retrospective study of program review which included the comparison of MDR-TB treatment outcome of cohort 2007 – 2011 and their intervention strategy. Cambodia has piloted community based care since 2008 and used nationwide since 2009 for programmatic management of drug resistant TB (PMDT). The patient receives comprehensive counseling prior starting treatment and throughout the treatment. The hospital discharges the patients as soon as they become stable. Then NGO partners sets up the community-based care component and management for them. Direct observation Therapy (DOT) is used to assure patients' adherence. Three trained people are assigned to be the DOT Watchers (DW) for each patient. First DW is a local health professional. He/she provides injection and morning dose to patients during injection phase, and monitors treatment side effects and supervises the second/third DWs throughout the treatment. The second/third DWs are village volunteers or neighbors. They provide daily DOT and monitor treatment side effects. Third DW is assigned to play role of second DW when the second DW is busy. The patients receive medical follow-up at MDR-TB treatment sites every quarter or when clinical indicated. A field nurse provides monthly follow up. In addition, a clinician provides medical follows at patients' home as needed. The case definitions of treatment outcomes and treatment regimen are in line with WHO guidelines.

**Results:** A total of 194 MDR-TB patients were put on treatment in 2007 - 2011. Out of them, 75.8% (n=147) were treated successfully, 15.5% (n=30) died, 6.2% (n=12) loss to follow up treatment, 2.1% (n=4) failed treatment, and 0.5% (n=1) were not evaluated. The proportion of HIV positive cases in the cohorts of 2007, 2008, 2009, 2010 and 2011 were 50.0%, 14.9%, 17.4%, 22.6%, and 16.1% respectively. The death rates were 14.3%, 14.9%, 17.4%, 29.0%, and 7.1% in the cohorts of 2007, 2008, 2009, 2010, and 2011 respectively, while the defaulter rate were 21.4%, 12.8%, 4.3%, 0.0%, and 1.8% in the same cohorts.

**Conclusion:** Cambodia has a high success rate (>75%) and low treatment defaulter rate among MDRTB cases. We attribute the sharp decrease in defaulter rates over the years to community-based approach to PMDT.



### PD-1175-01 The spectrum of drug-resistant pulmonary tuberculosis among foreign-born in Singapore

K M Kyi Win,<sup>1</sup> C Chee,<sup>1</sup> J Cutter,<sup>2</sup> LH Sng,<sup>3</sup> R Jureen,<sup>4</sup> Y T Tang.<sup>1</sup> <sup>1</sup>TB Control Unit, Tan Tock Seng Hospital, <sup>2</sup>Communicable Diseases Division, Ministry of Health, <sup>3</sup>TB Laboratory, Singapore General Hospital, <sup>4</sup>Laboratory Medicine, National University Health System, Singapore, Singapore. Fax: (+65) 62524057. e-mail: kyi\_win\_khin\_mar@ttsh.com.sg

**Background:** The availability of Xpert Rif (Cepheid, USA) in developing countries has enabled the rapid detection of presumptive MDR-TB. Phenotypic drug susceptibility testing is however still required to detect isoniazid and second-line drug resistance to guide individualized treatment to optimize treatment outcomes, and to prevent amplification of drug resistance. Among Singapore / Malaysia-born TB patients, the prevalence of isoniazid (without Rifampicin) resistance and MDR-TB was 2.6% and 0.3% respectively, while that among non-Singapore/Malaysia-born (referred to as "foreign-born") was 8.4% and 3.5% respectively. We describe the spectrum of MDR among foreign-born TB patients according to whether they were new or previously treated, and their country of origin.

**Method:** Singapore is served by two mycobacterial culture laboratories. Both laboratories routinely perform first-line drug susceptibility testing (DST) for all patients with positive *Mycobacterium tuberculosis* isolates, and second-line DST for isolates resistant to isoniazid (INH) and/or rifampicin (RMP). Both laboratories are linked electronically to the National TB Registry. Using data from the National TB Registry, we analyzed the spectrum of drug-resistant TB in new and previously treated pulmonary TB cases among foreign-born TB patients with culture and DST performed between 2002–2013.

**Results:** There were 5,015 foreign-born patients with positive TB isolates during our study period. The proportion of isoniazid (without rifampicin) resistance among new and previously treated cases was 8.4% and 8.4% respectively, while that of MDR-TB was 2.7% and 16.8% respectively. Analysis according to country of birth showed MDR-TB among new cases to be highest in those born in Myanmar (8%), followed by Viet Nam (4.9%), China (3.3%) and Philippines (2.5%). For previously treated cases, the highest rate of MDR-TB occurred among those born in Viet Nam (40%), followed by Indonesia (28.4%), Myanmar (25%) and India (22.2%).

Drug resistance	Myanmar	Indonesia	India	China	Vietnam	Philippines	Bangladesh
At least 4 first-line drugs	74.4%	53.7%	42.9%	61.3%	100.0%	18.8%	66.6%
Pre-XDR*	14.0%	17.9%	0.0%	3.2%	12.5%	0.0%	33.3%
XDR	0.0%	9.0%	0.0%	3.2%	12.5%	0.0%	0.0%

\* Pre-XDR-TB = MDR-TB resistant to either a fluoroquinolone or second-line injectable

**Conclusion:** We found generally high-grade MDR-TB among foreign-born cases in Singapore with the exception

of those born in the Philippines. This information may be useful to international authorities in their recommendation of standardized MDR-TB treatment regimens.

### PD-1176-01 Determinants of multidrug-resistance tuberculosis in selected hospitals in Addis Ababa, Ethiopia: a case control study

D Abebe,<sup>1</sup> B Seyoum,<sup>2</sup> L Hordofa,<sup>3</sup> L D'ambrosio,<sup>4</sup> R Centis,<sup>4</sup> G B Migliori.<sup>4</sup> <sup>1</sup>Disease prevention and Health promotion core process, Dire Dawa Administration Health Bureau, Dire Dawa, <sup>2</sup>Medical Laboratory, Haramaya University, Harar, <sup>3</sup>Epidemiology, Haramaya University, Harar, Ethiopia; <sup>4</sup>research, 3WHO Collaborating Centre for TB and Lung Diseases, Fondazione S. Maugeri, Care and Research Institute, Tradate, Italy. Fax: (+251) 251125278. e-mail: zikuni2000@gmail.com

**Background:** Multi-Drug Resistant Tuberculosis (MDR-TB) has been jeopardizing the global effort to control Tuberculosis. The major determinants for MDR-TB are still not clearly known or controversial and also vary across the regions. No strong evidence on the determinants of MDR-TB is presently available in Ethiopia. This evidence can guide the National TB Programme in designing an evidence-based algorithm to prioritize access to MDR-TB services (culture and DST) and tailor prevention and control strategies towards MDR-TB. Aim of this study is to identify determinants of MDR-TB in a cohort of patients managed in reference hospitals of Addis Ababa, Ethiopia from April 1, 2013 to June 30, 2013.

**Methods:** A health facility based case control study design was used. All Adult confirmed MDR-TB patients who have been on treatment at Addis Ababa St. Peter and Alert Hospitals during study period were selected as cases; whereas adult Pulmonary TB patients who had been on 1<sup>st</sup> line TB treatment and became cured or treatment completed during study period were selected as a control from 12 representative health centers of Addis Ababa. Data were analyzed using SPSS version 16.0 software package.

**Results:** A total of 710 patients (229 confirmed MDR-TB and 481 Susceptible TB patients) were enrolled in the study. Of these, 55% and 84% were male and below age 44 years, respectively. Identified independent determinants for MDR-TB were contact history with a known TB patient (Adjusted Odds Ratio (AOR): 1.9, 95% CI: 1.1–3.3), previous TB treatment history (AOR: 11.9, 95% CI: 6.8–21), history of hospitalization (AOR: 4.4 95% CI: 2.2–7.8), sputum-smear positivity (AOR: 1.9, 95% CI: 1.1–3.4), social stigma (AOR: 5.1, 95% CI: 1.8–14.4) and Chronic Obstructive Pulmonary Disease (AOR: 47.8 95% CI: 23.9–95.6). In addition, both HIV (AOR: 0.3, 95% CI: 0.2–0.7) and co-morbid diabetes-mellitus (AOR: 0.2, 95% CI: 0.05–0.8) had lower risk for MDR-TB.

**Conclusions:** As the determinants associated with MDR-TB are country-specific, this first MDR data from Ethiopia provides important information for both clinical management and public health action. The factors can be considered for use in future MDR-TB screening tools. As factors may vary, future studies need to be performed in

other Ethiopian centers and settings as these results are from Addis Ababa.

**Table 1: Bivariate and Multivariate analysis to determine the independent Determinants for MDR-TB in Addis Ababa, Ethiopia between April 2013 and June 2013**

Variables	Crude		Adjusted	
	COR (95%CI)	P-value	AOR (95% CI)	
<b>Sex</b>				
Male	1.00		1.00	
Female	1.51 (1.09-2.07)	0.011	0.96 (0.52-1.75)	
<b>Age</b>				
>=45	1.00		1.00	
0 - 44	2.76 (1.64- 4.64)	0.000	1.32 (0.55-3.16)	
<i>Mean age: 31.7 Years</i>				
<b>Marital status</b>				
Divorce & Widowed	1.00		1.00	
Single	2.84 (1.51- 5.35)	0.001	2.37 (0.88 -6.39)	
Married	1.62 (0.84 - 3.16)	0.154	1.47 (0.53-4.06)	
<b>Educational status</b>				
Illiterate	1.00		1.00*	
1-8 grade	0.89 (0.54-1.48)	0.66	0.75 (0.32-1.74)	
9-12 grade	1.03 (0.62-1.69)	0.92	0.60 (0.26-1.42)	
>12 grade	2.18 (1.27-3.74)	0.005	2.04 (0.85-4.89)	
<b>Imprisonment history</b>				
No	1.00		1.00	
Yes	0.45 (0.22-0.95)	0.035	0.67 (0.21-2.16)	
<b>Ever smoking history</b>				
No	1.00		1.00	
Yes	0.74 (0.49-1.09)	0.136	0.71 (0.38-1.34)	
<b>Previous alcohol drinking habit</b>				
No	1.00		1.00	
Yes	0.75 (0.52-1.08)	0.12	1.45 (0.69-3.05)	
<b>Known TB contact history</b>				
No	1.00		1.00	
Yes	1.92 (1.37-2.68)	0.000	1.96 (1.13-3.38)*	
<b>Previous TB treatment history</b>				
No	1.00		1.00	
Yes	13.9 (9.5-20.3)	0.000	11.95 (6.78 - 21.1)*	
<b>History of Hospital-ization</b>				
No	1.00		1.00	
Yes	6.51 (4.28-9.91)	0.000	4.14 (2.19-7.84)*	
<b>Smear result at the time of diagnosis</b>				
Negative	1.00		1.00	
Positive	1.72 (1.25-2.36)	0.001	1.95 (1.13-3.35)*	
<b>HIV status</b>				
NR	1.00		1.00	
R	0.63 (0.42-0.96)	0.029	0.33 (0.16-0.66)*	
Unknown	0.72 (0.31-1.66)	0.445	1.47 (0.43-5.01)	
<b>Diabetic status of the patient</b>				
No + Unknown	1.00		1.00	
Yes	0.45 (0.18-1.11)	0.084	0.20 (0.05-0.83)*	

#### COPD status of the patient

No + Unknown	1.00		1.00
Yes	47.33 (27.9 - 80.1)	0.000	47.8 (23.9-95.6)*

#### Psychiatric status of the patient

No	1.00		1.00
Yes	4.80 (1.65-13.99)	0.004	0.59 (0.08- 4.63)

#### Disclosure status of the patient

Disclosed	1.00		1.00
Didn't disclosed	3.72 (1.88 - 7.38)	0.000	5.14 (1.84-14.39)*

### PD-1177-01 Increasing trend in multidrug-resistant tuberculosis in the extreme north of Russia

MK Vinokurova,<sup>1</sup> SN. Kondakov,<sup>1</sup> GI Alekseeva,<sup>1</sup>

LP Iakovleva,<sup>1</sup> AF Kravchenko,<sup>1</sup> AA Kornilov,<sup>1</sup>

OE Dogorova,<sup>1</sup> NE Evdokimova.<sup>1</sup> <sup>1</sup>Organization and

Methodology, Research & Practice Center for Tuberculosis of the Sakha Republic (Yakutia), Yakutsk, Russian Federation.

e-mail: mkvin61@mail.ru

**Background:** Enormous area is the feature of Yakutia: it is sized one fifth of Russia, lies mostly in the Arctic zone, has low population density, and substandard infrastructure. Tuberculosis (TB) incidence rate is the same as in Russia, and is 1.5 times lower than in the Far Eastern Federal District. We aimed to study changes in the incidence and profile of multidrug-resistant (MDR) TB in the north of Russia.

**Design/Methods:** We analyzed data on patients with MDR TB for the years 2006 and 2013. Bacteriologic sputum tests were performed using conventional solid media and BACTEC-960.

**Results:** Number of MDR TB cases was 281 (14.2% of all TB cases) in 2006, and increased to 399 (24.4% of all TB cases) in 2013. For the study period, the increase in the incidence of MDR TB in rural districts (including Arctic districts) was 1.7 times higher, than in cities. In 2006, resistance to isoniazid (H) + rifampicin(R) associated with resistance to: streptomycin (S) (93.2%), kanamycin (K) (41.3%), etambutol (18.1%), etionamide (12.1%), capreomycin (9.6%), PAS (8.9%), fluoroquinolones (6.4%). Regional MDR profile showed resistance to HRSK in 40% of cases. In 2013, resistance to isoniazid+rifampicin associated with resistance to: streptomycin (98.7%), kanamycin (44.0%), etambutol (26.0%), fluoroquinolones (24.3%), capreomycin (17.0%), etionamide (9.2%), PAS (5.5%), cycloserine (9.2%). Regional resistance profile was still HRSK in 40% of cases. But alongside with that: a quarter of cases became additionally co-resistant to etambutol and fluoroquinolones; percent of cases co-resistant to capreomycin has increased; co-resistance to cycloserine has emerged.

**Conclusion:** We observed a dangerous increasing trend in the incidence of MDR TB alongside with worsening drug-resistance profile in Yakutia for the last years.

Timely study of the incidence and drug resistance profile of *M. tuberculosis* (MTB) in a given area enables adequate management of drug supply. Local MTB drug resistance profile must be considered in planning the work of anti-TB services and case management in the northern area, especially in patients living in remote Arctic districts.

#### PD-1178-01 Acquired resistance to second line anti-TB drugs among multidrug-resistant (MDR-TB) patients from eastern Europe

J Ershova,<sup>1</sup> E Kurbatova,<sup>1</sup> T Dalton,<sup>1</sup> B. Kazenny,<sup>2</sup> K Kliiman,<sup>3</sup> V Leimane,<sup>4</sup> G Volchenkov,<sup>5</sup> P Cegielski.<sup>1</sup>  
<sup>1</sup>Tuberculosis Elimination, U.S. Centers for Disease Control and Prevention, Atlanta, GA, USA; <sup>2</sup>Tuberculosis, Orel Oblast Tuberculosis Dispensary, Orel, Russian Federation;  
<sup>3</sup>Tuberculosis, Tartu University Hospital, Tartu, Estonia;  
<sup>4</sup>Tuberculosis, Riga East University Hospital Centre of Tuberculosis and Lung Diseases, Riga, Latvia; <sup>5</sup>Tuberculosis, Vladimir Oblast Tuberculosis Dispensary, Vladimir, Russian Federation. Fax: (+1) 404 639 1566. e-mail: jhe3@cdc.gov

**Background:** Acquired resistance to second-line anti-TB drugs (SLD) during MDR-TB treatment can lead to extensively drug-resistant tuberculosis (XDR-TB). The highest rates of MDR-TB worldwide are reported in Eastern European countries. In this study we described the rates of and identified risk factors for acquired resistance (AR) to SLD among MDR-TB patients from Eastern Europe enrolled in the Preserving Effective Tuberculosis Treatment Study, 2005–2008.

**Design/Methods:** Consecutive, consenting adults with locally confirmed pulmonary MDR-TB starting SLD treatment were enrolled in Estonia, Latvia and Russia. Drug susceptibility tests (DST) were performed at the U.S. CDC. We defined “acquired resistance” as drug resistance at the last DST after susceptibility to the same drug at the baseline DST with genetic analysis confirming the same strain. Clinical factors were analyzed in relation to AR to SLD using bivariate logistic regression.

**Results:** Of 346 enrolled patients, at least two isolates were shipped to the CDC for 266 (77%). Of these, 172 satisfied enrollment criteria. Thirty (17%) patients had resistance to any fluoroquinolone (FQ) at the start of treatment, 70 (41%) to any injectable SLD (SLI), 15 (9%) had XDR-TB. Resistance to FQ increased (DST results changed from susceptible to resistance) in 18/142 (13%) patients, in 11(8%) AR was confirmed by genotyping. Resistance to injectable SLD (SLI) increased in 22/102 (22%) patients, in 14(9%) AR was confirmed by genotyping. Nineteen of 157 (12%) patients developed XDR-TB; acquired XDR-TB was confirmed in 12 (7.6%). Among 12 patients with acquired XDR-TB, 11/87(13%) had baseline resistance to at least one SLD compared to 1/70(1.4%) patients without baseline SLD resistance ( $p=0.009$ ). AR to FQ was associated with previous treatment with bacteriostatic SLDs (OR=3.8;CI:1.0–14.5) and baseline resistance to any SLD (OR=4.9;CI:1.0–23.3). AR to injectable SLD was associated with cavitary disease (OR=0.2;CI:0.05–0.5).

Acquired XDR-TB was significantly associated with baseline resistance to any SLD (OR=8.7;CI:1.1–68.9).

**Conclusion:** Patients with resistance to at least one SLD at the start of treatment were at high risk for development of AR to another SLD. Additionally, only 60% of occurred resistance to SLD was acquired as confirmed by genotyping, suggesting mixed infections or reinfection. Providers should consider emergence of AR among MDR-TB patients and practice strict infection control measures.

#### PD-1179-01 Drug-resistant extra-pulmonary tuberculosis cases in a tertiary care hospital in Karachi, Pakistan

S Butt,<sup>1</sup> A Mashhadi,<sup>1</sup> N Baig-Ansari,<sup>2</sup> A Bhurgri,<sup>1</sup> N Salahuddin.<sup>1</sup> <sup>1</sup>MDR TB CLINIC, The Indus Hospital, Karachi, <sup>2</sup>Research, Interactive Research Development, Karachi, Pakistan. Fax: (+92) 213 5112 718. e-mail: shahid.butt@industbcontrol.org

**Objective:** To describe the demographics, sites, types and treatment outcomes of Drug Resistant Extra-Pulmonary Tuberculosis (DR-EPTB) cases in a tertiary care hospital in a high burden tuberculosis country.

**Method:** A retrospective case series study was conducted at The Indus Hospital, which is the largest private tertiary care hospital in Karachi, Pakistan. All cases diagnosed and treated as DR EPTB over five years between January 2008 and December 2013, were included. Demographics, clinical, laboratory, and outcome data were retrieved from medical records.

**Results:** A total of 11,861 patients were diagnosed with TB, out of which 8435 (71%) were drug susceptible pulmonary TB, and 2834 (29%) were drug susceptible EPTB. DR TB accounted for 591 (5%) of total TB cases, of which 563 (95%) had DR PTB and 28 (5%) had DR EPTB. Mean age of DR EPTB patients was 27 years, and 54% were female. *Mycobacterium tuberculosis* was cultured in all but one case of DR EPTB. The most common sites for DR EPTB were lymph nodes 14 (50%) and spine 10 (32%), while the other sites were meningitis 1 (4%), bone and joint 2 (7%), soft tissue 1 (4%). Twenty (74%) patients were Multi-DR, 4 (15%) were Poly-DR, 1 (3%) was Mono-DR, and 2 (7%) were Rifampicin resistant. One patient was diagnosed as EPTB of the spine despite negative culture, but improved only after receiving second line drugs (SLD). All enrolled patients were re-treatment cases after failure or default. Treatment was according to WHO Guidelines and progress was determined clinically. Fifteen (48%) of the DR EPTB cases have completed treatment, while 12 (43%) are still receiving treatment.

**Conclusion:** In our series EPTB accounted for 29% of all TB cases. DR EPTB was found to be only 5% of all DR cases at our site. Diagnosis of EPTB is often difficult to confirm with culture, as invasive procedures are required to obtain samples, and bacterial burden is usually low in most EPTB. Despite the difficulties in obtaining samples for culture, 28 cases were found to be drug resistant, and recovered only after SLDs were given. It is therefore



important to make full attempts to culture tissue or fluid for TB in all suspicious cases in high burden TB countries.

#### **PD-1180-01 Antituberculosis drug-resistance survey in pulmonary tuberculosis cases in Ankara and Istanbul, Turkey**

N Albayrak,<sup>1</sup> F Sezen,<sup>2</sup> A Yildirim,<sup>3</sup> H Simsek,<sup>1</sup> A Arslanturk,<sup>1</sup> N Ucarman,<sup>1</sup> MA Torunoglu,<sup>4</sup> S Ozkara<sup>5</sup> FD Agca,<sup>1</sup> Al Suer,<sup>1</sup> K Altunay,<sup>1</sup> AC Simsek,<sup>11</sup> S Koyman,<sup>1</sup> and the Tuberculosis Laboratory Surveillance Network Study Group. <sup>1</sup>National Tuberculosis Reference Laboratory, Public Health Agency, Ankara, <sup>2</sup>Department of Early Warning and Response, Public Health Agency, Ankara, <sup>3</sup>Department of TB Control, Public Health Agency, Ankara, <sup>4</sup>Department of Communicable Diseases Control and Surveillance, Public Health Agency, Ankara, <sup>5</sup>10th Clinic, Atatürk Chest Diseases and Chest Surgery Education and Research Hospital, Ankara, Turkey. e-mail: ozkaraseref@yahoo.com

**Aim:** After antituberculosis drug resistance surveillance (DRS) in Ankara, Istanbul is added to DRS in Turkey.

**Methods:** This DRS was done in Ankara and Istanbul provinces during 1st January to 31st December, 2012. The study was carried out by participation of health facilities providing tuberculosis diagnosis and treatment services (Provincial Health Directorate Tuberculosis Coordination Department; Tuberculosis Dispensaries; and laboratories of Provincial Public Health, Anti-TB Association, Chest Diseases Hospitals, Government and University Hospitals), by coordination of National Tuberculosis Reference Laboratory (NTRL). NTRL, evaluated the laboratory capacity by rechecking the DST results; EQA for microscopy, culture and DST; and by in site supervision with Laboratory Assessment Tool. **Results:** Totally 3,717 isolates from 3,086 pulmonary TB cases were received by the National Reference Laboratory. Cases from Ankara and Istanbul were 2,013. Another 88 cases were foreign born; 25 (28.4%) of them were MDR-TB, and 3 (3.4%) of them were XDR-TB cases. 93 (4.6%) cases from Istanbul and Ankara were MDR-TB cases (53 were new, and 40 were previously treated cases); one (0.04%) of them was a XDR-TB case. MDR-TB ratio in new and previously treated cases were 3.1% (53/1726), and 16.5% (37/224), respectively. 63 cases without previous treatment history were not included.

**Conclusion:** Drug resistance is low in new cases, and moderate in previously treated cases from the Istanbul and Ankara. But it is high in the foreign born cases. After this DRS in two biggest cities, DRS will be expanded to other provinces.

#### **PD-1181-01 High DR-TB prevalence and vulnerability in adolescent girls: the Indus Hospital TB control programme experience**

F Amanullah,<sup>1</sup> A Malik,<sup>2</sup> S Butt,<sup>1</sup> S Khawaja,<sup>2</sup> N Salahuddin,<sup>1</sup> A Bhurgri,<sup>1</sup> A Khan,<sup>2</sup> H Hussain.<sup>1</sup> <sup>1</sup>TB Control, The Indus Hospital, Karachi, <sup>2</sup>International Health, Interactive Research & Development, Karachi, Pakistan. e-mail: amyn.malik@irdresearch.org

**Background:** Pakistan had 1602 confirmed multidrug resistant tuberculosis (MDR TB) cases in 2012. Globally, apart from few center based studies, very little is known about drug resistant tuberculosis (DR-TB) rates in children.

**Objective:** To assess the gender demographics and treatment outcomes of children and adolescents with DR-TB, at the Indus Hospital Programmatic Management of Drug Resistant TB (PMDT)

**Design/Methods:** We retrospectively reviewed the medical records of all children and adolescents diagnosed and registered with DR-TB in the Indus Hospital PMDT from January 2008- March 2014.

**Results:** Children 0–18 years comprise (110/580) 19% of the DR-TB caseload at the Indus Hospital PMDT. Females comprised 65.5% of all DR-TB children and adolescents. Of the female DR-TB patients, 93% were culture confirmed compared to 79% culture confirmation among male patients (p-value <0.05). Among those with pulmonary TB the M:F ratio was 0.53, whereas all patients with extra-pulmonary TB were female. Females were more likely to be severely underweight 72% (52/72) compared to males 45% (17/38) (p-value < 0.01). Treatment success was 70.6% and 66.7% among males and females respectively, with a 5.6% default rate only in females. Females had a mortality rate of 8.3% compared to 5% among males (p-value 0.55).

**Conclusion:** DR-TB in children and adolescents accounts for a significant proportion of the total DR-TB caseload with more than half of the burden occurring in females. Females were more likely to be culture confirmed and severely underweight at presentation, indicating later presentation compared to males. Despite good treatment outcomes overall, female children and adolescents with DR-TB had higher mortality and default rates. Adolescent girls are a vulnerable population that need intensified efforts for early DR-TB diagnosis and enhanced social support.

### PD-1182-01 Alarming second-line drug resistance pattern in patients under XDR-TB treatment in Nepal

B Shrestha,<sup>1</sup> B Maharjan,<sup>1</sup> D B Pradhan,<sup>2</sup> H Hoffmann,<sup>3</sup> K. Avsar,<sup>3</sup> P Rajendra,<sup>4</sup> A Shrestha.<sup>4</sup> <sup>1</sup>OPD, German Nepal TB Project (GENETUP), Kalimati, Kathmandu, <sup>2</sup>Administration, Nepal Anti-TB Association, Kalimati, Kathmandu, Nepal; <sup>3</sup>Laboratory, Kuratorium Tuberkulose in der Welt e.V., München-Gauting, Germany; <sup>4</sup>Administration, National Tuberculosis Center, Thimi Bhaktapur, Nepal. Fax: (+977) 01-270019. e-mail: bhagwan.maharjan@yahoo.com

**Background:** The ambulatory standard XDR TB treatment approved by Green Light Committee to NTP, Nepal offers to all bacteriological confirmed XDR TB cases and the MDR TB Treatment failure with resistance to Fluoroquinolone group. The treatment regimen CM, Moxi, Cs, PAS, PZA, Amoxy/clav and clofazimine. In Nepal, we do have the facility of DST on Rifampicin, Isoniazide, Ethambutol, Streptomycin, Ofloxacin and injectable Aminoglycosides only. Overall, the treatment success rates of the 28 patients (registered between 2010 to 2012) with XDR treatment regimen is merely 14.3 %, with a high proportion of failure (25 %) and death (42.8 %) among them. Since the treatment outcome is very poor, some strains were sent to SRL, Gauting for further DST.

**Design/Methods:** This study reviewed the sputum status and the clinical judgment of 50 cases enrolled in XDR TB treatment (from 2010 to 2013). Among them, 22 samples were randomly selected and were sent to SRL, Gauting for further SLDST. The testing was performed by Conventional and MGIT of the following drugs: Ofx, Mfx, Cap, Kan, Ami, PTH, PZA, PAS, LZD, Cfz, and Cs.

Total No=22			
Resistant to	Name of Drugs	Nos.	Pts
2 drugs	PTH + PZA	1	1
3 drugs	KM+PTH+CFZ	1	2
	PZA+PAS+LZD	1	
4 drugs	Ofx+MOXI+PTH+PZA	1	2
	Ofx+PTH+PZA+CFZ	1	
5 drugs	Ofx+MOXI+PTH+PZA+PAS	1	2
	Ofx+MOXI+KM+PTH+PZA	1	
6 drugs	Ofx+MOXI+KM+PTH+PZA+CS	1	4
	Ofx+MOXI+KM+AM+PZA+CFZ	1	
	Ofx+MOXI+CAP+PTH+PZA+CFZ	1	
	Ofx+MOXI+PTH+PZA+PAS+CFZ	1	
7 drugs	Ofx+Moxi+KM+AM+PTH+PZA+CFZ	1	2
	Ofx+Moxi+CM+KM+AM+PTH+PZA	1	
8 drugs	Ofx+Moxi+KM+AM+PTH+PZA+PAS+CFZ	1	4
	Ofx+Moxi+CM+KM+AM+PTH+PZA+CFZ	2	
	Ofx+Moxi+CM+KM+AM+PTH+PZA+PAS+CFZ	1	
9 Drugs	Ofx+Moxi+CM+KM+AM+PTH+PZA+PAS+CS	1	2
	Ofx+Moxi+CM+KM+AM+PTH+PZA+PAS+CFZ	1	
10 Drugs	Ofx+Moxi+CM+KM+AM+PTH+PZA+PAS+CFZ+CS	3	3
			22

**Results:** The results showed an alarming number of resistances to the second line drugs. It was seen that there was one Linezolid-resistant strain and 3 strains with drug resistance to all tested drugs except Linezolid. Regarding the second line drugs, it was found to have a high number of resistance to Prothionamid and Pyrazinamide (90% & 95% respectively), whereas, the resistance rate to PAS

and Cycloserine were lower with 45% & 23% respectively. Meanwhile, the accordance of the ofloxacin DST and the Moxifloxacin DST was 100%.

**Conclusion:** The alarming situation is a big challenge to the management of XDR TB in Nepal. These results underline the need to detect the pattern of drug resistance in the earliest course of the disease. We do recommend the testing of the additional second line drugs before the starting of XDR treatment and the treatment regimen should be individualized depending upon the SLDST. The treatment should be done in the isolation settings.

### PD-1183-01 Multidrug-resistant tuberculosis in children in Kazakhstan

KS Serikbayeva.<sup>1</sup> <sup>1</sup>Pediatric Department, National TB Center, Almaty, Kazakhstan. Fax: (+7) 7272918658. e-mail: ncpt@bk.ru

**Setting:** The study of questions of MDR TB diagnostics in children and effectiveness of treatment with anti-TB drugs of the second line is topical for our country. Target of this study was to investigate the effectiveness of MDR TB treatment by standardized scheme in children.

**Materials and methods:** 79 patients with confirmed MDR TB from cohort of 2010–2012. Effectiveness of different methods of MDR TB diagnostics was investigated and cohort analysis of DOT therapy under standardized regimen was conducted.

**Results:** During last 15 years in Kazakhstan percentage of yearly registered pediatric TB cases decreased from 9.6% in 1999 to 4.0% in 2013. During 8 last years percentage of children among all registered MDR TB cases varied from 0.8% to 3.1% in 2013 and constituted 1.4% in 2014. Diagnostics of TB and MDR TB performs by conduction of the standard diagnostic minimum before chemotherapy start including bacterioscopy and cultural investigation of culturing on solid and liquid media including molecular genetic testing methods. Susceptibility of *M. tuberculosis* to anti-TB drugs of the first and second line. is determined. Effectiveness of the culturing constituted 15.6%, at this the resistant strains were identified in 20.2% of cases. Bacterioscopy confirmed the 8.7%, while culturing did in 32.8% among registered new cases. Contact with TB index case was stated in 60.0% of children, including MDR TB cases was the source of infection in 55.6%. Treatment is conducted by standardized scheme 6Cm+Lfx+Pto+Cs+PAS+Z/12Lfx+Pto+Cs+PAS. All the treatment is conducted under DOT regimen. In the process of the treatment symptomatic therapy is provided to cut the adverse reactions to anti-TB drugs. Analysis of effectiveness of treatment under regimen of IV category with anti-TB drugs of the 2<sup>nd</sup> line in the cohort of 2011 showed the high therapeutic effect up to 91.6%, while in 2010 it did 89.0%, 6.7% died, 1.7% were defaulters. In the cohort of 2010 outcome “treatment failure” occurred in 1.1%, that of “transferred” did in 4.4%.

**Conclusion:** Thus, at the earlier diagnostics and timely started adequate treatment of MDR TB in children it should reach to the high successful outcomes.

#### **PD-1184-01 Yield of contact investigation among multidrug-resistant tuberculosis patients from urban slums of New Delhi, India**

R Singh,<sup>1</sup> A Rawat,<sup>1</sup> V Shibu,<sup>1</sup> H Solanki,<sup>1</sup> G Srinivas,<sup>1</sup> S Sharma,<sup>1</sup> S Saini,<sup>2</sup> A Khanna.<sup>2</sup> <sup>1</sup>Public Health, German Leprosy and Tuberculosis Association India, Chennai, <sup>2</sup>RNTCP Health Department, Govt of Delhi, Delhi, India.  
e-mail: rajbir@glraindia.org

**Background:** World Health Organization recommends contact investigation for household and close contacts of MDR TB cases. It is crucial for early identification of active disease, reducing its severity and transmission to others. German Leprosy & TB Relief Association initiated a community development MDR TB home based care project to support TB services in the urban slums of New Delhi, India. This project has a key component to investigate contacts of the household members of the Multi-Drug Resistant Tuberculosis (MDR-TB) patients.

**Methodology:** The project implemented since July 2011 in urban slums of North-East and South Delhi, India. House hold contacts of 248 registered MDR-TB patients were investigated by a team of trained counselors who visited MDR-TB patient's home. A total 1034 house hold contacts were advised for screening at nearest TB clinic.

**Results:** There was an average of four family contacts per patient. Counselling was done to 92 % of contacts to be screened for TB. The contact investigation identified 28 (2.9%) Tuberculosis patients and among them 42.8% (12 out of 28) were found multi drug resistant. Median age of diagnosed cases is 21 years and men-women ratio is 60:40; majority were from lower socio-economic class. All the cases were put on appropriate regimen.

**Conclusion** The close agglomeration in urban slums resulted in high transmission. Yield of contact investigation reemphasizes the need of routine screening of contacts of MDR-TB patients. This will not only lead to early detection and timely initiation of Directly Observed Treatment Strategy interventions but prevent further transmission of resistant tuberculosis.

#### **PD-1185-01 Multidrug-resistant tuberculosis (MDR-TB) among refugees and local population in North Eastern Kenya**

A Nur Farah,<sup>1</sup> V Otieno.<sup>2</sup> <sup>1</sup>National TB and Leprosy Program, Ministry of Health, Garissa, <sup>2</sup>Africa Regional office, KNCV TB Foundation, Nairobi, Kenya.  
e-mail: ombeka@yahoo.com

**Background:** Kenya is faced with a high burden of TB and HIV with an emerging challenge of multi drug resistant TB (MDR-TB). In the North Eastern Province (NEP) of the country this is complicated by an influx of refugees mainly from the neighboring Somalia which has had a breakdown in health systems for over 20 years.

This study describes notified TB and MDR-TB rates and treatment outcomes in the local community and the refugees.

**Design/Methods:** In this descriptive study, we reviewed the patient records in registers and program reports between January 2009 and December 2013. All notified TB cases and bacteriologically confirmed MDR-TB patients diagnosed and enrolled on treatment were included. Policies for diagnosis and treatment were also reviewed. Rates were derived using the population estimates from the national bureau of statistics.

**Results:** Kenya employs passive case finding for TB among presumptive cases that present to health facilities. There is routine drug resistance surveillance which is limited to defined high risk groups (Previously treated cases, Contacts of MDR TB patients, new smear positive and new smear negative HIV positive patients). In the five year period a total of 11,302 and 2611 TB cases were notified among the locals and refugees respectively giving annual notification rates of 108 and 105 per 100,000 population respectively with an HIV co-infection 3.3% and 2.5% respectively. The proportion of retreatment cases was 6.8% and 6.5% among local and refugees respectively. There were 4 MDR-TB cases among the local population which were retreatment cases and 119 cases in the refugee group 2 of whom were new cases while the rest were retreatment cases giving an MDR-TB rate among notified cases of 0.04% and 4.6% respectively. In the 2009–2011 cohort that had finished treatment 100% were cured in the local group while 57% were cured in the refugee group with 10% completing treatment and 33% adverse outcomes.

**Conclusion:** The TB and TB-HIV co-infection rates and proportion of retreatment cases in the two groups are comparable. However there is significantly higher MDR-TB rates in the refugee population compared to the local community. The implication is that more investment in resources needs to be made in the management of MDR-TB among the refugees and more research needs to be done to identify the causes of the high MDR-TB among the refugees in order to mitigate it.



## 61. TB INFORMATION SYSTEMS: EVALUATING TREATMENT OUTCOMES

### PD-1186-01 Two third of TB cases missing in three months smear conversion report, have adverse treatment outcomes in Jharkhand India

V Ghule,<sup>1</sup> S Saruk,<sup>2</sup> R Dayal,<sup>3</sup> K Rade,<sup>1</sup> P Malik,<sup>1</sup> A Sreenivas,<sup>1</sup> B Prasad.<sup>3</sup> <sup>1</sup>TB Control Programme of India, World Health Organization country office for India, New Delhi, <sup>2</sup>Public Health, Government of Maharashtra, District General Hospital, Washim, Washim, <sup>3</sup>Ministry of Health & Family Welfare-Government of Jharkhand, State Tuberculosis Control Cell, Jharkhand, Ranchi, India.  
e-mail: ghulev@rntcp.org

**Background:** Tuberculosis (TB) is a major public health problem for Revised National Tuberculosis Control Programme (RNTCP) of India. TB patients are diagnosed and treated free under the programme. RNTCP of India notified 632 300 New Smear Positive (NSP) patients in 2012. 568 600 (90%) were sputum converted and ~52 700 (8%) were reported missing i.e. NA (Smear result Not available) while declaring sputum conversion (SC) at the end of 3 months. Smear Positive TB patients are potentially infective, but very little is known about the basic profile of such NAs at the very first and critical follow up sputum examination. This particular subset of missing NA patients aren't analysed dedicatedly in further reports. RNTCP of Jharkhand reported about 1400 (7.6%) of the 18000 NSP patients as NA in 2012. The SC Report stated 92% TB patients sputum converted. It was needed to evaluate the reported treatment outcomes of these missing TB cases.

**Design/Methods:** Jharkhand is predominantly tribal & poor geopolitical state of eastern India with 34.4 million population. This retrospective record review study of smear positive TB patients was conducted in Palamu district of Jharkhand covering 2.02 million population over July 2012 to June 2013. Data were extracted from TB treatment registers, analyzed in WIN PEPI and MS Excel software ensuring double entry. Differences between the groups were compared for statistical significance using Odd's ratio. P values less than 0.05% were considered statistically significant.

**Results:** 64% of the smear positive TB patients (reported NA in conversion) have unfavourable treatment outcomes while the parent cohort reported 8% unfavourable outcomes (O.R.19.08; 95% C.I. 12.39-29.38). 56% of the 25 deaths belong to 25-44 years age group & 84% Deaths occurred in first 3 months of treatment initiation.

**Conclusion:** Regular audits are needed for causal analysis of TB deaths. Verbal autopsy of being NA at the time of sputum conversion shall help to track and address the adverse outcomes earlier. A comprehensive understanding of patient-provider perceived barriers to adherence holds a scope of further qualitative research. This will help developing effective patient centred programme strategies to improve treatment success under TB control programme.

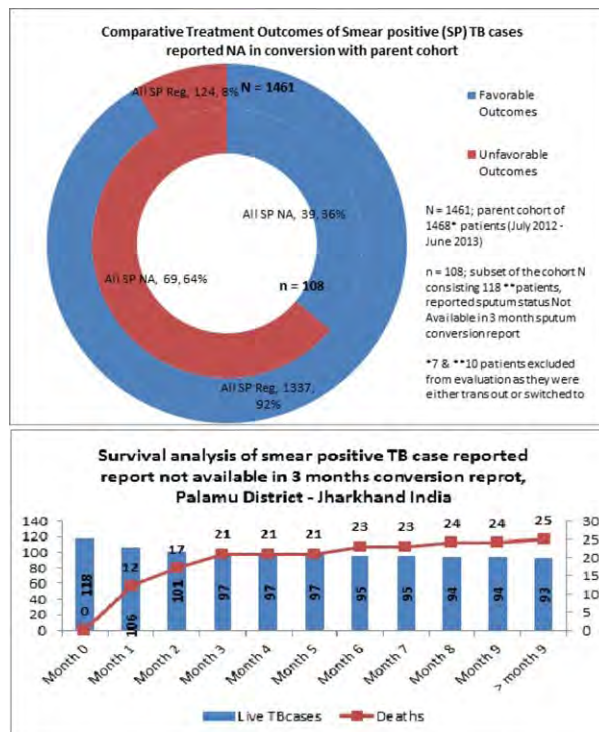


Table 1: Comparative Treatment outcome analysis of TB patients in Jharkhand-India

Study Population (July 2012 - Sep 2013)	Favourable Outcomes	Un-Favourable Outcomes	Total	Odd's Ratio
Subset cohort reported NA in conversion Report	39 (36%)	69 (64%)	108	19.08 (95% C.I. 12.39 to 29.38)
Parent cohort	1337 (92%)	124 (8%)	1461	

### PD-1187-01 Assessment of sputum microscopy monitoring in Uganda: a retrospective record review

P Nakaggwa,<sup>1</sup> R Odeke,<sup>2</sup> B Kirenga,<sup>3</sup> E Bloss.<sup>4</sup> <sup>1</sup>District Health Office, National TB and Leprosy programme, Kyankwanzi, <sup>2</sup>Health Services, US Centres for Disease Control and Prevention, Entebbe, <sup>3</sup>Medicine, Makerere College of Health Sciences, Kampala, Uganda; <sup>4</sup>Division of Tuberculosis Elimination, US Centers for Disease Control and Prevention, Atlanta, GA, USA. Fax: (+256)414321457.  
e-mail: rmodeke@gmail.com

**Background:** Monitoring of sputum results using smear microscopy at months 2 or 3, 5, and 6 or 8 during treatment of tuberculosis (TB) guides treatment decisions. However, monitoring (i.e. collection and testing) of sputum results is inconsistent in many settings. The factors related to incomplete sputum monitoring at different stages during treatment are unknown in Uganda. This study assesses the barriers to comprehensive smear microscopy monitoring for pulmonary TB patients in Uganda.

**Design/Methods:** The study was conducted in all 11 diagnostic and treatment units in Kiboga and Kyankwanzi districts. A retrospective review of TB treatment and laboratory registers was conducted for all pulmonary TB patients with positive sputum-smear microscopy results who started treatment 2009-2011. Patients with all results documented at 2 or 3, 5, and 6 or 8 months

were classified as having complete monitoring; otherwise, they were classified as having incomplete monitoring. Comparison was made between the number of sputum smears documented in TB treatment and laboratory registers. Patients with complete and incomplete monitoring were compared using odd ratios (ORs) and 95% confidence intervals (CI) in multivariate analyses. Health care providers and TB patients were interviewed about barriers to complete sputum monitoring.

**Results:** Overall, 272 (55%) of 492 patients had incomplete monitoring: 16% (78/492) at 2 or 3 months, 39% (181/465) at 5 months, and 28% (119/428) at 6 or 8 months of treatment. More sputum results were recorded in lab registers than in TB treatment registers. Incomplete monitoring was significantly associated with being from Kyankwanzi District (adjusted odds ratio [AOR] =2.0, CI=1.3-2.9), not receiving directly observed therapy (DOT) (AOR=1.6, CI=1.1-2.4), unknown HIV status (AOR=6.1, CI=1.4-27.2), and unsuccessful outcomes (AOR=2.5, CI=1.4-4.5). Patients' inability to produce sputum, long waiting times at the laboratory, and insufficient education were primary reasons reported by patients and providers for incomplete monitoring.

**Conclusion:** Incomplete sputum monitoring is common and related to poor treatment outcomes. Patients from Kyankwanzi District, not on DOT, and with unknown HIV status should be prioritized for more complete monitoring. The recording and reporting practices, the efficiency of laboratory services, and patient education must be improved.

### PD-1188-01 Improving patient treatment outcomes for tuberculosis using a iskr minimisation based approach

C Owunna,<sup>1</sup> A Kwiecien.<sup>1</sup> <sup>1</sup>Systems for Improved Access to Pharmaceuticals and Services, Management Sciences for Health, Arlington, VA, USA. Fax: (+1) 703 524 7898. e-mail: cowunna@msh.org

**Background and challenges to implementation:** All anti-TB medicines pose risks to patients, but many countries do not effectively manage known and preventable risks, which degrades treatment outcomes. The World Health Organization's TB pharmacovigilance handbook emphasizes the importance of identifying risk factors; however, most national TB control programs (NTPs) lack guidance on using low-cost risk identification approaches, and our literature review did not yield any helpful resources.

**Intervention or response:** To address this gap, we began by identifying five risk elements (adverse events, interactions, safe use indicators, drug integrity and supply chain, and chronic medicine use risk) with 25 sub-elements that affect treatment outcome. We adapted risk factors to resource-limited settings from resources including the US Food and Drug Administration's safe use initiative report and the European Medicines Agency's guidelines on good pharmacovigilance practice.

A tracer list of anti-TB medicines was selected, and package inserts and related resources were compared to known risk factors for 5 first-line and 20 second-line medicines. We quantified results with an equally weighted three-point rating scale and classified the risks by three impact levels: minor, moderate, and major.

**Results and lessons learnt:** The result of these analyses was the first risk management approach of its kind for anti-TB medicines. Preventing and Minimizing Risks Associated with Antituberculosis Medicines to Improve Patient Safety provides step-by-step instructions on developing risk-reduction strategies for TB treatment, particularly in countries with high prevalence of resistant TB. The approach describes how to identify and assess risk factors; develop and prioritize feasible interventions to improve identified risks; and implement, monitor, and evaluate activities to ensure successful mitigation interventions. At the core of this approach, which the figure illustrates, is effective communication and consultation with key stakeholders at every step of the process.

**Conclusions:** The approach provides a minimum set of criteria for assessing and introducing risk minimization strategies in resource-limited countries. It can help NTPs and pharmacovigilance professionals better manage risks associated with anti-TB medicines, save costs by preventing serious complications, and improve treatment outcomes and patient safety.

Figure1: Approach to Preventing and Minimizing Medicine Safety Risk



### PD-1189-01 Efficacy and safety of intensive intravenous chemotherapy using port-catheter in patients with MDR- and XDR-TB

S Cherenko,<sup>1</sup> N Lytvynenko,<sup>1</sup> O Reva,<sup>1</sup> O Hmel,<sup>1</sup> R Veremeenko,<sup>1</sup> M Pogrebna,<sup>1</sup> Y Senko.<sup>1</sup> <sup>1</sup>MDR TB, SO <<(National Institute of Phthisiology and Pulmonology named after F. G. Yanovsky NAMS of Ukraine)>>, Kyiv, Ukraine. e-mail: sprynsian@uf.ua

**Background and purpose.** To study the efficacy and safety of intensive intravenous chemotherapy with port-catheter for continuous intravenous infusion in patients with MDR and XDR TB.

**Materials and methods.** In a controlled study we compared the efficacy and safety of intensive 7-

component anti-TB chemotherapy regimens. In the main group (16 patients with MDR or XDR TB) 3 anti-TB drugs (moxifloxacin, PAS, linezolid) were administered via port-catheter for intravenous application. In the control group which was formed by a pair-matching method (according to the drug resistance profile) the same intensive chemotherapy regimens were used, and mentioned drugs were administered by daily IV infusions. In each group patients with relapses dominated (87.5 %). The duration of intravenous therapy course was 2–4 months.

**Results.** In the main group no cases of premature discontinuation of the infusions, no manifestations of phlebitis or complaints of pain in the injection site were observed, and only in 12.5% patients hematoma after setting port-catheter developed. All patients in the control group had complaints of pain and hematoma at the site of injection, in 43.7% phlebitis developed (due to impossibility to penetrate the vein in 56.2% patients) which caused the interruption of intensive intravenous treatment. At the end of the intensive phase of chemotherapy sputum conversion and disappearance of clinical symptoms were noted in 15 patients (93.7%) of the study group that was 26.7% higher vs. control ( $p > 0.05$ ). Time to sputum conversion in the main group was significantly better vs. control ( $2.2 \pm 0.1$  vs.  $3.7 \pm 0.3$  months, respectively).

**Conclusions.** Port-catheters is a safe and effective method to provide long-term daily intravenous anti-TB therapy. It was not accompanied by subjective patients' complaints and the development of phlebitis. In the control group where usual fashion daily IV infusions were provided 56.2% patients prematurely discontinued treatment through intensive local complications or phlebitis. Application of intensive treatment with the introduction of anti-TB drugs through the port-catheter allows to achieve more quickly sputum conversion.

#### PD-1190-01 Outcome and treatment among patients with multidrug-resistant tuberculosis in Spain

M Ramírez Lapausa,<sup>1</sup> J Pascual Pareja,<sup>1</sup> R Carrillo Gómez,<sup>1</sup> M Martínez Prieto,<sup>1</sup> MJ Jaras Hernández,<sup>1</sup> C García Cerrada,<sup>1</sup> A Noguero Asensio.<sup>1</sup> <sup>1</sup>Internal Medicine, Cantoblanco-La Paz Hospital, Madrid, Spain. e-mail: mrlapausa@yahoo.com

Multidrug-resistant tuberculosis (MDR-TB) is difficult and costly to treat. Prompt diagnosis and an adequate MDR-TB treatment with the use of directly observed treatment (DOT) are important strategies to control this disease. **METHODS** A retrospective study was performed to review the demographic and clinical characteristics, drug-resistance patterns and treatment outcome of MDR-TB patients in Madrid. During 16-yr period (from January 1998 through March 2014), all the patients diagnosed with pulmonary MDR-TB who were attended to in Cantoblanco-La Paz Hospital Isolation Internal Medicine Unit, were enrolled. **RESULTS** A total of 58 patients were identified with a mean age of 36 yrs.

66% were immigrants. Thirty-three patients (57%) were diagnosed as a new MDR-TB case. The isolated strains were resistant to a median of 4 drugs (RIQ 3–6.25), 3 patients had extensively drug-resistant tuberculosis. 55 patients began treatment in the Isolation Unit. The patients received a median of 5 induction drugs (RIQ 5–5) and 4 (RIQ 4–4) maintenance drugs. 53 patients (96%) received an appropriate aminoglycoside and 51 (93%) received fluoroquinolone. The patients received an aminoglycoside for a mean period of 4 months (RIQ 3–6.4). Cultures became negative after a median of 2.4 months (RIQ 1.9–3.1). The median length of hospitalization was 2.93 months (RIQ 2.1–4.7). They were treated during a median of 24 months (RIQ 16.4–24.4). 55 patients began treatment in the Unit, 5 were transferred to another hospital and 5 are awaiting treatment completion. The outcome assessment comprised of 45 patients, among whom 43 (96%) were cured or completed treatment, 1 died and 1 experienced treatment failure. DOT was carried out on 92% of patients. 42 patients (76%) had some adverse events. We recorded a total of 86 adverse effects. In 80% of the cases the effects were mild and moderate and did not need to discontinue the drug. The drug events more frequently observed were nausea in 22 patients (40%), arthralgias in 12 (22.8%), hepatitis in 10 (18.2%) and deafness in 7 (12.7%). 26 patients were followed up for a median of 12.5 (RIQ 6.6–43.5) and no clinical or bacteriological manifestation of disease was detected. **CONCLUSIONS** Early appropriate and intensive regimens treatment, comprising at least 4 effective drugs with fluoroquinolone and aminoglycoside, aggressive management of side effects and set up strategies to improve adherence to treatment, may improve the outcome for patients with MDR-TB.

#### PD-1191-01 Validated methods for identifying tuberculosis cases in health administrative databases: a systematic literature review

L Ronald,<sup>1,2</sup> D Ling,<sup>3</sup> JM Fitzgerald,<sup>2,4</sup> K Schwartzman,<sup>1,5</sup> JF Boivin,<sup>1</sup> G Bartlett-Esquillant,<sup>6</sup> A Benedetti,<sup>1,5</sup> R Menzies.<sup>1,5</sup> <sup>1</sup>Epidemiology, Biostatistics and Occupational Health, McGill University, Montreal, QC, <sup>2</sup>Centre for Clinical Epidemiology and Evaluation, Vancouver Coastal Health Research Institute, Vancouver, BC, <sup>3</sup>Clinical Prevention Services, BC Centre for Disease Control, Vancouver, BC, <sup>4</sup>Institute for Heart and Lung Health, University of British Columbia, Vancouver, BC, <sup>5</sup>Respiratory Epidemiology and Clinical Research Unit, Montreal Chest Institute, Montreal, QC, <sup>6</sup>Department of Family Medicine, McGill University, Montreal, QC, Canada. e-mail: ronaldal@shaw.ca

**Background:** Health administrative databases are generated through the routine administration of health care programs and record patients' contact with the health-care system. Strengths of such databases include the ease and low-cost of obtaining large datasets, near-complete coverage of the population, and reduced risk of selection bias compared to many primary data collection studies. An increasing number of studies are using health administrative databases for tuberculosis (TB) research



and surveillance, but few studies have reported on the accuracy of TB case definitions in such databases. Our objective was to conduct a systematic review of studies which have validated TB case definitions in health administrative databases

**Design/Methods:** We conducted a systematic review in two databases (Ovid Medline and Embase). We limited the search to diagnostic accuracy studies assessing drug prescriptions, diagnostic codes (International Classification of Disease, ICD codes) and procedure-based algorithms for identifying cases of active TB in health administrative databases. We evaluated studies for potential bias using the QUADAS-2 quality assessment tool for diagnostic accuracy studies.

**Results:** The search identified 717 unique citations. We accepted 25 for a full-text review, and 10 were included in our study. Diagnostic accuracy estimates varied widely across studies: positive predictive value (PPV) ranged from 1.3% to 100%, and sensitivity ranged from 20% to 100%. The most frequent reasons for false positive identification of active TB cases were non-tuberculosis mycobacteria (NTM), suspected (but not confirmed) TB, and latent TB infection (LTBI). More rigorous drug prescription-based algorithms to identify active TB, including 3 or more TB drugs, a marker to distinguish TB from NTM cases such as a prescription for pyrazinamide or a macrolide, and inclusion of a minimum treatment duration rule, provided the highest PPV measures.

**Conclusion:** Health administrative databases may be useful for TB research and surveillance, but more work is needed to validate case identification algorithms in different settings. Sole use of ICD codes to identify active TB cases in health administrative databases is likely to overestimate case numbers, particularly when including non-hospitalized populations.

#### PD-1192-01 Result of five years' experience of TB control services in central highland of Afghanistan

A Hamim,<sup>1</sup> MA Hemmat,<sup>2</sup> J Ahmad,<sup>2</sup> GA Ali Madad,<sup>3</sup> G Qader,<sup>1</sup> AA Mohammad,<sup>2</sup> D Ehsanullah,<sup>4</sup> F Habibuddin.<sup>4</sup> <sup>1</sup>TB CARE I, Management Science for Health (MSH), Kabul, <sup>2</sup>Leprosy Control (LEPCO), TB Department, Kabul, <sup>3</sup>Bakhtar Development Network, Baghlan, <sup>4</sup>Ministry of Public Health, National TB Control Programme, Kabul, Afghanistan. e-mail: ahamim@msh.org

**Background:** Afghanistan is one of 22 high burden TB countries with annual estimated prevalence of 358, incidence of 189 and death of 37 in 100,000 populations. In 2013, the case notification rate for all TB cases was 111 in 100,000 populations and treatment success rate of 90%. Almost 1,197 health facilities running TB control service in Afghanistan, and LEPCO is a German organization which assists NTP Afghanistan to achieve its strategic objectives on increasing access to TB services since 1998. LEPCO supports only TB and Leprosy services through nine clinics in five provinces by fix, campaign and active case finding at community level and

training of community volunteers. We assessed LEPCO's contribution on TB services from 2009 - 2013.

**Methodology:** This was a cross sectional study conducted between January–March 2014, we used the standard NTP recording and reporting formats as data collection tool. The technical teams from NTP/TB CARE collected and reviewed the data of 2009–2013 on TB case notification, conversion and cure rate.

**Results:** From January 2009 to December 2013, LEPCO was able to notify a total of 4,544 new sputum smear positive TB patients (1,788 male and 2,756 female) and it makes 10% of all SS+ cases identified all over Afghanistan. Out of them; 4,180 (92%) cases converted to sputum smear negative. Also, 3,421 smear positive cases (2009–2012) were put on treatment, out of them 3,113 (91%) patients cured {female (92.4%) and male (89.6%)}. In addition to above results, the contribution of LEPCO in TB services delivery is significantly important in Afghanistan because by running of 9 clinics out of 1,197 clinics in the country, LEPCO were able to notify almost 10% of all TB cases country wide.

**Conclusion:** This study discovered that LEPCO's interventions improved access to TB services in remote areas of Afghanistan and resulted in early case detection and improved cure rate. Thus, we strongly recommend the replication of this approach to other similar challenging settings.

Table: Result of five years TB control services in central highland of Afghanistan

Indicators/ Year	2009	2010	2011	2012	2013
No. of health facilities covered by DOTS (#)	9	9	9	9	9
No. of TB suspects identified/examined (#)	3,326	4,550	6,101	6,633	7,445
No. of new sputum smear positive cases notified (#)	609	740	988	1,011	1,196
Conversion rate of sputum smear positive cases (%)	85	86	88	92	92
Treatment cure rate of new sputum smear cases	85	87	89	90	91

#### PD-1193-01 From paper to digital: developing online TB information system in the largest archipelago country, Indonesia

DE Mustikawati,<sup>1</sup> Sulisty,<sup>1</sup> H Suryani,<sup>1</sup> C Natpratan,<sup>2</sup> R Palupy,<sup>2</sup> T Haryanto,<sup>1</sup> PN Wastu,<sup>2</sup> D Supriyadi.<sup>3</sup> <sup>1</sup>TB Sub-directorate, Ministry of Health Republic Indonesia, DKI Jakarta, <sup>2</sup>Clinical Services Unit, FHI 360 Indonesia, DKI Jakarta, <sup>3</sup>TB Program, WHO Indonesia, DKI Jakarta, Indonesia. e-mail: riniwpalupy@gmail.com

**Background:** Timely TB report with data quality is the challenge in Indonesia. Manual paper-based reporting system that has been used took TB staff's times to validate. The evolution of TB information system in Indonesia started in 2000 with transforming manual paper-based reporting into electronic reporting. In 2011, National TB Program (NTP), with assistance from TB CARE I/USAID, led the development of TB information system and collaborated with National Data Center of

Ministry of Health (MOH). National Data Center is responsible for integrity of data infrastructures.

**Intervention:** In 2000, TB reporting was designed in Excel-based (TB.03 Elektronik) and used by TB staff in district health offices to collect data. However, Excel has limitation to respond to complexity of TB data. In 2011, NTP led the design of electronic TB information system. The system is known as SITT (Integrated TB Information System). The SITT Phase 1 (2011–2013) emphasized on shifting of TB.03 elektronik data into web-based ([www.sitt.depkes.go.id](http://www.sitt.depkes.go.id)). Phase 2 started to develop in year 2013 emphasized on web-based system for data entry of TB cases, planning and stock of first line anti-TB drugs, data quality assurance of TB laboratory, and basic data about resources from health facilities that are implementing DOTS. SITT Phase 2 can be linked to data in E-TB manager, where PMDT data is recorded. Trainings and coaching were conducted to TB staff in provinces and districts

**Results:** SITT officially used in January 2013 by 33 provinces. SITT has changed the role of data entry from district TB staff to health facilities. Thus, the facility staff are encouraged to utilize their data. Still, some health facilities have obstacles to use or access to computer, TB staff in district level will continue to do data entry. A step wise adoption plan of SITT is needed and it will depend on the condition in each district and province. SITT shortens the time of data validation and sending report. While TB staff entry the data, software will do validation. Every time TB data is submitted into SITT in online mode, TB reports will automatically generate and can be assessed by TB team from district up to national level in the same time

**Conclusions:** SITT is the system that helps NTP to validate, collect, and store the data; before the data is analyzed. NTP continues to improve TB information system, particularly with the adoption on revision definitions and reporting framework for tuberculosis

#### PD-1194-01 Tuberculosis burden estimation using capture-re-capture study, Sitamarhi, India

K Rade,<sup>1</sup> S Jha,<sup>1</sup> N Kulshreshta,<sup>2</sup> R S Gupta,<sup>2</sup> K N Sahai,<sup>3</sup> P Malik,<sup>1</sup> BK Mishra,<sup>3</sup> A Sreenivas.<sup>1</sup> <sup>1</sup>Country Office for India, World Health Organization, New Delhi, <sup>2</sup>DGHS/MOHFW, Central TB Division, New Delhi, <sup>3</sup>Government of Bihar, State TB Cell, Department of Health and Family Welfare, Patna, India. e-mail: [drkiranrade@gmail.com](mailto:drkiranrade@gmail.com)

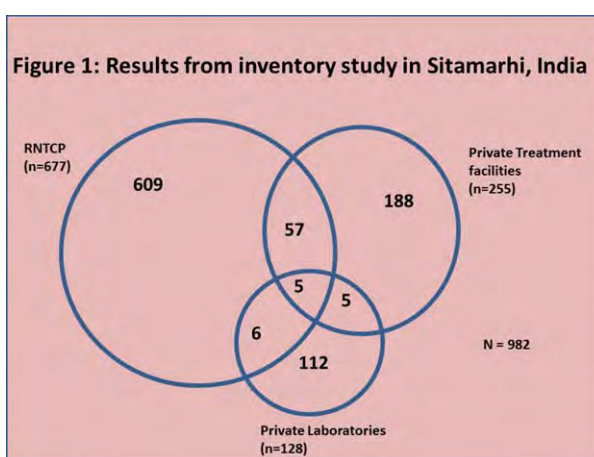
**Background:** Every fourth Tuberculosis patient being Indian, every eighth TB patient in the world is treated by private health sector in India. However, in the absence of precise estimates of TB burden, it is difficult to assess how many cases are outside the Revised National Tuberculosis Control Programme (RNTCP). Mandatory notification of all tuberculosis cases by each health facility and deployment of case based online surveillance system (Nikshay) for notification in India has given the platform to mount inventory studies.

**Design/Methods:** Retrospective inventory study with objective to quantify number of TB cases using capture-

re-capture technique in Sitamarhi district (population 3.5 million) in north India. All public and private health facilities were line listed. Officials and staff were sensitized with assistance from district health authorities and professional bodies. Health facilities were registered and followed up with standard notification format. Data collected by programme staff visiting each health facility at least weekly. Patient details were entered in Nikshay to create a database of all notified TB patients. Name alike function, Sex and Age  $\pm 5$  years were used to identify overlap in three databases of TB patients notified by public health facilities, private laboratories and private treatment facilities during August to December 2013. Additionally, all databases were checked manually to ensure complete deduplication.

**Results:** All 39 public health facilities and 261 private health facilities (22 laboratories, 239 treatment facilities) agreed for notification and participated in study. 168(56%) health facilities did not diagnose or treat any TB case. Total 982 cases were notified with total overlap of 7.6%. RNTCP notified 677(69%), Private practitioners notified 255(26%) and private laboratories notified 128(13%) cases. Using Chao et al.'s sample-coverage method for three independent sources, total 3514 (3399–3632) cases were estimated. 2417(73%) of total estimated cases were not captured by either of three systems.

**Conclusion:** With RNTCP performance of less than 33% of case detection and huge proportion (>73%) of cases not captured by either source; it plausible that considerable number of patients either are not seeking health care or seeking care from private sector outside the district. In either case, RNTCP need to strategize large scale health behavioral change towards universal access. .



### PD-1195-01 Impact of data completeness on reaching the 85% target for tuberculosis treatment success in the EU/EEA

B Karo,<sup>1</sup> Vahu Hollo,<sup>2</sup> B Hauer,<sup>1</sup> L Fiebig,<sup>1</sup> M Van Der Werf,<sup>2</sup> W Haas.<sup>1</sup> <sup>1</sup>Infectious Disease Epidemiology, Robert Koch Institute (RKI), Berlin, Germany; <sup>2</sup>Tuberculosis Program, European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden. Fax: (+49)30187543341. e-mail: karob@rki.de

**Background:** Very few EU/EEA countries achieved the 85% target of treatment success rate (TSR). In this study we analyzed the TB treatment outcome (TO) in the European Union and European Economic Area (EU/EEA) over a 10-year observation period and assessed the impact of data completeness on reaching the TSR target. **Methods:** We performed a descriptive analysis of data reported to the European Surveillance System (TESSy) between 2002 and 2011. In line with ECDC definitions, the cohort eligible for our analysis included new culture-confirmed pulmonary TB cases. Countries who did not report on TO for the whole study period were excluded. **Results:** Eighteen Member States reported information on TO for all years of the observation period. A total of 250,854 new culture-confirmed pulmonary TB cases were eligible for the TO analysis. The overall TSR was 78.2%. About 6.5% died while being treated for TB and 2.4% were still on treatment at the end of the 12-month follow-up. The proportion of cases with unsuccessful outcome was 8.9% (including 2.2%, with treatment failure, 5.7% had defaulted and 1.0% was transferred). Cases with unknown TO accounted for 4.0%. Analysis of trends shows that TSR increased from 75.4% in 2002 to 79.8% in 2006 ( $P=0.04$ ), but subsequently decreased to 76.6% in 2011 ( $P=0.07$ ). The proportion of cases with unknown TO showed a revers pattern, decreasing from 7.0% in 2002 to 2.6% in 200, then increased significantly to 4.5% in 2011 ( $P=0.04$ ). After excluding the cases with unknown TO, the TSR increased to be 81.4%. Patients of national origin had a higher proportion of death (6.9% in nationals vs. in foreigners) and treatment failure (2.7% in nationals vs. 0.2 in foreigners). In nationals also the proportion with advanced age was higher (patients aged >64 years accounted for 17.2% in nationals vs. 10.8% in foreigners). The TSR was slightly higher among nationals (78.7%) than foreigners (77.3%). After excluding cases with unknown outcome, the TSR in foreigners (82.8%) became higher than nationals (81.1%).

**Conclusion:** Missing information on TO remains a challenge in monitoring TB control in the EU/EEA. Our data showed that the proportion of cases with unknown TO has a strong impact on TSR and is potentially leading to underestimation of treatment success. Therefore, strengthening TO monitoring, particularly minimizing the proportion of cases with unknown outcome is a key element to reach the 85% target of treatment success in EU/EEA.

### PD-1196-01 Are patient data captured electronically under the national TB programme in Maharashtra, India quality-assured?

S Dapkekar,<sup>1</sup> A Kumar,<sup>2</sup> K Rade,<sup>1</sup> N Wilson,<sup>3</sup> A Jacob,<sup>2</sup> N Kulshreshtha,<sup>4</sup> M Pawar,<sup>5</sup> A Sreenivas.<sup>1</sup> <sup>1</sup>Tuberculosis, World Health Organization Country Office for India, New Delhi, <sup>2</sup>Research, The Union, South-East Asia Regional Office, New Delhi, <sup>3</sup>Public Health, Independent Public Health Consultant, New Delhi, <sup>4</sup>Central TB Division, Directorate General of Health Services, India, New Delhi, <sup>5</sup>State TB Office, Directorate of Health Services, Pune, India. e-mail: drshankardapkekar@gmail.com

**Background:** To improve the efficiency of recording and reporting under the national tuberculosis programme in India and enable real-time surveillance and patient monitoring, an electronic, case-based web-based system named "NIKSHAY" was introduced in 2012. Under this, patient-wise data of all TB patients registered are transcribed from the treatment card (paper-based) into NIKSHAY electronic database by health staff at district or sub-district level. Concerns have been raised about the possibility of data entry errors and the same has not been systematically studied yet. In this operational research from six districts of Maharashtra State, we aimed to determine the number (proportion) of records with data-entry errors.

**Methods:** In this cross sectional study, we compared the data of patients registered during January-March 2013 in NIKSHAY electronic database with that in the treatment card (gold-standard) with respect to selected demographic and disease related variables.

**Results:** There were a total of 2383 TB cases registered in the study period as per NIKSHAY. After omitting multiple entries for the same patient (69) and accounting for missing entries (53), data were available for 2261 TB Patients which could be compared with treatment cards. Of them, 659 (29%) had data-entry errors in any one of the variables (see Table). The extent of data-entry errors varied with each variable – age (10%), sex (4%), type of TB (5%), site of disease (7%), category of treatment (3%) and pre-treatment sputum microscopy results (9%).

**Table:** Proportion of records with data-entry errors among TB Patients registered in six districts of Maharashtra from January to March 2013 (N=2261)

Variables	Number (%) of records with discordance
Total Records	659 (29)
Age	234 (10)
Sex	91 (4)
Type of TB	124 (5)
Site of disease	159 (7)
Treatment category	62 (3)
Pre-treatment sputum microscopy result	201 (9)

**Conclusion:** It is concerning to note that nearly three in ten patient-records in NIKSHAY had data entry errors in study population. Using this data could lead to errors in decision making at patient and programmatic levels. Steps to address this need to be taken which include



creating internal quality checks to prevent duplicate entries, intensifying supervision and monitoring by programme staff and regular validation, considered a benchmark in ensuring data quality. We intend to examine the reasons for errors and challenges involved in data entry using qualitative methods in future.

### PD-1197-01 A brief review of remote monitoring tools for GeneXpert MTB/RIF: initial Implementation of GxAlert in Mozambique

J Cowan,<sup>1,2</sup> I Manhiça,<sup>3</sup> C Michel,<sup>2</sup> C Macek,<sup>4</sup> C Jacob,<sup>5</sup> E Jezierski,<sup>6</sup> S Gloyd.<sup>1,2</sup> <sup>1</sup>Global Health, University of Washington, Seattle, WA, <sup>2</sup>Mozambique, Health Alliance International, Seattle, WA, USA; <sup>3</sup>National Tuberculosis Program, Mozambique Ministry of Health, Maputo, Mozambique; <sup>4</sup>GxAlert, SystemsOne, Cambridge, MA, USA; <sup>5</sup>TB REACH, WHO, Geneva, Switzerland; <sup>6</sup>CEO, InSTEDD, Seattle, WA, USA. e-mail: jcowan22@uw.edu

**Background and challenges to implementation:** Mozambique is one of the 22 high burden tuberculosis (TB) countries that are in the process of scaling up GeneXpert MTB/RIF implementation in an effort to improve TB case-detection. In April, 2014 there were 18 Xperts in Mozambique, but there was no effective remote monitoring tool in place to aggregate testing results from all Xpert sites, to create monthly/quarterly M&E reports, to quickly communicate key results to providers, or to help manage the relatively valuable Xpert cartridge inventory. **Intervention or response:** We evaluated 3 remote monitoring platforms (compared in table 1) currently or soon to be available for GeneXpert MTB/RIF: Cepheid Remote Monitoring, XpertSMS, and GxAlert. Cepheid plans to release a remote monitoring tool in October, 2014. XpertSMS was developed by Interactive Health Solutions. GxAlert was developed by SystemsOne.

**Results and lessons learnt:** Cepheid's system integrates the best with the Xpert platform and will provide Cepheid with performance data if there are problems with any machines, but in the first iteration will not transmit fields that could contain patient identifying information. XpertSMS is particularly attractive when paired with electronic medical record system that can follow patients over time. However, Mozambique does not currently have a universal EMR system and would like to collect patient identifying information. Thus we chose to pilot GxAlert on 5 Xpert machines in Central Mozambique. Initial installation was moderately complex. Once installed, new Xpert test results are uploaded daily anytime the Xpert computer is connected to the internet via a USB modem or Ethernet. Test results are accessed by logging in online through gxalert.com where they are analyzed and filtered through a series of intuitive dashboards. Automated SMS or email messages can be sent to predefined contacts.

**Conclusions and key recommendations:** Remote monitoring and notification tools have the potential to be part of the backbone for the next generation of TB control strategies in developing countries. Current platforms are in their first generation, but already significantly improve

M&E and patient care. However, issues of patient confidentiality, secure data transmission and storage, reliable and constant internet connections, unique identifiers for patients, and long term sustainability from a financial and human resource perspective remain significant challenges and need to be improved.

Table 1. Comparison of 3 Remote Monitoring Tools for GeneXpert MTB/RIF

Product Features	Cepheid Xpert Remote Monitoring Tool*	XpertSMS	GxAlert
Secure Data Transmission and storage	Yes	Yes	Yes
Location of data server	Private Cloud	Cloud or in-country server	Cloud server – possible in-country in the future
Ability to Transmit Patient Identifying Data**	No (per current plan)	Yes	Yes
Uploads data automatically once connected to the internet	Yes	Yes	Yes
Compatible with OpenMRS EMR	No	Yes	No***
Supports automated SMS to Health Care Providers	No	Yes, if used with OpenMRS or other EMR	Yes
Allows uploading of data from different diagnostic companies	No	Yes	Yes
Can be configured to generate automatic reports	Yes	Yes, if used with OpenMRS or other EMR	Yes
Availability	Oct, 2014	Now	Now
Estimated cost	Free to low income countries, charge for middle and high income countries	Software is open source and free, additional fees for formal tech support if desired	Modest fee for initial pilot, costs not yet available
Developed by a Third Party Relative to Cepheid	No	Yes	Yes
Requires internet connection	Yes	Yes****	Yes
Results automatically uploaded when internet is connected	Yes	Yes	Yes
Xpert Cartridge Inventory Management Tool	Possibly*****	No*****	Yes

Allows downloading of all patient and test results into excel or csv file	No	Yes	Yes
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\*Not currently available. Data regarding Cepheid Remote Monitoring system based on personal communication with platform developer and Cepheid data management team.

\*\*Allows for upload of data from Patient ID, Sample ID or Notes field. Patient ID could be entered in this field, but is not always (one can use a unique patient identifying number).

\*\*\*One can develop a system for GxAlert to communicate with electronic medical records

\*\*\*\*XpertSMS allows for actual sending of results to server either from SMS or internet

\*\*\*\*\*But inventory management could also be done outside the system

## 62. TB IN SPECIAL POPULATION: RISKY PLACES AND OCCUPATIONS

### PD-1198-01 Role of DOTS Corner at tertiary level hospitals in identifying TB cases and their referral

M Akramul Islam,<sup>1</sup> S Islam,<sup>1</sup> S Munim,<sup>1</sup> M.M. Rahman,<sup>2</sup> K Fatema,<sup>1</sup> K Afsana.<sup>1</sup> <sup>1</sup>HNPP, BRAC, Dhaka, <sup>2</sup>TB, NTP, Dhaka, Bangladesh. e-mail: shayla.dhaka@gmail.com

**Background and challenges to implementation:** BRAC a development organization has been implementing community based TB control programme since 1984. Currently the organization is providing DOTS services in collaboration with national tuberculosis control programme (NTP) to 42 districts & different city corporations covering 93 million populations. BRAC has established 27 DOTS Corners in different tertiary level hospitals (both public and private) under the leadership of NTP. It enabled linkage with the health professionals of the hospitals to detect all types of tuberculosis cases specially smear negative, extra-pulmonary and child TB. An effective mechanism is essential for referral of diagnosed TB patients at peripheral DOTS centers and to ensure better treatment outcome.

**Intervention or response:** Presumptive tuberculosis patients reported at hospitals (both in-door and out-door) are referred to the hospital laboratory for diagnosis. After completion of diagnosis, TB patients resides closely to the hospital are registered and treated at the hospital DOT's corner. Free anti TB medicines supplied from NTP are given to the admitted TB patients without registration and discharging patients are referred to the peripheral DOTS centers according to patients' convenience. Proper counseling during referral is done so that the patient can report at referral center in time. Orientation sessions are held at hospital premises for intern doctors engaging the specialized clinicians from different department.

**Results and lessons learnt:** In 2012, A total of 3021 smear positive, 2592 smear negative, 6469 extra-pulmonary and 940 child TB cases diagnosed from different tertiary level hospitals which are 4%, 21%, 43% and 38% of all smear positive, smear negative, extra-pulmonary and

child TB cases diagnosed respectively in BRAC supported areas. In 2013, a total of 11,728 new TB cases diagnosed in these hospitals; among them 10,496 (89%) were referred to different peripheral DOTS centers for treatment.

**Conclusions and key recommendations:** Availability of diverse diagnostic facilities for TB and involvement of specialized health professionals enhanced the detection of smear negative, extra-pulmonary and child TB cases in tertiary level hospital. Proper referral and treatment of those patients are essential for universal DOTS coverage.

### PD-1199-01 Distinct modes of transmission of tuberculosis in aboriginal and non-aboriginal populations in Taiwan

Y-Y Chen,<sup>1</sup> F-C Tseng,<sup>1</sup> J-R Chang,<sup>1</sup> S-C Kuo,<sup>1</sup> J-J Lee,<sup>2</sup> J-J Yeh,<sup>3</sup> T-S Chiueh,<sup>4</sup> J-R Sun,<sup>4</sup> I-J Su,<sup>1</sup> H-Y Dou.<sup>1</sup>

<sup>1</sup>National Institute of Infectious Diseases and Vaccinology, National Health Research Institutes, Zhunan, Miaoli,

<sup>2</sup>Department of Microbiology, Hualien Tzu Chi Medical Center, <sup>3</sup>Department of Medical Research, Pingtung Christian Hospital, Pingtung, <sup>4</sup>Division of Clinical Pathology, Department of Pathology, Tri-Service General Hospital and National Defense Medical Center, Taipei, Taiwan.

e-mail: yihyuanchen@nhri.org.tw

**Background** Tuberculosis incidence amongst aborigines is 4- to 6-fold higher than for Han Chinese in Taiwan, but the extent to which *Mycobacterium tuberculosis* (MTB) strain characteristics and associated factors such as drug resistance patterns and clustering rates contribute to this difference is not well understood.

**Methods** MTB isolates from aboriginal and Han Chinese patients of two referral hospitals in eastern and southern Taiwan were analysed by spoligotyping and 24-loci MIRU-VNTR. Drug resistance was tested by the agar proportion method.

**Results** In eastern Taiwan, 60% of aboriginal patients were < 20 years old, significantly younger than the non-aboriginal (Han Chinese) patients there; aborigines were more likely to have clustered MTB isolates than Han Chinese (odds ratio (OR) = 5.98, p < 0.0001). In southern Taiwan, 50% of both ethnic groups (aborigine and Han Chinese) were older than 70 years; clustering rates between the two groups were similar (OR = 0.56, p = 0.19). MTB lineages with high clustering were EAI (59.7%) amongst southern Han Chinese, and Beijing (62.5%) and Haarlem (52.9%) amongst eastern aborigines, in which 5 of 8 and 5 of 5 clusters, respectively, involved patients < 20 years old. Whilst all clustering from southern aborigines also included Han Chinese, 5 of 14 clusters in the east were exclusively within aborigines. Resistance to first-line drugs and multidrug resistance (MDR) were significantly higher amongst eastern aborigines (> 15%) than in any other geographic and ethnic groups (p < 0.05); MDR was detected in 5 of 28 eastern aboriginal patients < 20 years old. Amongst patients from the eastern region, clustered strains (p = 0.01) and aboriginal ethnicity (p = 0.04) were independent risk factors for MDR.

**Conclusion** Patient age, MTB genetics and drug resistance profiles differed substantially by location and ethnicity. Significantly higher strain-clustering and MDR in eastern aborigines, especially amongst the youth, highlights weak TB control that warrants concentrated prevention strategies targeted towards this group.

#### PD-1200-01 TB screening in Bangladeshi garments workers

K Talukder.<sup>1</sup> <sup>1</sup>Department of Paediatrics, Centre for Woman and Child Health, Savar, Bangladesh.  
e-mail: khurshidtalukder@yahoo.co.uk

The garments industry is arguably the leading contributor to the rapid transformation of Bangladesh from a low to a middle-income country. The country's garments workers are however extremely vulnerable to tuberculosis because they are poor migrants working and living under crowded conditions. A study published in the Bangladesh Medical Research Council Bulletin in 2000 estimated pulmonary TB in RMG workers at 960 per 100,000 and a 2012 IJTLD paper estimated sputum positivity at 300 per 100,000 RMG workers in 2008-10. These figures were 3-4 times the national estimates at the time. Such high levels of TB in a vulnerable population led the Centre for Woman and Child Health (CWCH) in Bangladesh to design and implement a comprehensive garments TB screening and detection programme under TB Reach Wave 3 funding. Between April 2013 and September 2014 the CWCH plans to screen approximately 500,000 garments workers working in 500 factories in Savar/Ashulia, Dhaka – the garments heartland of Bangladesh. This work is being carried out under NTP stewardship. The CWCH team of 15 screening personnel and one doctor enters a garments factory with a mobile chest x-ray bus in the morning. In the course of the day these 15 screening personnel walk down the production lines and ask each of about 1,500 – 2,000 workers about 11 key features of TB including “cough for more than 3 weeks”. If a worker answers positively to either the 3 wk question or any three or more of the remaining questions, he/she is referred to the on-site CWCH team doctor who takes a more detailed history, examines the worker and orders a chest x-ray and/or sputum for AFB microscopy. The x-ray is done in the mobile x-ray bus and the sputum is collected at the factory and transported to the CWCH laboratory for AFB microscopy and Gene Xpert testing if necessary. The first year of this programme between the 8<sup>th</sup> of April 2013 and the 31<sup>st</sup> of March 2014 has resulted in screening for TB in 2,14, 094 garments workers, with detection and notification of 311 cases i.e. 145 all case detections per 1,00,000 workers. This rate of detection is much lower than the “estimated” national incidence of 220 all cases per 1,00,000. The sputum positive detections were also very low – 110 cases among 2,14,094 workers – i.e. 51.4 per 1,00,000. The Bangladesh Nationwide Tuberculosis Disease-cum-infection Prevalence Survey from 2007-09 showed an overall

adjusted prevalence of new smear-positive TB of 79 per 1,00,000 adult population.



#### PD-1201-01 TB intervention among prisoners in India

B Entoor Ramachandran,<sup>1</sup> S Chadha,<sup>1</sup> K Sagili.<sup>1</sup>

<sup>1</sup>Tuberculosis, International Union Against Tuberculosis and Lung Disease (The Union), New Delhi, India. Fax: (+91) 11 4605 4430. e-mail: ebaru@theunion.org

**Background:** Tuberculosis is an airborne disease and commonly spreads through close and prolonged contact with a smear positive TB patient. Given this scenario, the inmates in “Prisons” are at utmost risk of acquiring TB infection in a closed environment. Inmates of prisons are a moving population. They come to prison from community and go back to community or are transferred to other prisons. Evidence about TB prevalence in Prisons in India is limited.

**Intervention:** ‘Project Axshya’ (TB Free) is trying to engage all sectors to strengthen TB care and control in 300 districts across 21 states of India. Project Axshya is committed to serve Vulnerable and Marginalised with required TB services with support of Revised National Tuberculosis Control Programme (RNTCP). Project Axshya aimed “TB Care and Control among Prisoners” in all 300 Districts through a sensitization of prison staff and inmates during the period July – December 2013.

**Results:** Situation analysis findings - Project team tried to collect information from all 21 States and 300 Districts. Information was available from 176 (59%) project districts, 209 prisons including Central, District and Sub District level were reported. Totally, 1.2 million inmates were housed during the reporting period and there were 15471 (13%) females. 59% of the prisons were having Medical Officers (MOs) and 76% of MOs were trained about RNTCP its services. Only 40% of the prisons were following initial screening of new inmates. 50% of prisons were implementing regular screening for TB among inmates. 12% of the prisons having functional DMC inside the campus and 45% of the prisons are equipped with trained DOT providers. There were 1479 TB patients reported including 30 MDR TB patients during the period 2010-2013. Only 14% of the prisons reported they isolate Smear Positive TB Patients from rest of the inmates.



Outcome of Project Axshya Intervention - Out of 173 prisons and 97,227 inmates, 1013 prison staff and 15,808 inmates (16%) were sensitized on TB Care and Control directly by project staff during reporting period. Out of sensitized, 2410 (15%) inmates were screened to identify TB symptomatics and 526 (22%) were found with TB symptoms. 508 (97%) TB symptomatics were tested for TB and 21 (4%) TB patients were identified and initiated on treatment.

**Conclusion:** The outcome of the situation assessment and Axshya Interventions urges for sustained interventions among prisoners being vulnerable to TB.

#### **PD-1202-01 TB control services for homeless population at "Night Shelters" in Delhi**

S Arora,<sup>1</sup> D Kundu.<sup>2</sup> <sup>1</sup>Public Health Wing 1, Directorate of Health Services, Govt. of Delhi, New Delhi, <sup>2</sup>Delhi State RNTCP, Office of WHO Representative in India, New Delhi, India. e-mail: aroradrsk7@yahoo.com

**Background and challenges to implementation:** Apriority action required to accelerate progress towards 2015 global targets set within the contextof the Millennium Development Goals (MDGs)is to reach the 'missed' cases. Around three million people - equal to one in three people falling ill with Tuberculosis (TB) are not being detected globally, of which, overone million Indians with tuberculosis, are currently going undetected and being 'missed' by the country's health system. One such vulnerable group of population are homeless migrant and refugee communities who have special health needs, but 'missed' by the public health system due to obstacles for accessing health care such as language, stigmatization, psychological distress, disruption of families and social networks, and economic difficulties. Delhi, capital of India, despite being one of the most heavily populated metros in the country, attracts thousands of homeless migrants from all over the country, who arrive here in the search of a better livelihood stay.

**Intervention or response:** For the betterment of these homeless, the Delhi Government have established 'Night Shelters' where they are provided with basic amenities to stay. Delhi State RNTCP on World TB Day 24<sup>th</sup> March, 2013, started TB Control Services for the homeless population in the 25 'Night Shelters' located in in Delhi and linking up with the nearest chest clinic for pro-active screening of presumptive TB cases residing in these night shelters. Mechanism for sputum collection and transportation from the night shelters to the nearest microscopic centres of the linked Chest Clinic for diagnosis of TB, followed by categorization of treatment and administration of TB treatment by the night shelter staff were developed and operationalised. Night shelter staffs posted in these night shelters were given special training as community DOT provider at the State TB Office during the same year.

**Results and lessons learnt:** A total of 51 chest symptomatic residing in the night shelters in Delhi were screened for TB, of which 3 (6%) turned out to be positive in

smear examination, an additional case detected which was missed earlier by the public health system.

**Conclusions and key recommendations:** linking night shelters effectively with the public health system is one way local government can help in improving access to health care. Mandatory screening in 'Night Shelters' followed by DOTS if diagnosed, by trained staff to comply with treatment adherence

#### **PD-1203-01 Estimating the risk of latent tuberculosis infection in healthcare professionals of a general hospital in Brazil: a strategy to prevent the disease**

C Tietboehl-filho,<sup>1</sup> M Andrade.<sup>2</sup> <sup>1</sup>Service of Occupational Medicine, Hospital of Clinics of Porto Alegre, Porto Alegre, RS, <sup>2</sup>Institute Oswaldo Cruz Foundation, Ministry of Health of Brazil, Rio de Janeiro, RJ, Brazil. Fax: (+55) 51 3901 1084. e-mail: tietboehl@gmail.com

**Background:** There is a high risk of Tb infection in health professionals (HP) working at Hospital of Clinics of Porto Alegre, a general hospital notifying annually an average of 200 tuberculosis cases from the community. The delayed diagnosis of Tb is a potential risk of TB transmission to the health professionals (HP). We describe a longitudinal study designed to estimate the annual risk of tb infection in non-infected HP, enhancing the chance to treat latent Tb infection (LTBI) after tuberculin conversion..

**Design/Methods:** In November , 2010, five qualified nurses carried out the application and reading of tuberculin test (TT) in a population of HP that attended to the call for participation in two tuberculin surveys with an one-year interval. All the individuals responded to a self-administered questionnaire.A cohort of non-infected individuals was selected and tested again three weeks later (booster effect) and finally one year later (November, 2011).

**Results:** In the first survey 841 individuals were tested (40,5 ± 10,2 years-old, 82.5 %, women and 17.5 %, men). The TT result was above 10 mm in 206 (24.4% ) individuals and the others 635 (75.5 %) who were non reactors or weak reactors were emboldened to participate in a new survey scheduled to November, 2011. In the second survey only 90 (10.7%) individuals of the original cohort came along to a new test, of which 79 (87.7%) remained negative and 11 (12.2 %) became positive, revealing a high annual risk of infection in this group of HP, similar to the rates reported in other hospitals of Brazil.

**Conclusion:** We recommend tuberculin test as an annual routine procedure to the early detection of tuberculin conversion in tuberculine-negative HP at risk. It must be followed by the treatment with isoniazid in those tuberculin-converted. We emphasize the need of administrative, environmental and personal protective measures in these facilities to reduce the risk of tb transmission.

**PD-1204-01 Pre-entry TB screening: Is there a need for culture confirmation?**D Zenner,<sup>1</sup> M Muzyamba,<sup>1</sup> P Dhavan,<sup>2</sup> R Aldridge.<sup>3</sup><sup>1</sup>Centre for Infectious Disease Surveillance and Control, Public Health England, London, UK; <sup>2</sup>Manila Office, International Organisation of Migration, Manila, Philippines; <sup>3</sup>Research Department of Infection and Population Health, University College London, London, UK.  
e-mail: dominik.zenner@phe.gov.uk

**Background:** Pre-entry screening for active pulmonary TB (PTB) for UK-bound migrants has been established since 2006. Visa applicants are screened by chest X-Ray and individuals with suspicious lesions followed up with sputum microbiology. However, provider practices and UK technical instructions have changed over time. The aim of this study was to present TB case yield over time and the effect of screening practice changes on these trends to inform screening algorithms and best practice.

**Methods:** Data on all UK-bound migrants who underwent screening between 2006 and 2013 was studied using descriptive epidemiology and multivariable logistic regression analysis. We also adjusted our analysis for the potential clustering effect of culture protocol implementation at clinic level.

**Results:** A total of 709,933 migrants were screened between 2006 and 2013 and 633 (0.09%) were found to have active TB. Chest X-Ray referral rates for suspicious lesions after 2007 remained stable around 3.8%-4.5%, but screening yield increased significantly from 0.04% to 0.17% between 2006 and 2013 (chi square for trend  $p < 0.0001$ ). This correlated with a protocol change to mandate sputum cultures for suspected cases and the proportion of samples with cultures increased from 0% to 85% during the same period. The odds of case detection in sites with culture confirmation were more than double compared to sites with smear-only protocols (OR 2.26, CI 1.83-2.79). After accounting for important confounders including age, sex, contact to TB cases, world region and year, there remained a strong evidence for an association between the introduction of the screening protocol with culture confirmation, and the odds of detecting disease at screening (adjusted OR 2.37, CI 1.59-3.52).

**Discussion:** Our study shows that the introduction of a culture confirmation policy was a powerful predictor of TB case yield, even after adjusting for other relevant confounders. Because of the long lead times, applicants and providers are keen to avoid culture confirmation. Our findings suggest that many TB cases may not have been detected without a culture and robustly support our current policy of culture requirements.

**PD-1205-01 Latent tuberculosis infection among health-care workers in Portugal: national casuistic analysis of five years**M Gomes,<sup>1</sup> O Oliveira,<sup>2</sup> R Duarte.<sup>3,4,5,6</sup> <sup>1</sup>Occupational Health, Centro Hospitalar de Vila Nova de Gaia/Espinho, EPE, Vila Nova de Gaia, <sup>2</sup>Clinical Epidemiology, Predictive Medicine and Public Health, University of Porto Medical School, Porto, <sup>3</sup>Pulmonology, Centro Hospitalar de Vila Nova de Gaia/Espinho, EPE, Vila Nova de Gaia, <sup>4</sup>Chest Disease Centre, Chest Disease Centre, Vila Nova de Gaia, <sup>5</sup>Medical School University of Porto, Medical School University of Porto, Porto, <sup>6</sup>Institute of Public Health University of Porto, Institute of Public Health University of Porto, Porto, Portugal.  
e-mail: martacdgomes@gmail.com

**Background:** Health care workers (HCW) are at high risk of exposure to tuberculosis patients. Due to this occupational hazard, HCW represent an important group with higher risk of tuberculosis disease and infection. The aim of this study was to perform a casuistic analysis and assessment of the predictive factors for latent tuberculosis infection (LTBI) over a 5-years period in Portugal among health care workers.

**Design/Methods:** Retrospective study. All LTBI HCW cases registered in the national database (mandatory registration) between January 2008 and December 2012 were selected. Data about demographic situation (gender, age), job category (doctor, nurse, auxiliary nurse, others) and workplaces (hospital, primary care) were analyzed. LTBI was assessed by tuberculin skin test (TST) and interferon gamma release assay (IGRA). For a statistical analysis, the differences between groups were assessed by Chi-square test.

**Results:** In a total of 573 HCW, most were female ( $n=445$ ; 78%), Portuguese born ( $n=544$ ; 95%) with an average age of 38 years (SD 11 years). Most work in hospitals ( $n=348$ ; 84%) and the detection of LTBI was performed equally by routine and contact screening (50%). The highest prevalence was found in nurses (40%) and auxiliary nurses (33%). To each doctor registered ( $n=50$ ) there were 4 nurses ( $n=211$ ) and 3 auxiliary nurses ( $n=171$ ). The proportion of LTBI was higher in hospitals among auxiliary nurses compared to primary care (34% Vs 21%,  $p=0.03$ ). The proportion among the others job categories was similar.

**Conclusion:** Our study showed higher proportion of LTBI in nurses. The higher proportion of LTBI in hospitals was associated to auxiliary nurses. This data highlight adequate infection control measures should be undertaken.

# **PD-1206-01 Prevalencia de Enfermedad tuberculosa en Trabajadores de salud a nivel nacional, Republica Dominicana, 2005–2012**

M Genao Abreu,<sup>1</sup> B Marcelino,<sup>2</sup> A Rodriguez,<sup>2</sup> M Mercedes,<sup>2</sup> E Lebron Mendez,<sup>3</sup> J Medina.<sup>3</sup>

<sup>1</sup>Epidemiología, Hospital Salvador B. Gautier, Distrito Nacional, <sup>2</sup>Programa Nacional De Control de la Tuberculosis, Ministerio de Salud Publica, Distrito Nacional, <sup>3</sup>Unidad Ejecutora de Proyectos Fondo Mundial, Ministerio de Salud Publica, Distrito Nacional, Dominican Republic. e-mail: belkys\_tb@yahoo.es

**Background and challenges to implementation:** El objetivo general de este estudio fue determinar la frecuencia y distribución de la enfermedad tuberculosa en trabajadores de salud de Hospitales Provinciales en República Dominicana durante el período de 2005 a 2012.

**Intervention or response:** Se realizó un estudio analítico, observacional, retrospectivo, no controlado, de tipo longitudinal. Ámbito de estudio en 49 Hospitales Regionales y/o Provinciales del Ministerio de Salud de República Dominicana. obtuvo La información obtenida para el presente estudio se extrajo de: a) Libros de registro de los pacientes con TB b) Libros de registro o fichas epidemiológicas de las Oficinas o Unidades de epidemiología, c) Libros de registro de laboratorio de microbiología, d) Historias clínicas en el archivo del hospital e) Entrevista directa a los trabajadores de salud que contrajeron enfermedad TB f) Informes de exámenes radiológicos de tórax realizados a personal de salud con enfermedad TB g) Libros de registro de cultivos y pruebas de susceptibilidad del Laboratorio de Referencia Nacional para tuberculosis, participando en el estudio un grupo de personal de salud responsable de los programas de TB locales, con la participación y asesoría de los epidemiológicos de los hospitales de los servicios seleccionados para participar en el estudio extrayendo la información de 116 expedientes.

**Results and lessons learnt:** Se identificaron 116 casos de TB en persona de Salud ,75 femenino y 41 masculino. El grupo mayor fue de 40–49 años, Razón de casos según sexo fue de 3.85: 1 a favor del sexo femenino. Media de 43.5, varianza 160.7, desviación típica 12.6, mediana 43, edad mínima de 20 años, y una máxima de 77 años, moda de 49, un coeficiente de variación de 28.9. (26.7%), fueron enfermería con TB pulmonar, (17.2%), personal de limpieza y (11.2%) médicos. El Hospital José María Cabral y Báez con 19 casos (16.4%). Se diagnosticaron 18 casos con Tuberculosis Multidrogoresistente.

**Conclusions and key recommendations:** La TB en trabajadores de la salud es un problema de salud pública El riesgo incrementado de la infección y enfermedad tuberculosa en los hospitales también se ve expresado en la presentación de brotes de tuberculosis nosocomial en trabajadores de salud. Diseñar normas para seguimiento de la enfermedad TB en los trabajadores de la salud e implementar planes de control de infecciones con énfasis en TB en los hospitales.

# **PD-1207-01 Prevalence and risk factors for latent tuberculosis infection among primary health-care workers in Brazil: a multi-center study**

T Nascimento Do Prado,<sup>1</sup> F Souza,<sup>1</sup> R Locatelli,<sup>1</sup> K Gomes,<sup>1</sup> L Possuelo,<sup>2</sup> E Zandonade,<sup>1</sup> G Fregona,<sup>1</sup> E L Noia Maciel.<sup>1</sup> <sup>1</sup> Enfermagem, Universidade Federal do Espírito Santo, Vitória, ES, Brazil, <sup>2</sup>Farmacia, Universidade de Santa Cruz do Sul, Santa Cruz do Sul, RS, Brazil. Fax: (+55)2733357206. e-mail: tiagufes@yahoo.com.br

**Background:** Healthcare workers (HCWs) are one of the groups at increased risk of latent TB infection (LTBI), due to their occupational exposure to patients infected with this pathogen. The Brazilian Tuberculosis Program redirected efforts for TB control from the inpatient setting to primary healthcare facilities. With that comes a discussion on biosafety and risk of TB in healthcare workers who works at primary healthcare facilities. Here, we evaluate LTBI prevalence among primary HCW and analyzed the risk-factors associated in five Brazilian cities with a high-incidence of TB.

**Design/Methods:** A cross-sectional study was carried out from 2011 to 2013 in Cuiabá-MT, Manaus-AM, Salvador-BA, Porto Alegre-RS and Vitória-ES. The study population comprised primary HCW (physicians, nurses, nurse technicians and community HCW). The HCW were interviewed face-to-face and demographic data, as well as risk factors of LTBI were obtained. After, the Mantoux skin test was performed with 0.1 ml of PPD RT23 containing 2-TU (Tuberculin PPD Evans 2 TU), which was administered intradermally by trained nurses. The induration was measured and interpreted by the same nurses. The test was read 48–72 hours after the administration of the PPD, according to Brazilian National Institute recommendation, with positive results defined as indurations of  $\geq 10$  mm in the transverse diameter.

**Results:** 708 primary HCW were included in this study which the overall prevalence rate of LTBI among Brazilian primary HCWs according to TST cut-off points of  $\geq 10$  mm was 40% (285) [CI 95%: 36%–44%]. The multivariable analysis model confirmed the increased probability of a positive TST response among primary HCWs in Brazil were professional category-nurse technician [OR=2.02; CI 95%: 1.15–3.56], contact with a household member with TB [OR=2.08; CI 95%: 1.39–3.11], smoker [OR=1.79; CI 95%: 1.05–3.08] and alcohol abuse [OR=1.43; CI 95%: 1.04–1.98].

**Conclusion:** Our study suggests a substantial occupational risk of LTBI among Brazilian primary HCWs. Besides, demonstrated that the key factors driving LTBI among primary HCWs in Brazil were professional category (nurse technician), contact with a household member with TB, smoker and alcohol abuse. Besides, our findings highlight the need for implementing TB control activities at the primary facility in Brazil converging aspects of biosecurity with sociodemographic risk factors.



### PD-1208-01 Acceptance of IPT among health-care workers living with HIV in KwaZulu-Natal, South Africa

C Tudor,<sup>1</sup> M Van Der Walt,<sup>2</sup> J Ngozo,<sup>3</sup> J Golub.<sup>1</sup>

<sup>1</sup>Medicine, Johns Hopkins University, Baltimore, MD, USA;

<sup>2</sup>Tuberculosis Research, South African Medical Research Council, Pretoria, <sup>3</sup>Communicable Diseases, KwaZulu-Natal Department of Health, Pietermaritzburg, South Africa.  
e-mail: ctudor2@jhu.edu

**Background:** Health care workers (HCWs) are at a greater risk of TB than the general population and this risk is greater for HCWs living with HIV. The use of isoniazid preventive therapy (IPT) to treat latent TB infection has been recommended to prevent TB among people living with HIV.

**Methods:** A retrospective operational research study to assess process indicators of IPT implementation among HCWs living with HIV in 15 district hospital occupational health (OH) clinics across KwaZulu-Natal, South Africa.

**Results:** Eight hundred and sixty-five HCWs living with HIV were identified via chart review of OH clinical records. On average 7.1% of all HCWs working across the 15 hospitals had self-disclosed their HIV-positive status to the OH nurse. Nearly 42% (n=361) of HCWs had been treated for TB at least once. IPT was offered to 275 (31.8%) of HIV-positive HCWs and 198 (72%) of these accepted IPT. Twenty-eight percent (168/590) were ineligible for IPT because they were either currently on TB treatment (n=43) or had been treated for TB within the previous two years (n=125). HCWs with a CD4 count < 350 cells mm<sup>3</sup> were more likely to be offered IPT (OR 1.59 95% CI: 1.18–2.16), but not more likely to accept IPT (OR 1.24 95% CI: 0.72–2.15). Of the 198 who took IPT, 160 (80.8%) completed therapy, 21 (10.6%) stopped IPT, and 17 (8.6%) had no outcome recorded. Among those who took IPT 10 (5.1%) did not adhere to treatment, eight (4%) were diagnosed with TB while on IPT (two with multidrug-resistant TB (MDR-TB)), and one (4.8%) stopped due to side effects. An additional six (3.1%) were diagnosed with TB (two with MDR-TB) following the completion of IPT. The proportion of HCWs who accepted IPT did not differ significantly by age, sex, or occupation compared with those who did not accept. However, HCWs who worked in a hospital with an OH nurse with OH training were more likely to accept IPT (OR 6.35 95% CI: 2.9–13.92) but not to complete IPT (OR 2.36 95% CI: 0.82–6.77) compared with those working in hospitals with OH nurses without training.

**Conclusions:** While a small proportion of HCWs were offered IPT, the majority of them accepted IPT with low rates of reported default. However, there were several HCWs who had to stop IPT because they were diagnosed with TB or MDR-TB while on therapy. With high rates of TB among HCWs living with HIV in this sample, more effort needs to be made to protect HCWs from TB in the workplace.

### PD-1209-01 Tuberculosis indicator data from United States immigration screening, 2012

C Olson,<sup>1</sup> D Posey.<sup>1</sup> <sup>1</sup>Global Migration and Quarantine, U.S. Centers for Disease Control and Prevention, Atlanta, GA, USA. e-mail: colson@cdc.gov

**Background:** Applicants for US immigration (immigrants and refugees) are screened for tuberculosis (TB) before travel to the US. Physicians, known as panel physicians, conduct screening under a rigorous TB algorithm, the Culture & Directly Observed Therapy TB Technical Instructions (CDOT TBTIs), issued October 2009. The CDOT TBTIs require panel physicians to submit indicator data for their TB screening, diagnosis, and treatment to enable monitoring of the effectiveness and impact of the screening program. Information collected includes numbers of applicants screened and suspected of having TB disease, number of pulmonary TB cases, laboratory results, and treatment outcomes.

**Design/Methods:** Submitted data were reviewed for completeness and accuracy. When errors were identified, sites were contacted for clarification and correction. Data from panel sites were combined to produce aggregated, descriptive country-level data. Rates of TB disease diagnosed in 2012 were calculated and compared with 2012 World Health Organization (WHO)-published estimates.

**Results:** Fifty countries (124 panel sites) were required to submit TB data by January 1, 2013. We received data from panel sites in 78% of these countries and from 77 (62%) panel sites screening under the CDOT TBTIs at that time. A total of 454,679 applicants were screened by these 77 panel sites in 2012. Five percent (22,051) of applicants they screened were identified as having chest radiographs suggestive of TB (range 0.2% to 15.6%/panel site). A total of 1,155 applicants were diagnosed with TB disease (254 per 100,000 screened). The calculated incidence of TB disease reported by panel sites ranged from 0 to 1,038/100,000, compared with the range of 5 to 1,003/100,000 reported by WHO. In almost 30% of countries, panel sites reported higher rates of TB than the country rates reported by WHO.

**Conclusion:** The TB indicators contribute to assessment of the quality of the screening program. They also allow comparisons of rates of TB diagnosed during pre-immigration screening with country rates, which may be useful for TB programs in immigrants' countries of origin. Reasons that some panel sites report higher rates of TB than those reported by WHO include the use of active case-finding and cultures in the algorithm applied to applicants for US immigration compared with the general population. Populations undergoing immigration screening may also differ in clinically important characteristics from the general population.

### 63. ALL SMOKE FREE: FROM GOVERNMENT TO COMMUNITY

#### PD-1210-01 Public Health network to strengthen smoke free implementation at tourism cities in Viet Nam

NB Nguyen,<sup>1</sup> V Tran,<sup>2</sup> Lam Nguyen,<sup>2</sup> N M Tham.<sup>2</sup>

<sup>1</sup>Environmental and Occupational Health, Hanoi School of Public Health, Hanoi, <sup>2</sup>Tobacco Control Program, Viet Nam Public Health Association, Hanoi, Viet Nam. Fax: (+84)4373 66265. e-mail: nnb@vpha.org.vn

**Background and challenges:** Viet Nam is ranked among the 15 countries with highest prevalence of smokers in the world. It is also indicated that second hand smoke (SHS) exposure is also a significant issue with more than 33 million adults exposed to SHS at home and around 38 million being exposed to SHS at workplaces. Context and responses Nha Trang (Khanh Hoa Province) and Hue (Thua Thien – Hue Province) are tourism cities which attract millions of local and international tourists every year. Baseline survey showed that smoking is common in public settings at those cities especially at transportation and hospitality facilities. Series of training workshops were implemented to key leaders of different sectors (health, education, transportation, tourism), IEC materials including video clips, billboards, leaflets, posters, banners, band rolls and other manual like toolkit, media kit, guidelines, position statement, were produced to create useful, user-friendly and effective package for Tobacco Control (TC) local activists. Besides, enforcement campaigns and matches were also conducted to raise awareness and support from local residents. Local governments were also advocate to issue their own legal document and plan on TC

**Results and lessons learnt:** After two years implementing the program, Viet Nam Public Health Association (VPHA) together with local partners has achieved: - Develop a sustainable local taskforce on TC in targeted cities - Create supportive environment for smoke free implementation with involvement and participation of different local sectors - Make use project resources to support for advocacy for Draft TC Law and to disseminate for the Law - Raising awareness and support of the public and policy makers at city level as well as at national level to support for smoke free implementation; - Capacity building for TC focal points The involvement of PPCs and PC also directed different sectors in those cities to implement their task on the TC plan of PC

**Conclusions:** Experiences from the program showed that, involvement of local government was the key to success to mobilize the participation of different sectors in the cities. Results from post survey show significant changes on attitude and practice of local leaders as well as local resident in implementing and complying with smoke-free legislations. Experiences from two cities are also disseminated as evidences about supports of several provinces to TC Law, thus to convince policy makers about feasibility of TC Law

#### PD-1211-01 Smokefree city campaign: a case of Khulna Municipality in Bangladesh

A Bakul,<sup>1</sup> I Chowdhury,<sup>2</sup> Mr Aktar.<sup>3</sup> <sup>1</sup>ngo, Action In Development - AID, Dhaka, <sup>2</sup>Technical Advisor, International Union Against Tuberculosis and Lung Disease (The Union), Dhaka, <sup>3</sup>NGO, Action In Development - AID, Dhaka, Bangladesh. Fax: (+880)45161189(105). e-mail: aminulislambakul@gmail.com

**Background and Challenges to Implementation:** Action In Development- AID is working for smoke free Khulna division in Bangladesh since 2009. For the part of the activities AID is implementing the project: 'Smoke Free Khulna Division through Effective Enforcement of Smoke-Free Provision of Tobacco Control Law' with the financial support of The Union- France. One of the key objectives of the project is to make smoke free of the public places, government offices, institutions and transports through proper implementation of Tobacco Control Law of Bangladesh. For the implementing the activities it has faced several challenges including the ineffective lack of cooperation of the political and administrative personnel of KCC. Similarly the tobacco producing companies' illegal campaign and interventions were the challenges of the activities. But AID has overcome all the challenges and achieved its goal with a good accomplishment.

**Intervention or Response:** To implement the activities AID team developed collaboration with the KCC Mayor and the Deputy Commissioner of Khulna about the smoke free city campaign and several meeting, discussion with the authority then adopt smoke free city corporation guideline. Finally it was declared Khulna City as smoke free by the Mayor and the Deputy Commissioner with presence of mass people and others govt officials and law enforcement agencies. To comply the declaration AID has distributed the smoke free sign and declared the smoke free zone of the government offices, and other public places along with the concern authorities.

**Results and Lessons Learnt:** It has declared the 100% of the public places as a smoke free in KCC area. Along with these activities it has developed city corporation guideline, awareness and monitoring plan among the general people, public places, public transports drivers and assistants, government official to keep the smoke free zone as for their health concern. From the activities we have learnt that, for the smoke free public places strong and effective taskforce and enforcement of City Corporation is needed and the effective participation of the government officials must be needed.

**Conclusions:** Effective intervention of AID it has developed smoke free public places of the KCC areas. The public places are free from smoke and reduce the risk of the public health concern.

### PD-1212-01 Civic participation in smokefree policy-making and monitoring compliance with the national legislation

T Burieva.<sup>1</sup> <sup>1</sup>Project department, Arkhangelsk Centre of social technologies "Garant", Arkhangelsk, Russian Federation. Fax: (+7) 818 220 6510.  
e-mail: btanya75@hotmail.com

**Background and challenges to implementation:** The Russian national smoke-free law was introduced only in 2013. However, there is no enforcement policy or mechanism in place leading to rampant violations. Considering other issues, tobacco control is the least priority for the local authorities. The Northwest coalition on tobacco control (hereafter – Coalition), coordinated by the NGO "Arkhangelsk Centre of social technologies "Garant" and uniting different actors from 3 regions (Arkhangelsk, Murmansk and Pskov) of Russia, is oriented at introduction, test and ensuring practical application of mechanisms of civic participation in tobacco control policy-making and ensuring enforcement of the legislation.

**Intervention or response:** At first the coalition initiated establishment of the tobacco control public councils (hereafter- TC councils), uniting active citizens, NGOs, executive and legislative authorities, businesses, media and healthcare institutions in 3 regions of the Northwest to develop and adopt the regional tobacco control strategies, action plans and programs. Later TC councils' members took responsibility for monitoring implementation of tobacco control regional strategies, action plans and programs. For monitoring of compliance with smoke-free legislation the regional hotlines were launched to collect complaints of citizens on violation of TC legislation. The citizens' messages were passed to the surveillance authorities, later banning tobacco selling near schools, imposing fines, closing kiosks at bus stops. A separate hotline was organized at the Association of city transport in Arkhangelsk to control city bus-drivers' smoking. To enhance the system of civic control over implementation of the smoke-free legislation, the Coalition initiated and held training of active young citizens, NGOs in civic participation and control. Within the trainings, the civic control toolkit was prepared: a checklist for "sweeps" of public places, an Internet portal on violations of the smoke-free legislations. The TC councils' workshops have become the platform for discussion of results.

**Results and lessons learnt:** The system of civic participation in tobacco control policy-making and surveillance was developed in the Russian Northwest and integrated into the local policy-making and surveillance systems. The methods and toolkit were elaborated and tested.

**Conclusions and key recommendations:** The model can be easily applied in other regions of Russia.

### PD-1213-01 Polling in support to FCTC accession in Indonesia

R Mardhiati,<sup>1</sup> D Kurniawan,<sup>2</sup> F Nisma,<sup>1</sup> Y Yusuf,<sup>1</sup> N Andayani,<sup>1</sup> M A Malik,<sup>2</sup> T Ningsih,<sup>2</sup> IP Susanti.<sup>2</sup> <sup>1</sup>Public Health, Uhamka Research and Development Institute, Jakarta, <sup>2</sup>Public Health, Indonesia Institute for Social Development, Jakarta, Indonesia. Fax: (+62) 217 244461.  
e-mail: deni.wk@gmail.com

**Background:** The FCTC accession initiatives in Indonesia always hamper the tobacco industry interference, which always manipulate the tobacco farmers and tobacco industrial labor that will be mostly suffered as their front liners, whenever the FCTC will be acceded and enacted in Indonesia. In order to get the real pictures on how the Indonesian people in general perceives the accession and enactment of the FCTC in Indonesia, Indonesian Institute for Social Development (IISD) in partnership with the Research & Development Institute of the UHAMKA Muhammadiyah University, conducting a polling on the community perception to the FCTC accession. The objective of the polling is to explore the public knowledge on the effect of smoking and their opinion on tobacco control measures as stipulated by the FCTC.

**Design/Methods:** The study was conducted between May and June 2013 in 11 cities of 8 provinces in Indonesia. Direct interviews were made among 1,444 randomly selected respondents aged 18 years and above. A semi-structured questionnaire with demographic features, knowledge and perception about tobacco use, opinion on tobacco control measures and WHO FCTC accession.

**Results:** Total respondents was 1,444, with average 28.7 years of age (70.8% aged between 18 and 30 years), consisted of 60.1% male and 39.9% female, 64.3% was high school completed followed by under graduated 12.7%, with 32.2% respondents were current smokers, 12.1% ex-smokers and 55.7% were nonsmokers. The majority of respondent supports tobacco control measures such as ban smoking in all public places and workplaces (95%), pictorial health warning (87%), comprehensive ban of tobacco advertisements, promotion and sponsorship (82.8%), raise tobacco tax and prices (77%), policy on smoking cessation (84.9%). Respondents agreed to ban selling cigarette to minors (94.5%), to ban sale cigarette by stick (79%), to ban flavor in cigarette (80%) and plain packaging regulation (74%). Respondent also support FCTC accession (90%). The support to FCTC accession also high among current smokers (83.4%), ex-smokers (93.7%) and nonsmokers (95.4%).

**Conclusion:** The majority of Indonesia people supports FCTC accession and support for more tight tobacco control policies. Stronger support from young people (70.8% aged 18–30 years) indicating that Indonesian younger age group and productive age group supporting tobacco control policy.



### PD-1214-01 How to approach the creation of a smokefree environment at city level: Jinan City experience

S Ruan,<sup>1</sup> J Zhang,<sup>1</sup> Y Liu,<sup>1</sup> X Zhang,<sup>1</sup> S Liu,<sup>1</sup> X Wang.<sup>1</sup>

<sup>1</sup>Tobacco Control Office, Jinan municipal Center for Disease Control and Prevention, Jinan, China.

e-mail: jncdctco@163.com

**Objective:** To promote the revision of Jinan Municipality Provisions on Forbidding Smoking in Public Places; to drive the creation of smoke-free environment and reduce the exposure to secondhand smoking; and to increase public awareness of the hazards of smoking and secondhand smoking. [

**Methods:** To organize a specialized technical team of tobacco control for intensive training; to strengthen the construction of media networks, build a multidimensional TC propaganda platform; to create SF environment; to inspect and evaluate the creation work. [

**Results:** 1. In 2013, in accordance with Local Legislation Program (2013–2017) and Local Legislation Plan (2013) of Jinan Municipality NPC Standing Committee, Jinan Municipality Provisions on Forbidding Smoking in Public Places entered the list of the legislative research projects. The first draft has been finished. 2. To construct a three-dimensional propaganda network: Beginning with August 1, 2012, a propaganda campaign of TC was started on bus TVs and city TVs. The advertisement was rolling broadcast in over 16000 buses, 15 LED large screens, and 590 indoor terminals. From May 14 to June 14, 2012, a one-month touring exhibitions of tobacco health warning pictures were held. 3. There is a heavy exposure to secondhand smoking with a rate of 56.6%. The non-smokers are exposed mainly in public places and working places. Less than 70% of the respondents believed that the no-smoking provision in public places has been poorly implemented. The policy of forbidding smoking in public places in an all-round way is widely supported. 4. Out of the 268 on-the-spot respondents, 30% have read the “Secondhand Smoking: Invisible Killer” advertisement. Vast majority of the respondents have understood the hazards and taken related measures. [

**Conclusion:** Progress has been made in the SF legislation, but there is still a lot of work to do in this respect. The policy of forbidding smoking in public places in an all-round way is widely supported. Multi-dimensional propaganda activities are carried out to effectively improve the public awareness. Continuing inspection and evaluation are needed to improve the population's behavior.

### PD-1215-01 Smokefree hospitals in Jinan: a practice for comprehensive smokefree policies

J Han,<sup>1</sup> Jun Zhang,<sup>1</sup> RM Cao,<sup>1</sup> XW Li,<sup>1</sup> Y Jin,<sup>1</sup> SM Ruan.<sup>1</sup>

<sup>1</sup>Institute of Chronic and Non-communicable Disease, Jinan Municipal Center for Disease Control and Prevention, Jinan, China. e-mail: happyhanj16@yahoo.com

**Background:** In 2011, the Jinan government launched the Smoke-free Environment Project in hospitals. Hos-

pitals in Jinan were asked to ban smoking indoors and to provide advice and referrals for smoking cessation treatment.

**Objectives:** To assess the implementation of smoke-free environment policies in hospitals one year after the policies was introduced. The relationship between hospital grade and capacity of tobacco control was also studied.

**Methods:** The study was a descriptive research and was conducted at 20 hospitals including 8 primary hospitals, 7 secondary hospitals, and 5 tertiary hospitals using stratified random sampling method. Data collection included: 1) Field observations for 30 minutes including tobacco control infrastructure, presence of cigarette butts, and observed smoking incidents at a total of 317 locations on 20 hospital grounds. 2) Indoor fine particle PM2.5 [particulate matter <2.5µm in diameter] pollution measured by photometric devices for 30 minutes to assess second hand smoke exposure. 3) Survey of hospital staff on organized smoke-free environment activities, funding support, and tobacco cessation services.

**Results:** 75% of the 20 hospitals studied implemented smoke-free environment policies with smoking cessation services, smoke-free environment signs, designated outdoor smoking areas, and tobacco control bulletins. However, tobacco sales and butt bins are still visible in 2 hospitals. Smoking incidents were observed in 7 out of 317 locations observed and no staff attempted to dissuade the smokers. Markedly elevated PM2.5 levels were also observed at 4 indoor no-smoking locations: the outpatient building lobby, surgical waiting room, male restroom, and doctor's office in ward (mean 142.3µg/m<sup>3</sup> (±121.2) compared to that of other areas (76.4 µg/m<sup>3</sup> (±61.2)). Although attitudes of the hospital bans on smoking reflect strong support for smoke-free environment policies, the capacity for tobacco control decreased by hospital grade. Tertiary hospitals have a higher capacity for tobacco control than primary and secondary hospitals based on the percentage of full-time staff, staff with higher education degrees, funding support, and tobacco control research.

**Conclusion:** Many hospitals have implemented comprehensive smoke-free environment policies but the majority of them are still facing difficulties. Challenges and concerns need to be explored in depth and addressed to ensure the implementation and enforcement of 100% smoke-free hospital policies.

### PD-1216-01 Reduction in second-hand smoking with the implementation of COTPA, 2003 in Shimla Town

N Sharma,<sup>1</sup> P Lal.<sup>2</sup> <sup>1</sup>Civil Society, Himachal Pradesh Voluntary Health Association, Shimla, <sup>2</sup>Tobacco, The Union, South East Asia, Delhi, India. Fax: (+91) 177 2670346. e-mail: nar.sharma@gmail.com

**Background and challenges to implementation:** Second-hand smoke (SHS) also known as environmental tobacco smoke (ETS) is a mixture of 2 forms of smoke that come from burning tobacco, Sidestream smoke – smoke from

the lighted end of a cigarette, pipe, or cigar and Mainstream smoke – the smoke exhaled by a smoker. When non-smokers are exposed to SHS it's called involuntary smoking or passive smoking. Non-smokers who breathe in SHS take in nicotine and toxic chemicals by the same route as smokers do.

**Intervention or response:** India has a very high exposure to SHS. As per GATS, 2009, adults exposed to smoke were 52.3% and Himachal Pradesh was an alarming high of 83% at homes. Being primarily a rural state, effective implementation of smoke free laws was not enough, stakeholder sensitization had to be combined with awareness generation on harmful effects of tobacco and impact of SHS. HPVHA through concerted efforts focused on policy advocacy with grass root level officials through workshops and with the community through awareness generation in Gram Sabhas, poster display/IEC. 1800 smokers and 100 tobacco vendors in Shimla city with the main objective to gauge the change in the consumption of tobacco products, change in their smoking habits in the past 3 years i.e. whether they smoke within the office/office breaks/home/other places presently as well as 3 years back i.e. in 2014 and 2010 were questioned through a comprehensive developed protocol of international levels.

**Results and lessons learnt:**

**Results** indicate that about 71% of the respondents smoked within the office premises 3 years back and presently (2014), it is only 38%. The respondents not only include employees in private /government job but also include businessmen, labourers, unemployed and drivers. Digging deeper, we found that amongst those in service (Government/private) only 17% smokers still smoke secretly within the office premises i.e. in toilets, own cabins or in front of their peers who don't mind as compared to a 34% who smoked openly within the office premises in 2010 in front of their peers. About 35% of our respondents used to smoke at home in front of their family which has fallen to 18% currently.

**Conclusions and key recommendations:** Strict Compliance of rules and laws of 'No Smoking' and possibility/fear of challans along with increased awareness on ill effects of SHS among all stakeholders has significantly helped to reduce second hand smoke.

**PD-1217-01 Smokefree munger initiative: a gateway to tobacco free Bihar**

D Mishra.<sup>1</sup> <sup>1</sup>Tobacco Control, Socio Economic and Educational Development Society (SEEDS), Patna, India. e-mail: seedsdelhi@gmail.com

**Background and challenges to implementation:** According to GATS India report 2009-10, 53.5% adults use (30850882 million) tobacco in Bihar, out of which 14.2% of adult smoke (2710264 million), who expose nearly 25% of the rest of the population to secondhand smoke SHS at public places in Bihar (57665200 million).

**Intervention or response:** Efforts to institutionalize tobacco control by creating systems, advocacy with policymakers; capacity building of law enforcers, and

enforcement of the various provisions of India's tobacco control legislation were done. The media was used strategically to advance tobacco control at the district level. We measure the progress in the state and present the mid-term compliance studies done in the intervention district (13 of 38 districts in the state)

**Results and lessons learnt:** Compliance studies to measure smoking in a public place have shown tremendous improvement since the first interventions made in the state. Overall 89.3% of public places have been found to comply with the criteria identified to declare a public place as smoke free.

**Conclusions and key recommendations:** Good progress has been observed in the state of Bihar but challenges remain which threaten the sustainability of the interventions. widespread loc These include: one, the presence of India's largest tobacco industries (ITC) which dominates the policy space in the stae; two, domestic tobacco Industry's aggressively promotes its products locally; three, there is widespread local tobacco cultivation, and four limited funding and political support for tobacco control from the state government.

**PD-1218-01 Community perception on tobacco control in Cambodia**

SA Kong.<sup>1</sup> <sup>1</sup>National Center for Health Promotion, Ministry of Health, Phnom Penh, Cambodia. Fax: (+855)23432061. e-mail: saman@nchp.gov.kh

**Background:** In Cambodia, tobacco consumption consequences remain fatal to health and wellbeing of the public and government. With the leadership from the government and multi-disciplinary cooperation, the tobacco control efforts have produced significant success. The prevalence among adult male from 18 years of age, reduced from 54% in 2000, to 49% in 2005 and to 43.3% in 2010 and among adult female from 18 years of age, reduced from 24% in 2000, to 20.5% in 2005 and 17.2% in 2010 (NATSC 2011). According to the Global Youth Tobacco Surveys in Cambodia, the tobacco use prevalence among school children and teenagers remained very low over the last ten years. However, there are many viral work needed to be done.

**Objective:** This study aimed at determining the perceptions of community member about tobacco control and tobacco use and its harm.

**Methodology:** A qualitative research was conducted by using key informant interview with key individuals in the Cambodian government, NGO and community members. The research also conducted focus group discussion with community members to collect information related to the current situations of tobacco consumption.

**Results:** On the community level, the people need information on how to raise general awareness on tobacco harms through mass media campaign and community-based health education with use of, flyers, billboard and posters. The people fully support the prohibiting all tobacco advertising such as, stop employing cigarette promoter's girls to encourage adults smoking. They supported an investment in research to

identify an effective drug that can help smoker to quit smoking. V.

**Conclusion** In Cambodia, tobacco consumption prevalence is very high, in particular among male adult population, most of whom are rural with low education. This suggests that there is a correlation between low level of education and smoking prevalence in Cambodia. Hence, the provision of effective health education campaign to the households with low level of education can help to reduce the prevalence of smoking in Cambodia.

#### **PD-1219-01 Do smokefree policies harm the turnover and employment in the hospitality industry in Buenos Aires? Effects of the 1799 Act on tobacco control**

M C Angueira,<sup>1</sup> C Cañas.<sup>1</sup> <sup>1</sup>Tobacco Control, Ministry of Health Buenos Aires City, Buenos Aires, Argentina.  
e-mail: martaanguera@gmail.com

The analysis was based on: 1) The turnover and employment in bars, restaurants and pizza shops in the City of Buenos Aires compared to previous years. The method used for comparison was the difference estimation based on data from taxes. 2) The location of the City of Buenos Aires. The Province of Buenos Aires is next to de City of Buenos Aires. In the province there is no tobacco ban. The Association of Hotels, Restaurants and Coffee Shops argues that smokers move to the restaurants, bars and pizza shops in the Province of Buenos Aires generating the negative border effect.

**Results** from the work prove that the effect on both turnover and employment after the implementation of the law is positive. Establishments surveyed overall result is increased revenue (in real terms) on average about 570 pesos. This number represents an increase of almost 6% on the average turnover of establishments in the CABA in the year before the law was sanctioned. The result of this study corroborate the 1799 Act did not generate economic damage to bars, restaurants, pizza shops, bars and cafes. In addition it was found that there is no negative border effect.

#### **PD-1220-01 How good is compliance with smokefree legislation in India? Results of 38 subnational surveys**

R Kumar,<sup>1</sup> S Goel,<sup>2</sup> A D Harries,<sup>3</sup> P Lal,<sup>1</sup> R J Singh,<sup>1</sup> N Wilson,<sup>4</sup> A Kumar.<sup>1</sup> <sup>1</sup>Tobacco control, International Union Against Tuberculosis and Lung Disease, New Delhi, <sup>2</sup>Health Management, PGIMER School of Public Health, Chandigarh, India; <sup>3</sup>Operational Research, International Union Against Tuberculosis and Lung Disease, London, UK; <sup>4</sup>Tuberculosis, Independent consultant, New Delhi, India.  
e-mail: rkumar@theunion.org

**Background:** India has been implementing smoke-free legislation since 2008 prohibiting smoking in public places. We aimed to assess the level of compliance with smoke-free legislation (defined as presence of no-smoking signages and absence of active smoking,

smoking aids, cigarette butts/bidi ends and smoking smell) and the role of enforcement systems in Indian jurisdictions.

**Methods:** This was a cross-sectional retrospective review of reports and primary data sheets of surveys conducted in 38 selected jurisdictions across India in 2012-13.

**Results:** Of 20,455 public places (in 38 jurisdictions), 10,377 (51%) demonstrated full compliance to smoke-free law. Educational institutions and health care facilities performed well at 65% and 62% respectively while eateries and frequently visited other public places (like bus-stand, railway station, shopping mall, stadia, cinema hall etc.) performed poorly at 37% and 27% respectively. The absence of no-smoking signages was the largest contributor to non-compliance across all types of public places. Enforcement systems were present in all jurisdictions, but no associations could be demonstrated between these and smoke-free compliance.

**Conclusions:** Smoke-free compliance in public places in India was suboptimal and mainly related to absence of no-smoking signages. This warrants further pragmatic and innovative ways to improve the situation.

#### **PD-1221-01 Countering the tobacco industry interference: tactics in implementation of pictorial health warnings on all tobacco packs through media interventions**

C Ramakrishnan.<sup>1</sup> <sup>1</sup>Tobacco Control, Voluntary Health Association of India, Delhi, India.  
e-mail: binoymathew84@gmail.com

**Background and challenges to implementation:** Picture health warnings on tobacco packages effectively communicate the risks of tobacco use. Graphic warnings have greater impact and can be recognized by low literacy audiences and children – two vulnerable groups. Tobacco has a long history of killing and maiming people. In India, nearly 10 lakh people die of tobacco use every year. This is largely because of low levels of awareness about the hazards of tobacco use. Pictorial health warnings effectively communicates health hazards of tobacco use - consumers see warnings thousands of times. As per law (COTPA 2003, Section 7), it is mandatory to implement pack warnings across all tobacco products in India. Article 11 of the FCTC mandates that signatories should implement pack warnings within three years of ratifying the treaty. India ranks 128 among the 192 countries surveyed on warning size and fulfilment of requirements for picture-based warnings on cigarette packets. Multiple litigations filed by industry across India in various Courts challenging constitutionality and implementation, Using political clout to set up and influence the political leaders to dilute and delay PWs, Using livelihood card to influence political decision-making to its advantage and Coercing the Govt by announcing a closure of production and harping on loss of revenue incurred/day to exchequer

**Intervention or response:** Media Strategies were used to Counter Tobacco Industry through press statements, organizing press meets at national and state level,



collective advocacy with other public health and civil society organizations, releasing courtroom developments of PIL cases

**Results and lessons learnt:** Pro-active media advocacy resulted in nearly 650 stories on pictorial health warnings from the National & State Level, Extensive media coverage pan India (spanning national, regional and local media) , About 23 – 30 press releases were shared with the National & State Level Media and About 20 press meets held on pack warning at National Level & 15 states of India

**Conclusions and key recommendations:** Ensured implementation of stronger pictorial health warnings on all tobacco packs w.e.f the prescribed date of implementation.

#### **PD-1222-01 Exposure to second hand smoke in India: an analysis from Global Adult Tobacco Survey, 2009–2010**

D Sharma,<sup>1</sup> A Gupta.<sup>2</sup> <sup>1</sup>School of Public Health, Post Graduate Institute of Medical Education and Research, Chandigarh, Chandigarh, <sup>2</sup>Community Medicine, Indira Gandhi Medical College, Shimla, India.  
e-mail: drdeepakpgimer@gmail.com

**Background:** Exposure to secondhand smoke (SHS) from burning tobacco products causes disease and premature death among non-smoking adults and children.

**Aims and objectives:** To ascertain the level of exposure to second hand smoke and its socio-demographic correlates in various public places across India.

**Design/Methods:** The GATS India data 2009–2010 was analyzed to obtain the descriptive statistics on exposure to second hand smoke in India. Logistic regression model was then run to obtain the predictors of exposure to second hand smoke. Analysis was done using SPSS version 18.0 for windows.

**Results:** A region wise break up shows that more people residing in Central India (32%) were exposed to second hand smoke as compare to those residing in Eastern India(25%). Comparatively, more people in the younger age group were exposed to second hand smoke as compared to older people. More people residing in the urban area (31.6%) were exposed to second hand smoke as compare to those residing in rural areas (27.9%). Public transport system was the most frequent public place where people were exposed to second hand smoke.

**Conclusion:** Policy recommendations on protection from exposure to second-hand should be strictly implemented in India. Smoke free law needs to be more strictly implemented in urban areas. Public transport systems should be regularly monitored to enforce strictly the smoke free law in India and thus save people from the dangers of second hand smoke.

#### **PD-1223-01 Potential mortality averted from sub-national taxes in India**

C Rajeev.<sup>1</sup> <sup>1</sup>Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, USA.  
e-mail: rajeevrc2063@yahoo.com

**Background:** Tobacco excise taxes are the standard policy instrument governments use to raise the price of tobacco products relative to the consumption basket as a whole. This paper estimates the public health impact of taxes levied differentially on tobacco products by several states in India since 2010 under the label of value added taxes. The noteworthy feature of these taxes has been that they are not nominally excise taxes, but due to the discretionary power that states have over the rates they can levy on tobacco products they function as de-facto excise taxes.

**Design/Methods:** The modeling of potential mortality averted employs population data, sub national prevalence estimates by tobacco product type derived from the Global Adult Tobacco Survey, and estimates of the responsiveness of consumption to price increases, and of the impact of reduced consumption on mortality. A range of different parameter estimates is provided to examine the robustness of the estimates of mortality reductions to alternative assumptions of demand elasticities and of the pass-through of tax to final price.

**Results:** Between 2010 and 2013, prevalence-weighted mean state value-added taxes on cigarettes and smokeless products rose from 14.8% to 30.5% and 28% respectively, bidi taxes tripled from 5.4% to 15%. If state value-added taxes behaved like excise taxes and differentially raised the price of tobacco products relative to overall inflation, a conservative estimate of the impact using demand elasticities from the literature is that over 3.5 million potential premature deaths were averted across India over the period 2010-13.

**Conclusion:** State tobacco value-added taxes in India function like excise taxes to raise product prices. National and local market structure mediate the pass-through from tax to price. This affects whether prices rise similarly across states when tax increases vary across states, and attenuates or amplifies consumption reductions and modeled mortality reductions.

### **64. TOBACCO CONTROL LAWS: THE FORCE IS STILL WITH US!**

#### **PD-1224-01 Building tobacco control capacity in medical universities in China**

T Yang,<sup>1</sup> F Xueying,<sup>1</sup> Wu Dan,<sup>1</sup> Shuh Jiang.<sup>1</sup> <sup>1</sup>Center for Tobacco Control Research, Zhejiang University, Hangzhou, China. e-mail: tingzhongyang@zju.edu.cn

**Background:** Medical professionals play a critical role in policymaking, providing services and catalyzing social change. There are currently approximately 183 universities teaching medicine in China, from which 100,000 students graduate annually and go onto be employed at

medical institutions. The absence of tobacco control in their curriculum means that most graduates have no training related to tobacco reduction and smoking cessation. Our project addressed this issue by developing a tobacco control workforce via medical universities (Yang et al, Tobacco Control, 2010). Beginning in 2007 we have been deeply invested in “building tobacco control capacity”. Completed were two (China-1-15) (China- RI –15) projects in 2008 and 2011 respectively. The current project (China-RI-15B) similarly promotes the program scale up through a new mechanism. These projects cover all provinces, municipalities and autonomous regions in China, including 70 cities and 91 universities (see map).

**Objectives:** The overall objective of these projects is to increase the evidence based knowledge, skills and behavioral capacity of the medical faculty and students to implement and evaluate best practice tobacco control throughout China.

**Methods:** The project activities include several elements: 1) Identified culturally sensitive strategies that are appropriate for China Develop available and culturally relevant materials for a tobacco control course. 2) Implement tobacco control curricula training and smoke-free campus policy activities. 3) Conduct the tobacco control policy advocacy through project events.

**Results:** We developed culturally-appropriate materials for a tobacco control course which were published in <<Social Medicine Textbook>>and <<National Medical Exam Guide>>. So far 83,130 medicine students, and 648 medical professions have been trained through these projects, and their tobacco control knowledge, skills and behavioral capacity were built (Yang et al, Tobacco Control, 2011). Eighty percent of universities issued smoke free campus policies in prior two projects, totaling 890,000 staffs and students who have benefited from the program. The project generated strong media interest with 225 original media hits reported, including the Center Government website, etc. Our program advocacies positively impacted and influenced local and national policies by means of project events.



### PD-1225-01 Compliance assessment of section four of Indian tobacco control act in 4620 public places for evidence based advocacy

B Sharma,<sup>1</sup> J Pillai.<sup>2</sup> <sup>1</sup>Tobacco Control, Madhya Pradesh Voluntary Health Association, Indore, <sup>2</sup>Tobacco Control, Madhya Pradesh Voluntary Health Association, Indore, India. Fax: (+91) 7312877735. e-mail: silkdrops@rediffmail.com

**Background:** The Indian Parliament enacted the Cigarettes and other Tobacco Products Act (COTPA) in 2003. Section 4 of the act prohibits smoking in public places, mandatory display of smoke free signages, prohibition of promotional items of smoking etc. The study was conducted in order to understand the level of compliance of section 4 of Indian Tobacco Control Act and to assess the baseline status of compliance to do effective advocacy for implementation of (COTPA).

**Design/Methods:** It was an observational and cross sectional study conducted in 11 districts of Bhopal & Ujjain Division of Madhya Pradesh, India. The population of the divisions being surveyed was 16 million. The public places were divided into seven categories which were accommodation facilities, eating facilities, offices & workplaces, educational institutions, health care facilities, most commonly visited public places and public transport. A district was considered as one cluster and 60 public places were selected from each category in a district and a total of 420 public places were selected from each district. The total sample size of the study was 4620 public places from 11 districts. The field investigators visited and observed each of the sampled public places during peak business hours.

**Results:** No smoking signage were displayed at 13% of public places, availability of signages at prominent places was 7%, active smoking was observed at 36%, promotional materials like ash trays, lighters found in 26% public places, 45% public places had evidence of recent smoking, cigarette, bidi butts were found in 27% of public places. Display of signage was least in eating facilities(7%) and highest in accommodation facilities(26%). Active smoking was highest in eating facilities (57%) and least in healthcare facilities (22%). Promotional items like ash trays and lighters were found least in education and healthcare facilities (7%) and maximum in eating facilities (53%). Maximum cigarette bidi butts found in eating facilities (76%) and least in educational institutions (25%).

**Conclusion:** The results of the study shows that the compliance level of section 4 needs to be improved in Bhopal & Ujjain division and special efforts are required in order to implement the act. The results of the study used to do policy advocacy for effective implementation of Indian Tobacco Control Act.

**PD-1226-01 Smokefree cities - an innovative approach to tobacco control in challenging environments: case study, Tianjin**

GH Jiang,<sup>1,2</sup> W Li,<sup>1</sup> W Zheng,<sup>1</sup> Y Yang,<sup>1</sup> Yi Pan,<sup>1</sup> DZ Wang.<sup>1</sup> <sup>1</sup>Tianjin Centers for Disease Control and Prevention, Non-Communicable Disease Control and Prevention, Tianjin, <sup>2</sup>Tianjin Medical University, School of Public Health, Tianjin, China.  
e-mail: jiangguohongtjcdc@126.com

**Background:** The first smokefree legislation in Tianjin became effective in 1996. The legislation stated that the health bureau was the main enforcement agency and only several avenues were required to be smokefree. It was not consistent with the WHO FCTC.

**Intervention:** With the aim of protect more people avoid the harm of SHS, we implemented this project. Through strengthen the capacity on tobacco control and network building; Raise the public awareness about the harm caused by smoking and passive smoking via public communication and social mobilization; Modify the existing regulation to expand the non-smoking areas following the WHO FCTC; Systematically create 100% smokefree environments; Develop the best evaluation methodology and to evaluate the effects of interventions; monitor the implementation process.

**Results:** Tianjin Tobacco Control Regulation was formally implemented on May 31, 2012. Regulation covered 13 categories indoor area. Tianjin Municipal People's Government set up Tianjin Health Promotion Committee to organize, coordinate and guide the city's tobacco control efforts, and the deputy mayor is the director. In order to publicize the Regulations and the harm of tobacco, in collaboration with City Civilization Office, established a tobacco control media network, organized nearly 50 campaigns. Through TV, radio, LCD screen on buses & in downtown areas & building elevators to play tobacco control ads. Through advocacy, public awareness about smoking causes lung cancer was 90.9%, heart disease awareness reached 71.7%, while the awareness of SHS can cause children's lung disease was 83.9%. Established a comprehensive smoke-free environment in health, educational institutions, public transport and waiting places. The number was up to 6000. Established the monitoring system about the harm of tobacco in Tianjin. Monitoring results showed an overall decline about the smoking rate from 27.2% to 26.2% after two year implementation. Survey result also showed that public support for smoking ban in public places has increased to 95%.

**Conclusions and key recommendations:** Sum up results of the implementation will give guidance to other cities in China. All aspects have improved residents smoking rate showed a downward trend, but the key venues indoor exposure to SHS is still at a high level. The results also showed that we should promote the participation of various departments to intensify tobacco control efforts, and jointly create a smoke-free environment.

**PD-1227-01 Himachal a non NTCP (National Tobacco Control Programme) state as role model for the country**

G Chauhan.<sup>1</sup> <sup>1</sup>Health and Family Welfare, Office of the Chief Medical Officer Una Himachal Pradesh, Una, India.  
e-mail: drgopal7475@yahoo.co.in

**Aim:** Effective Tobacco control with minimum /available resources in existing settings. Background/challenges: Himachal Pradesh (68 lack population) was left out of the 28 States in India in 2006 in the list of NTCP (National Tobacco Control Program) States (21 states were identified) in spite of the fact that as per NFHS-iii 2005-06, the smoking prevalence in the State was higher (33.2%) than the Country (32.7%). In 2008 WHO, IUTLD and GOI conducted a zonal workshop on Tobacco Control and the representation of Himachal was the key to understand the issue.

**Interventions/response:** Identification of few but committed volunteers as ambassadors. Tobacco control in the state by utilizing the existing resources .Simple implementing procedures /guidelines(to discuss tobacco control with the existing programs, to fine violators of the tobacco control law with routine inspections, and to use funds collected as fine for anti tobacco activities). Developing good scientific database /reporting /monitoring. Evidence based smoke free model was tested in Shimla town in 2009-10 with technical support from IUTLD and replicated. Tobacco Industry in Hamirpur was closed within 6 months of its inception. Huge media support. The Incentive was in the form of recognition, rewards & motivation.

**Results/lessons learnt:** Smoke Free city Shimla with compliance of smoke free rules >90% in 2010, all 12 Distt. Headquarters as smoke free with compliance of >80% in 2012,All Distt. as Smoke Free/smoke free Himachal with compliance of >80% in 2013.A model for a Tobacco Free Distt. Una( >80% compliance of Program & Law) has been developed and tested .About 20 tobacco control related news items are appearing in leading newspapers in a month.>60000 persons has been fined and >60 lacs INR has been collected as fine out of which >80% has been spent on anti tobacco activities. Tobacco control has become a priority in the State. New partners are joining hands and providing funds for tobacco control in the State now. State has been awarded by WHO SEARO awards for tobacco control in 2011&2012. There is a healthy competition for better compliance amongst the jurisdictions. The states of Punjab,Utrakhand,Bihar,Rajsthan has declared more than 30 jurisdictions as smoke free on this pattern.

**Conclusion:** Effective tobacco control can be achieved with the existing resources within the Govt. /NGOs provided that we proceed in a strategic way.



### PD-1228-01 Developing a district level "Tobacco Free" model on the analogy of smoke-free in Himachal Pradesh, India

G Chauhan.<sup>1</sup> <sup>1</sup>Health and Family Welfare Department, Office of the Chief Medical Officer Una (Himachal Pradesh), Una, India. e-mail: drgopal7475@yahoo.co.in

**Background/challenges:** Una (.56 million population) is a semi hilly District out of total 12 in the State of Himachal Pradesh (6.8 million population). Distt. Una / Himachal is not covered under the NTCP (National Tobacco Control Program/no funds and guidelines). Una was declared as smoke free on 31.5.13 by the Distt. Administration with 82.95% compliance of the Smoke Free Rules (section 4) of Indian Tobacco Control Law/COTPA 2003.3044 violators were panelized (5 Lac INR collected as fine) in the Distt. whereas 60000 in the State (70 Lac INR collected as fine) in the last 5 years. The smoke free success encouraged to advance for Tobacco free with >80% compliance of the main provisions (section4, 5, 6 a&b, 7) of the Indian Tobacco Control law.

**Interventions/response:** Baseline/existing compliance, time/place specific IEC activities, awareness/sensitization, earned media coverage, to utilize the funds collected as fine for anti tobacco activities, oath by family heads for supporting tobacco free movement, involving good NGOs, political and administrative thrust, decentralization of powers/making 3–5 member teams at local levels for time bound raids / enforcement of the law, monthly reporting system, review and monitoring.

**Results/lessons learnt:** The half yearly progress shows that- 1. Compliance of Section 4(Smoke Free Rules) =85% 2. Compliance of Section 6(a) sale of tobacco products to the minors =36.15%, 3. Compliance of Section6 (b) Sale of Tobacco products near educational institutions=26.83 4. Compliance of Section-5 (Ban on direct and indirect advertisement of Tobacco) =88.46% 5. Compliance of Section-7 (Ban on sale of tobacco without pack warnings) =93.75% Tobacco free is the new attraction after Smoke Free. Each sub Distt. Unit/block is competing for better compliance. The result identified the grey areas also.

**Conclusion:** The tobacco free model after smoke free in relation to the reduction in tobacco use will encourage the policy/law makers to support or devise new strategies.

### PD-1229-01 Compliance study: a cost effective tool for strengthening smokefree policy

B Pandya,<sup>1</sup> P Lal,<sup>2</sup> R Parmar.<sup>1</sup> <sup>1</sup>Operations, Population Services International, Jaipur (Rajasthan), <sup>2</sup>Technical Advisor, International Union Against Tuberculosis and Lung Disease (The Union), New Delhi, India. e-mail: bhaskar@psi.org.in

**Background:** Population Services International implemented a tobacco control project in three districts (Jodhpur, Kota and Udaipur) of Rajasthan with the goal of creating smoke free districts by facilitating implementation of the Cigarette and Other Tobacco Products Act (COTPA). To qualify for the status of "Smoke Free and

Compliant with COTPA act", a district must be at least 80% compliant with requirements regarding no smoking signage, smoking bans in public spaces, availability of tobacco-related promotional items, availability of tobacco products in public spaces, sale of tobacco to minors and proximity of tobacco vendors to educational institutions. A third party assessment study was conducted in intervention areas to investigate the level of compliance with key sections of COTPA.

**Design/Method:** The study population was 77.53 lakh for three districts. Observation points were randomly selected from intervention project areas. Observational checklists and tobacco retailer questionnaires were developed based on guidance from the Campaign for Tobacco Free Kids, John Hopkins Bloomberg School of Public Health and International Union against Tuberculosis & Lung Disease. 987 public places and 178 educational institutions were observed, and 1158 tobacco retailers were interviewed in the three districts of Rajasthan.

**Results:** The study found the following:

Sr.	Indicators	Jodhpur	Kota	Udaipur
1	Availability of No Smoking Signage's	33.0%	23.9%	29.8%
2	Absence of active smoking in the public places	82.7%	83.2%	91.4%
3	Non-availability of promotional items of smoking	79.8%	87.7%	88.1%
4	Non-availability of cigarette and beedi butts in premises of public places	65.2%	65.7%	61.9%
5	No selling of any tobacco product to minors	74.0%	91.0%	93.8%
6	Non-availability of any tobacco vendors within 100 yards of education institutions	68.9%	82.1%	65.6%

**Conclusions:** This compliance assessment is an effective tool for helping to assess where districts are in relation to compliance with the law. The results provide direction to strengthen smoke free policy at district and state level. Results and recommendations from this study will be used to guide enforcement and public education resource allocation and efforts in all three districts.

### PD-1230-01 The compliance to local smokefree legislation in Bali Province, Indonesia

IWG Artawan Eka Putra,<sup>1</sup> A Swandewi,<sup>1</sup> IMK Duana,<sup>1</sup> K Suarjana,<sup>1</sup> KH Mulyawan,<sup>1</sup>

TA Pradnyadewi Ni Luh Nyoman,<sup>2</sup> T S Bam.<sup>3</sup>

<sup>1</sup>Epidemiology, School of Public Health, Faculty of Medicine, Udayana University, Denpasar, <sup>2</sup>Bali Tobacco Control Initiative, Center For Public Health Innovation, Denpasar, <sup>3</sup>Tobacco Control, The International Union Against Tuberculosis And Lung Disease, Jakarta, Indonesia. Fax: (+62)3617448773. e-mail: gedartawan@unud.ac.id

**Background:** Since 2011, the local government of Bali Province implement a local legislation no. 10/2011 regarding smoke-free area (local smoke-free legislation). The legislation is very important to reduce the harm of smoking and provide healthy air to the community. A comprehensive evidence is needed to support the

successful of the implementation. We aimed to describe the compliance to the legislation and identify the factors associated.

**Design/Methods:** We conducted two cross-sectional studies in Bali Province, Indonesia from July to August 2013 and February to March 2014. The population is all area that ruled in the legislation including education, health facilities, worship places, children's playground, work places and public places. Samples were selected by proportional probability to size (PPS). The compliance defined by 8 criteria that established in the legislation. The data were collected by observing the building and interviewing the managers using observation form.

**Results:** The study succeeded to observe 2647 building of 1100 smoke-free area selected at each study. The compliance to local smoke-free legislation is 11.8% in 2013 increasing to 17.2% in 2014. The 3 most infraction of smoke-free policy are found cigarette butts indoor (32.9% in 2013 and 32.6% in 2014), providing ashtray indoor (30.9% in 2013 and 29.6% in 2014) and smoking indoor (22.5% in 2013 and 27.8% in 2014). The no-smoking sign coverage is still low, 21.2% in 2013 increasing to 30.8% in 2014, which is the most important criteria effected to the compliance. Health facilities is the best area and Denpasar is the best city comply with the legislation. The factors associated to the compliance are the managers that have been informed the smoke-free legislation, the good knowledge of the managers regarding principal, responsibility, penalty of smoke-free implementation and application of internal monitoring.

**Conclusion:** The compliance to local smoke-free legislation is still lack and the increasing at the last 6 months period is not significant. We recommend to optimize the tobacco control team in each district/city to disseminating and mentoring the implementation of smoke-free policy and internal monitoring at each area.

#### **PD-1231-01 Smokefree cities - an innovative approach to tobacco control in challenging environments: case study, Harbin**

J Zhang.<sup>1</sup> <sup>1</sup>Tobacco Control Office, Harbin Center for Disease Control and Prevention, Harbin, China.  
e-mail: ccd0451@gmail.com

**Background and challenges to implementation:** In 2010, we joined in "Urban Smoke-free Environment Promotion Project" of Chinese Center for Disease Control and Prevention, started the cooperation for the first stage of the project with UNION, and launched the smoke-free environment promotion and the local smoking control law making of Harbin City. In 2011, Regulations for Preventing Harm of Environmental Tobacco Smoke of Harbin City was passed by the People's Congress of Harbin City and approved by the People's Congress of Heilongjiang Province. It was put into effect on May 31, 2012. At the same time, "Smoke-free Environment Promotion Project of Harbin City (reinvestment)" was launched to promote the smoke prevention law enforce-

ment and the indoor smoke-free environment construction of Harbin City.

**Intervention or response:** Promote the effective implementation of the local smoking control law, construct the smoke-free environment of indoor public places and work places, prevent the harm of environmental tobacco smoke, and protect the public health. Implement the project by policy management, publicity and advocating, construction of smokefree places, and social supervision and environment monitoring.

**Results and lessons learnt:** Through the cooperation for the reinvestment of the project with Chinese Center for Disease Control and Prevention and The Union, the implementation of Regulations for Preventing Harm of Environmental Tobacco Smoke of Harbin City has been effectively promoted, and the reinvestment project achievements have been obtained. At present, the indoor smoke-free environment of different kinds of no-smoking places has been improved greatly. According to monitoring investigations, the rate of places with possible smoking phenomena according to the prompt of environmental tobacco smoke monitoring of indoor air has dropped from 78% to 31%.

**Conclusions and key recommendations:** Regulation of Preventing Harm of Environmental Tobacco Smoke of Harbin City has been effectively implemented, "Smoke-free Environment Promotion Project of Harbin City (Second Stage)" has been carried out smoothly, and the smoke-free environment of indoor public places and work places has been comprehensively improved.

#### **PD-1232-01 Impact of effective implementation of tobacco control policies on consumption pattern in Shimla Town**

N Sharma,<sup>1</sup> R Kumar.<sup>2</sup> <sup>1</sup>Civil Society, Himachal Pradesh Voluntary Health Association, Shimla, <sup>2</sup>Tobacco, The Union, South East Asia, Delhi, India. Fax: (+91)01772670346.  
e-mail: nar.sharma@gmail.com

**Background and challenges to implementation:** Effective implementation of tobacco control policies has a long term impact on tobacco consumption pattern. Tobacco control policies can be implemented through tobacco taxation increase, implementation of smoke free laws and creation of awareness on ill effects of tobacco. The rationale behind these efforts is to encourage cessation among existing tobacco users, prevent initiation among potential users and to reduce the quantity of tobacco consumed. The implementation of smoke free laws through effective enforcement reduces the incidence of tobacco consumption.

**Intervention or response:** The tobacco industry is well aware that raising of taxes reduces the demand for tobacco most sharply in low and middle income countries where smokers are more responsive to price increases than in the high income countries, hence the industry tries to counter this policy initiative. But Himachal Pradesh Voluntary Health Association through proactive policy advocacy influenced the policy makers and taxes have been increased to 40% in last 3

years on tobacco products. HPVHA through concerted efforts of stakeholder sensitization, media advocacy, formation of enforcement mechanism effectively implemented COTPA, 2003 and the state of Himachal was declared as Smoke Free. To gauge the impact of tobacco control measures, HPVHA conducted a survey by developing a protocol of international standards and covered around 2000 stakeholders including the general public (consumers) and tobacco vendors across various localities in Shimla town.

#### Results and lessons learnt:

- 36.67% of the vendors claimed that there has been a decrease in tobacco sales in last 3 years.
- Out of these, 90.91% attribute the reduction in sales to the increase in prices of tobacco products.
- 72.72% feel that there has also been a significant impact of strict regulations on the tobacco sales.
- 70% of the vendors feel that consumers generally prefer buying loose cigarettes instead of the entire pack.
- 29.45% consumers feel that there has been a reduction in cigarette consumption in the last 3 years due to strict compliance of tobacco control policies.
- 26.31% consumers believe that the reduction in their cigarette consumption is due to increase in cigarette prices.

**Conclusions and key recommendations:** Survey findings clearly indicate that there has been a significant impact of the increase in tax rates and effective implementation of COTPA on the sales and consumption of tobacco products.

#### PD-1233-01 How compliant are tobacco vendors to India's tobacco control legislation on ban of advertisements at point of sale? A multi-centric study

S Goel,<sup>1</sup> R J Singh,<sup>2</sup> R Kumar,<sup>2</sup> J Tripathy.<sup>1</sup> <sup>1</sup>School of Public Health, Post Graduate Institute of Medical Education and Research, Chandigarh, <sup>2</sup>Tobacco Control, International Union Against Tuberculosis and Lung Disease, New Delhi, India. Fax: (+91) 17227 44993. e-mail: sonugoel007@yahoo.co.in

**Aim:** Section 5 of India's tobacco control legislation "Cigarettes and Other Tobacco Products Act (COTPA), 2003" comprehensively prohibits all kinds of tobacco advertisement, promotion and sponsorship (TAPS), however permits advertisements at the point-of-sale (POS) under certain conditions. This provision has been exploited by the tobacco companies to promote their products. We attempt to measure compliance to the provisions of Section 5 of Indian tobacco control legislation (COTPA, 2003) at point of sale in India.

**Methods:** A cross-sectional survey using an observation checklist was conducted in 1860 POS across three jurisdictions (Chennai city, District Vadodara and District Mohali) in India.

**Results:** The most common mode of advertisement of tobacco products was product showcasing (51.1%), followed by dangles (49.6%), stickers (33.8%) and boards (27.1%). More than one fourth of POS were

found violating legal provision for displaying advertisement boards in one or other forms (oversized, extended to full body length of POS, displayed brand name/package shot and promotional messages). Advertisement boards (16.3%) without health warnings were also found and wherever found, more than 90% health warning were not as per the specification in respect to size, font and background color.

**Conclusion:** Point of sale advertising is aggressively used by the tobacco industry to promote their products. There is an urgent need of effective implementation of comprehensive ban on tobacco product's advertisement, promotion and sponsorship at point of sale.

#### PD-1234-01 Tobacco smoke free Punjab: a government-civil society driven model for tobacco control in India

R Gupta,<sup>1</sup> R J Singh,<sup>2</sup> R Kumar,<sup>3</sup> S Goel.<sup>4</sup> <sup>1</sup>State Tobacco Control Cell, Health and Family Welfare Punjab, Chandigarh, <sup>2</sup>Tobacco Control, The Union, New Delhi, India, <sup>3</sup>Tobacco control, The Union, New Delhi, <sup>4</sup>School of public health, PGIMER Chandigarh, Chandigarh, India. Fax: (+91)1725012356. e-mail: rakesh60.mahajan@gmail.com

**Background:** Punjab (Population: 27.7 million; Area: 19,445 sq mi) is one of the states in northern part of India. It is a state of where most people are the followers of Sikh religion. Tobacco use in any form is totally prohibited in Sikhism. However, GATS India survey report 2009–2010 revealed that 12% of population in Punjab uses tobacco in any form; means there by there are about 33 lakh tobacco users in the state.

**Methods:** Present study was carried out with the objective to analyse the process undertaken in making 17 districts of Punjab- tobacco smoke-free with a compliance rate as high as 96.4%. The process for making 17 district tobacco-smoke free was assessed by the researchers by reviewing official documents at Tobacco Control Cell at Directorate of Health & Family Welfare Punjab, observing sensitization/law enforcers training workshops, scanning media reports, reviewing the monthly progress reports of program implementation and law enforcement and by interacting with key Stakeholders.

**Results:** It was observed that technical support and capacity building by the Union- South East Asia played a crucial role in the process. It was supported by strong advocacy movement and public awareness by local NGOs. Series of sensitization workshops and law enforcer's trainings were organized in each district. State level and Distt monitoring committees were notified. Government ensured strict law enforcement. All this led to challaning (fine) of 45000 violators of anti-tobacco law. Punjab became the first state to ban electronic cigarettes in India. Permanent District Task Force has been notified in Punjab to monitor implementation of Anti-Tobacco law and abuse of Nicotine in chemical form on a monthly basis. A total of 17 out of 22 districts are now declared as tobacco -smoke free till February 2014.

**Conclusions:** A synergistic and complimentary approach, mutual trust and synergistic collaboration between



Government institutions and civil societies is always vital for successful implementation of any public health initiative. The success of the tobacco- smoke free districts initiatives in Punjab showed the way for 100% tobacco free districts in next phase and a replicable model for others across India.

**PD-1235-01 Success story of intertabac Asia rejection in Bali, Indonesia: strong commitment from locals against the tobacco interference**

IMK Duana,<sup>1</sup> T S Bam,<sup>2</sup> TA Pradnyadewi Ni Luh Nyoman,<sup>3</sup> A Swandewi,<sup>1</sup> K Suarjana,<sup>1</sup> IWG Artawan Eka Putra,<sup>1</sup> KH Mulyawan.<sup>1</sup> <sup>1</sup>School of Public Health, Faculty of Medicine, Udayana University, Denpasar, <sup>2</sup>Tobacco Control, The International Union Against Tuberculosis And lung Diseases, Jakarta, <sup>3</sup>Bali Tobacco Control Initiative, Center for Public Health Innovations, Denpasar, Indonesia.  
e-mail: madekerta2na@yahoo.com

**Background and challenges to implementation:** Indonesia is the third country with the largest number of smokers in the world. Recently smokers reaching 60 million (28 % teenagers), due to massive advertising and promotion of cigarette. Plenty of the strategies have been taken by the government, the important one is regulations regarding smoking and tobacco products. Bali is province in Indonesia which has smoke-free law at provincial and district level. Tobacco industry targeting Indonesia as main venue of promotion for example in 2012 conducted the World Tobacco Asia in Jakarta. Since Indonesia becomes potential market and the regulation regarding tobacco control remain weak, similar activities will be carried out again in Bali (Intertabac Asia on 27 February 2014 which organized from Dortmund, Germany).

**Intervention or response:** Through Bali Tobacco Control Initiative (BTCl), various actions have been taken, such as: build networking (involving journalists and various media to blow up this event and get attention from the government, collaborating the actions with local organizations, local leaders, and academicians then sent letter of rejection to the local and central government and sign petition); advocating the policy makers (Bali Governor, Bali health office, Regent of Badung district, and the manager of the venue namely Bali Tourism Development Corporation (BTDC); Mass mobilization by conducting demonstration to emphasize our rejection to the public.

**Results and lessons learnt:** Following our efforts and actions, many rejection news blew up by various media, then official rejection stated by the Bali Governor and huge support from the community were gained. After the issuance of an official rejection letter either by the Bali governor or Regent of Badung district, these become a strong consideration for the managers of BTDC not to permit this event. Eventually, the committee of this event announced that Intertabac Asia is cancelled in Bali.

**Conclusions and key recommendations:** Commitment of locals needed against tobacco industry interference. Through our decentralization system, it is possible to make and maintain local policy with minimal interference from central government. It is proved by our success

to reject the Intertabac Asia in Bali. However, the local's commitment has to be maintain and even foster. Therefore, it is remain needed support and participation from all level of locals to cope the next challenges. .

**PD-1236-01 India's single cigarette economy: a back of the envelope assessment of its volume and size**

R Kumar,<sup>1</sup> P Lal.<sup>1</sup> <sup>1</sup>Tobacco control, International Union Against Tuberculosis and Lung Disease, New Delhi, India.  
e-mail: rkumar@theunion.org

**Background:** Sale of single cigarettes is an important factor for the initiation and persistence of tobacco use and a vital factor in smoking epidemic in India as it is globally. Singles stand to undermine public health effect of tax and distort fiscal policy and administration of tax, while creating opportunities for the sale of illicit cigarettes.

**Methods:** In February 2014, a 10 city survey estimated the sale of cigarettes in pack and sticks, by brands and price sold over a single day. Ethical Advisory Group of The International Union Against Tuberculosis and Lung Disease (The Union) provided guidance on ethical aspects of the study and granted ethical clearance to conduct the survey (application no: 213/2013).

**Results:** Nearly 74% of all cigarettes are sold as single sticks annually (worth nearly half a billion US dollars or 30 percent of the excise revenues from cigarette). This is the price which the consumers pay but is not captured through tax and therefore pervades in an informal economy.

**Conclusion:** The widespread existence of the single cigarette market buffers for any significant increase tax which is passed on to the consumer which defeats the public health goals and fiscal rationale of taxing cigarettes. Tracking price of single cigarette is an efficient proxy to determine cigarette tax (in the absence of any other rationale).

## 65. TB PREVALENCE ESTIMATIONS

**PD-1237-01 A modern approach to estimating incidence: re-writing Styblo's rule**

M Begun,<sup>1</sup> A Newall,<sup>1</sup> G Marks,<sup>2,3</sup> J Wood.<sup>1</sup> <sup>1</sup>School of Public Health and Community Medicine, University of New South Wales, Sydney, NSW, <sup>2</sup>Respiratory and Environmental Epidemiology, Woolcock Institute of Medical Research, Sydney, NSW, <sup>3</sup>South Western Sydney Clinical School, University of New South Wales, Sydney, NSW, Australia.  
e-mail: m.begun@student.unsw.edu.au

**Background:** Estimation of the true incidence is a challenging and important problem in the control of tuberculosis (TB). The model based approach proposed by Styblo in 1985 is known to be inaccurate in the modern era where there is widespread availability of treatment for TB. At present there is no clear and simple alternative to using Styblo's ratios in most settings. This

study re-examines the relationship between incidence and other disease indicators that may be derived from surveys with the aim of improving on Styblo's ratios in the presence of treatment programs. These revised ratios could potentially provide clinicians and epidemiologists with a cost effective and efficient means of estimating incidence from data that has already been collected.

**Design/Methods:** We adapt a simple, previously published model (Blower et al. 1995) that describes the epidemiology of TB in the presence of treatment to investigate a revised ratio-based approach to estimating incidence. We examine the behaviour of the ratios at different stages of the epidemic (increasing, declining, endemic), the impact of treatment and other condition changes, and the robustness of the approach to different realistic implementations of treatment programs.

**Results:** We show that, following changes to treatment programs for TB, the ratio of incidence to prevalence reaches an equilibrium value rapidly; long before other model indicators have stabilized. We also show that this ratio relies on few parameters but is strongly dependent on the efficacy and timeliness of treatment.

**Conclusion:** Our results show that a simple ratio based on equilibrium behaviour of the model can provide accurate estimates of modelled incidence from prevalence following changes to current treatment programs. We also show that this ratio relies on few parameters but is strongly dependant on efficacy and the timeliness of treatment. These findings demonstrate the potential for using model based approaches to find easy to use methods of accurately estimating incidence from data already in the process of being collected by planned cross-sectional surveys. This technique could provide epidemiologists with an efficient and cost effective method of estimating incidence of TB with data already being collected in national prevalence surveys in the areas they are investigating.

### PD-1238-01 Profil épidémiologique de la tuberculose en République Démocratique du Congo (2008–2012) et tendances prévisibles

N Aït-Khaled,<sup>1</sup> A Trébucq,<sup>1</sup> V Schwoebel,<sup>1</sup> G Koura,<sup>1</sup> G Lay,<sup>2</sup> G Bakaswa.<sup>2</sup> <sup>1</sup>Tuberculosis, The Union, Paris, France; <sup>2</sup>Unité Centrale, Programme National Tuberculose RDC, Kinshasa, Democratic Republic of Congo.  
e-mail: naitkhaled@theunion.org

**Objectif :** Etablir le profil épidémiologique de la TB en RDC et les tendances prévisibles.

#### Méthodes:

- Revue : documents, données du PNLT, rapports de visites de suivi/évaluation.
- Analyse des facteurs influant la TB et tendances épidémiologiques basée sur 3 graphiques (incidence et taux, variation annuelle, courbe des âges) pour la RDC et par province.
- Rapport de L'Union sur le profil épidémiologique de la TB, hypothèses de tendances.
- Validation du rapport par le PNLT et ses partenaires (Kinshasa, Novembre 2013).

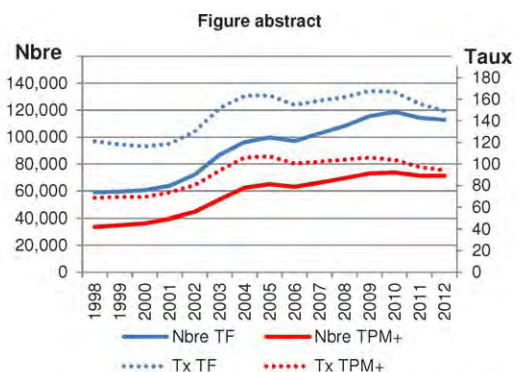
#### Résultats:

1. Fiabilité des données de par leur complétude et leur cohérence.
2. Facteurs favorables à une diminution de l'incidence de la TB : grande qualité du PNLT, du réseau de laboratoires, et du partenariat tant national (Fondation Damien, TLMI, CAD) qu'international (OMS, Union, USAID, AFD, Fond Mondial). Collaboration avec plusieurs Universités.
3. Facteurs favorables à la propagation de la TB : prévalence élevée du VIH, crise humanitaire et sociale, conflits armés, pauvreté, transmission élevée de la TB dans les mines...
4. L'incidence des cas déclarés de TB a doublée entre 1998 (33 442 TPM+Nx cas et TB 58 917), et 2012 (respectivement 71 124 et 112 786). 4 périodes ont été identifiées :
  - 1998–2000, suite aux conflits armés, le PNLT est désorganisé, augmentation faible (1% à 2%/an) ;
  - 2001–2004, soutien international (GDF, Union, USAID), réorganisation et expansion nationale du PNLT (augmentation d'au moins 10%/an culminant à 20% en 2003) ;
  - 2005–2009, augmentation d'environ 5% /an ;
  - 2010–2012, amorce de la stabilisation du nombre de cas déclarés.
5. Analyse des 3 graphiques
 

Pour la RDC : l'analyse suggère une tendance à la diminution du nombre de cas de la TB.

Mais les tendances sont différentes selon les provinces : diminution du nombre de cas (Bas Congo, Kinshasa), stabilisation (Bandundu, Equateur), ou augmentation (Kasai, Katanga, Maniema, Nord Kivu, Sud Kivu et Province Orientale).
6. Hypothèses sur les tendances épidémiologiques par extrapolation des résultats : augmentation annuelle de la TB de 0,27% dans l'hypothèse basse et d'environ 4% dans la haute avec une évolution variable selon les provinces.

**Conclusion :** En dépit de l'amorce d'une stabilisation de la déclaration des cas de TB en RDC, on ne peut pas encore prévoir une nette diminution des cas de TB dans les années à venir en raison de la persistance de facteurs favorables à l'expansion de la TB et de l'augmentation prévisible de la TB dans plusieurs provinces.



Incidence et taux d'incidence de la tuberculose en RD Congo, 1998 – 2012

### PD-1239-01 Incidence of smear positive TB in Dale district, Sidama, south Ethiopia

D Datiko,<sup>1</sup> E Woldemamayrat,<sup>2,3</sup> B Lindtjorn,<sup>3</sup> M Dangiso.<sup>3,4</sup> <sup>1</sup>Tropical Medicine, Liverpool School of Tropical Medicine, Liverpool, UK; <sup>2</sup>Public and Environmental Health, Hawassa University, Hawassa, Ethiopia; <sup>3</sup>Centre for International Health, University of Bergen, Bergen, Norway; <sup>4</sup>Sidama Zone Health Department, SNNPR Health Bureau, Hawassa, Ethiopia. e-mail: endromark@yahoo.com

**Background:** Incidence is one of the key indicators of tuberculosis (TB) burden. We aimed to estimate incidence of smear positive tuberculosis (PTB+) in Dale district, South Ethiopia.

**Design/Methods:** We did a census of 36,575 people in randomly selected six rural communities in Dale district, South Ethiopia. Based on interviews, we identified chronic coughers. We then did a prospective cohort study of 724 smear negative chronic coughers and 1448 neighborhood controls. Every third months, we interviewed them, and did sputum microscopy. During the same period, all PTB+ cases identified by TB REACH project (another study on active case finding) and health facilities report on self-presenting TB cases was taken.

**Results:** Between September 1, 2011 and June 30, 2012, over a total of 18,029 person-year of follow up, 56 PTB+ cases were diagnosed. Incidence rate of PTB+ in Dale was 310.6 cases per 10<sup>5</sup> person-years (95% CI 236.9 – 400.4). We observed higher incidence of PTB+ among chronic coughers, people in age group more than 34 years and those with no schooling than their counter part.

**Conclusion:** Compared to the national estimate and other reports, incidence of PTB+ is high in rural communities in South Ethiopia. Effective strategy is needed to decrease its burden. Improving health seeking behaviour of people and active case finding could help in reducing its transmission. Emphasis should be given to chronic coughers, people with no schooling and to those whose age is above 34 years.

### PD-1240-01 Tuberculosis among inhabitants of Rajshahi city of Bangladesh: an epidemiological study

M Kalam.<sup>1</sup> <sup>1</sup>Research, Siam Health Care, Dhaka, Bangladesh. Fax: (+88) 02 9138411. e-mail: med\_sociology\_jedcr@yahoo.com

**Background:** Tuberculosis is of huge concern for under developed countries and is the cause of millions of deaths each year. In this study we have researched epidemiological parameters of TB over a five year period in Rajshahi City, Bangladesh, highlighting the region's inefficient health systems.

**Methods and materials:** All participants referred to Rajshahi TB Clinic over a five year period (2008–2012) were studied. Questionnaires were completed by expert health care workers in Rajshahi TB Clinic for each patient. The demographic data Included: sex, age, name, address, nationality, residence, treatment, disease type

(pulmonary or extra pulmonary), success of treatment. Data after collection were analysed with SPSS Software. **Results** Two thousand and sixty eight cases were diagnosed over the five year total. The majority of cases (57%) were from urban areas and the majority of cases (83%) had pulmonary tuberculosis. Most of them were aged 21 to 30 years old. Treatment failed in a small minority patients (2.5%) due to pulmonary tuberculosis. In the patients with pulmonary tuberculosis the sputum smear before treatment in (16.5%) has not been done.

**Conclusion:** The majority of cases were urban and many of them are the workers and they are the major problem in the control of tuberculosis in Rajshahi TB Clinic, so much more case finding efforts should be done among them. The majority of cases are men with pulmonary tuberculosis. Although the majority of cases were treated successfully, the sputum smear the patients with pulmonary tuberculosis before treatment in (16.5%) has not been done so more attention should be given in this field.

### PD-1241-01 Tuberculosis in MERCOSUR border municipalities, 2011

R Maia,<sup>1</sup> M.S. Evangelista,<sup>1</sup> A De Paula Lobo,<sup>1</sup> C Oliveira Dantas,<sup>1</sup> M Jacobs,<sup>1</sup> H Barroso Bernal,<sup>1</sup> F Moherdau,<sup>1</sup> D Barreira.<sup>1</sup> <sup>1</sup>National Tuberculosis Control Program, Brazilian Ministry of Health (MoH), Brasilia, DF, Brazil. e-mail: maria.evangelista@saude.gov.br

**Background:** The South Common Market (MERCOSUR) is a block constituted to widen national markets through free trading of goods and services and the free movement of people and capital. This free movement brings possible public health issues in border areas and main migration routes. The Brazilian border area is still under economic development and the population has limited access to public goods and services. Living conditions in these areas and the large movement of people may favor the spread of the tuberculosis (TB) epidemic. The aim of this study was to describe TB diagnosed cases in the municipalities that are border with MERCOSUR countries (Brazil, Argentina, Paraguay, Uruguay and Venezuela).

**Design/Methods:** This is a descriptive study using secondary data from the National Surveillance Notification System (SINAN), covering 466 municipalities located in the border between Brazil and MERCOSUR countries. From this total, 7 municipalities are located in the North region, in the Venezuelan border; 39 are in the Midwest region, in the Paraguayan border; and 366 in the South region, in the border with Paraguay, Argentina and Uruguay. Sociodemographic data, clinical presentation, and retreatment cases were analyzed. Incidence rates (IR) were calculated per 100,000 inhabitants, according to sex, age and residence region.

**Results:** 1,757 TB cases were reported in the study population: 1,303 (74.2%) in the South, 374 (21.3%) in the North and 80 (4.6%) in the Midwest. The IR accounted 20.6, 52.5 and 43.2 per 100,000 inhabitants, respectively. From the total cases, 1,202 (68.4%) were male, 1,286 (73.5%) between 15–59 years old and 993 (56.5%) were white. With regards to the clinical



presentation of the disease, 1,463 (83.3%) cases were pulmonary TB. Regarding treatment closure, the cure rate was 76.6% and 7.2% defaulted. 228 cases were retreatment of pulmonary TB. From this total, 39.9% were sputum culture.

**Conclusion:** It is evident that TB remains a public health problem in border municipalities of MERCOSUR, which indicates the need for more effective disease surveillance, whereas the high traffic of people can hinder TB control, leading to the circulation of multidrug-resistant bacilli. Data from this study can contribute to the organization and strengthening of local health systems, in addition to the implementation of collaborative activities from the MERCOSUR TB Working Group.

#### PD-1242-01 Tuberculosis mortality survey in two selected townships in Myanmar

ST Aung,<sup>1</sup> KK Zaw,<sup>2</sup> T Lwin.<sup>3</sup> <sup>1</sup>Department of Health, National TB Programme, Nay Pyi Taw, <sup>2</sup>Department of Medical Research (Lower Myanmar), Nutritional Research, Yangon, <sup>3</sup>Department of Health, Disease Control, Nay Pyi Taw, Myanmar. Fax: (+95) 67-421201. e-mail: mywaddy@gmail.com

**Background:** National TB Programme (NTP) has never assessed TB mortality at the community level. The only information available in the country is the number of TB deaths among cohorts of registered TB patients. Vital registration is covering only one third of the country especially in urban. The aim of this study is to determine adult TB specific mortality rate in two selected townships: Padaung (Bago Region) and Kawkaireik (Kayin State).

**Design/Methods:** It is a cross-sectional study to ascertain causes of adult deaths that occurred during 1<sup>st</sup> January to 31<sup>st</sup> December 2012. Verbal autopsy interviews of relatives or main care givers of the deceased were done by trained interviewers. All deaths data were identified through death registries at respective Township Health Departments. Data collection was completed in May 2013. Verbal autopsy questionnaires were reviewed independently by 2 physicians to assign the causes of deaths. For discrepancies in diagnoses between these two physicians, 3<sup>rd</sup> physician gave the final decision. Pulmonary TB mortality per 100,000 population was estimated by using TB death data from verbal autopsy questionnaires and population data from respective township health management information.

**Results:** Out of total (448) persons aged  $\geq 15$  years, females comprised 61% of all deceased persons. The age of (448) deceased persons ranged from 15 to 99 years with the mean age of 83 years. About 40% of deaths occurred in people under 60 years. Most of deceased were ever married and most of deaths occurred at home. This study showed five leading causes of death: stroke, liver diseases, pulmonary tuberculosis, digestive neoplasms and other/unspecified cardiac diseases. But 22% of adult deaths had unknown cause. Pulmonary tuberculosis attributed to 7% of all adult deaths, which ranked 3<sup>rd</sup> in both townships. TB deaths occurred in males more than in females (61% vs. 39% of all adult TB deaths) and

in  $\geq 60$  years group more than  $< 60$  years group (61% vs. 39% of all adult TB deaths). TB mortality rate was 51 per 100,000 population and was higher in older age groups and males.

**Conclusion:** This study reasonably reflects the TB-specific mortality fraction among all deaths but it is confined to two selected townships and estimates of TB mortality per population have high level of uncertainty. However, the finding was quite close to WHO estimate, 48/100,000 population for 2012. Therefore, TB mortality survey of wider scope, a national scale, would not be necessary.

Table 4. Cause of death (physician-coded) for persons aged 15 years and above who died between Jan. and Dec. 2012 in the study areas of Kawkaireik and Padaung townships

Rank	Cause of death	Freq. (n=448)	Percent
1	Stroke	91	20.31
2	Liver cirrhosis	33	7.37
3	<b>Pulmonary tuberculosis</b>	<b>31</b>	<b>6.92</b>
4	Digestive neoplasms	28	6.25
5	Other and unspecified cardiac disease	26	5.8
6	Respiratory neoplasms	14	3.13
7	Diabetes mellitus	11	2.46
8	Renal failure	10	2.23
9	Other and unspecified neoplasms	9	2.01
10	Acute cardiac disease	9	2.01
11	Asthma	7	1.56
12	Malaria	6	1.34
13	Severe malnutrition	6	1.34
14	Chronic obstructive pulmonary disease	6	1.34
15	Road traffic accident	6	1.34
16	Accidental drowning and submersion	6	1.34
17	Acute abdomen	5	1.12
18	Sepsis	4	0.89
19	HIV/AIDS related death	4	0.89
20	Female reproductive neoplasms	4	0.89
21	Contact with venomous animals and plant	4	0.89
22	Intentional self-harm	4	0.89
23	Acute Respiratory infect including pneumonia	3	0.67
24	Abortion-related death	3	0.67
25	Other and unspecified infect disease	2	0.45
26	Breast neoplasms	2	0.45
27	Epilepsy	2	0.45
28	Exposure to force of nature	2	0.45
29	Diarrheal diseases	1	0.22
30	Meningitis and encephalitis	1	0.22
31	Oral neoplasms	1	0.22
32	Pregnancy-induced hypertension	1	0.22
33	Obstetric haemorrhage	1	0.22
34	Other transport accident	1	0.22
35	Accidental fall	1	0.22
36	Accidental poisoning and exposure to noxious substance	1	0.22
37	Assault	1	0.22
38	Other and unspecified external cause	1	0.22
39	Cause of death unknown	100	22.32

### PD-1243-01 Tuberculosis as a prevalence cause of pleural effusion in Akwa Ibom southern Nigeria

V Obot,<sup>1</sup> E Ekpe,<sup>2</sup> M Gidado.<sup>3</sup> <sup>1</sup>Public Health, Ministry of Health, Uyo, <sup>2</sup>Cardiothoracic Surgery unit, University of Uyo Teaching Hospital, Uyo, <sup>3</sup>Country Representative, KNCV/TBCARE 1, Abuja, Nigeria. Fax: (+234) 424 52 311. e-mail: valerie\_\_obot@yahoo.com

**Background:** Pleural effusion being excessive accumulation of fluid in the pleural cavity can occur as a result of lung, pleural or systemic disorders. Pleural TB is notoriously difficult to diagnose due to its paucibacillary nature yet it is the most common cause of pleural effusions in regions with high TB and HIV infections. For appropriate treatment, the specific cause of pleural effusion must be known. The aim of this study was to determine the common causes of non purulent pleural effusions.

**Design/Methods:** Retrospective chart analysis of medical records of 105 patients with non purulent pleural effusion who presented from January 2007 to December 2011 (5 years) at University of Uyo Teaching Hospital, a tertiary referred medical centre in southern Nigeria. Non purulent pleural effusion was defined as pleural effusion that was not grossly purulent fluid; but may have positive effusion culture; and positive Gram's stain for bacteria. 105 patients with non pleural effusion were analyzed for demography, symptoms, pleural fluid biochemical, microbiological, cytological, and pleural biopsy studies. Analysis was by comparative proportions and percentages.

**Results:** Of the 105 patients studied, there were 50 males and 55 females (M: F = 1:1.1) with age from six months to 69 years and mean 37.8 ( $\pm$  11.5). The most common symptoms were difficulty in breathing, cough and chest pain which were complained of by 100%, 97.1% and 92.4% of the patients. The pleural fluid was serous in about 75% (79 patients) and haemorrhagic in 26 patients (25%). Biochemical quantitative analysis of the pleural fluids for protein and lactate dehydrogenase differentiated the pleural effusion into 12 transudative and 93 exudative pleural effusions based on cut-off pleural fluid protein of 30g/L and LDH of 200U/L. Gram stains were suggestive of infection in 21 (20%) patients while cultures confirmed the infection in only nine (42.8%) of the 21 patients. Pneumonia was the most common cause of non purulent pleural effusion accounting for 31.4% of the cases while tuberculosis ranked second with 28.6% and breast cancers (all in women) ranked third with 10.5%

**Conclusion:** With appropriate facilities the cause of non purulent pleural effusion can be discovered to pave way for appropriate treatment. Tuberculosis should always be investigated as common cause of pleural effusions. Further research required to investigate the association between pleural effusions and immunosuppression.

### PD-1244-01 Biomass as a risk factor for tuberculosis among rural women of Sindh, Pakistan

Dr Asaad Nafees,<sup>1</sup> U Rabbani,<sup>1</sup> A Sahito,<sup>1</sup> A Kamran,<sup>2</sup> Z Fatmi.<sup>1</sup> <sup>1</sup>Department of Community Health Sciences, Aga Khan University, Karachi, Pakistan; <sup>2</sup>Princess Nora bent Abdallah Women Health Research Chair, King Saud University, Riyadh, Saudi Arabia. e-mail: unaib\_dr@yahoo.com

**Background & Objective:** There are certain established risk factors for pulmonary tuberculosis (TB) such as malnutrition, poverty, overcrowding, diabetes and tobacco smoke; however, association between biomass fuel use and TB is still unclear. Keeping in view fact that large proportion of rural population uses biomass fuel in Pakistan, we aimed to see association between biomass fuel and TB in local context.

**Methods:** Facility based, age and union council matched case-control study was conducted in taluka Gambat, district Khairpur between February and May 2013. Eligible women between 20–65 years of age with and without active TB were recruited as cases and controls respectively. Data was collected through structured questionnaire which was translated into local language and pre-tested before use. Conditional logistic regression was used to assess the association between biomass fuel and TB

**Results:** A total of 178 cases and controls each were interviewed. After controlling for potential confounders, multivariate conditional logistic regression found that those who were current biomass fuel users were at higher risk of TB (OR 2.3; 95% CI: 1.08-4.9). The association was also significant when the exposure was graded; (OR 4.0, 95% CI: 1.4–11.2) for non-biomass fuel use for less than 8 years and (OR 6.7, 95% CI: 2.7–17.1) for current biomass users compared to non-biomass fuel use for more than 8 years.

Table 1: Models of multivariate conditional logistic regression showing association of biomass fuel use for cooking with tuberculosis among rural women of Sindh, Pakistan.

Model 1	Adjusted mOR (95% CI)	Model 2	Adjusted mOR (95% CI)
Type of fuel used (Current)		Type of fuel used (Graded)	
Non-biomass	1	Non-biomass for more than 8 years	1
Biomass	2.3 (1.08-4.9)	Non-biomass for less than 8 years	3.9 (1.3–11.8)
		Current biomass users	4.3 (1.6–11.8)

Abbreviations: mOR, matched odds ratio, CI, confidence interval  
Adjusted for income, family history of TB and smoker in family

**Conclusions:** Our study suggests that there is strong association between biomass fuel and TB. This calls for preventive measures such as provision of alternate safe fuel to the households in the rural settings in order to reduce the burden of TB caused by biomass fuel. Our study demonstrates the feasibility of case control studies in rural populations of women to address this question,

and is an encouragement to larger and statistically more powerful investigations.

#### PD-1245-01 Epidemiological trend in tuberculosis in Romania between 2002–2012

A Golli,<sup>1</sup> M Nitu,<sup>2</sup> M Olteanu,<sup>2</sup> M Ghelase,<sup>1</sup> L Ciobanu Mitache,<sup>3</sup> F Turcu.<sup>4</sup> <sup>1</sup>Public Health, University of Medicine and Pharmacy Craiova, Craiova, <sup>2</sup>Pneumology, University of Medicine and Pharmacy, Craiova, <sup>3</sup>Epidemiology, County Clinical Emergency Hospital from Craiova, Craiova, <sup>4</sup>Nephrology, University of Medicine and Pharmacy Bucharest, Bucharest, Romania.  
e-mail: andreea\_golli@yahoo.com

**Background:** The actual epidemiological situation of TB in Romania shows the necessity of early detection and directly observed treatment application.

**Objective:** to analyze the evolution of TB epidemic in Romania between 2002–2012, compared with the registered European values, for the evaluation of TB control strategy in Romania.

**Design/Methods:** The study was retrospective, describing the evolution of the main epidemiological indicators of TB in Romania from 2002–2012. The dates were obtained from “Marius Nasta” Institute of Pulmology from Bucharest, Ministry of Public Health Report 2013, European health for all database (HFA-DB) 2014 and WHO Global TB Report 2013.

**Results:** The overall incidence decreased with 43%, after a peak in 2002 from 142.2/100.000 to 79/100.000 in 2012, which puts Romania in 2012 on the seventh place in WHO Europe Region after Republic of Moldova (125/100.000), Kyrgyzstan (113/100.000) Kazakhstan (111/100.000), Ukraine (90/100.000), Georgia (90/100.000), and Tajikistan (81/100.000) and on first place in European Union, since accession in 2007. From the new TB pulmonary cases in 2012, 73.5% were smear-positive. Incidence of TB in children 0–14 years dropped steadily from 47.2/100.000 (1784 cases) in the 2002 to 65.4/100.000 in 2012. The percentage of the extrapulmonary forms in children increased from 17.9% in 2002 to 59.1% in 2011. The number of severe cases of TB in children (meningoencephalitis, miliary, cavitary) still maintains a constant high annual rate (65 cases in 2011), which demonstrates the severity of endemic TB in our country. The incidence of relapses declined with 41.6% from 23.3/100.000 in 2002 to 13.6/100.000 in 2012. TB mortality was almost half in 2012 (6/100.000) from the registered value for 2002 (10.8/100.000). From all the registered cases, 533 were MDR TB cases and 30 XDR TB cases in 2011.

**Conclusion:** The decline in TB nationwide after 2002 confirms the effectiveness of the control measures, but the rates are still very high. Although the level of TB incidence in Romania is one of the highest in Europe and first in European Union (EU) countries, in the last 10 years of reported data it was observed a descending trend.

#### PD-1246-01 Prevalence of tuberculosis risk factors among tuberculosis patients in Kampala, Uganda: a cross sectional descriptive study

A Okwera,<sup>1</sup> B Kirenga,<sup>2</sup> M Joloba,<sup>3</sup> W Ssengooba,<sup>3</sup> F Mugabe,<sup>4</sup> S Kasozi,<sup>4</sup> M Boeree.<sup>5</sup> <sup>1</sup>Mulago National Referral Hospital, National Tuberculosis Treatment Unit, Kampala, <sup>2</sup>Department of Medicine, Makerere University College of Health Sciences, Kampala, <sup>3</sup>Medical Microbiology Department, Makerere University College of Health Sciences, Kampala, <sup>4</sup>National TB and Leprosy Programme, Ministry of Health, Kampala, Uganda; <sup>5</sup>Medical Centre, Radboud University Nijmegen, Nijmegen, Netherlands. Fax: (+256) 414 533 531. e-mail: A\_okwera@mucwru.or.ug

**Background:** Slow decline in TB incidence has been observed. To expand TB control strategies there is need to know the magnitude of the contribution of each TB risk factor to the current TB epidemic. Except HIV, other TB risk factors are poorly studied.

**Objective:** To determine the prevalence of reported well recognized TB risk factors among tuberculosis patients in Kampala district in Uganda.

**Design/Methods:** TB patients aged  $\geq 18$  years were consecutively enrolled in 2013. Data on socio-demographic, TB symptoms, cxr, sputum, poverty, overcrowding, history of TB contact, family h/o TB, smoking, alcohol use, HIV infection, history of cancer and diabetes were collected.

**Results:** Of 365 patients, 158 (43.29%) were males. Median age was 29 (IQR 28–30). PTB was found in 89.3% and 86.9% were new patients. MDR TB was found in 6.3% of the new patients and none of retreatment patients. The prevalence of TB risk factors was as follows: HIV infection 41.91% (151/365), smoking 26.4%, cancer history 1.4%, diabetes 5.4%, poverty 39.5%, overcrowding 57.3%, family history of TB 17.5%, TB contact 11.5% and alcohol use 50.7%.

**Conclusion:** The prevalence of TB risk factors is high among TB patients in Kampala. Adults should be targeted for TB screening.

#### PD-1247-01 Tuberculosis in Tunisia during the last thirteen years

S Ben Saad,<sup>1</sup> isla Mejri,<sup>1</sup> H Daghfous,<sup>1</sup> hela Cherif,<sup>1</sup> moun Ben Khelifa,<sup>1</sup> leil Slim,<sup>2</sup> F Tritar.<sup>1</sup> <sup>1</sup>Respiratory Department (C), Abderahmen Mami Hospital, Ariana, <sup>2</sup>Department of Bacteriology, Abderahman Mami Hospital, Ariana, Tunisia. Fax: (216) 7182 1184.  
e-mail: hafaoua.daghfous@yahoo.fr

**Introduction:** Tuberculosis (TB) reemerged as a major health problem.

**Aim:** Overview changes in epidemiology, clinical features and management of TB in Tunisia through decades.

**Method:** Three groups of TB cases registered between 1980–1983: G1 (n= 522), 1990–1993: G2 (n= 266) and 2010–2013: G3 (n= 100) were included in this retrospective and comparative study.

**Results:** Average age is about 35 years in all groups. However, the incidence rate in elderly patients (>65years) is 10% (G3) vs 2% (G1 and 2). According



to gender there is no statistical difference. Social characteristics: Urban residence represents 75% (G3) vs 60 % (G1). Low socio-economic status interests 34% (G3) vs 90% (G1). More than half of the studied cases are smokers. Chronic alcohol consumers are 35% (G3) vs 20% (G2) and drug users are 3% (G3) vs 0% (G1,2). BCG vaccine is done in 82 % of patients (G3) vs 30% (G1). More than 17% have diabetes (G3) vs 13% (G2) vs 7% (G1). Family transmission is 21% (G3) vs 15% (G1). TB features: Extra pulmonary symptoms are 16 % (G3) vs 2% (G1). This is due to more extra pulmonary localization of TB 14 % (G3) vs 4,5% (G1). Thus, severe forms with bilateral localization and lung destruction decreased from 34% (G1) to 13% (G3). Microscopic sputum smear is positive in 67% (G3) vs 73% (G1) with positive culture as well in half of cases. Unfortunately, positive diagnosis is delayed by 10 days (G3) vs 3 days (G1). All patients are treated under DOTS with less success 80% (G3) vs 97% (G1) and more side effects 48% (G3) vs 34% (G1). Consequently, clearing sputum smear is differed to 90 days in 9% (G3) vs 1.5% (G1). **Conclusion:** Although the importance advances in TB diagnosis and treatment, this disease continues to be a concern. There is still a lot to be done, especially in high burden countries where fast identification and early treatment represents the cornerstone for the best outcomes.

#### PD-1248-01 Increasing incidence of TB in Kyiv, Ukraine, and current challenges

V Petrenko,<sup>1</sup> R Prociuk,<sup>1</sup> G Radysh,<sup>1</sup> G Marchenko,<sup>1</sup> N Rybak,<sup>2</sup> T Flanigan.<sup>3</sup> <sup>1</sup>Dept of Tuberculosis and Lung Diseases, Bogomolets National Medical University, Kyiv, Ukraine; <sup>2</sup>Dept of Infectious Disease, Alpert Medical School of Brown University/ Rhode Island Hospital, Providence, RI, USA; <sup>3</sup>Dept of Immunology and Infectious Disease, Alpert Medical School of Brown University/Miriam Hospital, Providence, RI, USA. Fax: (+1) 401 444-5650. e-mail: tasharybak@gmail.com

**Background:** Ukraine is one of the 27 high burden countries for multi-drug resistant tuberculosis (MDR-TB) as identified by the WHO. Tuberculosis surveillance data in Ukraine is very important to assess the efficacy of TB program implementation and to address areas that need further intervention. Kyiv is the capital of Ukraine and has a high level of specialized care facilities for TB. **Design/Methods:** We analyzed surveillance data for Ukraine which included TB incidence, TB mortality, MDR-TB rates, and TB/HIV co-infection rates for both for the country of Ukraine and its capital Kyiv.

**Results:** The efforts of the Ukrainian national TB programme have resulted in a stable TB incidence (per 100,000) from 68,1 in 2012 to 67,9 in 2013. While the TB incidence is stabilizing in Ukraine as a whole, TB incidence in the capital of Kyiv has increased by 27,4% in 2013 and is now at 52,5. TB incidence is generally represented by pulmonary forms, however we are now seeing an annual increase of additional smear-positive forms. TB/HIV co-infection incidence in 2013 also increased by 46,3% in Kyiv (from 8,2 to 12,0 per 100,000 pop) while only from 10,4 in 2012 to 10,5 in

2013 in Ukraine. TB mortality rate in 2013 in Kyiv was high at 37,9%. MDR-TB accounts for 9,5% of all new cases, 38,8% of relapses and 30,5% of all other retreatment cases. In 2013, when compared to the previous year, there was a small decrease in treatment success rates for new smear positive cases from 53,3% to 52,5%. The rate for discontinued treatment for all new pulmonary TB cases is 14,0%, and for smear positive 11%. The rate of BCG vaccination for newborns is also steadily decreasing every year and currently is 87,1% among all newborns during 2013. This is 5,5% lower than the rate of BCG vaccination for the previous year. The child TB incidence has started to increase: from 8,4 per 100 000 in 2012 to 9,0 in 2013 in Ukraine while in the city of Kyiv it increased from 5,0 per 100 000 in 2012 to 11,6 in 2013.

**Conclusion:** Ukraine as in Europe shows some success in combating TB, but surveillance data reveals new challenges that are responsible for the recent TB country profile. These challenges include an increasing population of drug-resistant TB patients who serve as a potential reservoir of incurable cases also combined with a steady increase of the HIV/TB co-infection rate. These challenges have a huge impact on the general TB incidence in Ukraine.

Title: Increasing Incidence of TB in Kyiv, Ukraine and Future Challenges

Authors : Petrenko V.I., Prociuk R.G., Radysh G.V., Marchenko G.F., Krasniuk V.E., Rybak N. and Flanigan T.

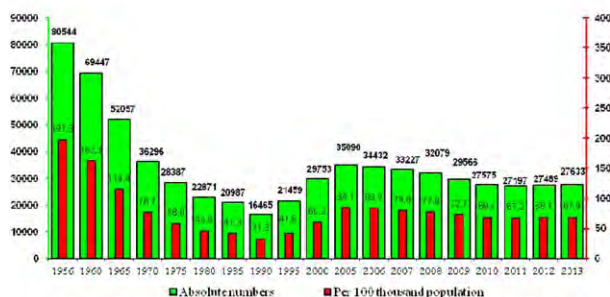


Figure 1. TB incidence in Ukraine for the period of 1956-2013 years

## 66. TB IN PRISONS

#### PD-1249-01 Profile of TB-HIV cases in inmate population, Brazil, 2007–2011

D Chaves Kühleis,<sup>1</sup> T Magalhães,<sup>1</sup> M Jacobs,<sup>1</sup> V Camargo Da Costa,<sup>1</sup> D Pelissari,<sup>1</sup> D Barreira.<sup>1</sup> <sup>1</sup>National Tuberculosis Program, Ministry of Health, Brasília, DF, Brazil. e-mail: daniel.chaves@saude.gov.br

**Background:** In Brazil's penitentiary units, people are more vulnerable to tuberculosis (TB) due to overcrowding of cells and poor facilities. TB incidence and human immunodeficiency virus (HIV) co-infection are very high. Apart from poor infrastructure, aggravating factors such as drug addiction, low socioeconomic status, health conditions and malnutrition, make TB and TB-HIV even

more lethal. The purpose of this paper is to describe the profile of TB-HIV cases within Brazil's inmate population, between the years of 2007–2011.

**Design/Methods:** A descriptive study of new TB-HIV cases among inmate population reported in the Disease Notification Information System, recorded between 2007 and 2011 was conducted analyzing the variable: HIV testing, clinical presentation, sex, ethnicity, outcome (cure/default) and directly observed treatment (DOT).

**Results:** In the period from 2007 to 2011, an average of 71,700 new TB cases was reported in the general population, in which 6.4% (3,935) were among inmates. In the same period, the percentage of new TB cases among inmates increased 68.4%, from 3.8% to 6.4%. In 2007, 38.6% of TB cases were tested for HIV among this population, and 64% in 2011, resulting an increase of 65.7%. In 2007, the TB-HIV coinfection rate was of 9.9%, moving to 9.4% in 2011, a decrease of 5.1% over the studied period. Most TB-HIV cases were male (85.8%), white (43.5%), with pulmonary TB (81.5%). There was an increase of 12% of DOT (from 44.4% in 2007 to 49.7% in 2011). For the cure rate, there was an increase of 19.5% (from 50% in 2007 to 59.8% in 2011) and a 20.9% default reduction (from 14% in 2007 to 11% in 2011).

**Conclusion:** The results presented show that TB-HIV coinfection cases represent approximately 8% of TB cases in inmate population. The availability of services such as HIV testing and DOTs increased in recent years, however it is still low considering the country's goals to test and monitor 100% of the cases. This scenario points to the need for the expansion of collaborative activities among institutions working on TB - HIV control in prisons, adopting different strategies to manage the diseases.

#### **PD-1250-01 Prevalence of pulmonary tuberculosis (TB) among inmates of three prisons and prison staff in Karnataka State, South India**

A Meundi,<sup>1</sup> B Dhabadi,<sup>1</sup> I Ismail,<sup>1</sup> A Sagara,<sup>1</sup> A G Kulkarni.<sup>1</sup> <sup>1</sup>Community Medicine, K V G Medical College, Sullia, India. e-mail: anandmeundi@yahoo.com

**Background:** Universal Access to Quality TB Diagnosis and Treatment includes special attention to high risk groups like migrants, homeless people and prison inmates etc. The present study was conceived in order to a) Estimate prevalence of pulmonary tuberculosis suspects and sputum positive pulmonary tuberculosis among prison inmates and prison staff at 3 major prisons in Karnataka State. b) To explore the health care seeking behavior of the identified pulmonary tuberculosis suspects for the current episode of cough.

**Methods:** Inmates and prison staff of three prisons in Karnataka (Belgaum and Mysore Central prisons and Mangalore district prison housing a total of 2450 prison inmates and 280 prison staff) were screened for cough for 14 days or more between September 2011 and February 2012. A semi-structured questionnaire was administered

only to the identified TB suspects (any person with history of cough for 14 days or more). Every TB suspect was subjected to 2 sputum smear (Ziehl Neelsen stain) examinations and fluorescent microscopy. A positive sputum result with either ZN staining or Fluorescent microscopy was considered as an evidence for initiating anti-TB treatment.

**Results:** Among 2450 prison inmates, 92 TB suspects were identified and none among the 280 prison staff. None of the 92 TB suspects had positive sputum. However, 10 TB suspects were already under anti TB treatment for pulmonary TB. This yields a prevalence of pulmonary TB and TB suspects of 4.02 and 37.55/1000 prison inmates respectively. Half of the TB suspects (47%) had history of previous incarceration. Majority of the TB suspects identified among the prison inmates had expectoration associated with cough. Majority of the TB suspects (77/92, 85%) had taken action after onset of cough and 96% (74/77) of them had obtained treatment from the prison medical officer. However, a majority of those treated (51/77, 66%) did not find relief after treatment. Two thirds of the inmates were active smokers (64%) and among the nonsmokers, 55% were exposed to passive smoking.

**Conclusions:** Relatively high prevalence of pulmonary TB and TB suspects, unresolved chest symptoms and almost universal exposure to smoking calls for a unique strategy to control TB in prisons. More detailed cohort analysis of TB suspects identified in prisons is imperative.

#### **PD-1251-01 Survey on the state of collaboration between prison institutions and public health centers in controlling TB among prisoners in Japan**

L Kawatsu,<sup>1</sup> N Ishikawa.<sup>2</sup> <sup>1</sup>Epidemiology and Clinical Research, Research Institute of Tuberculosis, Tokyo, <sup>2</sup>Director, Research Institute of Tuberculosis, Tokyo, Japan. e-mail: kawatsu@jata.or.jp

**Background and challenges to implementation:** Prisoners are at a higher risk of tuberculosis (TB) infection and disease in Japan. TB incidence among prisoners has been estimated to be around 220.2 per 100,000 populations, approximately 13 times higher than that of the general population in 2012. One of the key components of effective TB control in prisons is the collaboration between prison institutions and local public health centers (PHCs). Yet currently no relevant guidelines exist, and prisons and local PHCs are left to themselves to coordinate with one another.

**Intervention:** We conducted a first nation-wide survey on the state of collaboration between prisons and PHCs. Semi-structured interview was conducted via telephone with TB nurses of PHCs, which have one or more prison institutions within their local jurisdiction. Questions were asked about PHC practice regarding patient interview, pre-release conference and other aspects of collaboration.

**Results and lessons learnt:** Of the 31 PHCs which participated in the survey, 61% did not interview

patients at registration. Of them, 2 sought for interview but permission was not granted from the prison, and 17 had never given interview as they judged such was unnecessary. During treatment, 43% regularly communicated with prisons to exchange information regarding treatment, while 57% only contacted prisons "when necessary". 67% were able to gain release date and other relevant information, such as address and family details, prior to patients being released, while 19% were only let known of the release date, and 7% could not receive any information prior to release.

**Conclusions and key recommendations:** The results revealed not only inconsistency in the prisons' response to PHCs, but also discrepancy in PHCs' interpretation of their roles and responsibilities with regards to incidence of TB in prisons. This has resulted in much discrepancy in the state of collaboration between PHCs and thereby in both the quality and quantity of service offered to prisoner TB patients. A workshop was held among TB nurses, prison doctors and staff of the RIT to discuss the results of the survey, and a practical guideline for PHCs was established. The guideline will be introduced and its impact on PHC-prison collaboration will be monitored.

#### PD-1252-01 High prevalence of previously undiagnosed active TB among HIV-infected inmates upon entry into a Malaysian prison

H Al-Darraj, <sup>1</sup> F Altice, <sup>1,2,3</sup> A Kamarulzaman. <sup>1,2</sup> <sup>1</sup>Centre of Excellence for Research in AIDS (CERiA), University of Malaya, Kuala Lumpur, Malaysia; <sup>2</sup>Internal Medicine, Yale University School of Medicine, New Haven, CT, <sup>3</sup>Epidemiology of Microbial Diseases, Yale University School of Public Health, New Haven, CT, USA. e-mail: hdarraj@gmail.com

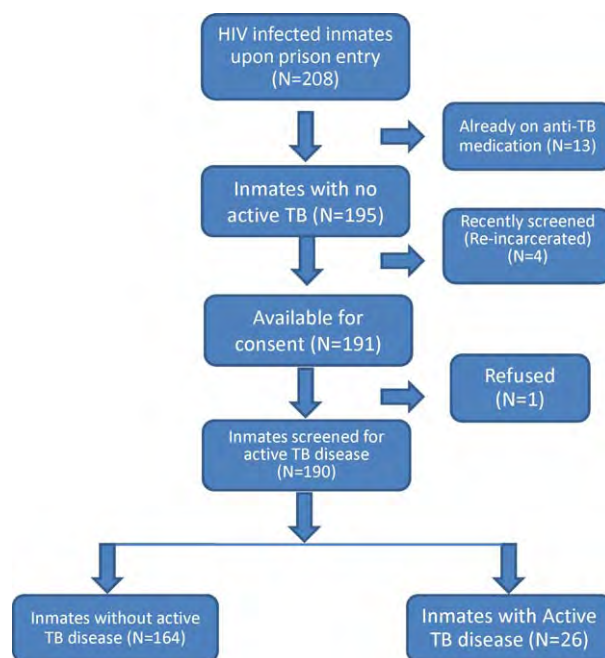
**Background:** Tuberculosis (TB)-related morbidity and mortality among prisoners, particularly those infected with HIV, remain high. Previous reports showed high prevalence of both latent TB infection and active TB disease among convicted prisoners in Malaysia, irrespective of the HIV status, but no data exists about the TB burden upon prison entry. This intensified case-finding study was conducted to determine the point prevalence of active TB at prison entry among HIV-infected prisoners.

**Design/Methods:** From July to December 2013, all newly entering male HIV-infected prisoners were invited to participate in a comprehensive TB screening study. Consented participants underwent a structured survey including demographic data, TB symptoms and body mass index (BMI) assessment, and were asked to submit two consecutive daily sputum samples. Sputum samples were tested using smear microscopy, Xpert MTB/RIF (Xpert) and BACTEC liquid culture, regardless of their presenting symptoms. CD4 count was assessed using point-of-care CD4 analyzer. A logistic regression model was explored to determine correlates of active TB disease, defined as being positive by either Xpert or culture methods.

**Results:** Among the 208 consecutive HIV-infected entering prisoners, 190 (91.3%) completed TB screening (Figure). Reason for exclusion included being on TB

treatment (N=13), recent TB screening (N=4) and refusal (N=1). Most participants were Malaysians (88.9%), age <40 years (62.6%) and had been previously incarcerated (83.7%). Most (73.7%) self-reported past drug injection, but only 48 (25.3%) had injected drugs within the 30 days before incarceration. Previous episodes of TB were reported by 33 (17.4%) prisoners. Median CD4 count was 389 (IQR 244–555) cell/mL and 19.5% were newly diagnosed with HIV upon entry. Most (70%) reported one or more of the World Health Organization's four-symptom TB screening method. Twenty six (13.7%) had evidence of active TB (Xpert (N=21) and culture (N=23)). On multivariate analysis, active TB was independently associated with being underweight (BMI <18.5 kg/m<sup>2</sup>; aOR 3.38, 95% CI 1.29–8.81), but not with CD4 count or any other independent variables.

**Conclusion:** Prevalence of active TB disease among HIV-infected prisoners entering Malaysia's largest prison was alarmingly high and associated with being underweight. Routine screening for active TB amongst HIV-infected prisoners and rapid institution of treatment for TB cases is crucial for TB and TB/HIV control.



#### PD-1253-01 Active case finding of pulmonary tuberculosis among prison inmates in Aba Federal prison in Abia State

O Okorie, <sup>1</sup> M Gidado, <sup>2</sup> E Ekundayo. <sup>3</sup> <sup>1</sup>Public Health and Disease Control, Ministry of Health, Abia, <sup>2</sup>TBCARE 2, KNCV Nigeria, Abuja, <sup>3</sup>Microbiology, MUOU Umudike, Abia, Nigeria. e-mail: onphil200@yahoo.co.uk

**Background and challenges to implementation:** The prevalence of tuberculosis among prisoners is always higher than general population. However TB in congregate settings remains a growing problem. There are Approximately 10 million individuals who are detained



worldwide. Inmates are at greater risk of developing TB disease due to prolonged indoor confinement and other associated conditions. TB incidence is 5 to 70 times greater in prisons than in communities. Prisons are overwhelmingly male, are typically aged 15–45 years, predominantly socioeconomically deprived sectors of the population where TB infection and transmission are higher. Prisons act as a reservoir for TB, pumping the disease into the civilian community through staff, visitors, and inadequately treated former inmates. However case-finding through self-referral may have limited successes in prisons. Some inmates may have been afraid to come forward, fearing the repercussions of diagnosis of tuberculosis, such as stigma. Periodically and systematically screening entire prison population can substantially influence the transmission of tuberculosis in prison. On this premise, the Abia State, TB control program conducted a pilot study to assess the contribution of active case finding in tuberculosis control in Aba Prison.

**Intervention or response:** This is a descriptive study. The entire inmates were clinically screened and the presumptive TB cases were screened AFB microscopy by direct smear light microscopy and HIV by rapid test kits.

**Results and lessons learnt:** Out of the total number of 447 prison inmates presents in the prison as of the time of study, 449 were clinically screened for history of cough of 2 week's duration. Fifty-two (10.42%) met the inclusion criteria for sputum smear microscopy. Eleven of the 52 (21.15%) tested for acid bacilli (AFB) by direct smear light microscopy were positive for AFB. One inmate already on anti-tuberculosis therapy and the eleven detected in the course of this study gave a total of 12 inmates of Aba prison with pulmonary tuberculosis. This gives a minimum point prevalence rate of 2,405 cases per 100,000 inmates. Four of the 11 prison cells had at least one smear positive case with 7 of the 11 cases concentrated in two cells. The age group of 25–34 had the highest number of sputum positive cases.

#### **PD-1254-01 A new way to advance STOP TB strategy in prisons**

E Gurbanova,<sup>1,2</sup> R Mekhdiyev,<sup>1</sup> A Ismayilov,<sup>1,2</sup> I Mammadova,<sup>2</sup> F Huseynov,<sup>1,2</sup> M Dara,<sup>3</sup> A Dadu,<sup>3</sup> J. Suleymanova.<sup>4</sup> <sup>1</sup>MMD MoJ, Main Medical Department of the Ministry of Justice, Baku, <sup>2</sup>MMD MoJ, WHO Collaborative Centre for TB control and prevention in prisons, Baku, Azerbaijan; <sup>3</sup>Communicable Diseases, Health Security, and Environment, WHO Regional Office for Europe, Copenhagen, Denmark; <sup>4</sup>Communicable Diseases, WHO Country Office in Azerbaijan, Baku, Azerbaijan.  
e-mail: e.gurbanova@prisonhealth.az

**Background:** Full range implementation of STOP TB Strategy is often a challenge in prisons. Along with infrastructural investments it requires strong government commitment and highly qualified personnel. The Main Medical Department of the Azerbaijan MoJ runs prison TB Control Programme which is internationally recognized as the best practice model for TB and MDR-TB Control.

**Intervention:** Internationally recommended strategy for TB control in Azerbaijan PS has been launched in 1995 and supported by WHO, ICRC, the Global Funds and other international stakeholders. A training center (TC) was established in the premises of the penitentiary TB hospital to address current needs in training of medical and non-medical personnel of the PS, promote WHO strategies and guidelines on TB control in prisons, provide support to WHO and give technical assistance to NTPs worldwide, including programmes in prisons. Along with theoretical modules, the trainees have a unique opportunity to share with the practical experience on case detection and treatment at 8 treatment wards, 23 sub-wards, high-level laboratory implementing all range of phenotypic and genotypic TB tests. The core mentors are active TB case managers and health care experts with high academic backgrounds, experienced in training delivery to diverse audiences. WHO experts' are regularly engaged in trainings for the international participants. The target audience includes physicians and nurses at primary, secondary and tertiary healthcare PS facilities; all levels laboratory technicians; and non-medical PS personnel. Last two years 37 training on more than 25 topics were performed. Trainings are provided on Azerbaijani, Russian and English languages. Basing on up-to-date WHO TB strategies and guidelines the TC offers a wide range of high quality, evidence based education on TB control in prisons (see [www.prisonhealth.az](http://www.prisonhealth.az) for more).

**Results:** During last two years participants from all Central Asia countries, Iraq, the Philippines, Belarus, and Georgia took advantages of the TC resources and pass the training curriculum. About 500 trainees acknowledged high training efficiency. The TB Training Center at the Main Medical Department of the Ministry of Justice of Azerbaijan has been designated as WHO Collaborating Centre.

**Conclusion:** The STOP TB Strategy implementation varies in different environments and population groups. Prison setting requires specific approaches to personnel's capacity building and education.

#### **PD-1255-01 Controlling pulmonary tuberculosis in the prisons of Bangladesh using active screening and strengthening the management and referral linkage**

S Ahmed,<sup>1</sup> MT Rahman,<sup>1</sup> R Khatun,<sup>1</sup> S Afrin,<sup>1</sup> Z Islam,<sup>1</sup> M.M. Rahman,<sup>2</sup> MA Husain,<sup>2</sup> S Banu.<sup>1</sup> <sup>1</sup>Centre for Communicable Diseases, International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka, <sup>2</sup>Directorate General of Health Services, National TB Control Program, Dhaka, Bangladesh. Fax: (+880) 2 9827062.  
e-mail: sbanu@icddr.org

**Background** Tuberculosis (TB), the second biggest killer among the infectious diseases worldwide, has long been a major public health concern in prisons. An earlier study revealed a staggering 20 times higher prevalence of TB in the largest prison of Bangladesh than that of corresponding general population stressing the need to conduct

further research involving more prisons to understand the TB burden in this setting.

**Methods** A symptomatic verbal screening system was established both at the entry point and inside the prison cells in four different prisons of Bangladesh to identify presumptive pulmonary TB cases. One large, two medium, and one small prison were selected based on their capacity. Three sputum samples were collected from the presumptive cases and were sent for microscopy in nearby DOTS Centre and also for culture in icddr,b laboratory. Additionally, a subset of microscopy negative suspects from Dhaka Central Jail (DCJ) was tested with GeneXpert. Socio-demographic data and clinical history were also recorded. All the identified cases were closely followed to ensure treatment registration and proper referral upon release or judicial transfer.

**Results** In all four prisons 85,719 inmates were screened. Of them, 3,084 (3.6%) presumptive cases were identified and tested. A total of 217 (7.04%) patients were identified of whom 125 (57.6%) were microscopy positive, 17 (5.7% of the 300 samples tested) were positive on GeneXpert in DCJ, and additionally 69 (31.8%) were found positive only on culture, 6 (2.76%) patients were diagnosed clinically. Of the 128 patients identified in DCJ, 13.3% was identified by GeneXpert. Of the 217 patients identified, 180 (83%) were registered for treatment inside prisons, 6 (3%) were traced back to their home and registered for treatment in their nearby facility, 9 (4%) refused treatment and 22 (10%) were lost. Of the 186 registered patients, 93 (50%) have already completed treatment, 29 (16%) are on treatment inside the prisons, 55 (29%) are referred out and are on treatment in their local facilities, 3 (2%) died while on treatment inside prison and 6 (3%) were lost to follow-up.

**Conclusions** Referral linkage between prisons and also with community treatment entities must be strengthened to improve the treatment outcomes. GeneXpert is feasible in prison TB care system and can be integrated to improve case detection considering the resource requirements for setting up culture facilities.

#### PD-1256-01 Computer-aided diagnosis of X-rays in a screening for pulmonary tuberculosis of a prison population in Tanzania

A Steiner,<sup>1,2,3</sup> F Mhimbira,<sup>1,2,3</sup> J Van Den Hombergh,<sup>4</sup> P Clowes,<sup>5,6</sup> C Mangu,<sup>6</sup> B Van Ginneken,<sup>7</sup> M Hoelscher,<sup>5,8</sup> K Reither.<sup>1,3</sup> <sup>1</sup>Medical Parasitology & Infection Biology, Swiss Tropical and Public Health Institute, Basel, Switzerland; <sup>2</sup>Research and Training Centre, Ifakara Health Institute, Bagamoyo, United Republic of Tanzania; <sup>3</sup>Tropical Medicine, University of Basel, Basel, Switzerland; <sup>4</sup>PharmAccess, PharmAccess Foundation, Dar es Salaam, United Republic of Tanzania; <sup>5</sup>Division of Infectious Disease and Tropical Medicine, Medical Centre of the University of Munich, Munich, Germany; <sup>6</sup>National Institute of Medical Research, Mbeya Medical Research Centre, Mbeya, United Republic of Tanzania; <sup>7</sup>Medical Center, Radboud University, Nijmegen, Netherlands; <sup>8</sup>DZIF, National Centre for Infectious Diseases of

Germany, Munich, Germany.  
e-mail: andreas.steiner@unibas.ch

**Background:** Recent studies have shown that computer-aided diagnosis (CAD) of chest X-rays (CXR) allows the detection of pulmonary tuberculosis (TB) with a performance similar to that of clinical officers. This study investigated the performance of the new CAD4TB system in a Tanzanian prison.

**Design/Methods:** Between August 2013 and June 2014, all inmates of the Ukonga Prison, Dar es Salaam, are screened for TB. X-rays are classified as "normal", "abnormal, not suggestive of TB", "abnormal, consistent with TB", and "abnormal, highly suggestive of active TB" by an assistant medical officer with two years of training in radiology (reader A) and processed by the software CAD4TB v3.07 (Diagnostic Image Analysis Group, Nijmegen University, The Netherlands). A subset of 517 consecutive images was re-evaluated by reader A, as well as by an independent clinical officer (reader B), and by a TB expert. The CXR findings of the TB expert, based on a case definition which included X-ray results either "consistent with TB" or "highly suggestive of active TB", determined the radiological reference that was used for CAD4TB and the two other readers.

**Results:** On the 466 negative and 51 positive images, readers A and B performed with a sensitivity of 52.9% and 43.1%, and a specificity of 92.4% and 77.5%, respectively. CAD4TB performed significantly better than reader B, but not as good as reader A (AUC 0.751, e.g. sensitivity 52.9% and specificity 83.5% for a defined threshold). The intra-reader agreement of reader A was good (Cohen's  $\kappa=0.80$ ), but the agreement between A and B was low ( $\kappa=0.36$ ). Although all readers, including CAD4TB, analyzed every CXR in under two minutes, human readers delayed 10% of images by more than 20 hours during the screening.

**Conclusion:** This first evaluation of CAD4TB in a real-world screening situation showed, in line with previous studies, that CAD4TB performs better than a clinical officer (B), but not as good as a more experienced X-ray reader (A). Moreover, the overall time to detection is kept predictably short, which is an important criterion in multistage screening algorithms.

#### PD-1257-01 Promoting good TB infection control in Cipinang detention center: a lesson learnt

YN Sumarli,<sup>1</sup> Y Yuniarti,<sup>2</sup> I Kurniaty,<sup>3</sup> N Tandirerung,<sup>4</sup> MR Christian,<sup>5</sup> D Setyawati.<sup>6</sup> <sup>1</sup>Clinic, Cipinang detention center, Jakarta, <sup>2</sup>TB HIV Program, Provincial office of Ministry of Law and Human Right, Jakarta, <sup>3</sup>Tuberculosis program, East Jakarta District Health Office, Jakarta, <sup>4</sup>National Tuberculosis Program, Ministry of health, Jakarta, <sup>5</sup>Tuberculosis Unit, World Health Organization, Jakarta, <sup>6</sup>Clinical services unit, Family Health International, Jakarta, Indonesia. e-mail: regina.loprang@gmail.com

**Background and challenges to implementation:** Tuberculosis is still a major health problem in prisons and detention center in Indonesia. Inmates represent dynam-

ic, low socioeconomic, low education, productive age, and undiscipline behaviour in a setting that exacerbates TB transmission. Over capacity is also a risk to accelerate TB transmission. Cipinang detention centre is currently housing around 3,500 inmates; a 300% of its actual capacity of 1,136 inmates. Security is the top priority when designing prison complex that it is difficult to have good ventilated rooms. An innovative approach to ensure TB infection control in prison setting is needed, and Cipinang DC will focus on administrative measure. **Intervention or response:** Cipinang DC have started TB infection control program since April 2012. The key strategies are : 1) TB screening to every new inmates; 2) Designation of well ventilated rooms for TB suspects and TB on treatment; 3) train volunteer inmates as cough officer to provide TB education, Triage; referring inmates for further TB screening; 4) provide mask depot in; 5) create smoke free environment and spit-free area. Moreover Cipinang DC team have conducted series of advocacy to the head of detention center and provincial office of ministry of law and human right.

**Results and lessons learnt:** Between December 2012 to March 2014, a total of 932 inmates were given masks and informed about TB. As many as 287 inmates were referred to the clinic for further examination and 20 smear positive and 1 MDR TB cases were put on treatment. Mask Depots and TB IEC were available in every blocks, smoke free environment and spit-free area were established on February 2014. A circulation letter of TB infection control in prison and detention center in Jakarta was issued. A good collaboration and strong network between Cipinang DC, pengayoman hospital, district health office have been built in order to ensure rapid diagnosis and access to treatment.

**Conclusions and key recommendations:** With strong commitment, maintaining good infection control in detention center is feasible. A good triage is needed to ensure that the TB patients are found in earlier stage and have prompt treatment. One of a promising method is promoting cough surveillance and provide access to TB information and masks.

#### PD-1258-01 Empowering community-based organisation to strengthen TB post release programme in prison system in DKI Jakarta

Y Gunawan,<sup>1</sup> M Revilia,<sup>1</sup> YI Hiola,<sup>2</sup> M Samsuri,<sup>3</sup> C Natpratan,<sup>3</sup> R Palupy,<sup>3</sup> DP Setyawati,<sup>3</sup> T Mahatmi Nisa.<sup>4</sup> <sup>1</sup>TB-HIV, Yayasan Partisan Club, DKI Jakarta, <sup>2</sup>Correctional Division, DKI Jakarta Provincial Office of Ministry of Law and Human Rights, DKI Jakarta, <sup>3</sup>Clinical Services Unit, FHI360 Indonesia, DKI Jakarta, <sup>4</sup>HIV Program, WHO Indonesia, DKI Jakarta, Indonesia. e-mail: msamsuri@fhi360.org

**Background and challenges to implementation:** TB Case holding in inmates after being released or transferred to other prisons is difficult to trace and remains problematic for TB in prison program in Indonesia . There are 2 big obstacles: TB referral form (NTP register TB 09) was seldom use and TB treatment outcome form (TB 10) also never returned back to referring prison/detention center.

In 2008, TB in prison program was implemented in 3 prisons and 3 detention center in Jakarta, there was no data regarding transferred out inmates. Since 2011, TBCARE I through FHI360 initiated a collaboration with one community based organization, named Partisan. They would then be supporting to strengthen external linkage for TB in the prison system in Jakarta.

**Intervention or response:** When inmates with TB were going to be released or transferred to other prisons, Partisan staff together with prison health worker provided pre-release education, which include where to continue their TB treatment after being released, and the importance of continuing their treatment. Partisan's roles were to ensure that patients/inmates coming to the referral health center to continue their treatment, and to ensure that after treatment completed/cured, the referral health center return the TB 10. Therefore, the referring facilities would then know their inmates treatment outcome.

**Results and lessons learnt:** Table 1 Post Release Data from 3 prisons and 3 detention centers in DKI Jakarta, January-December 2013

Prisons/DCs	#Post Release	#Feedback TB09	#Should Complete Treatment	#Feedback TB.10
Salemba Prison	19	13	13	0
Cipinang Prison	2	1	1	0
Narcotic Prison	3	1	1	0
Salemba DC	14	14	10	10
Cipinang DC	16	16	16	16
Pondok Bambu DC	1	1	1	0
TOTAL	55	46 (84%)	42	26 (62%)

Successful referral rate for 2013's transferred out inmates was 84%, and we managed to have treatment outcome feedback for 62%. TB.09 & TB.10 forms which could not be traced usually came from inmates that being referred outside Jakarta and neighboring cities.

**Conclusions and key recommendations:** Partisan, the community based organization works in Jakarta prison system, plays an important role to strengthen TB post release program so that we can ensure released inmates and inmates sent to other prisons continue their treatment until complete and finally get cured. More CBOs should be facilitated and encouraged to work with prison system based on the experience from Partisan.

#### PD-1259-01 Operational framework for tuberculosis management at Tihar central prison in Delhi, India

N Sharma,<sup>1</sup> S Chandra,<sup>2</sup> Ashw Khanna,<sup>3</sup> M Dhuria,<sup>4</sup> KK Chopra,<sup>4</sup> M Hanif.<sup>4</sup> <sup>1</sup>Community Medicine, Maulana Azad Medical College, New Delhi, <sup>2</sup>Revised National Tuberculosis Control Program, WHO Country Office for India, New Delhi, <sup>3</sup>State Tuberculosis Control Office, Directorate of Health Services, New Delhi, <sup>4</sup>State TB Training and Demonstration Centre, New Delhi TB Centre, New Delhi, India. e-mail: chandras@rntcp.org

**Background and challenges to implementation:** High levels of tuberculosis (TB) in prison inmates is attribut-



able to a disproportionate number of them representing high risk groups along with frequent movement of infectious prisoners between prisons which leads to treatment interruptions, drug resistance and increased transmission in the community. In order to curb the disease transmission, it is essential to detect TB early through a high sensitive tool keeping in consideration the positive predictive value of the diagnostic algorithm deployed along with the operational feasibility owing to variable stay duration of most of the convicts. This study situates itself at Tihar Central prison in Delhi (which is the largest prison of South East Asia housing around 12417 inmates- long/short term convicts and under trials) with the following objectives i) to estimate the burden of TB among prison inmates ii) to frame the operational modalities for early detection of TB and drug resistant TB iii) to mobilize standardized TB care practices among the inmates.

**Intervention or response:** The longitudinal study comprises of a pre study phase (3 months) wherein a detail review of Revised National Tuberculosis Control Program (RNTCP) implementation based on logic model of evaluation was undertaken. In the continuing study phase of one year (October 2013 onwards), an operational framework was designed for early detection of TB and drug resistant TB using clinical symptoms, Chest X-ray and CBNAAT technology with single good quality sputum specimen. TB medicine was disbursed through prolongation pouches and patient wise boxes for short term and long term convicts respectively. One Medical Officer, Laboratory technician and treatment provider was posted at Tihar premises under the referral unit pattern of RNTCP.

**Results and lessons learnt:** Preliminary data analysis from Oct-Dec 2013 shows that of the 6210 inmates screened during medical checkup, 73.9% (4589) were under trials and majority were male (96.1%). Of those screened, 254 (4%) were suspected of TB out of whom 31.8% patients belonged to outside Delhi, 62% (158 patients) got diagnosed with TB and registered for treatment while 30% were lost to follow up as they got released before treatment initiation. With deployment of a referral unit pattern, TB notification increased two times (when compared with 2012). The shift in notification trends and disease pattern was statistically significant ( $p < 0.01$ ). Also found significant was the 19% reduction in lost to follow up for treatment and the treatment success rates of 65% in new and retreatment TB patients in early cohorts of 2013 vis-à-vis 55% rates in 2012.

**Conclusions and key recommendations:** For effective disease containment efforts in prisons, strong policy inducements promoting replication of the operational framework deployed in the study with a dedicated referral unit support needs to be reckoned for TB control in such high risk settings.

## PD-1260-01 Tuberculosis screening in prisons in Rwanda using mobile digital x-ray machine

E Ruseesa,<sup>1</sup> M Gasana,<sup>1</sup> G Mutembayire,<sup>1</sup> J Mugabekazi,<sup>2</sup> CB Uwizeye.<sup>1</sup> <sup>1</sup>Rwanda Biomedical Center, Ministry of Health, Kigali, <sup>2</sup>TB, World Health Organization, Kigali, Rwanda. e-mail: ruseesa@yahoo.co.uk

**Background:** From 2005, Rwanda introduced the policy of Tuberculosis (TB) screening using TB clinical signs for every new prisoner entering the prison. Since December 2013, Rwanda National TB program started TB screening in high risk groups (especially in prisons) using mobile digital x-ray machine.

**Methods:** The implementation of the activity started in prisons. The screening is done using mobile digital x-ray machine where all inmates of the 14 prisons in Rwanda are expected to be screened for TB using chest x-ray. All inmates with abnormal chest x-ray images give sputum sample for both LED microscopy and GeneXpert examination.

**Results:** From December 2013 to April 2014, the activity has been implemented in 3 prisons of 14. A total of 16,902 out of 17,065 (99%) prisoners were screened for TB. Among them, 2,293 (13.5%) had an abnormal chest x-ray image and were therefore classified as presumptive TB cases (compared to 2,538 presumptive TB cases reported the whole year of 2013 using clinical signs in the same 3 prisons). 2,148 (93.7%) and 1,625 (70.9%) presumptive TB cases gave sputum sample for microscopy and GeneXpert examination respectively. A total of 107 new TB cases were diagnosed. 73 (68%) cases of them were diagnosed only by GeneXpert examination.

**Conclusion:** TB screening using x-ray machine detects many presumptive TB cases especially in TB high risk groups compared to TB screening using clinical signs. The role of GeneXpert in TB diagnosis is highly significant.

## PD-1261-01 Tuberculosis in prisons in Republic of Macedonia

M Zakoska,<sup>1</sup> B Ilievska Poposka.<sup>1</sup> <sup>1</sup>Epidemiology Department, PHI Institute for Lung Diseases and Tuberculosis, Skopje, Macedonia, Yugoslav Republic. e-mail: mzakoska@yahoo.co.uk

**Introduction:** Prison's population (yearly approximately 2600 prisoners) is group with higher risk of tuberculosis (TB) due to fullness of prisons, bad living conditions and inadequate medical care. Total population's notification rate decreases continuously but the rate of tuberculosis cases in prisons is still high (384/2005, 0/2006, 76/2007, 230/2008, 307/2009, 384/2010, 153/2011, 38/2012 and 307/2013).

**Aim:** To prove the situation with tuberculosis in prisons in Macedonia.

**Material and methods:** Data for this survey are taken from the Central TB Registry. The forms of tuberculosis, previous treatment, bacteriological confirmation and treatment outcome between 49 prisoners have been analysed.

**Results:** In the period 2005–2013, 49 cases of tuberculosis were registered 46 (93, 9%) male and 3 (6, 1%) female, the ratio man/women is 15:1. The age 25–34 years have biggest number of cases 26(53, 1 %). The pulmonary tuberculosis was identified at 43 (87, 7%), extra pulmonary tuberculosis at 6 (12, 3%) cases. From all cases, 43(87, 7%) were new and 6 (12, 3%) previously treated. Bacteriological confirmation of pulmonary tuberculosis with direct microscopy identified at 22(44, 9%) and bacteriological confirmation of culture at 30 (61, 2%) cases. The drug sensitivity test demonstrated multi drug resistance in 1 (2, 0%) of total 49 cases of pulmonary tuberculosis. Treatment outcomes from 2005–2012 were following: successful treated 35 (85, 4%), dead 1 (2, 4%), 4 (9, 8%) default treatment and 1 (2, 4%) lost from evidence. Drug addiction is finding in 21(42, 8%) prisoners with TB.

**Conclusion:** Rate of tuberculosis in prisons in Macedonia is higher than in total population. Among tuberculosis cases in prisons percentage of bacteriological confirmation is low. Appearance of multi drug resistant form of tuberculosis is bad prognostic sign

#### PD-1262-01 TB case finding in Nigerian prisons: using health system strengthening approach

M Gidado,<sup>1</sup> J Onazi,<sup>1</sup> Josh Obasanya,<sup>2</sup> R Eneogu,<sup>2</sup> T Odusote,<sup>3</sup> F. E Odiah,<sup>4</sup> E Udom,<sup>4</sup> O Omosebi.<sup>2</sup>

<sup>1</sup>Program, KNCV/TB CARE I, Abuja, <sup>2</sup>Public Health, National TB & Leprosy Control program, Abuja, <sup>3</sup>TB/HIV Unit, USAID, Abuja, <sup>4</sup>Health & Welfare, Nigerian Prison Services, Abuja, Nigeria. e-mail: gidadom@kncvnigeria.org

**Background:** TB is known to thrive in overcrowded small spaces akin to prison thus posing a challenge to TB control effort. Effective TB control in prison is contingent upon active case finding through intensive screening of inmates' during admission into the prison and on a routine basis as well as improvements in health care system services in the prisons. The prison community from studies conducted has a high TB case notification rate than in the general population; and TB disease surveillance is sometime suboptimal making the understanding of TB situation in the prisons unclear. Nigeria has about 234 prisons inclusive of satellite detention centres spread across the country. The study is aimed at assessing the impact of the health system strengthening approach in TB case finding in Nigeria prisons.

**Method:** A TB symptomatic screening tool was developed as part of health screening tool for all inmates. Capacity building; provision of microscopes; and logistics for sample movement in some cases was done within the period. All presumptive TB cases were screened using AFB microscopy; confirmed cases were commenced on treatment and notified to NTP. The study design consists of a retrospective review of routine data of the National TB program in 2013. All TB cases notified from Prison services have however been put on treatment.

**Results:** TB case notification rate for all forms of TB in Nigeria in 2013 was 61/100,000 population. There are about 53,000 prison inmates in the country. Evidence from routine surveillance indicates that all forms of TB

cases notified from the prison population in 2013 was 340 TB cases giving a case notification rate of 641/100,000 populations a rate 10 times the case notification rate for all forms of TB for the entire country. Furthermore of those notified, 237 were smear positive TB cases. Additionally, 64% (218) of patients were tested for HIV; 20(9%) were HIV positive; 11(55%) accessed CPT and 8(40%) accessed ART.

**Conclusion:** Routine screening of TB in the Nigerian prison is beneficial and of priority to halt transmission and prevent epidemic of much resistant strains. However due to the nature of prison the buy in of prison administration is crucial for early detection and management of TB in prisons.

## ORAL POSTER PRESENTATIONS

### 01. THE PROMISE OF LIFE: INITIATING TREATMENT IN COINFECTED PATIENTS

#### OPP-400-01 Delay in access to anti-retrovirus therapy among people living with HIV in Viet Nam

TA Nguyen,<sup>1</sup> D Do,<sup>2</sup> P Nguyen Anh,<sup>2</sup> Mai Quach,<sup>2</sup> Tran Van,<sup>2</sup> Xuan Cuong,<sup>2</sup> Cuon Nguyen,<sup>2</sup> Hien Hien.<sup>2</sup>

<sup>1</sup>Research, Woolcock Institute of Medical Research, Ha Noi, <sup>2</sup>Research, Viet Nam Network of People Living with HIV/AIDS, Ha Noi, Viet Nam. e-mail: thuanh.nguyen@sydney.edu.au

**Background:** Optimum HIV management requires people living with HIV (PLHIV) to visit health facilities for regular health checkups and follow ups soon after learning of their HIV infection status. This will help to increase treatment efficacy and reduce the risk of transmitting the HIV disease to others. This research is conducted to assess the stage when PLHIV having access to ART and factors that may promote or inhibit the early access among PLHIV in Viet Nam.

**Design/Methods:** This study deployed a cross-sectional survey method in 7 provinces using a structured questionnaire to interview 1,615 PLHIV. Participants of the study were recruited using the snowball sampling method. The data was collected from November 2012 to March 2013 by the Network of PLHIV in Viet Nam. Logistic regression was used to examine the factors affecting time to get access to health care among PLHIV.

**Results:** Access to ART at a late stage of HIV infection was due to a delay in access to health care facilities after initial HIV diagnosis. Of the 55% of respondents who reported not to have visited the health facilities immediately after learning of their HIV positive status, there was a wide range of time in delay for health check up with the mean delay of 4.4 years  $\pm$  2.6 years. At the health check up, PLHIV should be given a CD4 count test to assess the eligibility for ART. However, the result indicated that about 50% had their first CD4 count test within 6 months after initial diagnosis of HIV infection. Particularly 40% of respondents had their first CD4

count test results of equal or less than 200 cells/mm<sup>3</sup>, and 24.4% of respondents had the test result of 201–350 cells/mm<sup>3</sup>. There was a combination of factors associated with late access to health care. We observed that male respondents, people living in rural areas or small towns, and those with a history of illicit drug use tended to access health care at a late stage. In particular, people who have a monthly income of more than 10 million VND (approximately 500 USD) were more likely to access health facilities at a later stage.

**Conclusion:** This finding suggests that efforts to increase early initiation of HIV care and treatment should focus on hard-to-reach populations, including drug users, males living with HIV, people residing in rural areas and people with a high income.

### OPP-401-01 Role of tuberculosis infection control teams in reducing diagnostic and treatment delays among HIV patients in Uganda

D Nansera,<sup>1</sup> Y Boum li,<sup>2</sup> W Muyindike,<sup>1</sup> P Bibangambah,<sup>3</sup> P Elyanu,<sup>3</sup> D Mutaahi,<sup>3</sup> G Amanyire,<sup>3</sup> M Siedner.<sup>4</sup> <sup>1</sup>Infectious Diseases' Clinics, Mbarara Hospital, Mbarara, <sup>2</sup>Research, Epicentre Mbarara, Mbarara, <sup>3</sup>Infectious Diseases' clinic, Makerere University Joint AIDS Program, Mbarara, Uganda; <sup>4</sup>Medicine, Harvard Medical School, Boston, MA, USA. e-mail: dnansera@gmail.com

**Background and challenges to implementation:** There is need to reduce diagnostic and treatment delays for tuberculosis (Tb) among HIV patients. We describe the impact of a tuberculosis infection control team on reducing these delays among HIV patients suspected of tuberculosis co-infection.

**Intervention or response:** The intervention was implemented in the HIV clinic of Mbarara Hospital, with approximately 9,000 active adults. The hospital has an integrated TB/HIV clinic treating TB/HIV co-infected patients. The tuberculosis infection control team is composed of laboratory technicians, nurses and clinicians and was set up in March 2012. It conducts symptomatic screening for Tb using the intensified case finding (ICF) parameters for tuberculosis; fast tracks those who screen positive for Tb for expedited clinical evaluation and linkage of confirmed cases of Tb to the integrated TB/HIV clinic for the duration of Tb therapy. At completion of anti-tuberculosis treatment, it re-integrates them back into the HIV clinic. We use the ministry of health care guidelines and health management information tools to inform care and to document outcomes. We abstracted dates from clinic records of patients who had started and completed Tb treatment during a 12 month period before and after initiation of the infection control team. We calculated the median number of days from suspicion of Tb to diagnosis and from diagnosis to initiation of treatment for both the pre- and post-implementation periods. The medians were compared using non-parametric rank sum testing using STATA version 12.0.

**Results and lessons learnt:** A total of 155 and 96 patients initiated Tb treatment in the 12 months before and after

implementation of the program. The median time from suspicion of Tb to diagnosis declined from the pre – to post – intervention period from 7 days (IQR 4 – 14) to 0 (IQR 0 – 4),  $p < 0.00$ ; median time from diagnosis to initiation of Tb treatment pre – to post – intervention remained 1 day but with an improved IQR from 1 (IQR 0 – 4) to (IQR 0 – 2),  $p = 0.02$  and median time from suspicion of Tb to initiation of Tb treatment among the co-infected declined from 46 (IQR 31 – 87) to 4 days (IQR 1 – 8),  $p < 0.00$ .

**Conclusions and key recommendations:** Implementation of tuberculosis infection control programs at HIV clinics can reduce delays in diagnosis and initiation of Tb treatment among those with the co-infection. There is need to evaluate the feasibility and effectiveness of their large-scale implementation and impact on patient delays.

### OPP-402-01 Outcomes of tuberculosis/human immunodeficiency virus co-treatment in Kenya: a case study of Eastern Deanery Aids Relief Programme

N Kirui,<sup>1</sup> C Mwangi,<sup>1</sup> J Kirigha,<sup>1</sup> B Orangi,<sup>1</sup> S Kegoli.<sup>1</sup> <sup>1</sup>Clinical, Eastern Deanery AIDS Relief Program, Nairobi, Kenya. e-mail: nomischris@yahoo.com

**Background:** Tuberculosis (TB) is the most common opportunistic infection affecting HIV positive (HIV+) individuals, with HIV infection contributing to a significant increase in the worldwide incidence of TB; yet TB is preventable and curable. Although the recommendations for TB treatment among HIV+ individuals do not differ with those not infected with HIV, TB treatment in HIV-infected individuals is complicated by health system issues, drug reactions, and paradoxical drug reactions that occur after Highly Active Antiretroviral Therapy (HAART) initiation. The Kenya national guideline recommends that HAART in HIV+ patients be started after initiating TB treatment, regardless of their CD4 count or WHO stage. We seek to describe the outcomes of concurrent HAART and TB treatment in co-infected clients.

**Design/Methods:** We conducted a retrospective review from EDARP's electronic medical record to identify clients, aged 15 years and above, taking TB/HIV treatment between October 2011 and September 2013 in the 14 EDARP facilities located in the Eastern slums of Nairobi, Kenya. At each clinical visit, clients were assessed to determine their TB status by using a combination of TB symptom screening, physical examination, and if indicated, chest radiography, tuberculin skin test, and/or sputum evaluation. Descriptive and regression analysis was done. Data were analyzed using STATA 12.0.

**Results:** A total of 1,582 new TB clients were included in analysis. Median age at TB enrollment was 35 years (Interquartile Range (IQR) 29 – 41 years). Males were 702 (44%). By TB type, Pulmonary TB was the majority with 1,249 (79%) while extra pulmonary TB was 333 (21%). At the end of TB treatment follow up period, 1,203 (76%) clients completed their treatment success-



fully while 136 (8.6%) died before completion. The median CD4 count at start of TB treatment was 138 cps/ml and 244 cps/ml at the end of treatment. During TB treatment, 1,331 (84%) clients were on HAART. Clients on HAART were more likely to complete TB treatment successfully [Odds Ratio (OR) = 3.5 (95% CI: 2.6-4.6,  $P < 0.001$ )] and less likely to die [OR = 0.4 (95% CI: 0.3-0.6,  $P < 0.001$ )] than their counterparts. Clients who were not on HAART at TB registration were initiated within median 3 weeks (IQR: 2 – 4.6 weeks) of starting TB treatment.

**Conclusion:** It is feasible starting TB treatment among HIV/TB co-infected clients on HAART early thus improving outcomes and reducing TB associated mortality in people living with HIV.

### OPP-403-01 The impact of implementation fidelity on mortality under a CD4-stratified timing strategy for antiretroviral therapy in patients with tuberculosis

M Patel,<sup>1</sup> D Westreich,<sup>1</sup> J Eron,<sup>2,3</sup> M Yotebieng,<sup>1,4,5</sup> W Behets,<sup>1</sup> A Van Rie.<sup>1</sup> <sup>1</sup>Epidemiology, University of North Carolina at Chapel Hill, Chapel Hill, NC, <sup>2</sup>Medicine, Center for AIDS Research, University of North Carolina at Chapel Hill, Chapel Hill, NC, <sup>3</sup>Medicine, Division of Infectious Diseases, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; <sup>4</sup>Public Health, University of Kinshasa, Kinshasa, Democratic Republic of Congo; <sup>5</sup>Epidemiology, The Ohio State University, Columbus, OH, USA.  
e-mail: monitap@email.unc.edu

**Background:** The World Health Organization recommends a CD4-stratified timing strategy for antiretroviral treatment (ART) initiation in patients diagnosed with tuberculosis (TB), with earlier ART initiation in those with the low CD4 cell counts. Evidence from implementation of this type of strategy in resource-limited settings is limited.

**Design/Methods:** Prospective cohort study of 395 adult, ART-naïve patients diagnosed with TB and HIV at five primary care clinics in Kinshasa, Democratic Republic of Congo. ART was to be initiated at the end of the first month of TB treatment if CD4 count was below 100 cells/mm<sup>3</sup> or WHO clinical stage 4 (other than extrapulmonary TB) and at the end of the second month of TB treatment if CD4 count was between 100–350 cells/mm<sup>3</sup>. We used logistic regression and the parametric g-formula to estimate the effect of implementation fidelity to the CD4-stratified timing strategy for ART initiation on total mortality risk during the first 6 months of TB treatment.

**Results:** Of the 395 participants, only 183 (46.3%) initiated ART in time, as recommended by the CD4-stratified timing strategy. Among the 212 (53.7%) participants who did not initiate ART in time, 53 (25.0%) never initiated ART and 159 (75.0%) initiated ART after a median delay of 11 days (IQR: 4–24). Median delay did not differ by time of ART eligibility (12 days for month 1 v. 10 days for month 2,  $p = 0.62$ ). During the first 6 months of TB treatment, 33 deaths were observed, the majority ( $n = 26$ ) of which occurred in patients who did not initiate ART in time. The estimated

6-month mortality risk under observed implementation fidelity was 12.0% (95% CI: 8.2–15.7%). Complete implementation fidelity to the CD4-stratified timing strategy for ART initiation in this population was estimated to result in 6-month mortality of 7.8% (95% CI: 2.4–12.3%), corresponding to an absolute risk reduction of 4.2% (95% CI: 0.3–8.1%). The preventable fraction of mortality due non-fidelity to the CD4-stratified timing strategy for ART initiation was an estimated 35.1% (95% CI: 2.9–67.9%).

**Conclusion:** Strategies to achieve high fidelity to CD4-stratified timing of ART initiation for patients with TB at primary care clinics in resource-limited setting need to be developed as this could substantially reduce mortality among patients diagnosed with TB.

### OPP-404-01 Timing of death among TB patients: an in-depth view

G Kasera,<sup>1</sup> E Masini,<sup>1</sup> H Weyenga,<sup>1</sup> J Kioko.<sup>1</sup> <sup>1</sup>Division of Disease Prevention and Control, National Tuberculosis, Leprosy and Lung Diseases Unit, Nairobi, Kenya.  
e-mail: kadondikasera@gmail.com

**Introduction:** Tuberculosis (TB) is a global leading cause of morbidity and mortality. While the Kenya has met most of the Global TB control targets TB related mortality remains a major challenge. We analyzed the national TBHIV data to describe clinical characteristics and timing of death among TB patients enrolled in 2012. **Methods:** We imported data from the national web-based TBHIV surveillance system (TIBU) and removed all personal identifiers. We Computed point estimates, 95% confidence intervals and standard deviation using Epi Info™ 7 and SPSS® 21. A case of TB death was defined as any record of with mortality recorded as an outcome during the course of TB treatment.

**Results:** A total of 99,728 patients with a HIV prevalence of 36% were notified in 2012 and had treatment outcomes. Of these 41,760 (42%) were pulmonary TB (PTB) smear positive (SM+); 32,601 (33%) PTB smear negative (SM-); while 17,228 (17%) extra pulmonary TB (EPTB). Overall, 33,352 (33%) got cured; 51,572 (52%) completed treatment; 497 (<1%) failed treatment; 5,089 (5%) were lost to follow up; 3,673 (4%) were transferred out; and 5,545 (6%) died. Of the 5,545 that died, 4,997 (90%) had complete records of treatment start and outcome dates while 548 (10%) had incomplete records. Of the 4,997 with complete records, 4,764 (95%) had their treatment outcomes within 8 months of treatment initiation. Of the 4,764 the HIV prevalence was 59% and 1,254 (26%) were PTB SM+; 1,975 (41%) PTB SM-; and 1,077 (23%) EPTB. The median time of death was 2 month, with an interquartile range (IQR) of 1 – 3 months. There was difference in timing of death among those HIV infected compared to those uninfected and those initiated on early and late antiretroviral therapy

**Conclusion:** Half of the deaths among TB patients occur during the intensive phase of treatment. There is need to focus on reducing mortality among both the HIV infected

and uninfected individuals, Early Initiation of ART among HIV patients need to be further interrogated.

#### **OPP-405-01 Comparative analysis of the TB treatment outcomes among HIV positive and HIV negative TB patients in 2012 in Oyo state, Nigeria**

A F Omoniyi,<sup>1</sup> A Awe,<sup>1</sup> J O Obasanya,<sup>2</sup> T Oduosote,<sup>3</sup> N Chukwurah,<sup>2</sup> O Lawal,<sup>4</sup> M Gidado,<sup>5</sup> E Ubochioma.<sup>2</sup>

<sup>1</sup>TB, WHO, Abuja, Nigeria, <sup>2</sup>TB, NTBLCP, Abuja, <sup>3</sup>TB/HIV, USAID, Abuja, <sup>4</sup>TB, STBLCP Oyo State, Ibadan, <sup>5</sup>TB, TB CARE I, Abuja, Nigeria. e-mail: omoniyifadare@yahoo.com

**Background:** Oyo state with a population of about 6.6 million is one of the high burdened TB and HIV states in Nigeria. Oyo state is among the first set of states that started implementing TB/HIV collaborative activities in 2006. HIV Counseling and Testing (HCT) services are currently provided in all the 179 DOTS centers across the state. This study was conducted to test the Null hypothesis which states that the TB treatment outcomes in HIV positive TB patients is comparable to that of the HIV negative TB patients

**Design/Methods:** This is a retrospective study of 7,014 TB patients registered for TB treatment between January and December 2012 in Oyo state, Nigeria. All the TB patients were offered HCT. The HIV status of the patients and the history of ARV and cotrimoxazole intake were recorded in the Patient's cards and the registers. TB Treatment outcomes of the patients were assessed in relation to the HIV status of the patients and were captured using the revised quarterly summary forms in line with the National Guidelines.

**Results:** 915 (13%) of the TB patients were HIV positive; 99.9%(914) of the HIV positive TB patients received CPT and 61.5%(563) received ART. The Treatment Success Rate(TSR) among HIV positive TB patients was 85.2% , while the TSR was slightly higher among HIV negative TB patients (92.9%); the death rate among HIV positive-TB patients was 8.2%, while it was 2.9% in HIV negative-TB patients. Further analysis of the death rate among HIV positive-TB patients revealed that HIV positive patients with Extra Pulmonary TB (EPTB) has a higher death rate, 26.5%(22) of the HIV positive EPTB patients(34) died; The failure and default rates among the two groups of patients appear similar.

**Conclusion:** The treatment outcomes among HIV positive and HIV negative TB patients appear similar. The national target of 85% TSR was achieved among both HIV positive-TB patients (85.2%) and HIV negative-TB patients(92.9%). Though Mortality rate in HIV positive TB patients (8.2%) is still slightly higher than in HIV negative TB patients (2.9%); Mortality rate was particularly higher among HIV positive patients with EPTB. HIV positive patients with EPTB must be closely monitor while on treatment. HIV and TB programme must collaborate to ensure early initiation of ART among TB/HIV co-infected patients to reduce the mortality rate; National HIV programme must scale up ART services using wider network of the TB programme.

#### **OPP-406-01 Factors affecting antiretroviral therapy uptake by HIV-infected tuberculosis patients in Uganda: a comparative study of two districts**

F Mugabe,<sup>1</sup> B Kirenga,<sup>2</sup> A Katamba,<sup>2</sup> E Bloss.<sup>3</sup> <sup>1</sup>Central Unit, Uganda National TB and Leprosy Programme, Kampala, <sup>2</sup>College of Health Sciences, Makerere University, Department of Medicine, Kampala, Uganda; <sup>3</sup>Division of TB Elimination, US Centers for Disease Control and Prevention, Atlanta, GA, USA. e-mail: vtu3@cdc.gov

**Background:** Antiretroviral therapy (ART) reduces morbidity and mortality among HIV infected tuberculosis (TB-HIV) patients. Nationally 46 percent of TB-HIV patients in Uganda were on ART in 2012. We investigated reasons for the low ART uptake in Uganda by comparing factors affecting uptake in one high uptake district (Nebbi) and one low uptake district (Masaka).

**Design/Methods:** Nebbi and Masaka districts were selected based on HIV service indicators reported to the National TB and Leprosy Program (NTLP) in 2011. TB and ART treatment registers were reviewed to capture demographic and clinical data for all TB-HIV patients registered for treatment during January 1 – December 31, 2011. Structured interviews were conducted among health workers and TB-HIV patients to seek their views on barriers to ART uptake.

**Results:** A total of 382 registered TB-HIV patients (157 from Nebbi and 225 from Masaka) were included. Even though staffing levels and the number of facilities providing ART per capita were higher in Masaka than Nebbi, a significantly greater proportion of TB-HIV patients were on ART in Nebbi (41%) than Masaka (27%) ( $p=0.004$ ). TB-HIV patients in Nebbi were more likely to be accurately recorded in both TB and ART registers compared with patients in Masaka ( $OR=5.1$ , 95%  $CI=2.7-9.6$ ). All 33 TB-HIV patients interviewed (23 from Nebbi and 10 from Masaka) knew that TB and HIV should be treated concurrently. All patients from Nebbi and eight (35%) from Masaka reported receiving TB-HIV education from a health worker ( $p=0.031$ ). Among the 37 health workers interviewed (12 from Nebbi and 25 from Masaka), there were no significant differences between providers in Nebbi and Masaka in terms of their access to (8% vs 28%,  $p=0.17$ ) and knowledge of the current ART guidelines (92% vs. 92%,  $p=0.97$ ), whether they received training in TB-HIV (25% vs 28%,  $p=0.85$ ), and whether they worked in integrated TB-HIV clinics (67% vs 68%,  $p=0.93$ ). However, shortages of antiretroviral drugs were more frequently reported as a barrier to ART uptake by health workers in Masaka (44%) than Nebbi (17%) ( $p=0.10$ ).

**Conclusion:** Overall ART uptake was low despite high levels of patient and provider knowledge of TB-HIV treatment guidelines. Poor recording, lack of patient education, and shortage of antiretroviral drugs were more frequent in Masaka. Training in recording and reporting and improvements in patient education and drug supply may increase ART uptake in Masaka.

### OPP-407-01 Uptake of ART among TB-HIV co-infected clients in Nairobi, Kenya

E Ndungu.<sup>1</sup> <sup>1</sup>TB Control, Ministry of Health, Nairobi, Kenya.  
e-mail: eunice.wambui@gmail.com

**Summary:** Kenya has high burden of tuberculosis with about 50% of all the TB patients being co-infected with HIV. National TB/HIV guidelines stipulate that all TB-HIV co-infected clients should be put on life-long antiretroviral therapy (ARV). In Kasarani Zone T, one of the TB control zones in Nairobi, only 29% of TB-HIV co-infected patients received ART in early 2010. This was because a quarter (26%) of clients were lost due to poor intra-facility transfers, no special attention was provided to the clients newly diagnosed with HIV at the TB clinic and poor data flow from HIV clinic to feedback the TB clinic. Selected high impact interventions (ranging from improved linkage to care to improved customer care) were implemented. This resulted to rapid uptake of ART up to 80% by end of 2013.

**Introduction:** Zone T comprises 8 facilities which diagnoses about 90 new TB cases every month, of which almost half (43%) are co-infected with HIV. Without treatment, many of these clients would not survive to complete their full course of TB treatment. For long time the zone had a great challenge in ART uptake. In early 2010, only 1 in every 3 TB patients co-infected with HIV were put on ART, this informed the need to have concerted efforts to improve ART uptake among HIV positive.

**Methodology:** To improve ART uptake among TB patients, the following interventions were implemented: Intra-facility client follow-ups whereby TB/HIV collaboration was initiated and the staff working at TB clinic liaised with those at the HIV comprehensive care clinic (CCC). Friendly escorts by facility based community health workers who were sensitized and mandated to escort patients from TB clinic to the CCC, ensure they are enrolled in care and provide feedback to TB clinic with their unique CCC identifier. Competitive engagement of health care workers/inter-facility competitions

**Results:** ART uptake rose from a 2010 baseline of 29% to 80% by end of 2013.

**Lessons learnt:** It requires a mix of bottom-up and top-bottom approaches to diffuse national policies in patient care and break from a tradition.

**Conclusion:** In resource limited settings, it is possible to improve ART uptake among HIV co-infected TB patients cost effectively by ensuring data ownership, intra-facility client follow-ups, setting targets and encouraging inter-facility competition. Scaling up this approach has the potential to achieve universal access to ART for HIV co-infected TB patients in Kenya and similar settings.

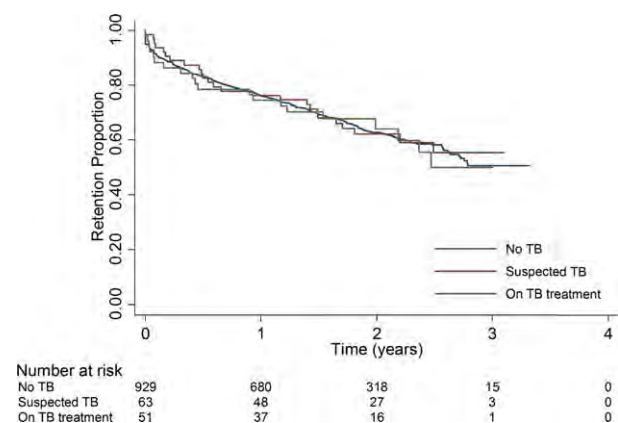
### OPP-408-01 Retention of HIV-positive patients on antiretroviral therapy in Nigeria is not affected by tuberculosis status

EK Dokubo,<sup>1</sup> S Agolory,<sup>1</sup> R Shiraishi,<sup>1</sup> S Odafe,<sup>2</sup> D Onotu,<sup>2</sup> I Dalhatu,<sup>2</sup> A Auld,<sup>1</sup> A Bashorun.<sup>3</sup> <sup>1</sup>Division of Global HIV/AIDS, US Centers for Disease Control & Prevention (CDC), Atlanta, GA, USA; <sup>2</sup>Division of Global HIV/AIDS, CDC, Abuja, <sup>3</sup>National AIDS and STI Control Program, Federal Ministry of Health, Abuja, Nigeria.  
e-mail: vic8@cdc.gov

**Background:** Retention of HIV-positive patients in antiretroviral therapy (ART) programs is essential to optimize treatment outcomes; however, some studies suggest an increased incidence of attrition among HIV-positive TB patients in ART programs. Nigeria has an estimated 3.5 million people living with HIV (PLHIV), is ranked 9<sup>th</sup> among the 22 high-burden tuberculosis (TB) countries, and 23% of TB patients in the country are infected with HIV. We sought to assess the impact of TB status on retention of PLHIV initiated on ART in Nigeria.

**Methods:** A retrospective study was conducted among a nationally representative sample of adults enrolled in U.S. President's Emergency Plan for AIDS Relief (PEPFAR)-supported care and treatment programs. Data were abstracted from medical records of patients from 35 sites selected using probability-proportional-to-size sampling. Among PLHIV started on ART from January 2010 to February 2013, Kaplan-Meier estimates were calculated to determine the impact of TB status at the time of ART initiation on patient retention.

**Results:** Of 1043 patients, 929 (89.1%) were classified as not having TB, 63 (6.0%) were TB suspects, and 51 (4.9%) were on TB treatment at ART initiation. Retention at 6 months after initiating ART was 83.1%, 82.5%, and 78.4% in the three groups respectively, and declined to 76.2%, 76.2%, and 74.4% at 12 months after ART initiation. By 30 months after being on ART, 58.1% of PLHIV without TB, 55.4% of TB suspects, and 49.9% of PLHIV on TB treatment at ART initiation were still retained in the ART program (Figure).



**Conclusion:** Retention of HIV-positive patients in the Nigeria ART program is high in the initial months of treatment and is similar to that of other sub-Saharan



African countries. Attrition due to loss-to-follow-up, treatment discontinuation, and patient deaths does not appear to differ among PLHIV without TB at ART initiation, PLHIV suspected to have TB, and HIV-positive TB patients on TB treatment. Continued efforts are needed to sustain high retention in care and improve patient outcomes.

#### **OPP-409-01 Expanding access of HIV-positive TB patients to antiretroviral therapy (ART) services in Nigeria: lessons learnt from 2008–2013**

A F Omoniyi,<sup>1</sup> A Awe,<sup>1</sup> T Odusote,<sup>2</sup> J O Obasanya,<sup>3</sup> N Chukwurah,<sup>3</sup> E Ubochioma,<sup>3</sup> E Oyama,<sup>1</sup> M Gidado.<sup>4</sup>  
<sup>1</sup>TB, WHO, Abuja, <sup>2</sup>TB, USAID, Abuja, <sup>3</sup>TB, NTBLCP, Abuja, <sup>4</sup>TB, TB CARE I, Abuja, Nigeria.  
 e-mail: omoniyifadare@yahoo.com

**Background and challenges to implementation:** Nigeria ranked high among the 22 high TB burden countries globally, the burden of TB in the country is further compounded by the high HIV prevalence of 4.1%. The current guidelines stipulate ART for all HIV positive TB patients (TB/HIV co-infected patients) irrespective of their CD4 count. There has been an increase in the number of ART centers in the country with the number rapidly increasing in the past two years with associated expansion of ART services also into PHC facilities where majority of the DOTS centers are located. However the number of ART centers in the country is still suboptimal. This study aimed at reviewing lessons learnt in scaling up access of HIV positive TB patients to ART from 2008 to 2013 with aim of informing better programming.

**Intervention or response:** The reporting and recording formats for TB programme were revised by the programme to capture HIV information. A retrospective analysis of the TB cases registered from 2008 to 2013 by the National programme from all the facilities providing DOTS services in all the 37 states were analyzed according to the HIV status and their access to ART in line with the National guidelines.

**Results and lessons learnt:** The proportion of TB patients tested for HIV increased from 63% in 2008 to 88% in 2013, 22% of the TB patients tested for HIV in 2013 were HIV positive. The proportion of co-infected patients accessing ART also increased from 17% in 2008 to 67% in 2013. The ART uptakes among TB patients varies from state to state, in 2013 it ranges from 33% to 100%. It is higher in states with higher number of ART services and in facilities where the services are co located. The proportion accessing ART which has been relatively stable at 43% as at 2011 rapidly increased in 2012 with the commencement of decentralization of ART services and is currently at 67%. Uptake of ART service in private health care is very low as most of them are currently not providing ART services.

**Conclusions and key recommendations:** HIV programme must rapidly scale up ART services in the country using the wider network of TB programme. This will increase uptake towards the 100% target for co-infected patients

to be placed on ART. HIV programmes must include Private health care facilities in the HIV expansion plan. National programme must put in place measure to ensure all TB/HIV co-infected patients on ART are captured irrespective of when the test was done.

## **02. COMMUNITY ENGAGEMENT IN TB CONTROL**

#### **OPP-410-01 Advocacy, public art and social mobilisation: 'Nuestra Casa'— a case study of TB action on the US-Mexico Border**

E Moya,<sup>1</sup> S Silvia Maria Chavez Baray,<sup>1</sup> B Lomeli.<sup>2</sup> <sup>1</sup>Social Work, The University of Texas at El Paso, El Paso, TX, <sup>2</sup>SOLUCION TB, Project Concern International, San Diego, CA, USA. e-mail: emmoya@utep.edu

**Background:** Nuestra Casa (Our Home, in Spanish) is a touring project for tuberculosis Advocacy, Communication and Social Mobilization (ACMS). Nuestra Casa is a three-dimensional house that reflects the life and stories of people affected by TB on the U.S.-Mexico border. It is a tool to promote awareness among decision makers, health providers, and the public to get involved in concrete action to prevent the spread of TB, reducing the suffering, the number of cases, and deaths caused by it. Realizing that the community of persons affected by TB must be involved and their real-life situations addressed if efforts to combat the disease are to be effective. With support from the USAID, PCI adapted the concept of 'The Shack' developed in South Africa by Damien Schumann. The original exhibit traveled to four states in Mexico and two in the U.S. reaching more than 25,000 visitors. In 2012, Nuestra Casa returned to the University in El Paso and launched a 12-month initiative.

**Intervention:** Intended to provide a new perspective on the TB, increasing political will to improve prevention and care and mitigate stigma and discrimination experienced by the persons affected by TB. The exhibit became a vehicle for the Voices and Images of TB Photovoice exhibition. Local community and social research programs around Mexico have exhibited Nuestra Casa. Videos were produced, media stories were published, a webpage was created, and a regional award for community-academic engagement was received in 2013.

**Results:** Nuestra Casa reached 50,000 school children, farm workers, promotoras, university students, educators, and persons affected by TB, through education, social mobilization and a call to action. Lessons learned, personal testimonies, photographs, examples of community participation and involvement of PATB, the call to action, as well as the impacts will be presented.

**Conclusion:** The need to explore multiple forms of venues and forms to engage the public for bringing about public health education and ultimately structural social change is critical. Nuestra Casa has been referred as one of the finest examples of how universities and educational institutions connect with a community on an

important public and social issue and does so with the engagement of the students, faculty, persons affected and with aesthetic sensibilities.

### OPP-411-01 Effective advocacy to increase local government budget for TB control: Stop TB Partnership (STBP) Cimahi City, West Java, Indonesia

R Arifin Panigoro.<sup>1</sup> <sup>1</sup>National Board, Indonesian Association Against Tuberculosis, Jakarta, Indonesia. Fax: (+621)7397494. e-mail: henry.ppti@gmail.com

**Background:** Indonesia is in top five among high TB burden countries; majority of TB program funding is from international sources, while national funding is increasing but still in small proportion. To achieve targets set for MDGs and beyond, the large financial gaps must be filled. Stop TB Partnership Cimahi City conducted comprehensive advocacy to the Mayor and parliament to increase city budget for supporting TB program.

**Intervention:** PPTI (secretary of STBP) worked collaboratively with District Health Office of Cimahi City to raise the TB control importance to the City Mayor via organizing regular meetings with the Mayor Office. The TB “Champion” (well-known as public figure) frequently promoted TB program in every occasion and influential way to advocate the policy makers. The increasing of budget allocation mostly aimed to empower community and strengthen implementation of TB activities by community volunteers. Quarterly coordination was done by PPTI and DHO. Once a year, all the activities were evaluated and presented to the parliament for endorsement of next year proposal. Many resources, from other sources (private sector, donation, etc.), also supported TB program.

**Result:** The City’s budget to support TB program increased from IDR 42,691,500 (2010) to IDR 194,424,550 (2011), IDR 272,536,150 (2012), and IDR 236.677.500 (2013). The budget supported to empower community involvement and operation costs of community volunteers.

**Conclusion:** Advocacy to local government should be comprehensive and continuous. The TB “Champion” is the most effective advocate to increase local budget in Cimahi City.

### OPP-412-01 Partnership in approaching “community free of tuberculosis” in a hill-tribe village, Chiang Rai, Thailand

T Kantima,<sup>1</sup> S Luangjina,<sup>1</sup> J Wongyai,<sup>1</sup> S Boonyamanonukul,<sup>2</sup> A Wiriyaprasobchok,<sup>2</sup> S Nedsuwan,<sup>2</sup> P Poosang,<sup>3</sup> J Ngamvithayapong-Yanai.<sup>1</sup>  
<sup>1</sup>JATA-Project, TB/HIV Research Foundation, Chiang Rai,  
<sup>2</sup>Chiang Rai Regional Hospital, Chiang Rai, <sup>3</sup>Meakorn Sub-district Administration Organization, Chiang Rai, Thailand. Fax: (+66) 5375 2448. e-mail: ritcr@tbhiv.org

**Background and challenges to implementation:** Nong Khiew, a village of hilltribe minorities migrated from Myanmar in 1990s was one of the highest TB incidence

(1284/100K) and the poorest community of Chiang Rai province. Of the 623 community people, 8 had TB, 1 died, and 2 defaulted (lost follow up > 2 months) in 2007. Delay seeking care and treatment interruption were related to poverty. Almost 30% people were not eligible for the universal health insurance due to lacking of Thai citizen cards.

**Intervention or response:** In recognition of poverty and TB problems, since 2008 a group of active community volunteers in collaboration with the local partners including the Sub-district Administration Office, a hospital, a local non-governmental organization and the volunteer ladies against TB have implemented three interventions for community TB care and control. Firstly, raising awareness and reduce TB stigma by involving the cured ex-TB patients and the school students in TB education campaign; secondly, twice a year conducting TB symptom screening and referring the symptomatic cases with travel support and a green-light channel to access the hospital service and thirdly, establishing a revolving TB patient fund and empower TB patients by home visit, support travel expense to the hospital, including lending money for patients who are too sick to work. Moreover, the household contact cases were also supported for TB screening at the hospital.

**Results and lessons learnt:** Table 1 shows outcome of the community’s effort to control TB in 2008–2013. The volunteers early detected 8 active TB cases and achieved 100% treatment completion. Moreover, 26 household contacts received TB screening and TB preventive therapy for children under five years. The patients who borrowed money from the TB patient fund could resume to work and returned money. Nong Khiew village is approaching the stage of “community free TB”, i.e. zero TB death, zero default, and zero new TB case.

**Conclusions and key recommendations:** Through the constant commitments of the community volunteers and the partners, a “community free TB” seems to be possible. Social protection interventions are needed for the extreme poor population.

**Table 1:** Number of TB patients (all types, all age group) of Nong Khiew community 2007-2013

Year	Number of TB patients recorded in TB register	Number of TB patients identified by the community volunteer group and recorded in TB registry	Completed treatment and cured	Treatment interruption and loss of follow up	Deaths
2007	8	Not yet started the activities	5	2	1
2008	3	1	2	0	1
2009	2	0	2	0	0
2010	6	5	6	0	0
2011	2	2	2	0	0
2012	1	0	1	0	0
2013	0	0	0	0	0

### OPP-413-01 Engagement of the provincial, district and religious leaders as strategies to be successful in advocacy for TB CEPAT program in Indonesia

H Delyuzar,<sup>1</sup> R Yunita,<sup>2</sup> M Thompson.<sup>3</sup> <sup>1</sup>Health, JaringanKesejahteraan/KesehatanMasyarakat(JKM), Indonesia, Medan, <sup>2</sup>Microbiology, Faculty of Medicine, University of Sumatra, Medan, Indonesia; <sup>3</sup>Health Study, Westat, Rockville, MD, USA.  
e-mail: meklathompson@westat.com

**Background and challenges to implementation:** Tuberculosis infection (TB) remains the biggest health problem in Indonesia. Several programs were designed and implemented to decrease TB prevalence and increase the success rate of TB treatment. To be successful and sustainable it must engage the local government at the start of the project. JKM launched CEPAT TB project funded by USAID in three provinces: North Sumatra, West Sumatra and DKI Jakarta. The project has two main goals: community mobilization to increase awareness of TB problem and advocacy to involve more stakeholders' participation. In the community setting, it needs a strong commitment from government, parliament, and community leaders who can afford the proper policy, resources and budget for the program sustainability. The aspect presented focuses on advocacy.

**Intervention :** The project covers 14 districts in DKI Jakarta, North and West Sumatra provinces. Advocacy activities operate in all provinces. The cornerstone of advocacy activities are the program's launch involving the the Governors of the 3 provinces, US Embassy, USAID officer, Head of Provincial Health Offices, District and subdistrict leaders, and other important TB stake holders attending the ceremony. Through the ceremony, the project was introduced and more importantly began building a commitment to participate. After the launch at the province level advocacy continued within the district and subdistrict levels which involved district or subdistrict government and also parliament. At the community level advocates reached religious leaders and other key persons in the community.

**Results and lessons learnt:** Cooperation and commitment are gained between JKM and Governors of 3 provinces. The Governors are committed and enthusiastic to control the TB program through the project. The ceremony bridged cooperation sinergically between JKM and TB stakeholders in those three provinces, such as in North Sumatra where JKM cooperated with the Provincial Ministry of Health to build a free of charge referral system for TB patients from PUSKESMAS to a hospital funded by government so the patient does not pay for TB treatment while JKM supports the budget for patients' transportation cost including their home care. The government raised TB budget to 16%.

**Conclusions:** Advocacy to TB program stakeholders increase the commitment from government, parliament and community leaders who have the proper policy, resources and budget for program sustainability.

### OPP-414-01 An assessment of IEC intervention to increase the awareness on early detection and treatment seeking of tuberculosis in six states of India

S Pandurangan,<sup>1</sup> S Chadha,<sup>1</sup> S Mohanty,<sup>1</sup> B Entoor Ramachandran,<sup>1</sup> D Lekharu.<sup>2</sup> <sup>1</sup>TB care and control, International Union Against Tuberculosis and Lung Disease (The Union), New Delhi, <sup>2</sup>Project Axshya, Population Services International, New Delhi, India. Fax: (+91) 11 46 05 40 30. e-mail: sripriya14@gmail.com

**Background:** India has the world's highest burden of Tuberculosis. Lack of awareness about TB is one of the main reasons for such huge TB burden in the country. The Union South-East Asia Regional office, through the project Axshya conducted a mass media campaign to improve the awareness level among the general population in six states of India. The campaign was conducted through a combination of mid-media, static media and mass media campaign in the programme states. The first and second round of campaign was conducted during March 2012 and December 2012 respectively. This paper presents the impact of the IEC campaign in increasing the knowledge about early diagnosis of Tuberculosis and its treatment services.

**Methodology:** Two rounds of cross sectional community based survey adopting multistage systematic random sampling was conducted in 30 districts of 6 states of India. The impact of the campaign was assessed by looking the status of key indicators among exposed and not exposed groups and with those from baseline. Baseline figures and those not exposed during end line have been compared with those exposed during end line to see the impact of campaign over a period of time. A structured pretested questionnaire was administered to capture information on Media exposure and awareness.

**Results:** There was significant increase ( $P < 0.05$ ) in awareness about TB among those exposed (96%) to IEC campaign during end line in comparison to not exposed (91%) and from baseline (87%). Similarly, significant improvement in awareness among those exposed observed in relation to place of TB diagnosis and TB treatment. Awareness about DOTS has also increased significantly but still only one-fifth of the exposed population is aware about DOTS. There is overall significant increase ( $P < 0.05$ ) in knowledge levels among those endline exposed (88%) and non-exposed group (82%) from base line (78%). However when compared to exposed and non-exposed at end line knowledge indicators like only TB is a contagious disease, coughing more than 2 weeks is a symptom of TB, simple cough cannot be symptom of TB, and TB drugs are provided free of charge showed the significant changes ( $p < 0.05$ ).

**Conclusion:** The significant change in the knowledge indicators among the exposed population highlights the effectiveness of community focused IEC campaigns in improving the knowledge about tuberculosis.



### OPP-415-01 From community advisors to scientific partners: lessons on strengthening community engagement in research from the community research advisors group

C Lee,<sup>1</sup> M Frick,<sup>1,2</sup> E Lessem,<sup>2</sup> D Von Delft,<sup>1</sup> L Ruiz Mingote,<sup>1</sup> D Namutamba,<sup>1</sup> S Goldberg,<sup>3</sup> P Nahid.<sup>4</sup>  
<sup>1</sup>TB, Community Research Advisors Group, New York, NY,  
<sup>2</sup>TB/HIV, Treatment Action Group, New York, NY, <sup>3</sup>TB Elimination, US Centers for Disease Control and Prevention, Atlanta, GA, <sup>4</sup>School of Medicine, University of California San Francisco, San Francisco, CA, USA. Fax: (+1) 212.253.7923. e-mail: mike.frick@treatmentactiongroup.org

**Background:** Growing consensus points toward community engagement as an essential component of ethical TB clinical trials. Yet few investigators involve communities at the earliest stages of scientific development when they are framing research questions, debating strategies and drafting protocols. The Community Research Advisors Group (CRAG) is an international, community-based advisory body to the US CDC's Tuberculosis Trials Consortium (TBTC). Here we describe how the CRAG and TBTC developed a mechanism to engage community representatives in protocol development for an upcoming phase III treatment-shortening trial for drug-sensitive TB.

**Intervention:** In 2013, CRAG and TBTC investigators piloted a system in which CRAG members reviewed early drafts of study protocols. These reviews occurred in parallel with investigator consultations with other TBTC committees and before IRB and regulatory reviews. Principal investigators presented successive protocol drafts to the CRAG during in-person meetings and teleconferences. A CRAG representative served on the protocol team and Core Science Group, which sets the TBTC's scientific agenda. The CRAG reviewed presentations through structured group discussions, checking for member understanding and communicating concerns back to the protocol team.

**Results:** CRAG feedback on early protocol drafts contributed to several changes, including a statement that results dissemination would occur through means informed and approved by the CRAG. The CRAG representative on the protocol team successfully advocated for the inclusion of adolescents as well as people with HIV at a lower CD4 count in the study. Early and repeated engagement gave investigators multiple opportunities to explain the study design, clarify questions and solicit community feedback. CRAG members built their capacity to engage with investigators and review scientific documents.

**Conclusions:** Research institutions should create avenues for community advisors to serve as scientific partners in protocol development. Earlier involvement of communities in the scientific process may enable community advisors to better prepare communities for studies; strengthen feelings of community ownership over research; and relay community perspectives on the inclusion of vulnerable populations. The impact of earlier community involvement in protocol development deserves formal assessment from groups seeking to

demonstrate the value of community engagement for TB research.

### OPP-416-01 Improving clinical research at the community level: an evaluation framework for good participatory practices in TB drug trials

K Macqueen,<sup>1</sup> N Eley,<sup>1</sup> M Frick,<sup>2</sup> L Ruiz Mingote,<sup>3</sup> A Chou,<sup>4</sup> S Seidel,<sup>5</sup> S Hannah,<sup>6</sup> C D Hamilton.<sup>7</sup> <sup>1</sup>Social & Behavioral Health Sciences, FHI 360, Durham, NC, <sup>2</sup>TB/HIV, Treatment Action Group, New York, NY, USA; <sup>3</sup>Institutional Development, Planeta Salud, Barcelona, Spain; <sup>4</sup>Project Manager, Reagan-Udall Foundation for the FDA, Washington, DC, <sup>5</sup>Community Engagement, TB Alliance, New York, NY, <sup>6</sup>Senior Program Manager, AVAC, New York, NY, <sup>7</sup>Scientific Affairs, FHI 360, Durham, NC, USA. Fax: (+1)9195447261. e-mail: kmacqueen@fhi360.org

**Background:** In October 2012 the Stakeholder and Community Engagement Workgroup of the Critical Path to TB Drug Regimens issued Good Participatory Practice Guidelines for TB Drug Trials (GPP-TB), based on similar guidelines for HIV. Despite growing acceptance of the importance of community engagement and participatory strategies in clinical research, empirical assessment of the benefits and burdens has languished. Development of an appropriate evaluation framework is a critical step in building an evidence base for and strengthening desired outcomes of GPP-TB.

**Design/Methods:** Working with a diverse group of global TB stakeholders that included advocates, scientists, and ethicists we used a Theory of Change approach to develop an evaluation framework for GPP-TB. Steps included defining the pathway from current practices to those set out in GPP-TB, specifying what is needed for enhanced ethical goals to be achieved, and articulating underlying assumptions that can be tested and measured.

**Results:** The resulting evaluation framework includes a clearly defined ethical goal, a set of powerful strategies derived from GPP-TB practices for achieving the goal, and intermediate outcomes connecting strategies to goals. The ethical goal was defined as "TB clinical trials demonstrate social value, achieve increased access across stakeholders, and meet standards of acceptability." Five powerful strategies for achieving the goal were identified: accountability mechanisms, community mapping, shared learning, responsible advocacy, and deliberation. Each strategy reinforces and supports responsibilities of both researchers and communities. We identified short term outcomes for the strategies that provide the foundation for GPP-TB principles to be realized along with intermediate and long term outcomes that document results of enactment of GPP-TB principles. Causal chains linking strategies, outcomes, and principles to the ethical goal were hypothesized. The framework will inform development of process and outcome measures to evaluate GPP-TB implementation and the extent to which practices achieve the ethical goal.

**Conclusion:** GPP-TB is a valuable resource for strengthening TB clinical trials research by fostering practices that engage communities and ensure results are understood and utilized. Through use of established evaluation

tools and strategies, advocates and scientists can work together to strengthen the positive impact of GPP-TB.

POWERFUL STRATEGIES	Accountability Mechanisms	Community Mapping	Shared Learning	Responsible Advocacy	Deliberation
SHORT TERM OUTCOMES provide the foundation for GPP-TB principles to be realized	Increased transparency and integrity in representing individual and stakeholder group interests & expectations, and in maintaining scientific and ethical standards	Increased identification of needs and understanding of context: local community, research community, global public health community	Increased shared stakeholder knowledge: literacy on community context, research context, and TB	Increased awareness, political will, and resources for TB clinical trials and community engagement	Increased use of formal discussion & negotiation with all stakeholders to ensure options for mutual gain are pursued when trade-offs in principles or benchmarks are needed
GPP-TB PRINCIPLES					
GPP-TB BENCHMARKS demonstrate that GPP-TB principles are realized	<b>Respect / Fairness / Integrity / Transparency / Accountability / Autonomy</b> <b>Mutual Understanding:</b> <ul style="list-style-type: none"> <li>Sociocultural competency: understanding of cultural norms, practices, beliefs; social circumstances; diverse stakeholder perspectives; appreciation of implications of power differences</li> <li>Research competency: understanding scientific process; developing appropriate trial designs; collecting, analyzing &amp; disseminating data to ensure valid results</li> </ul> <b>Complementarity:</b> Funders, sponsors, research teams & local public health systems partner to maximize the impact that research and health care have on local populations				
INTERMEDIATE & LONG TERM OUTCOMES document results of enactment of GPP-TB principles	<b>Efficiency:</b> Eliminating wastes of time and effort as much as possible Stakeholders are empowered to decide together if a given trial is appropriate in a given community				
ETHICAL GOAL	TB clinical trials demonstrate social value, achieve increased access across stakeholders, and meet standards of acceptability.				

# **OPP-417-01 Engaging public music advertisers in creating TB awareness in the communities in Oyo State, Nigeria**

O Lawal,<sup>1</sup> O Oladimeji,<sup>2,3</sup> O Eltayeb,<sup>4</sup> O Daniel,<sup>5</sup> A Awe,<sup>5</sup> M Gidado,<sup>6</sup> J O Obasanya,<sup>6</sup> T Odusote.<sup>7</sup> <sup>1</sup>Tuberculosis, Oyo State Ministry of Health, Ibadan, Nigeria; <sup>2</sup>Research, Liverpool School of Tropical Medicine, Liverpool, UK; <sup>3</sup>Tuberculosis Research Unit, Zankli Medical Center, Abuja, <sup>4</sup>Tuberculosis, Damien Foundation Belgium, Ibadan, <sup>5</sup>TUB, World Health Organization, Abuja, <sup>6</sup>Tuberculosis, Federal Ministry of Health, Nigeria, Abuja, <sup>7</sup>TB-HIV, United States Agency for International Development, Abuja, Nigeria. e-mail: droladfb@gmail.com

**Background and challenges to implementation:** Improved accessibility to TB care and diagnostic services is very important to TB control as this would track the missed cases, improve the case finding and minimise delay in TB case notification in the rural communities and peri-urban settlements. Poor awareness of availability of screening and treatment services in the state contribute to low case finding. This study was done to objectively showcase how public music advertisers have provided assistance in improving TB case detection in the community through playing of TB audio CD and cassettes in different languages.

**Intervention or response:** The project was conducted in 11 LGAs, TB jingles were produced on audio CD and cassettes. There were increased advocacy activities among the association of PMAN to facilitate awareness building among the members. This was followed by training of 77 members of the association on TB strategies and referrals linkages. IEC TB referral forms and materials were deposited with the selected members in their shops. Each was given 1 audio CD and cassette containing the TB jingle in local language. The TBLS monitored the playing of the jingle 8–9, 12–1 and 5–6pm in various LGAs. The PMA are abound in all the towns and villages selling audio and video CD as well as playing this music in markets and major junctions of towns and villages.

**Results and lessons learnt:** A total of 11TBLS, 66 PMAs were involved in the project resulting in referral of 3,512 suspects in 1<sup>st</sup> quarter of 2013 compared to 2215 screened in 4<sup>th</sup> quarter 2012. The case notification also increased by 15% from 1415 patients in 4<sup>th</sup> quarter 2012 with male preponderance. Referral patterns show, TB-HIV co-infection-20% . Of the 342 new smear positive TB cases detected, 10% were referred by PMA and 35% by those hearing the jingles.

**Conclusions and key recommendations:** The findings has been found to have positive impact for creating awareness in the community and is cost effective, religious friendly and culturally acceptable to use in improving TB case finding in our various communities. There is a need to scale up the implementation of the approach in other LGAs of the state and Nigeria to improve TB case detection in Nigeria.

# **OPP-418-01 Caring for the “carer”: rights-based approaches to promote patient-centered approaches**

L Mabote.<sup>1</sup> <sup>1</sup>HIV, TB and Human Rights Advocacy, AIDS and Rights Alliance for Southern Africa (ARASA), Cape Town, South Africa. Fax: (+27) 21 4225483. e-mail: lynette@arasa.info

**Setting:** Integrated occupational risk and compensation guidelines for healthcare workers remain absent in resource-restrained settings and hampers patient-centred approaches to health care service delivery. A study in Kwazulu Natal, South Africa revealed that health care workers were at a 6 to 7 times higher risk of contracting MDR/XDR TB than patients. There are no official figures for healthcare workers infected with TB in most Southern African countries. SADC has seen an upsurge in the number of strikes for better occupational health and safety measures, as well as compensation.

**Intervention:** Between 2011 and 2013, ARASA, with the support of OSF, commissioned a study in Botswana and Swaziland focusing on “Perceptions of nurses, TB patients and community members on infection control and nurse-patient relationships”.

**Results:** 30% of the healthcare workers interviewed acknowledged that in settings where they worked with TB patients, nosocomial spread of TB was high, but remained unreported. It was observed that most of them do not wear N95 respirators, when attending to TB and DR-TB patients. There was poor knowledge about the importance of infection control (IC) among patients, assistant healthcare workers and community members, as well as poor implementation of infection control protocols at health care facilities. The Swaziland Democratic Nurses Union (SWADNU) did not have data on nurses who contracted TB in the workplace and admitted that it needed to document evidence of the level of infection among its members in order to effectively advocate for the development and implementation of adequate policy measures to address the issue.

**Conclusion:** The research recommended that healthcare workers be considered as a high-risk group. Targeted

interventions are needed to encourage health-seeking behaviour on the part of healthcare workers to reduce to nosocomial spread of TB. Legislation governing workplace compensation in Botswana is sufficiently worded to include both HIV and TB as scheduled occupational disease for which compensation was payable. Similar legislation in Swaziland fails to adequately entitle healthcare workers to who contract TB in the workplace to compensation. It recommended that civil society work with patient groups and the community to support advocacy prompting government to incorporate better occupational health and safety and compensatory measures (such as minimum service level agreements) for healthcare workers.

### OPP-419-01 Axshya villages play role model in promoting RNTCP and sustaining TB control services in Chhattisgarh, India

G Mallick,<sup>1</sup> S Chadha,<sup>1</sup> S Mohanty.<sup>1</sup> <sup>1</sup>TB, The Union, Delhi, India. e-mail: gmallick@theunion.org

**Background and implementation challenges:**  $\geq 70\%$  Indian population live in villages. TB remains a major public health problem amongst the general populace living in the villages and there is a need to maintain and further strengthen TB control measures on a sustained and long-term basis. With 25.5 million populations scattered over to 20235 villages (2011 Census),  $\geq 80\%$  of Chhattisgarh's population live in its villages.

**Intervention:** Global funded Project Axshya promotes engagement of community-based providers in improving TB services among the villagers besides marginalized, vulnerable and TB-HIV co-infected populations. Project Axshya takes up the theme "Reach the three million; a TB test, treatment and cure for all" and marches with the civil society to transform it into reality by selecting and helping villages to move towards elimination of TB step by step. "Axshya Village" (AV) is a community generated activity implemented in the project to create awareness about TB and to ensure that every adult member of the identified village and secondary school children get knowledge about TB suspect, its spread & diagnosis, information about the nearest DMC, DOT, duration of treatment, importance of adherence to treatment, reduction of stigma. Any TB patient identified in this village should follow treatment as per DOTS guidelines. Community-Intensive Programs are conducted regularly in these focussed villages by Axshya Mitras (AM) as identified from the village.

**Results:** 250 AVs have been formed in 10/27 Axshya districts thru its three sub-recipient partners during Apr 2013-Mar 2014 period. Covering 14.8 million populations in 9577 villages of the 10 project districts, 6531 chest symptomatics have been examined by referral and sputum collection & transportation initiatives as taken by the trained CVs and AMs from the 250 designated villages. The 290 NSP cases as diagnosed from the sputum examination have been put on DOTS successfully. 17 CVs & AMs are giving DOTS to 23 patients.

**Conclusions and key recommendations:** AVs as modelled by the project played a major role in promotion of TB care and control by involvement of the local communities. Local self-government and NGOs will be encouraged thru concerted project initiatives to develop AVs in rest of the areas on priority basis to reach out to every common people of the village with the key message of "a TB test, treatment and cure for all".

*Project Axshya performance at a glance from Apr 2013 – Mar 2014 thru Axshya Village (AV) interventions*

Sl. No.	District	Popln (in mil-ions)	No. of vil-lages in the district	Com-munity meet-ings con-ducted	Axshya Villages formed and in-volved in RNTCP	Symp-tomatics refer-red & sputum col-lected/trans-ported	TB pa-tients diag-nosed and put on Rx	% of sputum referal, sputum col-lected/trans-ported & Rx in AV
1	Bastar	0.9	602	267	35	673	42	70
2	Raigarh	1.5	1435	145	24	1999	75	90
3	Janjgir	1.7	913	220	27	127	2	50
4	Korba	1.2	742	146	19	895	34	70
5	Kaward-ha	0.9	1009	138	17	478	21	70
6	Raipur	2.1	545	110	13	251	9	50
7	Mahasa-mund	1.0	1132	290	35	592	26	70
8	Bilaspur	2.1	638	217	29	879	73	60
9	Rajnand-gaon	1.6	1685	225	26	513	5	90
10	Durg	1.8	876	202	25	124	3	50
	<b>Total</b>	<b>14.8</b>	<b>9577</b>	<b>1960</b>	<b>250</b>	<b>6531</b>	<b>290</b>	<b>67</b>

Source: Ax-Real (Project Axshya official site) data as reported by District Coordinators from the respective Axshya districts, Chhattisgarh

### 03. TUBERCULOSIS PROGRAMMES: FROM LAB TO BEDSIDE

#### OPP-420-01 Treatment of pulmonary tuberculosis with first line anti-TB drugs: a non all-inclusive approach that should be matched with molecular findings

B Honarvar,<sup>1</sup> M Moghadami,<sup>2</sup> A Behbahani,<sup>3</sup> A Emami,<sup>4</sup> A Roudgari,<sup>4</sup> G Sami Kashkoli,<sup>4</sup> M Rezaee,<sup>4</sup> M Kalari.<sup>4</sup>

<sup>1</sup>Shiraz University of Medical Sciences, Health Policy Research Center, Shiraz, <sup>2</sup>Shiraz University of Medical Sciences, HIV/AIDS Research Center, Shiraz, <sup>3</sup>Shiraz University of Medical Sciences, Diagnostic Laboratory Sciences and Technology Research Center, School of Paramedical Sciences, Shiraz, <sup>4</sup>Shiraz University of Medical Sciences, Shiraz-Enghelab Health Center, Shiraz, Islamic Republic of Iran. Fax: (+98) 7112309615. e-mail: honarvarbh32@yahoo.com

**Background** The incidence of tuberculosis (TB) continues to decline worldwide. However, the incidence of



multiple drug resistant (MDR) TB is increasing. The aim of this study was to determine existence of IS 6110 gene and frequency of gene mutation in patients afflicted with pulmonary TB.

**Method** This molecular study comprised new cases of pulmonary TB that did not respond to first line anti-TB drugs in the tertiary level TB center in Shiraz, southern Iran. Data were analyzed by SPSS.

**Results** A total of 92 patients (mean age  $45.4 \pm 15$  years) of which 75 (81.5%) were Iranian nationals were included in this study. Conventional drug sensitivity test showed that 16 (17.4%) patients were resistant to isoniazide (INH), 19 (20.7 %) refractory to rifampin (RIF) and 24 (26.1%) were resistant to both INH and RIF. Polymerase Chain Reaction (PCR) identified IS 6110 gene in 71 (77.2%) patients. The number of mutations detected by PCR included 3 (3.2%) in Kat G, 3 (3.2%) inh A, 9 (9.7%) both Kat G and inh A, 17 (18.4%) rpo B and 20 (21.7%) in kat G, inh A and rpo B genes. INH resistant patients were more common among RIF resistant ones (OR= 7.1).

**Conclusion** Nearly 75% of patients non-responsive to first line anti-TB drugs had IS 6110 gene, typical of *Mycobacterium tuberculosis*, while 25% were MDR-TB. PCR by detection of gene mutation can accelerate the diagnosis and treatment of MDR-TB patients and prevent the use of unnecessary medication in patients with non-resistant TB.

#### OPP-421-01 Prescripción de corticoides en pacientes con patrón miliar tuberculoso

R Martinez,<sup>1</sup> C Jimenez,<sup>2</sup> A Valencia,<sup>1</sup> C Bueno.<sup>3</sup>

<sup>1</sup> Enfermedades Infecciosas, Comfamiliar Risaralda, Pereira,

<sup>2</sup> Medico, Grupo VIHDA, Pereira, <sup>3</sup>Medico, Union HAART, Pereira, Colombia. e-mail: ricardoamartinezg@hotmail.com

**Background:** El inicio de terapia antituberculosa se puede asociar a presencia de injuria pulmonar y síndrome de dificultad respiratoria agudo del adulto secundaria al componente inflamatorio tras la destrucción bacilar en pacientes con componente miliar tuberculoso. Es el objetivo del presente trabajo establecer el factor protector aportado por los corticoides en esta situación

**Design/Methods:** Se realizó estudio de cohortes entre 72 pacientes con patrón miliar radiográfico de origen tuberculoso ( 36 pacientes por cohorte) atendidos en Comfamiliar Risaralda (Centro hospitalario del occidente de Colombia )entre enero del 2003 y diciembre del 2013. Se consideró como cohorte expuesta a pacientes con inicio de terapia antituberculosa y esteroides( prednisona 2 mgs /kg / día o su equivalente por 5 días), la cohorte no expuesta solo recibió terapia antituberculosa , el desenlace buscado fue requerimiento de ventilación mecánica (VM)

**Results:** El diagnóstico de tuberculosis se estableció por baciloscopia en 80% de los casos(confirmación posterior mediante cultivos) 20% por métodos moleculares; El promedio de edad fue 32 años ; 20 pacientes presentaban infección por el virus de la inmunodeficiencia humana ;

La mediana de la relación Pao2/Fio2(presión arterial de oxígeno/fracción inspirada de oxígeno) previo a terapia antituberculosa era 210; Mediante regresión logística al uso de esteroides aportó un RR : 0.45 IC 0.04 – 0–98; No se evidenciaron diferencias en características clínicas o demográficas entre ambas cohortes previas a prescripción farmacológica

**Conclusion:** La prescripción de esteroides se comportó como un claro factor protector ante el potencial desarrollo de injuria pulmonar y requerimiento de ventilación mecánica en pacientes con patrón miliar de origen tuberculoso tras el inicio de la terapia antimicrobiana y su uso debería ser considerado al igual que en forma rutinaria se hace en pacientes con compromiso pulmonar por *pneumocystis jiroveci* e hipoxemia

#### OPP-422-01 Diagnostic process for smear-negative pulmonary tuberculosis in Cambodia

S Saint,<sup>1</sup> K Okada,<sup>2,3</sup> N Yamada,<sup>2</sup> S Tieng,<sup>1</sup> T E Mao.<sup>1</sup>

<sup>1</sup>National Center for Tuberculosis and Leprosy Control (CENAT), Ministry of Health, Phnom Penh, Cambodia;

<sup>2</sup>Research Institute of Tuberculosis (RIT), Japan

Anti-Tuberculosis Association (JATA), Tokyo, Japan; <sup>3</sup>JICA/ CENAT National TB Control Project, Japan International Cooperation Agency (JICA), Phnom Penh, Cambodia. e-mail: okadak@jata.or.jp

**Background:** While the 2nd national prevalence survey in Cambodia showed that symptomatic (cough  $\geq 2$  weeks) cases with smear-negative pulmonary TB (SNTB) are as prevalent as those with smear-positive TB (SPTB) in the community, SNTB cases notified under the NTP are nearly a half of SPTB in number.

**Objectives:** To propose revised diagnostic algorithms for SNTB in the context of patient-centered approach

**Methods:** Two studies were conducted in selected districts in Battambang province: 1) retrospective cohort study to examine what medical practices or examinations presumptive TB with negative results of the 1st set of smears received, and 2) retrospective study to examine what diagnostic process registered SNTB cases underwent from negative results of the 1st set of smears till diagnosis.

**Results:** 556 (92%) of 605 presumptive TB with negative results of the 1st set of smears received antibiotics or other medicines. Of these, 321 (58%) persons had no further examinations. These findings validate that an antibiotic trial is useful in reducing the number of subjects who proceed with further medical examinations in resource-limited settings. Two thirds of presumptive TB with CXR underwent the CXR exam at private sector by their own decision, with most of them not having received the 2nd set of smear exams. This was probably because they were unable to wait for the lengthy process for diagnosis. During the time between the 1st set of smears and the interview, 16 subjects developed TB diseases (11 SPTB and 5 SNTB or extra-pulmonary TB). The incidence rate of all forms of TB was 3.5%/person-year with an average observation period of 8.6 months. The retrospective study for registered SNTB cases showed that 96 out of 97 cases included in the analysis

were taken for CXR at public sector, and 69 (71%) answered to have been treated with antibiotics before TB diagnosis. The median from the 1st set of smears to registration was 33 days and the 2nd set of sputum exams was significantly associated with longer delay in TB diagnosis.

**Conclusion:** An antibiotic trial soon after the 1st set of negative smear results, followed by CXR exam for non-responder could be beneficial to reduction in the cost and time for presumptive TB to be diagnosed, and it also may lead to earlier case detection. Operational researches on the validation of the proposed diagnostic algorithms are needed to carry out.

### OPP-423-01 C- reactive protein as biomarker in diagnosis for pleural effusions

P Kapiszyzi,<sup>1</sup> D Argjiri,<sup>1</sup> A Mitre,<sup>2</sup> G Burazeri,<sup>3</sup> R Hasa,<sup>1</sup> M Tabaku,<sup>2</sup> O Nuredini,<sup>1</sup> R Light.<sup>4</sup> <sup>1</sup>First Clinic, University Hospital Of Lung Diseases 'Sh Ndroqi', Tirana, <sup>2</sup>Clinical biochemistry, University Hospital "Mother Tereza", Tirana, <sup>3</sup>Statistic Department, University Hospital "Mother Tereza", Tirana, Albania; <sup>4</sup>Pulmonary, Vanderbilt University, Nashville, TN, USA. e-mail: eritjantashi@gmail.com

**Background:** Our objective was to determine the usefulness of pleural effusion C reactive protein levels in the diagnosis of pleural effusions.

**Patients and Methods:** A comparison of serum and pleural fluid C-reactive protein (CRP) levels in different subgroups of 286 patients with pleural effusion was made. We assessed prospectively the sensitivity, specificity, positive and negative predictive values, accuracy, Youden index, likelihood ratio and ROC curve of the test, for a period from February 2008 to November 2011.

**Results:** Among 286 patients with pleural effusion, 67 patients were included in the transudate group, 219 patients were included in the exudate group. In transudates the cut-off value of pleural fluid CRP  $\leq 15$  mg/L had a Youden index of 0.678 and the area under curve = 0.86 comparing with exudative pleural effusions. In malignant pleural effusions, the cut-off value of pleural fluid CRP  $\leq 20$  mg/L had a Youden index of 0.728 and the area under curve = 0.89 comparing with tuberculous effusions. In tuberculous effusions, the cut-off value of pleural fluid CRP  $> 20$  mg/dl had a Youden index of 0.45 and the area under curve = 0.96 comparing with malignant effusions. The values of pleural fluid/blood CRP ratios had a very small Youden index and the area under curve in all subgroups of patients with pleural effusion.

**Conclusions:** Levels of CRP in exudative pleural effusions less than 20 mg/L are strongly suggestive of malignant effusion and chronic tuberculous effusion. A CRP pleural fluid level  $> 20$  mg/L almost excludes transudative pleural effusion while the levels of CRP above 30 mg/L are suggestive of an inflammatory etiology and almost exclude malignant pleural effusion.

### OPP-424-01 Don't ignore extra-pulmonary tuberculosis! The epidemiology of extra-pulmonary tuberculosis in Israel, 1999–2010

Z Mor,<sup>1,2</sup> N Cedar,<sup>1,3</sup> G Pinsker,<sup>1</sup> M Lidji,<sup>4</sup> I Grotto.<sup>5,6</sup> <sup>1</sup>TB and AIDS, Ministry of Health, Jerusalem, <sup>2</sup>Ramla department of Health, Ministry of Health, Ramla, <sup>3</sup>Public Health Laboratory, Ministry of Health, Tel Aviv, <sup>4</sup>Tel Aviv Lung Clinic, Tel Aviv Lung Association, Tel Aviv, <sup>5</sup>School of Public Health, Ben Gurion University in the Negev, Beer Sheva, <sup>6</sup>Public Health Services, Ministry of Health, Jerusalem, Israel. Fax: (+972) 368 36632. e-mail: turkiz1@netvision.net.il

**Background:** Recurrent tuberculosis (TB) is one of the factors hampering eradication efforts, and be related to the quality of the National TB program. This study aims to assess the incidence of recurrent-TB in Israel and identify the associated risk factors in order to support eradication efforts.

**Methods:** This study included two components of all Israeli TB cases from 1999 and 2011: (a) a retrospective cohort study comparing those recurred to those who did not in the Cox regression model, generating hazard ratio (HR) and 95% confidence interval (CI); (b) a matched case-control component to perform in-depth analysis to identify demographic and behavioral variables associated with recurrent-TB in the logistic regression, generating odds ratio (OR) and 95% CI.

**Results:** During the 11-years of follow-up of all 3515 Israeli citizens who were cured of TB, comprising of 23,805 person-year, 37 cases (1.05%) recurred (1.5 recurrent-TB per 1000 person-years). Factors which were independently associated with a greater risk of recurrent-TB included being a male (HR 3.2, 95% CI 1.4–7.4), co-infection with HIV (HR 3.9, 95% CI 1.5–10.4), having positive sputum culture (OR 2.7, 95% CI 1.1–6.9) and avoiding more than 25% of the directly observed therapy meetings (OR 3.2, 95% CI 1.1–10.27).

**Conclusion:** TB recurrence was identified in ~1% of cure cases. The low incidence in Israel suggests satisfactory performance of the National TB Program. It is recommended that males, HIV-infected patients and those with positive sputum culture or do not adhere to anti-TB treatment should be followed-up after treatment completion to prevent recurrent-TB.

### OPP-425-01 Tanzanian X-ray score for the detection of active pulmonary TB on chest radiographs: a comparison with subjective assessment

M Breuninger,<sup>1,2,3</sup> J Van Den Hombergh,<sup>4</sup> J Dharsee,<sup>5</sup> L Jugheli,<sup>1,2,6</sup> J Hella,<sup>2</sup> D Wagner,<sup>3</sup> K Reither.<sup>1,2,6</sup> <sup>1</sup>Medical Parasitology and Infection Biology, Swiss Tropical and Public Health Institute, Basel, Switzerland; <sup>2</sup>Bagamoyo Research and Training Centre, Ifakara Health Institute, Bagamoyo, United Republic of Tanzania; <sup>3</sup>Center for Infectious Diseases and Travel Medicine, University Hospital Freiburg, Freiburg, Germany; <sup>4</sup>PharmAccess International, PharmAccess International, Dar es Salaam; <sup>5</sup>AgaKhan Hospital, AgaKhan Hospital, Dar es Salaam, United Republic of Tanzania; <sup>6</sup>University of Basel, University of Basel, Basel, Switzerland. e-mail: marianne.breuninger@posteo.de

**Background:** The Tanzanian X-ray Initiative developed a structured reporting and scoring system, the Tanzanian X-ray Score (TXS), to assist readers in the evaluation of chest radiographs (CXR) for the presence of active pulmonary tuberculosis (PTB). Does the TXS provide a better diagnostic accuracy and inter-reader agreement compared to structured, but subjective assessment of CXRs?

**Methods:** Three readers (2 experts<sup>\*,#</sup>, 1 clinical officer<sup>\*</sup>) rated 427\*/237# digital CXRs of presumptive adult PTB patients enrolled in two cohort studies at the Ifakara Health Institute in Bagamoyo, Tanzania. Readers were blind to clinical, microbiological and radiological results. The TXS provides a computerized form with a list of radiographic findings and their location. Depending on the combination of radiological features determined by the reader, a score is assigned and translated into the conclusion categories: 1.normal, 2.abnormal, not suggestive for active TB, 3.abnormal, consistent with active TB and 4.abnormal, highly suggestive for active TB (=score conclusion). In our test version, the reader was unaware of the score conclusion and instead was asked to subjectively assess the radiograph using the same 4 categories (=manual conclusion). All patients were clinically and microbiologically characterized and followed up for  $\geq 5$  months. Culture-confirmed patients and fully recovered non-TB patients were used as cases (194\*/118#) and controls (233\*/119#). We calculated the sensitivity, specificity and weighted kappa agreement for the manual and score conclusion.

**Results:** The figure shows the sensitivity and specificity to distinguish TB cases and controls: ROC curves for the TXS performance and symbols with different fill for the manual conclusion (empty=any abnormality, crossed=TB consistent, filled=highly suggestive for TB). Agreement between the manual and score conclusion was very good (0.83, 0.80) for the expert readers, but only moderate (0.30) for the clinical officer. The inter-reader agreement for the manual and score conclusion was 0.68, 0.29, 0.30 and 0.66, 0.26, 0.28, respectively.

**Conclusion:** The score-generated conclusion corresponds reliably to the expert's manual conclusion. In its current state it does not further enhance the diagnostic accuracy or the inter-reader agreement of the interpretation of CXRs for active PTB compared to structured, subjective

assessment. Further studies should determine whether remodeling of the score can improve the diagnostic tool.

### OPP-426-01 Intra-cellular lipid bodies, bacillary persistence and clinical outcomes during treatment of pulmonary tuberculosis in Malawian adults

D Sloan,<sup>1,2,3,4</sup> HC Mwandumba,<sup>1</sup> N J Garton,<sup>5</sup> S H Khoo,<sup>6</sup> A E Butterworth,<sup>2</sup> L Corbett,<sup>1,2</sup> M R Barer,<sup>5</sup> G R Davies.<sup>1,2,6</sup> <sup>1</sup>Malawi-Liverpool-Wellcome Trust Clinical Research Programme, Blantyre, <sup>2</sup>College of Medicine, University of Malawi, Lilongwe, Malawi; <sup>3</sup>Liverpool School of Tropical Medicine, Liverpool, <sup>4</sup>Liverpool Heart and Chest Hospital, Liverpool, <sup>5</sup>Department of Infection, Immunity and Inflammation, University of Leicester, Leicester, <sup>6</sup>University of Liverpool, Liverpool, UK. Fax: (+44) 151 7065944. e-mail: djsloan@liverpool.ac.uk

**Background:** Drug-tolerant persisters bacilli may adversely affect TB treatment outcomes. Currently, persister organisms cannot be identified in clinical samples but accumulation of intracellular lipid bodies (LBs) within a sub-population of TB cells is proposed as a phenotypic marker of persistence. We evaluated relationships between the presence of LBs within acid-fast bacilli (AFB) in sputum samples and the response to TB therapy of Malawian adults.

**Design/Methods:** Previously untreated adults with smear positive pulmonary TB received standard 6 month therapy and were followed-up for a further year. Clinical outcomes were defined as favourable (sustained cure) or unfavourable (failure/relapse). Sputum was repeatedly collected during the first 8 weeks. Bacteriological outcomes were generated by calculating intensive phase bacillary elimination rates from liquid culture Time-to-Positivity and Serial Sputum Colony Counting data. A fluorescence microscopy technique with auramine O and a neutral lipid dye (LipidTOX Red) was used to detect intracellular LBs. The acid-fast-Lipid-Body (af-LB) count of each sputum sample was defined as the mean percentage of AFBs containing  $\geq 1$  LB in two smears of the specimen. Relationships between af-LB counts and clinical or bacteriological outcomes were assessed by logistic regression.

**Results:** Baseline af-LB counts were available for 69 patients. 42 (61%) were HIV-infected and 10 (15%) had unfavourable clinical outcomes. The median baseline af-LB count was 28% (IQR: 13–44%). There was a trend towards higher baseline af-LB counts in patients who cooked indoors with biomass fuel (OR: 10.19, 95% CI: 0.91–113.55,  $p=0.059$ ). There were no associations between baseline af-LB counts and clinical or bacteriological outcomes. However, serial af-LB counts from day 0–28 of therapy for a sub-set of 38 patients revealed a trend towards consistently higher af-LB counts amongst individuals whose ultimate clinical outcomes were unfavourable (OR: 1.21, 95%: 0.87–1.50,  $p=0.088$ ).

**Conclusion:** For the first time, a sub-population of LB positive AFB has been related to treatment response in patients with pulmonary TB. No associations were described between baseline af-LB counts and clinical or



bacteriological outcomes, but the serial trend towards higher af-LB counts in patients with unfavourable final outcomes suggests that LB accumulation deserves further investigation as a phenotypic marker of bacillary persistence.

### OPP-427-01 Tuberculosis cutánea: experiencia en la consulta monográfica de tuberculosis de un hospital de tercer nivel

J Díaz Tantaleán,<sup>1</sup> A Villar,<sup>1</sup> MA Seminario,<sup>2</sup> F Morell,<sup>1</sup> N Saborit.<sup>1</sup> <sup>1</sup>Pneumología, Hospital Universitari Vall d'Hebron, Barcelona, <sup>2</sup>Unitat de Tuberculosi de Drassanes, Hospital Universitari Vall d'Hebron, Barcelona, Spain. e-mail: anibaldt@hotmail.com

**Introducción:** La tuberculosis cutánea (TC) es una forma poco frecuente de enfermedad tuberculosa con una prevalencia de hasta el 5.9% en nuestro medio. La presentación clínica es variable, pudiendo pasar desapercibida. En el presente trabajo, se describe una serie de pacientes diagnosticados de TC.

**Pacientes y métodos:** Estudio retrospectivo descriptivo observacional de pacientes diagnosticados de TC en la consulta monográfica de tuberculosis de un hospital terciario entre octubre 2011 y marzo 2014.

**Resultados:** Se incluyeron 7 pacientes, con una edad media de 53 años, de los que 6 (85.7%) fueron mujeres. 2 (28.6%) eran naturales de países endémicos. El tiempo de enfermedad fue de  $3 \pm 2$  años. En el momento del diagnóstico se demostró positividad del PPD en todos los casos y del Quantiferón en los 3 en los que se realizó la determinación. Un paciente (24.3%) había realizado tratamiento de infección tuberculosa latente y otro tratamiento de Eritema Indurado de Bazin (EIB) hacía 5 años. La lesión cutánea predominante fue nódulo eritematoso violáceo en 5 (71.4%) pacientes, y nódulo supurativo en 2 (28.6%). En un paciente (14.3%) se objetivó afectación mediastínica con estudio anatomopatológico sugestivo de linfadenitis granulomatosa necrotizante y en otro (14.3%) adenopatía axilar no supurativa, con estudio inespecífico. La biopsia de las lesiones cutáneas mostró paniculitis lobulillar compatible con EIB en los 7 (100%) pacientes, de los cuales 6 (85.7%) presentaron granulomas necrotizantes. El estudio microbiológico fue negativo en todos los casos, realizándose PCR de biopsia cutánea en 3, de los cuales 2 fueron negativos y 1 positivo para *Acinetobacter iwoffii*. El tratamiento utilizado fue 2RHPE/4RH en 4 (57.1%) pacientes, 9RH en 2 (28.6%), y 12RHE en un (14.3%) paciente, tratándose este último de un retratamiento. De los 4 pacientes que han finalizado el tratamiento, 2 (2RHPE/4RH y 9RH) presentaron remisión completa, y los otros 2 (9RH y 12RHE) presentaron recurrencia de las lesiones tras 6 meses. Tres pacientes (42.9%) están actualmente en tratamiento sin reaparición de nuevas lesiones.

**Conclusiones:** En nuestra serie la forma más frecuente de TC fue el EIB con respuesta al tratamiento variable. La ausencia de aislamiento microbiológico y de PCR en la mayoría de los casos, no permite realizar estudio de

resistencias, que si bien son poco frecuentes, serían de ayuda en el manejo terapéutico de estos pacientes.

### OPP-428-01 C-reactive protein for pulmonary tuberculosis: a systematic review and meta-analysis

L Chaisson,<sup>1</sup> C Yoon,<sup>1</sup> P Drain,<sup>2</sup> S Patel,<sup>1</sup> A Cattamanchi.<sup>1</sup> <sup>1</sup>Medicine, University of California, San Francisco, San Francisco, CA, <sup>2</sup>Medicine, Massachusetts General Hospital, Boston, MA, USA. Fax: (+1)415-695-1551. e-mail: chaissonl@medsfgh.ucsf.edu

**Background:** The current symptom-based tuberculosis (TB) screening strategy recommended by the WHO is impractical; nearly all persons living with HIV (PLHIV) in sub-Saharan Africa screen positive. The consequence for patients is missed or delayed IPT initiation, and for HIV/AIDS programs a large volume of unnecessary TB testing. We performed a systematic review and meta-analysis to determine whether C-reactive protein (CRP), which can be measured using a point-of-care assay, could improve TB screening among PLHIV.

**Methods:** We searched multiple databases using pre-specified search terms to identify all studies evaluating the diagnostic accuracy of elevated CRP ( $\geq 10$  mg/L) for active TB among PLHIV. We assessed the quality of included studies using the QUADAS tool and obtained pooled estimates of sensitivity and specificity using hierarchical logistic regression.

Table 1. Study characteristics.

Authors	Year	Country	Population	Total N	Sensitivity	Specificity
Lawn et al.	2013	South Africa	Outpatient HIV clinic	496	85% (75%-92%)	58% (53%-62%)
Sage et al.	2010	United Kingdom	Inpatients with TB symptoms	247	89% (72%-98%)	22% (17%-28%)
Wilson et al.	2011	South Africa	Outpatients with TB symptoms	250	98% (93%-100%)	59% (51%-67%)
Drain et al.	2014	South Africa	Outpatients with TB symptoms	84	95% (83%-99%)	51% (36%-66%)
Yoon et al.	2014	Uganda	Outpatient HIV clinic	201	80% (28%-99%)	87% (82%-92%)
Pooled estimate					93% (35%-76%)	57% (35%-76%)

**Results:** Five studies met eligibility criteria. All five were cohort studies, and were of medium quality according to QUADAS. Of the 5 studies, 4 were conducted among outpatients and 4 were performed in high TB-burden countries. Three studies enrolled people with TB-related symptoms and 2 studies enrolled all PLHIV regardless of symptoms. Overall, there were a total of 1278 PLHIV (range 84–496) and 234 confirmed TB cases (range 5–81). Pooled sensitivity of CRP for active TB was 93% (95% CI 84%-97%), and pooled specificity was 57% (95% CI 35%-76%). In the four studies conducted among outpatients, pooled sensitivity was 92% (95% CI

79%–97%), and pooled specificity was 66% (95% CI 48%–80%).

**Conclusion:** CRP has high sensitivity and moderate specificity for active pulmonary TB, and may be a useful screening tool for PLHIV. Pooled sensitivity is comparable to that of the WHO-endorsed symptom-based screen, and pooled specificity is higher, suggesting that CRP could be used to improve the efficiency of intensified case-finding activities and IPT initiation among HIV-infected individuals worldwide.

#### **OPP-429-01 C-reactive protein and erythrocyte sedimentation rate for diagnosis and treatment response of pulmonary tuberculosis in an HIV-endemic setting**

P Drain,<sup>1</sup> L Gounder,<sup>2</sup> F Sahid,<sup>3</sup> Y Moosa.<sup>4</sup> <sup>1</sup>Medicine, Massachusetts General Hospital; Harvard Medical School, Boston, MA, USA; <sup>2</sup>Virology, Inkosi Albert Luthuli Central Hospital, Durban; <sup>3</sup>Medicine, University of Witwatersrand, Johannesburg; <sup>4</sup>Infectious Diseases, King Edward Hospital; University of KwaZulu-Natal, Durban, South Africa. e-mail: pkdrain@gmail.com

**Background:** We evaluated acute inflammatory markers, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), to diagnose AFB smear-positive and/or culture-confirmed pulmonary tuberculosis (TB) and to monitor response to anti-TB treatment.

**Design:** We conducted a prospective study of adults ( $\geq 18$  years) suspected of pulmonary TB based on characteristic clinical symptoms in Durban, South Africa. We obtained a nebulized sputum sample for AFB microscopy and mycobacterial culture before treatment. CRP and ESR testing were performed at baseline, after 2 weeks of therapy, and then monthly for 6 months. We assessed diagnostic accuracy of ESR and CRP, alone and in combination, for AFB smear-positive and culture-confirmed pulmonary TB, and assessed changes over 6 months of anti-TB treatment.

**Results:** Among 90 participants, 49% were female, mean age was 36.9 years, 93% (82/88) were HIV-infected with a median CD4  $168/\text{mm}^3$  (IQR 89–256/ $\text{mm}^3$ ), and 63% had culture-confirmed pulmonary TB. Mean baseline ESR was  $104 \pm 46$  mm/hour for culture-negative and  $129 \pm 23$  for TB culture-positive participants ( $p=0.009$ ); mean baseline CRP was  $42 \pm 50$  mg/L among culture-negative and  $77 \pm 66$  among TB culture-positive participants ( $p=0.006$ ). Serum ESR  $\geq 100$  mm/hour had a sensitivity and specificity of 93% (95% CI 83–98%) and 39% (95% CI 22–58%) for culture-positive pulmonary TB, while sensitivity and specificity were 100% (95% CI 75–100%) and 22% (95% CI 13–33%) for smear AFB-positive TB. Serum CRP  $\geq 10$  mg/L had a sensitivity and specificity of 91% (95% CI 80–97%) and 45% (95% CI 27–64%) for culture-positive pulmonary TB, while sensitivity and specificity were 100% (95% CI 75–100%) and 24% (95% CI 15–37%) for smear AFB-positive TB. When using a combined strategy, ESR  $\geq 100$  mm/hour or CRP  $\geq 10$  mg/L, sensitivity and specificity were 100% (95% CI 94–100%) and 23% (95% CI 10–41%) for culture-positive TB. Mean ESR and CRP

remained significantly higher among TB culture-positive participants until the 3<sup>rd</sup> month of treatment, and decreased significantly during the 6-month treatment period (Figure).

**Conclusions:** In our setting, participants with smear-positive and/or culture-positive TB had high acute inflammatory markers, which decreased significantly during the course of anti-TB therapy. Our findings suggest that lower ESR ( $<100$  mm/hour) and/or lower CRP ( $<10$  mg/L) identify patients with non-infectious disease, and therefore may be valuable when triaging patients for respiratory isolation. They might also be valuable biomarkers to monitor response to treatment.

#### **04. PAEDIATRIC TB, PNEUMONIA AND ASTHMA**

##### **OPP-430-01 Treatment initiation and outcomes of children diagnosed with tuberculosis based on a positive gastric aspirate (GA), Botswana, 2008–2012**

T Lo,<sup>1</sup> T Arscott-mills,<sup>2,3,4</sup> L Ntshimane,<sup>3</sup> T Lere,<sup>5</sup> K Mugisha,<sup>5</sup> A Ho-foster,<sup>3</sup> A Steenhoff,<sup>2,3,4</sup> R Ncube.<sup>5</sup>

<sup>1</sup>Division of Global HIV/AIDS, Centers for Disease Control and Prevention, Atlanta, GA; <sup>2</sup>Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA;

<sup>3</sup>Botswana-UPenn Partnership, Botswana-UPenn Partnership, Gaborone, Botswana; <sup>4</sup>The Children's Hospital of Philadelphia, The Children's Hospital of Philadelphia, Philadelphia, PA, USA; <sup>5</sup>National TB Programme, Botswana Ministry of Health, Gaborone, Botswana. e-mail: tgl8@cdc.gov

**Background:** Since 2008, the Botswana National Tuberculosis (TB) Control Program and the Botswana-University of Pennsylvania Partnership have sought to improve the diagnosis of pediatric ( $<15$  years) TB through the use of gastric aspiration performed at local health facilities. Children with  $>1$  symptom of TB and a gastric aspirate (GA) that is smear positive for acid fast bacilli or culture positive for *M. tuberculosis* are referred for treatment. Children diagnosed and treated are recorded in facility TB registers and entered into Botswana's National Electronic TB Registry (ETR). We aim to describe the treatment initiation and outcomes of children with a positive GA.

**Design/Methods:** Treatment initiation and outcomes were assessed for children with a positive GA from 2/2008 through 12/2012 through name-based matching of the GA database with the ETR or facility TB registers in 6/2013. We used a matching algorithm that accounted for name misspellings, ages, and facility locations to identify matches. Children with a positive GA who could not be matched with the ETR were assessed by record searches at local clinics and interviews with families. Treatment outcome data were analysed for those initiating treatment prior to 6/2012. Analyses included descriptive statistics and multivariate regression models to identify factors related to treatment initiation.

**Results:** Among 213 children diagnosed with TB via GA, 145 (68%) initiated treatment; of these, 113 (78%) had matching ETR records and 32 (22%) were found in facility TB registers. Among the 68 children for whom we found no evidence of treatment initiation, 9 (13%) moved out of the area, 5 (7%) retested, and 50 (74%) had no documentation in ETR or TB registers. In multivariate regression, known HIV status was significantly associated with documentation of treatment initiation (adjusted Odds Ratio=3.1; 95% Confidence Intervals=1.5–6.4) while gender, age, having a household TB contact, and TB symptom history were not. Among 96 matches with treatment outcome data, 85 (89%) completed treatment or were cured, 10 (10%) were currently on treatment, and 1 (1%) defaulted.

**Conclusion:** We could not find documentation of treatment for 32% of children with laboratory-confirmed TB. Clinicians often have few diagnostic options beyond smear to diagnose TB in children. The failure to initiate and promote treatment completion warrants investigation and urgent action. Almost all children that initiated went on to complete treatment. The relationship between having known HIV status and initiating TB treatment needs further exploration.

#### OPP-431-01 Experiences in offering upfront Xpert MTB/RIF testing to pediatric presumptive TB and DR-TB cases

N Raizada,<sup>1</sup> KS Sachdeva,<sup>2</sup> A Sreenivas,<sup>3</sup> R Thakur,<sup>1</sup> S Kulsange,<sup>1</sup> C N Paramasivan.<sup>1</sup> <sup>1</sup>India, Foundation for Innovative New Diagnostics, New Delhi, <sup>2</sup>Central TB Division, Ministry of Health and Family Welfare, Government of India, New Delhi, <sup>3</sup>India, World Health Organisation, New Delhi, India. e-mail: drneerajraizada@gmail.com

**Background:** Diagnosis of tuberculosis in children is difficult and globally a large proportion of cases are diagnosed clinically. Bacteriological confirmation of TB diagnosis in children is challenging due to difficulty in obtaining good quality sputum specimen as well as paucibacillary nature of disease in children. Xpert MTB/RIF, a highly sensitive and specific rapid tool, offers a promising solution in addressing these challenges. Through this study, we are sharing our experiences of implementing upfront Xpert MTB/RIF testing for presumptive TB and DR-TB cases in pediatric groups under programmatic settings in India.

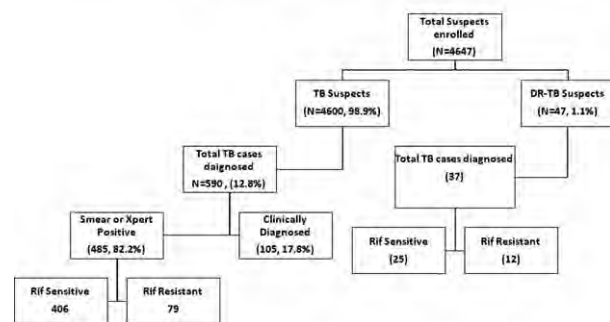
**Methods:** The study covered a population of 8.8 million across 18 different sub-district level tuberculosis units (TU), with one Xpert MTB/RIF lab established at each study TU, from March 2012 till December 2013. Pediatric presumptive TB cases accessing public health facilities in study area were prospectively enrolled in the study and tested on Xpert MTB/RIF, following a standardized diagnostic algorithm.

**Results:** Of the 4600 pediatric pulmonary presumptive TB cases were enrolled in the study and offered upfront testing on both Xpert MTB/RIF and smear microscopy. A total of 590 (12.8%, CI: 11.8–13.8) pulmonary TB cases (PTB) were diagnosed of which 485 (82.2%, CI: 78.9–85.1) were bacteriologically confirmed, 262 (54.9%, CI:

50.4–59.3) being smear negative. Further, upfront Xpert MTB/RIF testing of pediatric presumptive TB and presumptive DR-TB cases, resulted in the diagnosis of 79 and 12 rifampicin resistance cases, respectively; Positive predictive value (PPV) for rifampicin resistance detection was high (97.9% CI 89.1–99.6) and with no statistically significant variation with respect to past history of TB treatment.

**Conclusion:** Upfront access to Xpert MTB/RIF testing in pediatric presumptive TB cases lead to significant increase of bacteriologically confirmed TB and rifampicin resistant TB cases under field settings. Results from our study clearly demonstrate that Xpert MTB/RIF testing at peripheral settings can be instrumental in meeting the present day challenges of diagnosis of TB in pediatric patients.

**Figure 3: Flow chart on presumptive pediatric TB cases enrolment under the study**



#### OPP-432-01 Stool sampling for the diagnosis of intrathoracic tuberculosis in children

E Walters,<sup>1</sup> C Bosch,<sup>1</sup> M Van Der Zalm,<sup>1</sup> S Friedrich,<sup>2</sup> R Gie,<sup>3</sup> A Hesselning.<sup>1</sup> <sup>1</sup>Paediatrics and Child Health, Desmond Tutu TB Centre, Stellenbosch University, Cape Town, <sup>2</sup>Division of Medical Physiology, Biomedical Sciences, Stellenbosch University, Cape Town, <sup>3</sup>Paediatrics and Child Health, Tygerberg Academic Hospital, Cape Town, South Africa. Fax: (+27)021 938 9719. e-mail: ewal@sun.ac.za

**Background:** The diagnosis of intrathoracic tuberculosis (TB) in children is challenging due to the paucibacillary nature of the disease and the difficulty in obtaining adequate sputum samples from young children. Bacilli present in ingested sputum are detectable in stool: our study explores the diagnostic value of microbiological and molecular analysis of stool samples to detect paediatric TB.

**Methods:** Children <13 years of age presenting as in- or outpatients with suspected intrathoracic TB were consecutively enrolled from Tygerberg and Karl Bremer hospitals, Cape Town, April 2012–February 2014. Children were eligible if they presented with 1 of: prolonged and persistent cough, fever, lethargy or failure to thrive, OR any duration of cough with 1 of a) close contact with TB index case, b) reactive Mantoux, or c) chest radiograph compatible with intrathoracic TB. Investigations included a minimum 2 respiratory samples



(gastric aspirates/sputum, induced sputum or nasopharyngeal aspirate) and a single stool sample for smear microscopy, liquid mycobacterial culture and GeneXpert MTB/RIF (Xpert). Stool samples were homogenised with sterile water, decontaminated and concentrated prior to Xpert analysis.

**Results:** Of 178 children enrolled, 148 (83%) submitted a stool sample [72 (49%) female, median age 14 months, 22 (15%) HIV-infected]. A clinical diagnosis of TB was made in 74 (50%): 34/74 (46% of TB cases; 23% of total) were confirmed by either culture or Xpert on any sample. Respiratory cultures were contaminated in 42/685 (6%) samples; Xpert gave invalid/error results in 13/685 (2%) samples. Stool culture was positive in 6 (4%) children and contaminated in 59 (40%). Stool Xpert was positive in 11 (7%), and invalid/error in 16 (11%) samples. Stool culture and Xpert each added one diagnosis to the total confirmed cases: both cases had supporting clinical evidence of TB. Eleven (7%) children had positive Xpert on either a single gastric aspirate or a single induced sputum, similar to stool Xpert. Fifteen of 17 children with positive stool culture or Xpert had severe intrathoracic or disseminated TB.

**Conclusion:** The low sensitivity and high rate of contamination of stool culture limit its utility for the diagnosis of TB. However, sensitivity of Xpert on a single stool sample was equivalent to a single respiratory sample. The incremental value and impact of a second stool Xpert for the diagnosis of intrathoracic TB in children should be explored.

#### **OPP-433-01 Tuberculosis bacteremia more prevalent in adult than pediatric populations: a systematic review and meta-analysis**

P Pavlinac,<sup>1</sup> E Lokken,<sup>1</sup> J Walson,<sup>1,2,3,4</sup> B Richardson,<sup>2,5</sup> G John-Stewart.<sup>1,2,3,4</sup> <sup>1</sup>Epidemiology, University of Washington, Seattle, WA, <sup>2</sup>Global Health, University of Washington, Seattle, WA, <sup>3</sup>Pediatrics, University of Washington, Seattle, WA, <sup>4</sup>Medicine, University of Washington, Seattle, WA, <sup>5</sup>Biostatistics, University of Washington, Seattle, WA, USA.  
e-mail: ppav@u.washington.edu

**Background:** Tuberculosis (TB) is the most common cause of morbidity and mortality in HIV-infected children and contributes to substantial pediatric morbidity globally. We conducted a systematic review and meta-analysis to compare the prevalence of TB bacteremia in adult and pediatric patient populations.

**Design/Methods:** We searched PubMed for publications between 1980 and 2013 describing culture-confirmed TB bacteremia among patients with suspected TB or febrile illness. Case reports/series, retrospective chart reviews, and non-English articles were excluded. Estimates of TB prevalence and BCG vaccine coverage by country and enrollment period were obtained for each citation from the WHO Global Health Observatory data repository. Multivariable meta-regression using log-transformed prevalence was used to determine whether study-level confounders (average blood quantity, year of enrollment, Africa vs. non-African setting, BCG coverage, and adult

TB prevalence estimates) explained the association between age group and TB bacteremia.

**Results:** Of 905 reviewed abstracts, 25 citations met inclusion criteria and were included, yielding 27 independent TB bacteremia prevalence estimates (22 adults/5 pediatric). Most (66.7%) studies were conducted in Africa and 37% included only HIV-infected participants. The median age in adult studies was 33 years (range: 13 to 95 years) and in pediatric studies was 2.7 years (range: 2 months to 15 years). There was substantial heterogeneity between TB prevalence estimates in adult ( $I^2$ -statistic 86.3%), but not pediatric studies ( $I^2$ -statistic 2.4%). The pooled TB bacteremia prevalence in adult studies was 13.5% (95% CI: 10.8–16.2%) and in pediatric studies was 0.8% (95% CI: 0–2.0%) (p-value for difference between adults and pediatric studies = 0.004). Restricting analyses to HIV-infected participants, pooled TB bacteremia prevalence from 21 adult and 3 pediatric studies were 15.5% (95% CI: 12.5–18.5%) and 0.8% (95% CI: 0–1.8%), respectively (p=0.001). Inclusion of pre-determined study-level confounders did not account for observed differences in pooled TB prevalence between adult and pediatric studies.

**Conclusion:** While TB bacteremia appears relatively common in adults, particularly those with HIV infection, bloodstream TB appears to be rare in children. Reasons for differences in risk of detected TB bacteremia may include degree of immunosuppression, TB reactivation vs. primary infection, and/or timing or volume of blood culture.

#### **OPP-434-01 When TB Reach eliminates cost, other barriers to screening child household TB contacts are revealed in Eldoret, Kenya**

D Szkwarko,<sup>1</sup> P Owiti,<sup>2</sup> N Buziba,<sup>2,3</sup> E J Carter.<sup>2,4</sup> <sup>1</sup>Family Medicine, Memorial Hospital of Rhode Island, Pawtucket, RI, USA; <sup>2</sup>AMPATH, Academic Model Providing Access to Healthcare, Eldoret, <sup>3</sup>Hematology, School of Medicine, College of Health Sciences, Moi University, Eldoret, Kenya; <sup>4</sup>Warren Alpert Medical School, Brown University, Providence, RI, USA. e-mail: szkward@gmail.com

**Background:** Tuberculosis (TB) programs globally continue to experience operational challenges in fulfilling World Health Organization recommendations for child contact management and screening. At a TB clinic in Eldoret, Kenya, a child contact register (CCR) revealed that fewer than 1% of child contacts under age five exposed to a smear positive TB index case underwent clinical review. Staff surveys revealed the cost of screening and transportation to be the major screening barrier. Design Funded by TB Reach, child contacts under five years exposed to smear positive TB index cases at the Moi Teaching and Referral Hospital TB clinic became eligible for a 'child contact screening package' in April 2012. The package includes screening chest x-ray, transport fees for index case and child, and registration fee. Outcomes included the number of identified child contacts who initiated screening as well as their diagnoses (active TB or isoniazid preventive therapy initiation). Possible variables influencing child contact

screening initiation after cost elimination were assessed. Variables included index case age, gender, HIV status, and relationship to child as well as child contact age and symptom status.

**Results:** In 14 months, 169 exposed child contacts under five were identified by the TB clinic CCR. 146 (86.4%) were brought in for screening. Of these, 43 (29.5%) were diagnosed with active TB disease. Children with a male index case were at increased risk of not being brought in for screening relative to children with a female index case [RR 3.4 (95% CI: 1.2–9.7),  $p=0.01$ ]. Asymptomatic children were at increased risk of not being brought in for screening relative to symptomatic children [RR 17.8 (95% CI: 2.4–129.9),  $p<0.000$ ]. Child contact age, index case age, index case HIV status, and index case relationship to child were not found to be variables influencing the risk of a child not being brought in for screening. (Table 1)

**Conclusion:** Child contact management, screening, and treatment remain challenges for TB programs. Eliminating cost improved child contact screening at our site by 85 % and increased identification of pediatric TB disease. Once cost was eliminated, bivariate analyses revealed that child contacts with a male index case or who are asymptomatic are at increased risk of not presenting for screening. Further qualitative work is needed to identify strategies that can target these vulnerable child contacts and ensure that they access care.

**Table 1: Variables influencing child contact screening after a TB Reach 'child contact screening package' eliminates cost in Eldoret, Kenya**

Variable	CC Screening Yes Variable/ Total Screened	CC Screening No Variable/ Total Screened	Relative Risk (95% Confidence Interval)	P-value
Index case is male	79/146 (80.6%)	19/23 (19.4%)	3.4 (1.2–9.7)	0.01*
Index case gender unknown = 0				
Index case HIV positive	67/132 (82.7%)	14/20 (17.3%)	2.1 (0.8–5.0)	0.1
Index case HIV status unknown = 17				
Index case age > median age (32yrs)	52/114 (80.0%)	13/20 (20.0%)	2.0 (0.8–4.6)	0.1
Index case age unknown = 35				
Index case is not mother	106/140 (83.5%)	21/23 (16.5%)	3.0 (0.7–12.1)	0.09
Index case relationship is unknown = 6				
CC > 1 year of age	129/146 (86.6%)	20/23 (13.4%)	0.9 (0.3–2.7)	0.8
CC age unknown = 0				
CC is asymptomatic	61/138 (77.2%)	18/19 (22.8%)	17.8 (2.4–129.9)	<0.000*
CC symptom status unknown = 12				

\*statistically significant,  $p < 0.05$ , CC = child contact

### OPP-435-01 Intensified TB case finding among child attendants of Indra Gandhi Institute for Child Healthcare (IGICH) in Kabul City, Afghanistan

A Sanaie,<sup>1</sup> M Seddiq,<sup>2</sup> A Nasrat,<sup>3</sup> L Manzoor.<sup>4</sup> <sup>1</sup>TB, ACREOD, Kabul, Afghanistan, <sup>2</sup>NTP, MoPH, Kabul, <sup>3</sup>TB, ACREOD, Kabul, <sup>4</sup>TB, ATLDs, Kabul, Afghanistan.  
e-mail: sanaie.as@gmail.com

**Background and challenges to implementation:** Afghanistan is one of the 22 world's high TB burden countries with highest children mortality rate in the world. 46% of the population is aged 0–14 years and TB is one of the causes of child mortality. Within the routine surveillance system of NTP, 10–15% of TB all form are notified among children and this notification is much lower than the expected cases. Still presumptive TB cases identification rate among child attendant of the health facilities is less than 1%.

**Intervention or response:** Under the project titled "Innovation towards zero TB deaths among children in Kabul City of Afghanistan" ACREOD with support of TB REACH Wave 3 grants initiated procedures to intensify child TB case finding in IGICH. The efforts resulted dramatic achievements and huge number of additional cases detected. Under the TB REACH Wave grant, hospital's 30 OPD doctors were trained, a TB unit with 5 members was assigned, hospital was equipped with mobile digital X-ray and LED microscopy, TST was supplied, TB education for parents in-placed, presumptive child TB referral mechanism in-placed. Intensified TB case finding was started in late Q3 2013 and accordingly each child attendants of the hospital was monitored for TB.

**Results and lessons learnt:** The data of Q2-Q4 2013 and Q1 2014 was reviewed and compared with The data of Q2-Q4 2012 and Q1 2013 and we found that a huge number of additional TB cases has been found with TB REACH project's efforts. During mentioned period, 132,000 children (0–14 years) were presented in IGICHs' OPDs. Among them 2,640 presumptive child TB cases were identified and out of that 2,376 of them were screened for TB as per recommended diagnostic algorithm. As result 581 confirmed child TB cases were detected which was 4 times higher than the 143 child TB cases detected in Q2-Q4 2012 and Q1 2013.

**Conclusions and key recommendations:** The study findings indicated that large number childhood TB cases were missing in in IGICH before TB REACH project. NTP and NGOs working in TB control need to improve the quality of childhood TB diagnosis services.

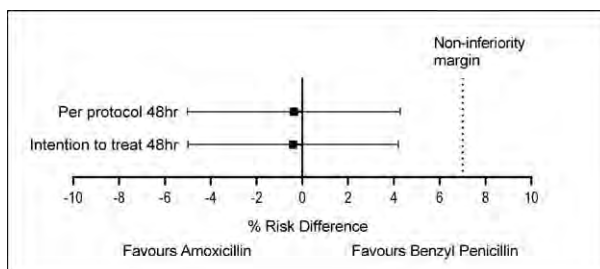
### OPP-436-01 Oral amoxicillin versus benzyl penicillin for severe childhood pneumonia among Kenyan children: a randomised controlled non-inferiority trial

A Agweyu,<sup>1</sup> D Gathara,<sup>1</sup> J Oliwa,<sup>1</sup> N Muinga,<sup>1</sup> T Edwards,<sup>2</sup> E Allen,<sup>2</sup> E Obimbo,<sup>3</sup> M English.<sup>1,4</sup> <sup>1</sup>Health Services Unit, KEMRI-Wellcome Trust Research Programme, Nairobi, Kenya; <sup>2</sup>Medical Statistics, London School of Hygiene and Tropical Medicine, London, UK; <sup>3</sup>Paediatrics and Child Health, University of Nairobi, Nairobi, Kenya; <sup>4</sup>Paediatrics, University of Oxford, Oxford, UK.  
e-mail: agweyu@gmail.com

**Background:** To determine whether the risk of treatment failure among children with severe pneumonia (World Health Organization 2005 definition) treated with oral amoxicillin is non-inferior to parenteral benzyl penicillin within a margin of 7%.

**Design/Methods:** We conducted an open-label multi-centre randomised controlled non-inferiority trial at six Kenyan hospitals and randomised eligible patients to oral amoxicillin and injectable benzyl penicillin. Recruited children were followed up for the primary outcome of treatment failure at 48 hours, and cumulative treatment failure five days after enrolment or upon hospital discharge (whichever occurred sooner) and treatment failure at day 14 as secondary outcomes.

**Results:** We enrolled 527 children from September 2011 to September 2013 including 302/527 (57.3%) children with co-morbidity. Treatment failure was observed in 20/260 (7.7%) and 21/261 (8.0%) of patients in the amoxicillin and benzyl penicillin arms respectively (risk difference -0.3%, 95% confidence interval (CI) -5.0 to 4.3) in per protocol analyses. These findings were supported by intention to treat analyses. Treatment failure by day 5 post-enrolment was 11.4% and 11.0% and rising to 13.5% and 16.8% by day 14 in the amoxicillin versus benzyl penicillin groups respectively. The most frequent cause of cumulative treatment failure at day 14 was clinical deterioration within 48 hours of enrolment (33/59; 55.9%). Four patients died (overall mortality 0.8%) during the study, three of whom were allocated to the benzyl penicillin group. The presence of wheeze was found to be independently associated with less frequent treatment failure.



**Conclusion:** Previous trials suggesting oral amoxicillin is non-inferior to benzyl penicillin for the treatment of severe pneumonia failed to influence Kenyan policy as decision makers doubted their generalisability to a high mortality setting. Our findings confirm non-inferiority,

provide estimates of risk of treatment failure in Kenya and offer important additional evidence for policy making in sub-Saharan Africa.

### OPP-437-01 Caregiver's knowledge, attitude and practices regarding home management of acute respiratory infections in children under five years in Issele-Azagba

T Idaboh,<sup>1</sup> kofo Odeyemi,<sup>1</sup> S Olarewaju.<sup>2</sup> <sup>1</sup>Department of Community Medicine, Lagos University Teaching Hospital, Lagos, <sup>2</sup>Department of Community Medicine, Ladoke Akintola University Teaching Hospital, Ogbomosho, Nigeria.  
e-mail: oolarewaju7@gmail.com

**Background** Inappropriate management of Acute Respiratory Infections (ARIs) by caregivers among under-five year old children worldwide has resulted in preventable mortality and morbidity from treatment failure, unnecessary adverse effects of the antibiotics used, waste of health care and family resources, and an increased emergence of bacterial resistance. Assessment of the Knowledge Attitude and Practices (KAP) of caregivers of under five year old children on home management of childhood ARIs is important in enabling policy makers plan and provide appropriate education interventions to reduce mismanagement of ARIs and its consequences. **Aims & Objectives:** This study assesses the KAP of caregivers of under-five year old children on management of ARIs in Issele-Azagba Community, Nigeria.

**Materials and Methods:** This is a cross sectional descriptive study. Multistage random sampling procedure was used to select 278 caregivers of children aged 0 – 59 months. The instrument of the study was semi-structured, pre-tested interviewer administered questionnaires adapted from UNICEF (IMCI tool). Data entry and analysis were carried out using SPSS version 16.

**Results:** Most of the respondents were females (i.e. 98.2%), mothers (81.3%) with mean age  $33.3 \pm 10.0$  years. Majority (97.1%) have heard of ARIs but their comprehensive knowledge on its causative agent, mode of prevention and transmission was low. Likewise, almost all the respondents (i.e. 97.1%) had negative attitude towards home management of ARIs. Inappropriate use of antibiotics had been practiced by 75.9% of the respondents, other practices observed included rubbing menthol/balm on the nostrils, neck and chest of the under-fives, and sometimes dissolving the menthol/balm in water for the under-fives to ingest the concoction.

**Conclusion:** Caregiver's knowledge in home management of ARI is inadequate, attitudes were inappropriate and subsequent practices were poor. Necessary steps to improve care givers knowledge, attitude and practices towards home management of ARIs are recommended.



### OPP-438-01 Targeting vaccines against respiratory pathogens: deaths in hospitalised infants in a developing country

P Acosta,<sup>1,2</sup> A Erviti,<sup>2</sup> D Sucker,<sup>3</sup> H Ves Losada,<sup>3</sup> F Polack.<sup>2</sup>

<sup>1</sup>Virology, CONICET, CABA, <sup>2</sup>Immunology, INFANT, CABA,

<sup>3</sup>Epidemiology, Secretary of Health, , CABA, Argentina.

e-mail: patricionoel@hotmail.com

**Background:** Acute respiratory infections are the main cause of hospitalization in infants and young children in industrialized and developing countries. Among all cases of ARI, >50% are caused by respiratory syncytial virus (RSV). A disproportionate number of severe RSV cases and 99% of fatalities occur in the developing world. But while infants at risk for fatal RSV infections should be primary targets for protective interventions against the virus, limited information is available about ARI and RSV-associated deaths to identify and protect this population.

**Design/Methods:** We conducted a prospective study in a catchment population of ~56,560 children <2 years during three RSV seasons (2011–2013) in an underserved region of Argentina. Children in the region were hospitalized in a network of 12 public hospitals. Mortality due to acute respiratory illness (ARI) was assessed prospectively in all institutions. Demographic, clinical and laboratory data were collected and compared to that of infants surviving hospitalization. RSV infections were assayed by RTPCR in nasal aspirates.

**Results:** From 2011 to 2013, 4,875 infants and young children <2 years with ARI and an oxygen saturation in room air <93% were hospitalized in the region. Thirty-six patients died. Population-based mortality rates based on hospitalized patients were 0.7 per 1,000 in 2011, 0.56 per 1,000 in 2012 and 0.7 per 1,000 in 2013. In addition, available information from 2011 and 2012 suggests that infant home deaths equaled those in admitted patients. Forty four percent of fatalities among hospitalized infants and young children were infected with RSV. Other diagnoses among fatal respiratory cases included infections with adenovirus (n=1), human metapneumovirus (n=1), pertussis-like (n=3), *S. aureus* sepsis and ARDS. Off-respiratory season, prevailing diagnoses included trauma, poisoning, and drowning.

Infants with fatal ARI had a mean (and range in) age on admission of 5.5 (0.5–23.9) months vs. 6.4 (0.5–24) months among survivors. Median age in fatal cases was 3.6 months. Fifty percent of fatal ARI cases and 54% of hospitalized ARI were male. Mean survival time at the hospital was 12.5 (1–46) days, with a median=7.5 days. Extreme poverty characterized the population, but did not overtly identify families of dead, hospitalized infants. Over 30% of fatal cases visited an emergency room during the episode with respiratory symptoms and were discharged home. Moreover, >80% of fatalities lived <1 hour away from a hospital. Importantly, 13/36 (35%) children who died with an ARI had a clinically significant pneumothorax during hospitalization vs. 5/4,840 inpatient survivors (p<0.001).

**Conclusion:** • Infants and children with fatal ARI had lower birth weights and more frequent comorbidities

than those surviving infections. Other indicators of vulnerability, including younger age on admission and younger gestational age, lower rates of up-to-date vaccinations, and intrauterine growth retardation may also characterize this population. from a tertiary care center, and more than 50 consulted a physician due to respiratory symptoms before admission (although consultations were less frequent than those of surviving infants). Most of fatalities had symptoms for >48 hs before admission.

- 35% of children with fatal ARI experienced a clinically significant pneumothorax during disease.
- RSV was the most frequent (>50%) agent isolated in fatal cases.

### OPP-439-01 Paediatric asthma in The Gambia: the case for better care

K Clarkson,<sup>1,2</sup> B Camara,<sup>1</sup> K Bojang,<sup>1,3</sup> S Anderson.<sup>1,4</sup>

<sup>1</sup>Clinical Services, Medical Research Council - The Gambia Unit, Fajara, Gambia; <sup>2</sup>Medicine, King's College London, London, UK; <sup>3</sup>Paediatrics, Edward Francis Small Teaching Hospital, Banjul, Gambia; <sup>4</sup>Paediatrics, Imperial NHS Trust, London, UK. Fax: (+22) 449 4154.

e-mail: kevin.clarkson@nhs.net

**Background:** Little information exists regarding paediatric asthma in The Gambia. To date, no research has reviewed current management practices or assessed the availability and affordability of treatment. We aimed to evaluate asthma control and management in Gambian children, including the use of healthcare services, prescribing practices, access to medication and awareness of health information.

**Design/Methods:** A consecutive outpatient case series of children with asthma was carried out from July to September 2012. Children presenting for treatment were recruited from four centres near Banjul. Data were drawn from structured interviews and examinations based on guidelines from the Global Initiative for Asthma (GINA) concerning diagnosis, disease stratification and management. Regional and local guidelines were audited. Local pharmacies were surveyed for the availability and cost of inhaled  $\beta_2$  agonists and corticosteroids.

**Results:** 111 children with asthma were identified of which 96% met the GINA criteria for uncontrolled disease and 65% had moderate or severe airflow restriction. In the preceding year, participants reported a median of 6 (range 1–30) clinic visits due to asthma and 58% had missed school. 48% had been admitted to hospital for asthma treatment on a least one occasion during their lifetime. One child died during the study due to asthma exacerbation. No children were prescribed inhaled corticosteroids and provision from local pharmacies was limited and prohibitively expensive. 76% of parents could not identify any risk reduction strategies recommended by GINA and 61% were unaware of the need for immediate access to bronchodilator therapy with the onset of symptoms. No existing regional strategy or local guidelines were identified for the management of paediatric asthma.

**Conclusion:** Asthma control and health awareness in this group was poor, management was sub-optimal, health-care utilisation was frequent and the morbidity impact was high. These findings suggest the need for national diagnostic and treatment protocols, health awareness campaigns and cost-effective drug procurement.

## 05. HIGH AND LOW: THE SEARCH FOR TB CASES

### OPP-440-01 Engaging the mining sector in tuberculosis diagnosis in Quang Ninh province, Viet Nam

HK Pham,<sup>1</sup> B H Nguyen,<sup>2</sup> C Hennig.<sup>1</sup> <sup>1</sup>Stop TB, World Health Organization, Ha Noi, <sup>2</sup>Programme Management Unit, National TB control Programme, Ha Noi, Viet Nam.  
e-mail: phamh@wpro.who.int

**Background and challenges to implementation:** Viet Nam ranks 12nd among 27<sup>th</sup> high burden TB countries with 130,000 new cases and 18,000 TB deaths each year (Global TB report 2013). A TB epidemiology evaluation (Jan 2013) revealed although the MDG for TB can be achieved by 2015, the slow decline TB prevalence and incidence at 4.4% and 4.6% annually, respectively—calls for more efforts to enhance TB case finding. Continued passive case finding in the general population in combination with active case finding among risk groups followed by TB treatment are the principal public health strategies to obtain a steeper decline in TB incidence and mortality. Miners are at high risk for developing tuberculosis (TB), but they are often outside of the purview of the national TB control programme. Novel approaches are required to find lingering TB cases spreading the disease in these confined spaces underground. Both the scientific world and popular media have reported on and raised awareness about a potential high burden of TB in the miners (South Africa). The study showed the PTB prevalence was 19.4% on history alone, and 35.2% on history or on chest X-ray.

**Intervention or response:** In order to investigate TB among coal miners in Quang Ninh, the National TB programme conducted an active case finding campaign in 2013 in collaboration with the health centre of the coal industry and Quang Ninh TB hospital with support from WHO. All people at risk were screened by questionnaires and chest X-ray. Sputum of those who had either abnormal chest X-ray or history of TB disease were submitted for an Xpert MTB/RIF test. Quality assurance for X-ray reading and Xpert testing was in place. All confirmed TB cases were referred to Quang Ninh TB hospital for treatment registration.

**Results and lessons learnt:** Among 7401 miners from the two biggest coal mines, 385 (4.2%) either had an abnormal chest x-ray or history of TB disease and submitted sputum for an Xpert MTB/RIF test. 15 (4.0%) cases of TB were identified, one of which also had resistance to the drug rifampicin. All confirmed TB patients were referred for TB treatment

**Conclusions and key recommendations:** A These cases represent a TB rate of around 203/100,000, nearly double that seen in the surrounding province. If the provincial TB programme and the coal industry continue to collaborate and routinely screen TB among coal miners, this potent source of transmission can be virtually eliminated.

### OPP-441-01 Active case finding with mycobacterial culture and drug susceptibility testing for TB diagnosis in a refugee camp

S Jonnalagadda,<sup>1</sup> O Gorbacheva,<sup>2</sup> Raz Wali,<sup>3</sup> L Ortega,<sup>1</sup> W Zhou,<sup>1</sup> J Painter.<sup>1</sup> <sup>1</sup>Division of Global Migration and Quarantine, Immigrant, Refugee and Migrant Health Branch, Centers for Disease Control and Prevention, Atlanta, GA, USA; <sup>2</sup>Migrant Health Division, International Organization for Migration, Bangkok, Thailand; <sup>3</sup>Migrant Health Division, International Organization for Migration, Damak, Nepal.  
e-mail: wau4@cdc.gov

**Background:** Over 100,000 Bhutanese refugees living in camps in Nepal since 1990s have been offered resettlement to the United States (US) and other countries. Tuberculosis (TB) diagnosis in the camps occurred through passive surveillance, relying on symptomatic case-patients seeking medical attention at UNHCR camp medical centers (CMC), and confirmed by sputum smears. Since 2007, TB screening for refugees opting to resettle in the US has been conducted by International Organization for Migration (IOM), as per mandatory technical instructions (TB TI) provided by the US Centers for Disease Control and Prevention (CDC). As per TB TI, refugees must undergo active screening for TB using smear, culture, and drug susceptibility testing on three sputum samples from all individuals  $\geq 15$  years with an abnormal chest radiograph (CXR) suggestive of TB. These services were not available to the non-resettlement population. **Response:** To improve TB control at the camp level, IOM extended TB TI to all refugees, including those not in the resettlement process, since October 2008, with funding from US Department of State. Individuals presenting at CMCs with symptoms suggestive of TB are referred to IOM for sputum testing. To further improve TB detection, active case finding among contacts was initiated in the camp population in November 2012.

**Results:** As of December 2013, 3403 TB suspects were referred to IOM for sputum testing. Of these, 518 (15%) had lab-confirmed TB and 54 had drug resistance. Annual incidence of TB in the camp population was 1/4<sup>th</sup> compared with the incidence in the resettlement population through universal screening (Table 1). Of the 518 case-patients, 23% were smear negative (s-) and culture positive (c+), compared with 58% of 681 lab-confirmed TB cases in the resettlement screening, suggesting fewer of the non-resettlement s-, c+ cases were being identified. From November 2012 to December 2013, an additional 371 contacts of 80 TB case-patients were screened. Of these, 9 (2%) were c+, s- and 3 (1%) were c+, s+.

**Conclusions:** This project demonstrates implementation of improved TB diagnosis protocol in a refugee camp with low resource and high TB burden by leveraging resources between camp service provider and resettlement agencies (with high quality medical and laboratory infrastructure and capacity). To maximize the impact of a sensitive diagnostic protocol, active case finding could be considered in this setting.

#### **OPP-442-01 FAST reveals the hidden cause of prolonged high incidence of TB in Bangladesh**

LR Khan,<sup>1</sup> P Daru,<sup>1</sup> M Alam,<sup>1</sup> AE Barrera-cancedda.<sup>2</sup> <sup>1</sup>TB CARE II Bangladesh, University Research Co., LLC, Dhaka, Bangladesh; <sup>2</sup>TB, Partners In Health, Boston, MA, USA. e-mail: kchakraborty@urc-chs.com

**Background and challenges to implementation:** Since the initiation of DOTS strategy in 1994 in Bangladesh, the incidence of pulmonary positive TB found to have been high. Though the NTP target for case detection rate and cure rate have been achieved for the last couple of years, it is clear that there are some other sources of infection yet to notice.

**Intervention or response:** A longitudinal study has been done in NIDCH from September 2013 to December 2013. All newly admitted cases in NIDCH were sputum tested by GeneXpert under the Finding TB cases Actively, Separating safely, and Treating effectively (FAST) strategy. We have divided the patients in two groups. One group that constituted TB patients but not known as MDR cases were screened for MDR TB and the other group included 'Other lung disease' patients but not known as TB cases were screened for TB/MDR TB. Known MDR TB patients were excluded.

**Results and lessons learnt:** During this period, total 557 patients of other lung disease cases were tested. Out of them 90 cases were detected MTB of which 17 were Rif. resistant. In the same period, out of a total of 247 known TB cases being treated with first line anti-TB drug (cat-1 and 2), 19 MDR TB cases were detected. A significant number of new TB cases and MDR cases detected from among patients of other lung diseases and MDR cases detected from normal TB cases. Without the FAST strategy these patients would have remained unnoticed and act as a source of infection of TB and MDR TB.

**Conclusions and key recommendations:** According to this study we can conclude that all patients with lung diseases, which are not known TB cases, with or without signs and symptoms of TB (more than three weeks cough) should be screened for TB by GeneXpert. The student also suggests that screening all pulmonary positive TB cases by GeneXpert would be an effective approach for early diagnosis and infection control of MDR TB. This study evaluated only four months' of data that is a too short period. Moreover the study place is the specialized national lung disease hospital where usually critical cases are referred. So a study in broader aspect is needed.

#### **OPP-443-01 TB burden in Tanzanian prisons: active screening with X-pert MTB/Rif® assay and establishment of associated characteristics for MTB infection**

C Mangu,<sup>1</sup> Jan Van Den Hombergh,<sup>2</sup> D Kowour,<sup>1</sup> L Maboko,<sup>1</sup> C Kasang,<sup>3</sup> J Malewa,<sup>4</sup> M Hoelscher,<sup>5,6</sup> P Clowes.<sup>1,5</sup> <sup>1</sup>Operational Research and Interventions, NIMR-Mbeya Medical Research Centre, Mbeya, <sup>2</sup>PAI, Stichting PharmAccess International, Dar es Salaam, United Republic of Tanzania; <sup>3</sup>HQ, Medical Mission Institute, Wuerzburg, Germany; <sup>4</sup>HQ, Tanzania Prisons, Dar es Salaam, United Republic of Tanzania; <sup>5</sup>Division of Infectious Diseases and Tropical Medicine, Medical Centre of the University of Munich (LMU), Munich, <sup>6</sup>DZIF, German Centre for Infection Research, Munich, Germany. Fax: (+255) 25 2503134. e-mail: pclowes@mmrp.org

**Background:** There is consensus that penitentiary institutions are a permanent source for active MTB infections, but conclusive data on TB prevalence in prisons, as well as associated risk factors for prisoners, are scarce and hard to come by, especially in Africa where 26% of all newly diagnosed cases occur. Consistent and sustainable TB screening methods are urgently needed to get reliable baseline information to effectively reduce TB transmission in these settings.

**Design/Methods:** As part of a TB REACH grant, all inmates and new admissions to 4 central Tanzanian prisons are actively screened for TB by using a proven effective diagnostic technology, the X-pert MTB/Rif® assay. Furthermore, a short screening algorithm with chest X-ray followed by a confirmatory Xpert MTB/Rif® assay is employed in one prison in Dar es Salaam. Short questionnaires are applied to all to collect information on possible risk factors. Due to the high burden of HIV among the prison population, PITC is offered as an opt-out strategy.

**Results:** A total of 5,182 prisoners were screened between July 2013 and April 2014. 67.95% (3,521 prisoners) were inmates and 32.05% (1,661) new admissions. TB prevalence amongst inmates and new entries was 1.16% and 1.02%, respectively. Only 26 of 59 MTB positive clients (44.1%) reported any TB symptoms prior to being diagnosed by Xpert MTB/Rif assay. Just under 50% ever had an HIV test before being diagnosed with MTB and merely 4 of 59 (6.8%) were already on ARTs. The median stay in prisons for MTB pos inmates was 64 months (0 to 165 months). PITC uptake was highest in prisons where PITC was already established prior to the intervention. TB prevalence in 4 out of 5 prisons, where active screening was newly introduced, was similar with just under 1.5%, but significantly higher than in the fifth prison where routine inmate and entry screening was established in November 2010 and prevalence could be reduced to 0.75%.

**Conclusion:** Routine TB screening activities followed by effective treatment can significantly reduce TB prevalence in prisons over a period of only a few years. Although TB prevalence in inmates is slightly higher than in new admissions, both groups contribute substantially to the TB problem in correctional facilities. The absence of classical TB symptoms does not exclude active MTB



infection and mass screening amongst inmates, followed by ongoing routine screening of new entries should therefore become part of prison health programmes.

# **OPP-444-01 Contribution of Public-Private Mix (Urban DOTS) in TB control services in Kabul, Afghanistan**

A Hamim,<sup>1</sup> SM Sayedi,<sup>1</sup> Ghul Qader,<sup>1</sup> M Rashidi,<sup>1</sup> M Shefa,<sup>1</sup> A Momand,<sup>1</sup> L Manzoor,<sup>2</sup> P Suarez.<sup>3</sup> <sup>1</sup>TB CARE I, Management Science for Health (MSH), Kabul, <sup>2</sup>National TB Control Program, MoPH, Kabul, Afghanistan; <sup>3</sup>TB CARE I, Management Science for Health (MSH), Arlington, VA, USA. e-mail: ahamim@msh.org

**Background** Kabul, the capital of Afghanistan, has approximately 4 million inhabitants. In 2009, 106 health facilities existed in Kabul but only 22 of these facilities provided TB services. As a result, the TB indicators in Kabul were very poor: the TB case notification rate was just 26%, the conversion rate was 43%, and the TB treatment success rate was 46%. In 2009, to overcome these challenges, Afghanistan's National TB Control Program (NTP) began implementing an urban DOTS program with support from the USAID-funded TB Control Activity Project (TB CAP) and its follow on, TB CARE I. This program sought to engage both public and private sector facilities in TB service delivery.

**Interventions:** To implement urban DOTS, the NTP and TB CAP/ TB CARE I strengthened coordination mechanisms between private and public health facilities and trained health care staff on TB service delivery. The partners also distributed anti-TB drugs, laboratory reagents, and DOTS packages to the participating health facilities. DOTS packages included education materials on TB control for health workers, patients, and communities. They also included materials for transferring patients' sputum samples and medication boxes that included patients' entire treatment regimens. To ensure staff were using these materials and providing consistent, high-quality TB services, the NTP and TB CAP/TB CARE I conducted regular monitoring and supervision visits to the participating health facilities. In 2013, the NTP and TB CARE I conducted an assessment to evaluate the role of urban DOTS activities in improving TB control indicators in Kabul. The assessment team reviewed the TB data that was collected at the participating health facilities during the intervention period (2010 to 2013) and compared it with national TB surveillance data from prior 2009.

**Results** The study revealed that the participating health facilities identified five times as many TB suspects in 2013 as they had in 2009. Similarly, the number of TB cases notified (all forms) at the facilities increased by 84%, the number of newly identified TB sputum smear positive cases increased by 48%, the conversion rate improved by 29%, and the TB patient treatment success rate improved by 32% to reach 76%.

**Conclusion** Urban DOTS contributed to significant improvements in Kabul City's TB case notification rate, sputum smear conversion rate, and treatment success

rate. Urban DOTS should be scaled up in Kabul and similar urban settings worldwide.

**Table: Results of PPM (Urban DOTS) approach in TB control services, 2009–2013**

Indicators	2009	2010	2011	2012	2013	% improvement
No. of health facilities with TB laboratory services	106	111	111	111	111	111
No. of health facilities with DOTS services	22	48	53	68	73	232%
No. of TB suspects identified/ examined at the health facilities	2,856	10,150	11,900	13,644	14,181	396%
No. of all TB cases notified at the health facilities	1,934	2,738	2,728	3,208	3,548	84%
No. of new sputum smear positive (SS+) TB cases notified at the health facilities	814	1,022	1,082	1,173	1,204	48%
Conversion rate among SS+ TB cases at the health facilities	43%	65%	70%	74%	72%	29%
Treatment success rate among new SS+ TB cases at the health facilities	44%	62%	74%	76%	NA	32%
Transferred out rate among new SS+ TB cases at the health facilities	46%	26%	16%	19%	NA	27%

### OPP-445-01 Perspectives on community-based approaches for tuberculosis case finding in douthern Ethiopia: a qualitative analysis

G Asnake,<sup>1</sup> D Datiko,<sup>1</sup> M A Yassin,<sup>2</sup> O Tolluch,<sup>3</sup> P Markos,<sup>1</sup> L E Cuevas,<sup>4</sup> Tade Mamo,<sup>1</sup> S Theobald.<sup>3</sup>

<sup>1</sup>LSTM TB REACH, REACH Ethiopia, Hawassa, Ethiopia;

<sup>2</sup>Tuberculosis and Malaria, The Global Fund, Geneva, Switzerland; <sup>3</sup>Social sciences and international health, Liverpool School of Tropical Medicine, Liverpool, <sup>4</sup>Clinical Research, Liverpool School of Tropical Medicine, Liverpool, UK. e-mail: girumasnake2006@yahoo.com

**Introduction:** Since 2010 an innovative community-based TB intervention project has been implemented in Sidama Zone, southern Ethiopia with female community based health extension workers (HEWs) and their supervisors. The project doubled the number of TB cases identified and improved treatment outcome among rural populations with limited access to health services.

**Objectives:** Qualitative research was used to understand the experiences and perspectives of key participants in the project, support the ongoing intervention and assess its sustainability.

**Methodology:** Qualitative interviews were undertaken with purposively sampled participants: community members with TB symptoms (n=21), HEWs and promoters (n=20) supervisors (n=4) and laboratory technicians (n=13). Focus group discussions were also conducted with separate groups of HEWs and laboratory technicians (n=3). A framework analysis approach was undertaken.

**Results:** Women and men at the community level: had learnt about TB from HEW mobilization activities, they found free community-based TB services acceptable and convenient. Prior to the intervention many patients with chronic cough remained without care. Poverty was a major barrier to diagnosis in the past, especially for women, and the elderly. Smear negative cases were anxious about next steps. Providers: All types of providers spontaneously referred to the positive impact the community based intervention had on vulnerable groups' access to diagnosis, care and treatment for tuberculosis. They found the positive feedback from, and visible impact on, communities very motivating. HEWs were successfully able to take on new tasks (collecting sputum and preparing smears) in partnership with promoters and with additional training and ongoing support from supervisors and laboratory technicians.

**Conclusions:** Service users and providers found the intervention highly acceptable and most challenges were overcome with training and regular feedback. HEWs' role in the community based intervention was supported and facilitated through the structures and processes established within the Health Extension Programme and the intervention itself alongside the high visible impact on health in their community. Developing context embedded strategies to support, sustain and motivate this critical cadre is important.

### OPP-446-01 Intensified TB case finding in primary health-care clinics of Swaziland

L Dlamini Mdluli,<sup>1</sup> E Phiri.<sup>2</sup> <sup>1</sup>National TB Control Program, Ministry of Health, Manzini, <sup>2</sup>National TB Control Program, Ministry of Health, Manzini, Swaziland. Fax: (+268)5053248. e-mail: mdluli\_lindiwe@yahoo.com

**Background and challenges to implementation:** Swaziland has a population of 1.1 million and the highest prevalence of HIV in the world of 26% among individuals aged 15–45 years (Swaziland DHS 2007; 10). The HIV epidemic has significantly contributed towards the huge TB burden being experienced in the public health sector which had a TB case notification rate of 717/100000 population, TB/HIV co-infection rate of 80%, high death rate above 5% and low treatment success rate of less than the global target of 85% (NTCP annual report 2012; 25). In response to the dual epidemic of TB and HIV and the unfavourable TB treatment outcomes, Swaziland is implementing a National Multi-sectorial Strategic Framework to expand HIV and TB interventions. One of the strategies is to strengthen early TB case detection by implementing Intensified TB Case Finding (ICF) in all ART and Pre-Art departments in the primary health care clinics in Swaziland.

**Intervention or response:** Individuals with a minimum of secondary school level of literacy who were already working as volunteers in health care settings were identified. A training curriculum and monitoring tools for this cadre were developed. Recruitment was conducted; selected candidates were trained on TB ICF and deployed in different primary health care clinics where they were strategically placed in ART, Out Patient and Antenatal departments. Their duties included: triaging, TB screening, sputum collection, ensuring early TB treatment initiation of confirmed cases, recording and reporting. All samples collected were examined through Gene X-pert. Confirmed TB cases were promptly initiated on TB treatment, initial defaulters were tracked and initiated on treatment. At the health care facilities these officers worked under the supervision of a nurse manager, and TB Coordinators provided mentorship as well as supervision.

**Results and lessons learnt:** TB screening among pre-ART and ART patients was scaled up from less than 20% in 2010 to above 70% in 2012. Treatment success rate increased from 68% in 2010 to 73 % in 2012. Death rate was reduced from 12% in 2010 to 6% in 2012.

**Conclusions and key recommendations:** Intensified TB Case finding promotes early enrollment of TB patients into treatment thus reducing deaths and improving treatment outcomes.

### OPP-447-01 Substantial impact of a culture-based screening algorithm among U.S. bound immigrants and refugees on reducing the incidence of tuberculosis

Y Liu,<sup>1</sup> J Painter,<sup>1</sup> D Posey,<sup>1</sup> M Cetron.<sup>1</sup> <sup>1</sup>Division of Global Migration and Quarantine, Centers for Disease Control and Prevention, Atlanta, GA, USA. Fax: (+1) 404 639 4441. e-mail: jpainter@cdc.gov

**Background:** Prior to 2007, overseas tuberculosis (TB) screening in U.S.-bound immigrants and refugees was based on a smear-based algorithm which could not diagnose smear-negative and culture-positive TB. In 2007, CDC revised the smear-based algorithm to include mycobacterial culture, drug-susceptibility testing, and directly observed therapy for TB treatment. As of 2011, the new culture-based algorithm had been implemented in 52 countries.

**Methods:** We conducted a descriptive epidemiologic analysis of U.S.-bound immigrants and refugees diagnosed with TB by the culture-based algorithm during 2007–2011.

**Results:** During 2007–2011, the culture-based algorithm screened 42.7% (1,134,151) of the 2,655,502 U.S.-bound immigrants and refugees, and diagnosed 3,003 (265 cases/100,000 persons) TB cases, including 1,587 (140 cases/100,000 persons) smear-negative and culture-positive cases. Of the 3,003 TB cases, 52.5% (1,587) were smear-negative and culture-positive TB. Prior to implementation (2002–2006) of the culture-based algorithm, the annual number of reported cases among foreign-born persons within 1 year of arrival in the United States was relatively constant (annual mean of 1,504 cases). By comparing to the mean of annual number of the reported cases prior to implementation, there was a cumulative decline of 1,667 cases among foreign-born persons within 1 year after arrival in the United States during 2007–2011. This cumulative decline was approximately the same of the cumulative cases (1,587 cases) of smear-negative and culture-positive TB diagnosed and treated overseas among U.S.-bound immigrants and refugees during the same period.

**Conclusions:** The implementation of the culture-based algorithm in U.S.-bound immigrants and refugees substantially reduced the incidence of TB among newly arrived foreign-born persons in the United States.

### OPP-448-01 Screening for tuberculosis among adults newly diagnosed with HIV in sub-Saharan Africa: a cost-effectiveness analysis

A Zwerling,<sup>1</sup> M Sahu,<sup>2</sup> L G Ngwira,<sup>3</sup> M Khundi,<sup>3</sup> T Harawa,<sup>3</sup> L Corbett,<sup>4</sup> R E Chaisson,<sup>5</sup> D Dowdy.<sup>1</sup>

<sup>1</sup>Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, <sup>2</sup>Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA; <sup>3</sup>Blantyre, Malawi-Liverpool-Wellcome Trust Research Programme, Blantyre, Malawi; <sup>4</sup>Department of Infectious & Tropical Diseases, London School of Hygiene & Tropical Medicine, London, UK; <sup>5</sup>Center for Tuberculosis Research, Johns

Hopkins University School of Medicine, Baltimore, MD, USA. e-mail: azwerlin@jhsph.edu

**Background:** Intensified case finding (ICF) for TB is increasingly recommended for those newly diagnosed with HIV as a tool to reduce TB mortality. Unfortunately, the tool most widely used for TB ICF has limited sensitivity among HIV infected persons. New tools, including light emitting diode (LED) fluorescence microscopy and the molecular assay Xpert MTB/RIF® (“Xpert”, Cepheid, Inc., Sunnyvale, CA, USA) offer increased sensitivity for TB over traditional SSM and can be performed in under 2 hours, but can be expensive.

**Methods:** We used cost and operational data from a trial of LED microscopy and Xpert for rapid TB screening among people newly diagnosed with HIV in rural Malawi to explore the potential cost-effectiveness of on-demand screening for TB in low-income countries of sub-Saharan Africa. Patients newly diagnosed with HIV would be screened for TB by one of three strategies: Xpert, LED or standard of care (i.e., at the discretion of the treating physician). We assumed that those diagnosed with TB received standard first line treatment, while those diagnosed with rifampin-resistant TB by Xpert received appropriate second line therapy.

**Results:** Cost-effectiveness of intensified TB case finding among individuals newly diagnosed with HIV was largely determined by two factors: prevalence of active TB among patients newly diagnosed with HIV and volume of testing. In facilities that could screen at least 50 people with a 6.5% prevalence of TB, or at least 500 people with a 2.5% TB prevalence, TB screening with Xpert is likely to be cost-effective at a willingness to pay of per-capita gross domestic product per DALY averted (Figure 1). At somewhat lower prevalence – including that observed in Malawi – LED microscopy may be the preferred screening strategy, whereas in settings of lower TB prevalence or small numbers of eligible patients, no screening may be reasonable (such that resources can be deployed to other interventions). These results provide important guidance to low-income countries in sub-Saharan Africa as they contemplate the most appropriate approaches to implementing novel TB diagnostic tests for screening among people newly diagnosed with HIV.

**Conclusion:** Using novel diagnostics to screen for TB at the point of HIV diagnosis may be cost-effective in low-income countries of sub-Saharan Africa, but only if a relatively large population with high prevalence of TB can be identified for screening.

### OPP-449-01 Using internet services for targeted TB screening in Ukraine

P Lychovyd,<sup>1</sup> M Bachmaha,<sup>2</sup> N Rybak.<sup>3</sup> <sup>1</sup>Tuberculosis Department, Lviv Communal Municipal Medical Unit “Phthysiopulmonology”, Lviv, <sup>2</sup>Brown University Ukraine Collaboration, Lviv Education Foundation, Lviv, Ukraine; <sup>3</sup>Department of Infectious Disease, Rhode Island Hospital, Providence, RI, USA. e-mail: bachmaham@gmail.com

**Background and challenges to implementation:** Intensified case finding is one of goals for identifying and



treating people affected by TB. This intervention aimed to use an easily accessible free Internet technology to make a switch from generalized population screening for TB to a targeted screening of at-risk populations in Lviv, Ukraine. Despite the adoption of the Stop TB Strategy by the National TB Programme in 2012, the incidence and prevalence of TB and MDR-TB in Ukraine continue to rise. WHO has identified that ongoing mass general population screenings are ineffective for TB control. Policymakers, however, remain uncommitted to making a change in TB screening methods within Ukraine. The model used in this intervention empowered primary healthcare providers responsible for TB detection to use everyday technology to improve case detection.

**Intervention:** The most populated district of the city of L'viv, Ukraine with 15,370 residents, most of who live in multi-apartment buildings was selected. A multi-layer map of the district was created using the online map service <https://www.google.com/>. The map contained a detailed street view with each apartment building and its address displaying clearly. Two TB physicians at the Lviv Municipal Phthisiatry Hospital participated in the intervention. From January until April 2014 the physicians marked each case of sputum-positive TB in their practice from the selected district on the map. Since no electronic medical database is available, the interactive map became the only tool allowing physicians to immediately see if an apartment building contained 2 or more TB cases. If 2 or more cases were found, the physicians promptly alerted the primary health care provider overseeing that building. The primary health care provider was then able to target residents from these buildings for TB screening at their local health clinic.

**Results and lessons learned:** Over the duration of four months, four buildings with 2 sputum-positive TB cases and one building with 3 sputum-positive TB cases were identified. The TB physicians were able to contact the local primary health care providers for those buildings and recommend targeted screening for TB.

**Conclusions:** Free and easy to use Internet map can be used as an interim tool to carry out targeted TB screening until electronic databases are adopted. This model can be even more efficient in cities with denser populations like Donetsk in Eastern Ukraine or large cities in Russia.

## 06. MANAGING MDR-TB: PROBLEMS AND SOLUTIONS

### OPP-450-01 Surveillance of the second-line drug resistance among multidrug-resistant tuberculosis in Taiwan, 2007–2013

MH Wu,<sup>1</sup> HY Chang,<sup>1</sup> TF Wang,<sup>1</sup> YM Deng,<sup>1</sup> R Jou.<sup>1,2</sup>

<sup>1</sup>Institute of Microbiology and Immunology, Centers for Disease Control, Taipei, <sup>2</sup>Institute of Microbiology and Immunology, National Yang-Ming University, Taipei, Taiwan. Fax: (+886) 2-2653-1387. e-mail: [rwj@cdc.gov.tw](mailto:rwj@cdc.gov.tw)

**Background:** A DOTS-plus program was implemented in 2007 for better management of multidrug-resistant

tuberculosis (MDR-TB) cases in Taiwan. To understand the extent of resistance to the second-line drugs among MDR-TB cases, we conducted a population-based analysis.

**Design/Methods:** We retrospectively analyzed drug susceptibility testing (DST) results of the second-line drugs, ofloxacin (OFX), kanamycin (KM), para-aminosalicylate (PAS), ethionamide (EA) and rifabutin (RBT), of MDR *Mycobacterium tuberculosis* complex isolates tested in 2007–2011, and amikacin (AM) tested in 2008–2011; while moxifloxacin (MOX), gatifloxacin (GAT) and cycloserine (CS) tested in 2010–2011. One isolate of each case per year was included in this study. DST was performed using either the Middlebrook 7H10 agar or a liquid-based proportion method. Of the 1,108 MDR *M. tuberculosis* isolates tested, 144, 353, 238, 197 and 176 isolates were tested in 2007, 2008, 2009, 2010 and 2011, respectively.

**Results:** In this survey, 19.3–43.1% were resistant to OFX, 22.3–22.7% resistant to MOX, 6.3–6.6% resistant to GAT, 11.2–13.4% resistant to KM, 6.8–9.7% resistant to AM, 6.1–8.5% resistant to CAP, 1.5–1.7% resistant to CS, 10.8–23.6% resistant to PAS, 15.9–42.0% resistant to EA, and 83.3–89.2% resistant to RBT (Figure). Thirty extensively drug-resistant (XDR) TB were identified in 2008–2011. Since GAT was not available in Taiwan, resistant to GAT might be resulted from cross-resistance with other fluoroquinolone. Significant decrease of the OFX resistant rate ( $P < 0.01$ ) and PAS resistant rate ( $P < 0.01$ ) were observed in 2008. A policy implemented in 2007 to restrict the prescription of fluoroquinolone was proved to be effective.

**Conclusion:** Substantial proportion of MDR-TB isolates were resistant to OFX and MOX, thus signaling the emerging of XDR-TB. This survey needed to be extended to analyze patient's clinical data to reveal causes of drug-resistance.

### OPP-451-01 A novel therapeutic vaccine against tuberculosis in the cynomolgus monkey model and clinical trial

M Okada,<sup>1</sup> T Nakajima,<sup>2</sup> Y Kaneda,<sup>3</sup> Y Inoue,<sup>1</sup>

K Tomono,<sup>3</sup> A Kumanogoh,<sup>3</sup> K Tsuyuguchi,<sup>1</sup> S Shoji.<sup>4</sup>

<sup>1</sup>Clinical Research Center, National Hospital Organization Kinki-chuo Chest Medical Center, Osaka, <sup>2</sup>Ikedo Laboratory, Genomidea Co., Osaka, Japan, <sup>3</sup>Medical School, Osaka University, Osaka, <sup>4</sup>Internal Medicine, NHO Tokyo Hospital, Tokyo, Japan. Fax: (+81) 722 512 153. e-mail: [okm@kch.hosp.go.jp](mailto:okm@kch.hosp.go.jp)

**Background:** Multi-drug resistant (MDR), especially extremely drug resistant (XDR), *Mycobacterium tuberculosis* (M. TB) is a big problem in the world. We have developed novel TB therapeutic vaccine (HVJ-Envelope/HSP65 +IL-12 DNA vaccine) to eliminate MDR-TB.

**Design/Methods:** DNA vaccine (so called HSP65 vaccine) expressing M.TB heat shock protein 65 and IL-12 was delivered by the hemagglutinating virus of Japan (HVJ)-envelope. Human M.TB ( $5 \times 10^2$  CFU) was intratracheally instilled into cynomolgus monkeys and then

the monkeys were treated with the vaccine by the injection i.m. 9 times, three times a week.

**Results:** HSP65 vaccine provided remarkable protective efficacy and strong therapeutic efficacy against MDR-TB and XDR-TB in murine models (prolongation of survival time and the decrease in the number of MDR-TB in the lungs, liver and spleen). This vaccine exerted synergistic therapeutic effect by the combination of chemotherapy (INH) in TB infected mice. Furthermore, we extended our studies to a cynomolgus monkey model, which is currently the best animal model of human tuberculosis. HSP65 vaccine provided therapeutic efficacy of prolongation of survival time (100% survival) compared to saline control group (60% survival) of TB infected monkeys. The proliferation of PBL from the monkeys treated with the vaccine was more augmented than that from control group. This vaccine augmented the immune responses (IL-2 production) in TB-infected monkeys. In addition, the IL-2 production from PBL after the stimulation with PPD or HSP65 antigens correlated with the survival after TB challenge. Therefore, we have planned to do clinical phase I trial after keeping the good laboratory practice (GLP) by safety pharmacology and toxicology test. Targets are human patients with MDR-TB. 8 weeks after 6 times injection of this vaccine, the number of MDR-TB, sputum-culture conversion of MDR-TB and the augmentation of immune responses against TB are defined as an efficacy (primary efficacy of end point) of the vaccine. Adverse events will be also examined.

**Conclusion and recommendations:** These data indicate that our novel vaccine might be useful against tuberculosis including XDR-TB and MDR-TB for human therapeutic clinical applications. (Co-worker Ayako Mikami, Tomoshige Matsumoto, Takefumi Saito, Yoko Kita, Satomi Hashimoto, Yasuko Nishida, Hitoshi Nakatani, Shiho Nishimatsu, Yumiko Kioka, Seiji Hayashi, Paul Saunderson, Esterlina V. Tan, David McMurray.)

#### **OPP-452-01 Non-tuberculosis mycobacteria: trend of isolation rate and characteristics of NTM in Cambodia during 2011–2013**

S Khann,<sup>1</sup> T E Mao,<sup>2</sup> K Tan,<sup>2</sup> Y Rajendra.<sup>1</sup> <sup>1</sup>STOP TB, World Health Organization, Phnom Penh, <sup>2</sup>National Center for Tuberculosis and Leprosy Control, Ministry of Health, Phnom Penh, Cambodia. e-mail: khann.sokhan@yahoo.com

**Background:** The evidence of increase in the prevalence of NTM is being reported around the world. In Shanghai, China it rose from 4% to 6% in year 2005 to 2008. Cambodia is one of the 22 high TB burden countries. The NTM isolation rate among pulmonary smear positive previously treated TB and new smear positive non-converter at month 2 or 3 was 25% in 2011.

**Objective:** To determine the trend of NTM isolation rate from presumptive multi-drug resistant tuberculosis (MDR-TB) cases during 2011–2013 and their characteristics.

**Method:** A retrospective cross-sectional study which included all presumptive MDR-TB patients whose samples reached two main mycobacterial culture laboratories of National TB Program during 2011–2013. Each of the two samples were examined by smear microscopy with Ziehl Neelsen, cultured with Lowenstein Jensen and BACTEC MGIT 960, and identified for mycobacteria with ICA test. Possible cases were defined as a single positive NTM isolate, and definite cases were defined as two positive NTM isolates. The NTM isolation rate and the relationship of NTM and smear result were analyzed.

**Results:** A total 6,115 sputum samples of 3,338 patients were cultured, of which 32.3% (n=1079) patients have at least one positive culture with median age of 51 years (IQR: 40–62) and male 59.5%. Out of these, 36.9% (n=398) were NTM isolates with median age of 56.5 years (IQR: 46–65) and male 51.0%. Of these, 39.7% (n=158) were defined as NTM cases. The isolation rate of NTM among culture positive of presumptive MDR-TB patients were 26.1%, 31.5%, and 46.9% in year 2011, 2012, and 2013 respectively. This isolation rate was strongly correlated with grade of smear result but not TB treatment history. The proportion of NTM by grade of smear results were 62%, 53%, 27%, 15%, and 6% among smear negative, scanty, 1+, 2+, and 3+ respectively and the proportion of NTM by type of TB patients were 66.7%, 53.0%, 38.5%, 34.4%, 30.9%, 29.4%, and 2.7% among pulmonary TB smear negative previously treated cases, non-converter of new smear positive cases, symptomatic close contacts of known MDR-TB patient, failure, HIV/TB new smear positive, relapse, and return after defaulter respectively.

**Conclusions:** The isolation rate of NTM in Cambodia among presumptive MDR-TB patients were found to be remarkably high and increasing of the last 3 years and strongly correlated with grade of smear result. Further studies and appropriate managements should be done for those patients.

#### **OPP-453-01 Factors associated with loss to follow up among multidrug-resistant tuberculosis patients at drug-resistant TB center, central Gujarat: 2010–2013**

K Shringarpure,<sup>1</sup> P Isaakidis,<sup>2</sup> K Sagili,<sup>3</sup> R Baxi.<sup>1</sup>

<sup>1</sup>Preventive and Social Medicine, Medical College Baroda, Baroda, <sup>2</sup>Operational Research, Médecins Sans Frontières, Mumbai, <sup>3</sup>Research, The UNION, South East Asia Office, Baroda, India. e-mail: keyurbrahme@gmail.com

**Background:** MDR-TB is a rising global threat to public health and concerted efforts for its treatment are diluted if the outcomes are not successful-Loss to follow up (LTFU) being one of them. It is therefore necessary to know the proportion and reasons associated with these LTFU cases and devise effective patient-centred strategies to improve retention in care.

**Methods:** Retrospective cohort study was conducted at the DR-TB Site for Central Gujarat on all patients registered between January 2010 to June 2013 using pre-

designed structured data capture instrument. Necessary permissions were taken from the concerned institutions. Data sources used were individual patient treatment cards validated with the DR-TB treatment register. Anonymous double data entry using password protection was done in EpiData 3.1. Analysis was done using EpiDataAnalysisV2.2.182. Multivariate modelling and Kaplan Meier survival analysis was done.

**Results:** The proportion of LTFU patients is 19.1% of the total 796 patients registered between 2010–2013 and 40.53% of the poor outcomes (death, LTFU, switched to XDR). Proportion of LTFU among males (32.9%) is higher than in females (29.6%). 19.5% of the below poverty line and 23.1% of patients residing in tribal areas were LTFU. Factors associated with LTFU are: adverse drug reactions (ADR) in Intensive Phase (IP) and Continuation Phase (CP); change in DOT provider in IP and CP, hospitalizations in CP [ $p < 0.05$ ]. There was significant difference in the actions for retrieval that were taken by the DOT provider from the program as compared to health department in IP ( $p < 0.03$ ) and in CP ( $p < 0.01$ ). Maximum likelihood estimation for LTFU due to ADR in CP is 7.37. Multivariate analysis shows that treatment initiation at the district instead of the DRTB site was a risk factor (AOR 5.69 CI 2.08–15.5). Short current duration of treatment (AOR 0.996, CI 0.994–0.997), continuation phase (AOR 0.23, CI 0.09–0.54) and lesser duration of previous treatment (AOR 0.93, CI 0.86–0.99) prevented loss to follow up. The time to event survival analysis is shown in the figure.

**Conclusion:** Adverse drug reactions and DOT provider based factors are associated with LTFU. Improving training of DOT providers and proper counselling and aggressive management of ADR may help reduce LTFU.

#### OPP-454-01 Treatment outcomes of MDR-/XDR-TB and efficiency of resection surgery among patients with risk factors of unfavorable outcomes

Y Batyrshina,<sup>1</sup> T Petrenko.<sup>1</sup> <sup>1</sup>Microbiology, Novosibirsk TB Research Institute, Novosibirsk, Russian Federation. Fax: (+383) 203-83-62. e-mail: batirshina@inbox.ru

**Background:** High prevalence of MDR-TB in Novosibirsk Oblast (NO) (Russian Federation) - 55,8 on 100000 population in 2013 - requires for search of optimal treatment methods for these patients.

**Objectives** of the study were evaluation outcomes of treatment patients with MDR-TB in NO, determination of risk factors (RF) of unfavorable outcomes and impact of resection surgery (RS) on outcomes.

**Methods:** Retrospective cohort study. The sample included 476 patients (69,1% male, 30,9% female, middle age 35,8 (SD 12,9) years) with newly diagnosed MDR-TB, residents of NO in 2003–2010. Initial drug resistance was MDR 68,7%, pre-XDR 29,6%, XDR 1,7%. Outcomes were defined after completed treatment course as a cure (culture conversion, elimination cavity) and unfavorable (failure, death) with follow-up of 1–6 years in 294 patients. Collected clinical and socio-

demographic patients' data were evaluated for potential RF of unfavorable outcomes by odds ratio (OR) with 95%CI calculation. Additionally use of RS among patients with identified RF was evaluated by same method.

**Results:** 342(71,8%) patients were cured, 26(5,5%) died during treatment and 108(22,7%) had treatment failure. Relapses occurred in 15 of 185 cured (9,6%), 18 of 109 patients with treatment failure (16,5%) died during follow-up time. RF of unfavorable outcomes were: treatment interruptions (OR 7,3(4,6–11,8),  $p < 0,0001$ ), noncompliance with national standards of anti-TB chemotherapy (OR 2,2(1,4–3,4),  $p = 0,001$ ), smear-positivity (OR 3,14(2,01–4,88),  $p < 0,0001$ ), presence of cavity(s) (OR 10,0(2,39–41,9),  $p = 0,002$ ), pulmonary lesions > 2 segments (OR 6,8(3,9–11,9),  $p < 0,0001$ ), pre-XDR (OR 1,9(1,3–2,9),  $p = 0,002$ ), alcoholism or/and drug addiction (OR 4,8(3,1–7,5),  $p < 0,0001$ ), TB-pre-treatment history > 3 months (OR 2,0(1,3–3,1),  $p = 0,002$ ), imprisonment history (OR 2,2(1,3–3,6),  $p = 0,003$ ), low income (OR 3,4(2,1–5,5),  $p < 0,0001$ ), rural residence (OR 2,0(1,3–3,7),  $p = 0,0008$ ). Surgical resections were performed in 96(20,2%) patients. Outcomes among patients with RS and without one were: cure 91,7% vs 66,8%, treatment failure 7,3% vs 26,6%, death 1,1% vs 6,6%,  $p < 0,0001(\chi^2)$ . Table demonstrates risk decrease of unfavorable outcomes in patients with these RF due to RS. Percentage of relapses during follow-up time was 8,8 in patients with RS and 7,3 without one,  $p = 0,967(\chi^2)$ .

**Conclusions:** Use of RS in the MDR/XDR TB-treatment may improve treatment results especially in patients with RF of unfavorable outcomes.

#### OPP-455-01 Prevalence and risk factors for multidrug-resistant tuberculosis in Catalonia, Spain

A Rodes Monegal,<sup>1</sup> N Follia,<sup>1</sup> & Orcau Palau,<sup>2</sup> I Barrabeig,<sup>1</sup> L Clotet,<sup>1</sup> M Jané,<sup>1</sup> J Alvarez,<sup>1</sup> P Godoy.<sup>1</sup>

<sup>1</sup>Catalan Public Health Agency, Catalan Health Department, Barcelona, <sup>2</sup>Barcelona Public Health Agency, Barcelona City Hall, Barcelona, Spain. Fax: (+34) 9355 17506. e-mail: anna.odes@gencat.cat

**Background:** Multidrug-resistant tuberculosis (MDR-TB) has become a serious problem in the WHO European Region and its increasing prevalence represents a global public health emergency. Although TB incidence in Catalonia is moderate, 16,2 cases per 100.000 population in 2012, the prevalence and risk factors for MDR-TB are not well known. The purpose of this study is to assess the prevalence of MDR-TB and its determinants in Catalonia using its surveillance system.

**Design/Methods:** Retrospective cohort of TB cases reported to the TB control program from 2006 to 2012. MDR-TB was defined as resistance to at least both rifampicin and isoniazid of the first isolate. A multivariable logistic approach was used to assess predictors of MDR-TB, calculating the odds ratios (OR) and its 95% confidence intervals (CI).



**Results:** During the study period, 10,368 TB cases were reported, 6,631 of them were cultured confirmed with drug susceptibility testing (DST) results available (64%). Among all isolates, 91 (1.4%) were MDR (1% among isolates from new cases and 7.1% among retreated cases). 61.5% of MDR-TB cases were men, 79.1% in the 15–44 age group, 76, 9% foreign-born, 8% never treated cases, 15,4% HIV infected and 14,3% injecting drug users (IDU). After controlling for age, sex and HIV infection, risk factors independently associated with MDR-TB included: previous TB treatment (OR: 8.32, CI: 5.22–13.24), being born in Eastern Europe (OR: 6.96, CI: 3.28–14.76), Latin America (OR 3.81, CI: 1.83–7.94), Sub-Saharan -Africa (OR 3.69, CI: 1.38–9.84) or Asia (OR 3.60, CI: 1.53–8.49) and being IDU (OR 4.59, CI: 1.90–11.11).

**Conclusion:** In Catalonia, MDR-TB prevalence remains low, probably a reflection of the generally good management of patients with TB. Previous treatment was the strongest determinant of MDR-TB, and a detailed study of the reasons for inadequate treatment, especially in immigrants from TB high-burden countries could improve control strategies. Surveillance data on resistance to drugs is a cornerstone of any TB control program since they are needed to track the effectiveness of prevention and control activities.

#### OPP-456-01 Emergence of drug resistance following introduction of novel first-line TB treatment regimens: a modeling analysis

M Fofana,<sup>1</sup> S Shrestha,<sup>1</sup> G Knight,<sup>2</sup> T Cohen,<sup>3</sup> F Cobelens,<sup>4</sup> R White,<sup>2</sup> D Dowdy.<sup>1</sup> <sup>1</sup>Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA; <sup>2</sup>Centre for Mathematical Modelling of Infectious Disease, London School of Hygiene and Tropical Medicine, London, UK; <sup>3</sup>Division of Global Health Equity, Brigham and Women's Hospital, Boston, MA, USA; <sup>4</sup>Amsterdam Institute for Global Health and Development, Amsterdam Medical Center, Amsterdam, Netherlands.  
e-mail: mariam.fofana@gmail.com

**Background:** For the first time in decades, new first-line regimens for active TB treatment are in development. The inclusion of fluoroquinolones in these regimens raises concerns for future drug resistance, especially “pre-XDR” TB strains resistant to isoniazid, rifampin, and fluoroquinolones, with implications for the development and deployment of future TB treatments and drug sensitivity assays.

**Methods:** Using a dynamic compartmental model, we projected possible trajectories of TB transmission and drug resistance from 2014 to 2034. We used fixed parameters for model inputs relating to the natural history of TB, and randomly sampled inputs for parameters that are highly relevant to TB drug resistance but for which data are unavailable or of poor quality (probability of acquiring drug resistance during treatment, relative transmission fitness of drug-resistant strains, and treatment outcomes for drug-resistant strains compared to drug-sensitive TB). We analyzed the most significant driving factors for the prevalence of “pre-

XDR” TB 20 years after the introduction of a fluoroquinolone-based first-line regimen using multivariable linear regression.

**Results:** Out of 5,000 trajectories, 84 were consistent with current epidemiologic data on TB incidence, prevalence and drug resistance. Although all trajectories had a prevalence of “pre-XDR” TB in 2013 that was between 0.3% and 1.6% of all incident TB, the proportion of “pre-XDR” among all TB cases by 2034 varied widely, from 0.5% to 51% (median 2.3%). Among retreatment cases, the proportion of “pre-XDR” ranged from 2% to 80% (median 9%). In comparing trajectories with high levels of pre-XDR to those with slow pre-XDR emergence, the most important predictors were the transmission fitness and the treatment outcomes for drug-resistant TB relative to drug-susceptible TB. The rate of acquiring drug resistance while on treatment was less important.

**Conclusions:** Current data are insufficient to predict the trajectory of *M. tuberculosis* drug resistance following introduction of a new fluoroquinolone-containing first-line regimen. Within 20 years of launch, it is possible that pre-XDR TB could account for anywhere from 0.5% to 50% of all TB – and each trajectory is consistent with existing data. To better predict the future of emerging drug-resistant TB, more data is needed on relative transmission fitness and treatment outcomes among people with drug-resistant TB.

#### OPP-457-01 Strategy for reducing hearing loss in patients on drug-resistant TB therapy, Namibia

E Sagwa,<sup>1</sup> N Ruswa,<sup>2</sup> E Muundjua,<sup>3</sup> R Jacobs,<sup>4</sup> J-P Musasa,<sup>3</sup> A Shaker.<sup>3</sup> <sup>1</sup>Pharmacoepidemiology & Clinical Pharmacology, Utrecht Institute for Pharmaceutical Sciences, Utrecht, Netherlands; <sup>2</sup>National Tuberculosis & Leprosy Programme, Ministry of Health & Social Services, Windhoek, <sup>3</sup>Erongo Region, Ministry of Health & Social Services, Walvis Bay, <sup>4</sup>ENT, Windhoek Central Hospital, Ministry of Health & Social Services, Windhoek, Namibia. Fax: (+264) 220361.  
e-mail: esagwa@yahoo.com

**Background:** Namibia has a high per capita burden of drug-resistant (DR) TB, with 307 cases started on treatment in 2013. Erongo region ranks 5<sup>th</sup> in the country, with 49 cases reported in 2013. DR-TB therapy includes administration of an injectable aminoglycoside (amikacin, kanamycin) or capreomycin, which are known to cause hearing loss. In 2008, Namibia changed from amikacin to kanamycin as the preferred aminoglycoside and introduced capreomycin as an option. From 2007, Erongo region commenced the systematic audiometric monitoring of patients on DR-TB therapy for early detection of hearing loss and early intervention. Our aim was to determine the effect of this strategy on the incidence of hearing loss in Erongo.

**Design/Methods:** We reviewed records of patients treated for DR-TB in Erongo from June 2004 to March 2014. The patients were assessed using pure tone audiometry at baseline and every 3 months until completion of DR-TB treatment. Patients who had

completed treatment before 2008 had audiometry performed in 2008. Descriptive statistics, including incidence of hearing loss by year of treatment initiation, were calculated.

**Results:** A total of 175 records were retrieved, with a male: female ratio of 61:39. All patients had no documented pre-treatment hearing impairment. Baseline age and weight were  $35.7 \pm 10.8$  years and  $52.3 \pm 12.0$  kilograms respectively. 48 (27%) of the patients had been exposed to amikacin, while 100 (57%) had been on kanamycin. Capreomycin exposure accounted for 9 (5%) of the cases, while 18 (10%) records did not have documentation of the injectable drug used. The incidence of audiometrically confirmed hearing loss (all grades) declined from 88 cases/100 in 2004–2007; to 23 cases/100 in 2011 and 40 cases/100 in 2013 (Figure1). Switching from amikacin-based standard regimen to kanamycin based one was associated with a 51% drop in risk of hearing loss ( $p < 0.001$ ), while simple introduction of quarterly audiometry also drastically reduced hearing loss ( $RR = 0.4$ ,  $p < 0.001$ ).

**Conclusion:** Switching from amikacin to kanamycin, coupled with intensified audiometric monitoring of DR-TB patients resulted in a marked decline in the incidence of hearing loss. This was probably due to early audiometric detection of hearing loss and the follow-up intervention. This strategy should be scaled-up to the rest of Namibia. Also, DR-TB treatment programs should invest in resources and skills for routine audiometric monitoring.

#### **OPP-458-01 Sputum culture conversion and treatment outcomes in patients with XDR-TB in two provinces in South Africa**

M Van Der Walt,<sup>1</sup> C Kvasnovsky.<sup>1,2,3</sup> <sup>1</sup>Office of Tuberculosis Research, Medical Research Council of South Africa, Pretoria, South Africa; <sup>2</sup>Department of Surgery, University of Maryland Medical Center, Baltimore, MD, USA; <sup>3</sup>Department of Colorectal Surgery, King's College Hospital, London, UK. e-mail: ckvasno@gmail.com

**Background:** We set out to examine sputum culture conversion and treatment outcomes for patients with XDR TB in an area of high HIV prevalence.

**Methods:** A retrospective cohort of patients initiating treatment for XDR TB in Eastern Cape (EC: 10/06-6/08) and KwaZulu-Natal Provinces (KZN: 10/06-1/08). Patients who had 2 consecutive negative sputum cultures taken at least 30 days apart after treatment initiation were considered to have achieved culture conversion. We compared first-time culture conversion at different time points. We assigned treatment outcomes after 2 years treatment using standard definitions: patients who were cured or completed treatment were considered to have favorable outcomes, while those who died, defaulted, or failed treatment were considered to have unfavorable outcomes.

**Results:** Overall, 344 adult patients initiated XDR TB treatment (220 patients from EC and 124 patients from KZN). In total, 230 patients (63.0%) were HIV-positive at treatment start, with 112 patients (50.9%) on ARVs at

treatment start. After 2 years of treatment, 39 patients (10.1%) met the definition for cure and an additional 13 patients (3.4%) met the definition for treatment completion, such that 13.5% of patients had a favorable treatment outcome. An additional 61 patients (15.8%) were alive but failing treatment after two years. In total, 221 patients (57.4%) died and 30 patients (7.8%) defaulted treatment. A total of 70/344 patients (20.3%) achieved culture conversion during the study period, 43 within 4 months of treatment start (55.8%) and 57 within 6 months of treatment start (74.0%). Sputum culture conversion within the first 6 months of treatment had a 44.6% positive predictive value for favorable treatment outcome (sensitivity 73.5% and specificity 89.5%, Figure). The negative predictive value for patients who had not converted to negative sputum culture within 6 months of treatment was 96.7%.

**Conclusions:** Sputum culture conversion within 6 months of XDR TB treatment start was predictive of a favorable treatment outcome, but overall outcomes were poor. These results would support lengthening the intensive phase of XDR TB treatment to improve overall outcomes, even in those patients who achieved culture conversion. Further analysis will focus on predictors of early and late sputum conversion, as well as overall treatment outcome.

#### **OPP-459-01 Treatment outcomes and time to sputum smear and culture conversion for extensively drug-resistant tuberculosis patients in Latvia, 2000–2010**

L Levanovica,<sup>1,2</sup> L Kuksa,<sup>1,2</sup> V Riekstina.<sup>1</sup> <sup>1</sup>MDR TB, Riga East University Hospital; Centre of Tuberculosis and Lung Diseases, Riga, <sup>2</sup>Faculty of Continuing Education, Riga Stradins University, Riga, Latvia. Fax: (+371) 670 48256. e-mail: liga.kuksa@aslimnica.lv

**Background:** By systematically addressing program deficiencies, Latvia reduced the number of multidrug-resistant tuberculosis (MDR-TB) from 332 cases in 1997 to 110 cases in 2012. However the control of MDR-TB remains challenging due to growing proportion of extensively drug-resistant tuberculosis (XDR-TB) 5% in 2003 to 18% in 2013. During last 10 years NTP introduced new diagnostics and ensured access to additional medications such as newer generation fluoroquinolones and linezolid and participated in novel medication clinical trials. The aim of this study was to analyze treatment outcomes, time to sputum smear (SS) and culture conversion (SC) and treatment duration for XDR-TB patients in Latvia.

**Design/Methods:** Retrospective cohort analysis of all patients who began individualized XDR-TB treatment between January 1, 2000 and December 31, 2010. Data from the Latvian national TB registry and patient's medical records were analyzed. IBM SPSS Statistics version 20.0 was used for statistical analysis.

**Results:** 130 pulmonary XDR TB patients started individualized treatment: out of them 66 (51%) were cured, 39 (30%) failed, 17 (13%) defaulted and 8 (6%)

died. In the first 4 years cure rate was below 50 %. Starting from 2004 the percentage of cure was between 50 and 73. Average duration of treatment for cured patients was 643 days (Median 608). In patients who initially were SC positive (49 patients) treatment duration was 692 days (Me=644), among them were SS positive patients (33 patients) whose treatment duration was 732 days (Me=700). SS conversion time was 157 days (Me=93), SC time was 191 days (Me=125). Treatment duration in cured patients declined steadily from 1006 days in 2000 to 582 in 2010 and correlate positively and strongly with SC time ( $r<0.8$ ). (Figure 1.) **Conclusion:** Patients with SS positive in the beginning of treatment has to follow infection control measures for almost 5 months and have longer treatment duration than SS negative patients. Although XDR-TB cases shows increase there is stable decrease in treatment duration. SC conversion time and percentage of cure in last years were between 50 and 73 percent. To improve cure rate and reduce spread of XDR-TB we need to enforce early case detection, develop more reliable sensitivity testing for 2nd line medications, ensure infection control measures and introduce new treatment regimens for M/XDR TB.

## 07. DEVELOPING NEW REGIMENS FOR TREATING MDR-TB

### OPP-460-01 Patient follow-up under the nine month MDR-TB regimen in Burundi

M Sawadogo,<sup>1</sup> F Ciza,<sup>2</sup> T Ndikumana,<sup>2</sup> G Kamamfu,<sup>3</sup> E Declercq.<sup>1</sup> <sup>1</sup>Health, Damien Foundation, Brussels, Belgium; <sup>2</sup>Ministry of Health, National Tuberculosis Control Programme, Bujumbura, <sup>3</sup>Centre Hospitalier Universitaire de kamege, University of Burundi, Bujumbura, Burundi. Fax: (+257) 22.21.85.85. e-mail: sawadgom@yahoo.fr

**Background:** Burundi is one of the nine African countries involved in the assessment of the efficiency and tolerance of a short 9 months regimen for multi-Drug resistant tuberculosis (MDR/TB) treatment. Before, a 12 or 15 months regimen with an ambulatory follow-up was applied. The short 9 months regimen began from May 2013; about thirty patients had already been enrolled from several tuberculosis treatment facilities of the country. All patients are hospitalized for the whole course of treatment in the National Reference Center for MDR/TB in Kibumbu, at 75km from Bujumbura and having served as a Regional Anti-Tuberculosis Center since 1953. This center has been chosen in 2009 to serve as a National Reference Center to treat all MDR/ TB cases. The objective is to show the results of the patients' follow-up under a short 9 months regimen to treat MDR/ TB patients in Burundi.

**Design/Methods:** A multicentric survey is in progress in 9 francophone African countries since May 2013 aiming to measure the efficiency of a 9 months regimen for multi-drug resistant patients based on Moxifloxacin (4KmMfxPtoHCfzEZ/5MfxCfzEZ).

**Results:** 31 patients have already been received for hospitalization since May 2013 in the National Reference Center for MDR/TB and among them, 29 cases have been enrolled under the 9 months regimen and 2 cases, a 12 months regimen: 16 cases of failure category 1, 13 cases of failure category 2 and 02 cases of MDR/TB relapse. 29 cases have been confirmed and 21 of them by Gene-Xpert. The HIV status had been screened: 13 seropositive cases are under ART and Cotrimoxazole preventive therapy (41, 9%) and 18 cases are negative (58, 1%). About the patients' origin, 77, 4% of them are coming from Bujumbura and its area. The follow up shows good results and 50% of patients had smears conversion from positive smears to negative at the first month of treatment, 83, 3% at the second month and 85, 7% at the third month of treatment. Secondary effects during the treatment are few: 2 cases of hypoacusis, 14 cases type of nausea, vomiting, epigastralgia, especially in the first month of treatment and 2 cases of cutaneous pruritus.

**Conclusion:** A 9 months regimen for multi-drug resistant patients based on Moxifloxacin (4KmMfxPtoHCfzEZ/5MfxCfzEZ) seems to have good preliminary results based on smear conversion at the intensive phase and secondary effect. It remains necessary to ensure a suitable follow-up until the end of the treatment and surveillance.

### OPP-461-01 Multidrug-resistant tuberculosis in Myanmar: results of the third nationwide drug resistant survey (2012–2013)

ST Aung,<sup>1</sup> T Lwin,<sup>2</sup> WW Nyunt,<sup>3</sup> TL Swe,<sup>4</sup> AA Thwe,<sup>5</sup> D Ti Ti.<sup>6</sup> <sup>1</sup>Department of Health, National TB Programme, Nay Pyi Taw, <sup>2</sup>Department of Health, Disease Control, Nay Pyi Taw, <sup>3</sup>National TB Programme, National TB Reference Laboratory, Yangon, <sup>4</sup>National TB Programme, Upper Myanmar TB Reference Laboratory, Mandalay, <sup>5</sup>Department of Health, National TB Programme, Nay Pyi Taw, <sup>6</sup>Expand TB Project, Foundation for Innovative New Diagnostics, Yangon, Myanmar. Fax: (+95) 67-421201. e-mail: mywaddy@gmail.com

**Background:** Myanmar is one of the (27) high Multi-drug-resistant tuberculosis (MDR-TB) burden countries and MDR-TB is a major threat to TB control in Myanmar and globally. Two previous nationwide drug resistance surveys revealed that the proportion of MDR-TB among new and previously treated TB patients was 4.0 and 15.5% in 2002–2003, and 4.2% and 10.0% in 2007–2008. The third nationwide survey was conducted in 2012–2013 to obtain updated information on the magnitude of MDR-TB, determine trends in MDR-TB epidemiology and explore MDR-TB risk factors.

**Design/Methods:** Sputum samples were collected from a nationally representative sample of new sputum smear-positive TB patients registered at public health centers from October 2012 to December 2013 using a weighted cluster sampling method. At the same sample collecting period, the previously treated enrolled at the same health centers were collected. Culture and drug susceptibility testing to first-line anti-TB drugs were performed at the



national TB reference laboratories in Mandalay and Yangon.

#### Patterns of resistance to first-line anti-TB drugs

Drug-resistance pattern	No. (% [95% CI])		
	New (n = 1,103)	Previously treated (n = 58)	Total (n = 1,161)
Susceptible to all drugs			
Any drug resistance			
- Any resistance to H	8.3 (6.4–10.8)	32.8 (21.0–46.3)	9.5 (7.4–12.0)
- Any resistance to R	4.8 (3.3–7.0)	27.6 (16.7–40.9)	5.9 (4.2–8.3)
- Any resistance to E	2.5 (1.7–3.7)	10.3 (3.9–21.2)	2.9 (2.0–4.2)
- Any resistance to S	8.5 (6.7–10.7)	31.1 (19.5–44.5)	9.7 (7.8–12.1)
Total any drug resistance	10.7 (8.5–13.3)	37.9 (25.5–51.6)	12.1 (9.9–14.8)
Mono drug resistance			
- Mono resistance to H	0.1 (0.0–2.0)	1.7 (0.0–9.2)	1.0 (0.5–2.1)
- Mono resistance to R	0	0	0
- Mono resistance to E	0	0	0
- Mono resistance to S	2.1 (1.3–3.3)	5.2 (1.1–14.4)	2.4 (1.4–3.9)
Total mono drug resistance	3.0 (2.0–4.5)	6.9 (1.9–16.7)	3.4 (2.2–5.1)
Multi drug resistance			
- HR	0.7 (0.3–1.6)	3.4 (0.4–11.9)	0.8 (0.4–1.7)
- HRE	0.2 (0.0–0.7)	0	0.2 (0.0–0.6)
- HRS	2.3 (1.4–3.6)	15.5 (7.3–27.4)	2.9 (1.8–4.5)
- HRES	1.6 (1.0–2.6)	8.6 (2.9–19.0)	2.0 (1.3–3.0)
Total multi drug resistance	5.0 (3.1–6.8)	27.1 (15.0–39.2)	6.1 (4.1–8.0)
Polydrug resistance			
- HE	0.4 (0.1–1.0)	1.7 (0.0–9.2)	0.4 (0.2–1.0)
- HS	2.1 (1.3–3.3)	1.7 (0.0–9.2)	2.1 (1.3–3.2)
- ES	0.2 (0.0–0.8)	0	0.2 (0.0–0.7)
- HES	0.2 (0.0–0.7)	0	0.2 (0.0–0.7)
- RE	0	0	0
- RS	0.1 (0.0–0.8)	0	0.1 (0.0–0.8)
- RES	0	0	0
Total polydrug resistance	2.9 (1.9–4.4)	3.4 (0.74–11.9)	2.9 (2.0–4.3)

**Results:** A total of 1,510 sputum smear-positive cases were enrolled from 30 clusters. Complete results were available for 1,161 (77.7%) patients following removal of mycobacteria other than tuberculosis (15 samples), culture contamination (187 samples) and no culture growth (147 samples). After imputation of missing values, MDR-TB was detected in 5.0% (95% CI 3.1–6.8) of new TB cases and 27.1% (95% CI 15.0–39.2) of retreatment cases. MDR-TB was significantly associated with previous TB treatment (adjusted OR 6.9, 95% CI 3.1–15.0), living in Yangon Region (adjusted OR 3.0, 95% CI 1.5–5.8) and HIV positive status (adjusted OR

4.2, 95% CI 0.9–19.4). Although MDR-TB among previously treated TB patients was 27.1%, it needs careful interpretation, since the sample size was not representative.

**Conclusion:** The third nationwide drug resistance survey (2012–2013) in Myanmar reveals the highest MDR-TB rates in the South East Asian Region. Efforts to diagnose, treat and prevent the spread of MDR-TB are to be urgently scaled-up, particularly in Yangon Region. MDR-TB patients found in this survey were planned to be enrolled in existing programmatic management of MDR-TB for treatment with approval of national expert MDR-TB committee.

#### OPP-462-01 Multidrug-resistant tuberculosis among persons born in the former Soviet Union living in the United States, 1993–2012

J Ershova,<sup>1</sup> P Moonan,<sup>1</sup> E Kurbatova,<sup>1</sup> P Cegielski.<sup>1</sup>

<sup>1</sup>DTBE, U.S. Centers for Disease Control and Prevention, Atlanta, GA, USA. Fax: (+1) 404 639 1566.  
e-mail: jhe3@cdc.gov

**Background:** Since 2001, more than 50% of tuberculosis (TB) cases reported in the United States occurred among foreign-born persons. Countries in Eastern Europe and Central Asia that emerged from the former Soviet Union (FSU) republics have the highest prevalence of multidrug-resistant tuberculosis (MDR-TB) in the world. Reported TB cases in the U.S. among persons born in the FSU may have higher rates of MDR-TB as compared to other foreign-born and U.S.-born TB cases. The objectives of our study were to assess and compare the rates and trends of MDR-TB among TB cases from the FSU, United States and other countries reported in the United States National TB Surveillance System.

**Design/Methods:** We analyzed data from all culture-positive pulmonary TB cases reported in the United States during 1993–2012. MDR-TB was defined as resistance to at least isoniazid and rifampicin on the initial isolate collected. Cases with missing data on country of birth or born as U.S. citizens outside of the United States were excluded from analysis. We used chi-square tests to detect differences in proportions and assess trends in MDR-TB rates.

**Results:** Of 212,783 eligible TB cases reported, 3,256 (1.5%) had MDR-TB. The proportion of MDR-TB was 7.4% (90/1,210) in cases among persons born in the FSU as compared to 2.0% (1,879/94,263) and 1.1% (1,287/117,310) in cases among persons born in other countries and in the United States, respectively ( $p < 0.0001$ ). The proportion of MDR-TB among persons with TB born in the FSU significantly increased from 2.1% in 1993 to 18.8% in 2012 ( $p < 0.0001$ ); this trend consistently decreased from 3.2% to 1.5% ( $p < 0.0001$ ) among persons born in other countries and from 2.6% to 0.5% ( $p < 0.0001$ ) among those born in the United States (Figure).

**Conclusion:** The proportion of MDR-TB was significantly higher in reported TB cases in the U.S. among persons born in the FSU than other foreign countries and

the U.S. The proportion of MDR-TB increased 9 fold among TB cases from the FSU during the study period. Providers should consider rapid drug-susceptibility testing of persons with TB born in the FSU before selecting treatment regimens.

#### **OPP-463-01 Evaluation of sputum culture conversion as a prognostic marker for end-of-treatment outcome in patients with multidrug-resistant tuberculosis**

E Kurbatova,<sup>1</sup> P Cegielski,<sup>1</sup> and Global Petts

Investigators and Dots-plus Pilot Projects Case-based.

<sup>1</sup>Division of TB Elimination, CDC, Atlanta, GA, USA. Fax: (+1) 404-639-1566. e-mail: ies3@cdc.gov

**Background:** The objective of this analysis was to examine the validity of sputum culture conversion (SCC) and time to culture conversion as prognostic markers for treatment outcome in MDR TB patients. To the extent that SCC is a valid prognostic marker, the secondary objective was to identify optimum time points at which SCC can be considered a marker for outcome.

**Methods:** Data on 2,043 MDR TB patients from two large cohort studies, the prospective "Preserving Effective TB Treatment Study" (PETTS), 2005–2008, and the retrospective "DOTS-Plus Pilot Projects Case-Based Study," 2000–2003, were analyzed. Measures of association were determined using random effects multivariable logistic regression estimated via the penalized quasi-likelihood method. Predictive values were calculated using a bivariate random-effects linear mixed model. Time to event was analyzed using survival techniques.

**Results:** Among MDR TB patients, time to culture conversion and SCC at 6 months were significantly associated with end-of-treatment outcomes. SCC at 2 months was significantly associated with end-of-treatment outcomes among patients without known HIV infection. The overall association of SCC with treatment outcome was substantially stronger at 6 months (aOR=14.07) than at 2 months (HIV-negative patients: aOR=4.12; HIV unknown: aOR=3.59, HIV-positive: aOR=0.38). The 2-month definition of culture conversion had low sensitivity (27%) and high specificity (90%) for predicting treatment success compared to failure or death, while the sensitivity of 6-month SCC definition was high (92%), but specificity was moderate (58%). The maximum combined sensitivity and specificity was reached for SCC status assessed between the 6<sup>th</sup> and 10<sup>th</sup> month of treatment. Predictive values of 2-month and 6-month SCC had high variability geographically and across levels of individual patient characteristics. Given approximately 60% prevalence of successful outcome reported in cohorts of MDR TB patients, PPVs were relatively high: 80% for 2-month SCC and 77% for 6-month SCC.

**Conclusion:** Time to SCC on solid media, SCC at 6 months, and SCC at 2 months among patients without known HIV infection can be considered as valid proxy markers of end-of-treatment outcome in MDR TB patients, but the overall association with outcome is

substantially stronger for 6-month compared to 2-month SCC. These results will have implications on the choice of the surrogate end-point in phase IIb clinical trials on MDR TB.

#### **OPP-464-01 Salvage regimen containing meropenem plus clavulanic acid for extensive pulmonary XDR-/pre-XDR-TB: a case-series of 16 patients**

M-C Payen,<sup>1</sup> S Callens,<sup>2</sup> G Groenen,<sup>3</sup>

O De Arazolla Wouter,<sup>4</sup> F Mouchet,<sup>5</sup> I Muylle,<sup>6</sup>

n Clumeck,<sup>1</sup> S De Wit.<sup>1</sup> <sup>1</sup>Infectious Diseases, CHU

Saint-Pierre, Brussels, <sup>2</sup>Infectious diseases, UZ Gent, Gent,

Belgium, <sup>3</sup>Coordination, BeltaTB Net, Brussels, <sup>4</sup>Medical

Direction, Vlaamse vereniging voor respiratoire

gezondheidszorg and tuberculosebestrijding, Brussels,

<sup>5</sup>Paediatrics, CHU Saint-Pierre, Brussels, <sup>6</sup>Pneumology, CHU

Saint-Pierre, Brussels, Belgium. Fax: (+32) 2 535 32 50.

e-mail: christine\_payen@stpierre-bru.be

**Background:** Multidrug-resistant tuberculosis (MDR-TB) underlines the need for new therapeutic options. As new and effective drugs are scarce, the potential antimycobacterial activity of established drugs, e.g. carbapenems, is explored. Several studies have shown the combination carbapenems plus clavulanic acid has a potent bactericidal activity in vitro against drug-susceptible as well as extensively drug-resistant (XDR)-TB strains. Carbapenems mechanism of action against *M.tuberculosis* through inactivation of L, D transpeptidases confirms potential efficacy. In Belgium, regimens containing Meropenem/Clavulanic acid (MRP/CLAV) were used since 2009 for pre-XDR/XDR-TB patients.

**Design/Methods:** Retrospective analysis of MDR-TB treated with MRP/CLAV during the period 2009–2013. Data are collected by the BELTA-TB Net project which provides treatment for free to all MDR-TB patients in Belgium.

**Results:** Sixteen cases were included: 13 XDR-TB and 3 pre-XDR-TB. All are asylum seekers from the former Soviet Union (9 males, 7 females, 15 to 46 years old) and presented with extensive pulmonary disease. All but 2 were previously exposed to 2<sup>nd</sup> line drugs in their country of origin. Extensive resistance profile is illustrated in fig 1. Of the 13 XDR cases, 5 still showed susceptibility to capreomycin while one patient had linezolid resistance. Intra-venous MRP/CLAV (2g x 3/day during hospitalization and then 2g x 2/day during ambulatory phase) was used in association with available drugs based on drug susceptibility testing for the total treatment duration. One patient received bedaquiline. Patients were hospitalized until 3 consecutive negative sputum cultures were obtained and MRP/CLAV was administered by a dedicated nurse during ambulatory phase. Thirteen patients completed treatment, 1 case continues treatment, but sputum culture became negative. Two patients died (1 XDR case with linezolid resistance and 1 pre-XDR). Median time to sputum culture conversion was 52 days. Median total duration of MRP/CLAV was 21,7 months.

**Conclusion:** A successful treatment outcome is observed in 13 out of 16 pre-XDR/XDR-TB patients with a regimen including MRP/CLAV. One patient continues treatment and shows clinical improvement. The success rate (>80%) exceeds current XDR-TB cohorts (<50%). Given the extensive resistance profile of the strains (in particular the lack of potent known 2<sup>nd</sup> line drugs in 8 cases), we conclude that MRP/CLAV may prove to be a valuable addition for desperate cases.

#### OPP-465-01 Ofloxacin resistance among *Mycobacterium tuberculosis* isolates from retreatment cases at a tertiary care institute

J Arora,<sup>1</sup> A K Verma,<sup>1</sup> Gavi Kumar,<sup>1</sup> R Sarin,<sup>1</sup> V Myneedu.<sup>1</sup> <sup>1</sup>Microbiology, National Institute of Tuberculosis and Respiratory Diseases, New Delhi, India. e-mail: arojyoti@gmail.com

**Background:** The fluoroquinolones (FQ) are an important class of antibiotics and with the global emergence of multidrug resistant TB (MDR- TB), they are used in combination with other drugs for the clinical management of MDR TB patients. The pre exposure of this drug for other infectious diseases and its availability without prescription has resulted in acquisition of FQ resistance among *Mycobacterium tuberculosis* (*M. tuberculosis*) strains. The retrospective study was carried out to describe the occurrence of ofloxacin resistance among previously treated (failure/relapse/return after default) pulmonary TB patients at a reference hospital.

**Design/Methods:** We determined the prevalence of ofloxacin resistance among 1548 pulmonary *M. tuberculosis* complex isolates from retreatment patients whose samples were received for culture and DST between January 2011- December 2013. 991 (64.0%) patients were male and 557 (36%) were female with a male female ratio of 1.8: 1. The mean age of patients was 31 year. Drug susceptibility testing was performed by Mycobacterial growth indicator tube (MGIT) 960 liquid culture system (Becton Dickinson, Franklin Lakes, NJ, USA) in a BSL III lab at the following critical concentrations: streptomycin 1.0 µg/ml, isoniazid 0.1 µg/ml, rifampicin 1.0 µg/ml, ethambutol 5.0 µg/ml and ofloxacin.0 µg/2ml. The DST results were analyzed for ofloxacin resistance among isolates pan susceptible to four first line drugs and isolates with resistance to one or more drugs. The z-test for proportion (for comparing differences in proportions) was performed for statistical analysis.

**Results:** A total of 102 (6.6%) isolates were infected with *M. tuberculosis* strains susceptible to all four I line drugs of which 11(10.85%) were resistant to ofloxacin. Among isolates resistant to one or more first line drugs 66% (954/1446) were ofloxacin resistant. The resistance increased to 70.60% (879/1245) among MDR TB cases. When z test was applied p value was statistically significant among pan susceptible and resistant isolates (p<0.001). The present analysis shows alarming rate of ofloxacin resistance among previously treated TB patients 965/1548 (62.3%). The high frequency may be due to the fact that 1245/1548 (80.42%) of isolates were

MDR. Furthermore, since the hospital is a referral centre sampling bias cannot be ruled out.

**Conclusion:** There is a need to control the use of FQ and potential acquired FQ resistance during anti-TB therapy, especially in populations where MDR TB occurs. Addition of ofloxacin in the treatment regimen of MDR-TB patients without susceptibility testing would have less benefit and might increase the risk of XDR-TB development or render treatment ineffective. A simple and rapid method for detection of FQ is required to identify the pre XDR patients for their proper management.

#### OPP-466-01 Mutations in the GyrB Subunit of *M. tuberculosis* DNA gyrase: consequences on resistance to fluoroquinolones can be tricky to interpret

M Le Goff,<sup>1</sup> E Capton,<sup>1</sup> A Pantel,<sup>1</sup> V Jarlier,<sup>1</sup> C Mayer,<sup>2</sup> S Petrella,<sup>2</sup> A Aubry.<sup>1</sup> <sup>1</sup>NRC for mycobacteria, CIMI-Paris, U1135, UPMC, Paris, <sup>2</sup>Unité de Microbiologie Structurale, Pasteur Institute, Université Paris Diderot, Paris, France. Fax: (+33) 01 45 82 75 77. e-mail: alexandra.aubry@upmc.fr

**Background:** As a consequence of the use of fluoroquinolones (FQ) to treat multidrug-resistant tuberculosis (MDR-TB), resistance to FQ linked to mutations in DNA gyrase (GyrA2GyrB2) emerged leading to nearly untreatable extensively drug resistant TB (XDR-TB). Despite gyrA mutation are more common than gyrB mutations, the latter are more and more described. Our objective was to investigate whether various GyrB alterations described in *M. tuberculosis* strains occurring at a single amino-acid position (486 or 543) altered the quinolone susceptibility of *M. tuberculosis* DNA gyrase.

**Design/Methods:** Mutant GyrB proteins bearing mutations of interest were generated by site specific mutagenesis of GyrB alleles. *M. tuberculosis* wild type (WT) and mutant GyrA and GyrB subunits were overexpressed in *E. coli*, purified and used to reconstitute active gyrase complexes. Enzyme inhibition as well as MICs on clinical strains carrying mutations were studied for moxifloxacin (MXF), ofloxacin (OFX) and levofloxacin (LVX).

**Results:** Depending on the amino-acid substitutions, the impact of gyrB mutation at a same position varied from no impact on FQ-susceptibility (S486F, A543E) to a low level of resistance to FQ (S486F, A543T, A543V) when applying the WHO definition of FQ-resistance (i.e. MIC ≥ 2 mg/l). Furthermore, strains harbouring GyrB 543T mutation remain susceptible to MXF.

Mutations in GyrB	MIC/IC <sub>50</sub> <sup>a</sup> (MG/L)		
	OFX	LVX	MXF
WT	1/10	0.5/8	0.5/2
S486Y	2/32	1/28	1/8
S486F	1/12	0.5/13	0.25/2.5
A543E <sup>b</sup>	nd/20	nd/6	nd/2
A543T	2/36	1/13	0.25/1
A453V	2/20	1/32	1/6

<sup>a</sup>IC<sub>50</sub> is the drug concentration that inhibit DNA supercoiling by 50% and MIC is defined as the drug concentration at which the bacterial growth was reduced to <1% of the drug-free control <sup>b</sup>described by Ginsburg and coll (AAC, 2005)



**Conclusion:** These data showing that mutations occurring at a single residue can have various consequences on FQ-susceptibility are of high importance to (1) interpret molecular detection of resistance, (2) improve our molecular comprehension of the mechanisms of resistance to FQ which is an indispensable first step for developing a reliable molecular test for the detection of FQ resistance in *M. tuberculosis*.

#### OPP-467-01 Bedaquiline and clofazimine in a second-line regimen for tuberculosis in mice

T Gevers,<sup>1</sup> N Lounis,<sup>1</sup> K Andries.<sup>1</sup> <sup>1</sup>Antimicrobial Research, Janssen Research & Development, Beerse, Belgium.  
e-mail: kandries@its.jnj.com

**Background:** One of the shortcomings of the current standard for treating multidrug resistant tuberculosis (MDR-TB) with second-line drugs is its long duration. We wanted to study the sterilizing efficacy of shorter durations of combinations of bedaquiline with some key drugs used to treat MDR-TB (clofazimine, amikacin, pyrazinamide, moxifloxacin, and levofloxacin) in a mouse model of TB infection.

**Design/Methods:** 14 groups of 20 mice per group were infected intravenously with strain H37Rv of *Mycobacterium tuberculosis*. Two weeks after infection, treatment was started with various combinations of clofazimine (C, 20 mg/kg/day), amikacin (A, 150 mg/kg/day), levofloxacin (L, 300 mg/kg/day), moxifloxacin (M, 100 mg/kg/day), pyrazinamide (Z, 150 mg/kg/day) and bedaquiline (B, 25 mg/kg/day). Mice were treated 5 days a week for 4, 6 or 9 months, and then left untreated for an additional 3 months before they were sacrificed and investigated for the presence of bacilli in their lungs (relapse). Undiluted lung homogenates, and 10 and 100-fold dilutions were plated on 7H11 agar plates containing 0.4% charcoal (to prevent carry-over effects).

**Results:** Mice treated for only 4 months with BCL and BCMA were relapse-free 3 months after stopping treatment. Groups treated with BCA and BCLA had respectively 26% and 16% relapsers after 4 months, but none after 6 months of treatment. Groups treated with BLA, BZL and CLA had 28%, 17% and 5% relapsers respectively after 6 months of treatment. In groups treated with BCA and BCLA, BDQ resistant strains were isolated from three mice that received only 4 months of treatment, but no BDQ resistant strains were isolated from the groups that received 6 months of treatment with the same regimens. The BDQ resistant isolates had 3 to 10-fold increases in the MICs for both BDQ and clofazimine, compared to the MIC at baseline.

**Conclusion:** Drug combinations including both bedaquiline and clofazimine were able to cure mice in just 4 months. The observed selection of resistant strains from mice relapsing after only 4 month of combination treatment, and their apparent elimination by longer treatment, underscores the risk of resistance selection upon premature discontinuation of therapy in patients.

#### OPP-468-01 ABC-type efflux pumps polymorphisms and their potential implication in the resistance of *Mycobacterium tuberculosis* to levofloxacin

V Gómez,<sup>1,2</sup> A Nataly,<sup>1,2</sup> A Anderson,<sup>3</sup> J Robledo,<sup>1,2</sup> F Rouzard.<sup>1,4</sup> <sup>1</sup>Antioquia, Corporación para Investigaciones Biológicas (CIB), Medellín, <sup>2</sup>Antioquia, Escuela de Ciencias de la Salud, Universidad Pontificia Bolivariana (UPB), Medellín, <sup>3</sup>Antioquia, Programa de Estudio y Control de Enfermedades Tropicales (PECET), Universidad de Antioquia, Medellín, Colombia; <sup>4</sup>Montgomery, Equal Opportunity Life Sciences (EQUOLS), Rockville, MD, USA.  
e-mail: verogomez@cib.org.co

**Background:** Levofloxacin (LVX) is a fluoroquinolone (FQ) recommended by the WHO as a second line drug for the treatment of multidrug-resistant tuberculosis (MDR-TB). Poor adherence to prescribed regimen as well as the increased use of LVX in the treatment of a variety of bacterial infections including MDR-TB have led to the recent emergence of resistant isolates. The majority of FQ-resistant MDR-TB isolates are characterized by mutations in the *gyrA/B* genes coding for the DNA gyrase subunits. However, 15–60% of FQ-resistant MDR-TB isolates harbor no mutation in these genes suggesting that other mechanisms may be involved, one of them being an efflux pump system capable of extruding a broad range of molecules.

**Objective:** To evaluate the correlation between polymorphisms in 29 genes encoding ABC-type efflux pumps and the LVX-resistant phenotype of MDR-TB clinical isolates collected from pulmonary TB patients in Medellín, Colombia, between 2004 and 2009.

**Design/Methods:** 104 MDR-TB isolates were screened for LVX susceptibility by the proportion method. The minimum inhibitory concentration (MIC) was determined by the BACTEC MGIT 960 system. Sequencing was used to identify mutations in the *gyrA/B* genes among the totality of the MDR-TB isolates as well as to screen for polymorphisms in the 29 genes encoding the ABC-type efflux pumps.

**Results:** Of the 104 MDR-TB isolates, 3 (2.8%) were LVX-resistant. For those 3 isolates no mutation was found in the *gyrB* gene. Two isolates had mutations in *gyrA* (Asp94Gly and Ser91Pro) and displayed the highest MIC whilst one isolate had none. The 3 LVX-resistant isolates were further investigated and 29 genes coding for ABC-type efflux pumps were amplified and sequenced. Two of them, displayed non-synonymous polymorphisms in 8 genes encoding ABC-type efflux pumps (Rv0194c, Rv1217c, Rv1218c, Rv1272c, Rv1458c, Rv1463c, Rv1819c, and Rv2688c) when compared to LVX-sensitive MDR-TB isolates.

**Conclusion:** We hypothesize that non-synonymous polymorphisms in genes encoding ABC-type efflux pumps can modify LVX accessibility to the DNA gyrase. Further studies are necessary to understand the relationship between ABC-type efflux pumps polymorphisms and LVX action and MICs. Also, further investigations are needed to understand whether ABC-type efflux pumps polymorphisms alone can be responsible for LVX

resistance and/or if they act synergistically with gyrA mutations to increase LVX MICs.

#### OPP-469-01 Molecular analysis of isoniazid- and ethionamide-resistance in multidrug-resistant clinical isolates of *Mycobacterium tuberculosis*

R Johana,<sup>1,2</sup> T Realpe,<sup>1,2</sup> M Mejia,<sup>2</sup> J Robledo.<sup>1,2</sup>

<sup>1</sup>Antioquia, Corporación para Investigaciones Biológicas, Medellín, <sup>2</sup>Antioquia, Universidad Pontificia Bolivariana, Medellín, Colombia. Fax: (+57). e-mail: jrueda@cib.org.co

**Background:** Multidrug resistant-isolates of *Mycobacterium tuberculosis* (MDR-TB) have been described with a variable proportion of concomitant Ethionamide (ETH) resistant. It is important to determine whether resistance to Isoniazid (INH) and ETH is a cross or independent event in isolates from a specific area.

**Design/Methods:** we sequenced ethA, ethR, ndh, inhA promotor, inhA, katG and mshA genes in 30 MDR-TB isolates resistant to ETH, three MDR-TB isolates susceptible to ETH and four MTB isolates susceptible to INH and ETH. Drug susceptibility tests were done in a BACTEC MGIT 960® using low and high concentrations for INH and ETH. We also used the commercial kit GenoType® MTBDRplus version 1 to evaluate the presence of mutations in katG gene and inhA promotor.

**Results:** resistance to INH associated to mutations in katG and ndh was found in 100% of the 30 MDR-TB isolates that were resistant to ETH, in 93% resistant to ETH (ethA and mshA mutations), and in 43% cross-resistant to INH and ETH (inhA promotor and inhA mutations). We found resistance to INH in 100% of MDR-TB isolates susceptible to ETH (katG mutations), in 66% resistant to ETH (ethA and mshA mutations) and in 33% cross-resistant to INH y ETH (inhA mutations). Mutations in these genes were not found in four MTB isolates susceptible to INH and ETH. We found mutations not previously described in ethA (E36Q, T44A, C403W, F302S, M409I, L374R, and F157L), katG (I248M, V442G, W397Y and S652A) mshA (S352F and I460R) and ndh (N316K) genes. Concordance between phenotypic, sequencing and genotype test (for katG gene and inhA promotor) was 94.6%.

**Conclusion:** we found mutations not previously described in ethA, katG, mshA, and ndh genes. The high concordance between phenotypic and genotypic tests, as well as between sequencing results and the commercial kit, suggest that GenoType® may provide results to guide early anti-TB treatment. Special attention must be given to second line therapeutic schemes that includes ETH due to the frequent cross-resistance found between INH y ETH.

## 08. NON TUBERCULOSIS MYCOBACTERIA AND IDENTIFICATION

#### OPP-470-01 Incidence of pulmonary tuberculosis and non-tuberculous Mycobacteria (NTM) positive cultures in a cohort of 1419 patients with respiratory symptoms

M Ramos,<sup>1</sup> J Couto,<sup>1</sup> E Bensi,<sup>1</sup> P Panunto,<sup>1</sup> T Zaccariotto.<sup>1</sup>

<sup>1</sup>Internal Medicine, Faculdade de Ciencias Medicas/ UNICAMP, Campinas, SP, Brazil. e-mail: mramos1951@gmail.com

**Objective:** To determine the incidence of tuberculosis (TB), accuracy of smear microscopy, and frequency of NTM isolation in sputum samples in a cohort of patients with respiratory symptoms. Genotypic susceptibility against Rifampin and Isoniazid of *M. tuberculosis* (MTB) isolates was also determined. The investigation took place in a large general hospital in Campinas, SP, Brazil.

**Methods:** From 2008–2011, a cohort of 1419 patients attending to the Emergency Department and outpatient services from the “Hospital das Clínicas da UNICAMP”, SP, Brazil was investigated for pulmonary tuberculosis. 2345 sputum samples were submitted for staining and liquid culture. IS6110/hsp65-Multiplex/PCR was done to identify isolates to the complex level, and PRA-PCR to identify NTM species isolated. Genotypic susceptibility of MTB strains was determined using a line probe assay.

**Results:** 857 patients submitted one, 198 patients two, and 364 three sputum samples for examination. Mycobacterium was recovered from 104 patients (66 MTB strains and 32 NTMs). Based on culture results, the incidence of tuberculosis in this population was 4.7%. The smear positivity rate was 65% for the first sputum drawn%. For those who had two sputum samples examined, the combined sensitivity was 51.9%, and 66.7% for three sputum samples. Microscopic examination of the second and third sputum samples was negligible, one additional TB case was revealed after the microscopic examination of the second sputum drawn, and another after the third. MTB was isolated from 59 patients from the first sputum sample (89% of the total number of cases), and the remaining 7 TB patients from the second sputum sample. This confirms the contribution of liquid culture for the diagnosis of TB. 70% of smear negative TB/HIV co-infected patients, and 83% of non-HIV TB patients had positive MTB cultures in the first sputum sample submitted. Smear positivity rates for patients with an NTM was 12.5%. 17 NMTs species were identified, mostly *M. avium*, from 32 patients. In nine individuals an NTM was isolated from 2 or 3 sputum samples.

**Conclusion:** When liquid culture is performed, only one sputum sample examination is adequate for the diagnosis of most TB patients, anticipating the adequateness of Genomic point-of-care techniques performed in one sputum sample for the diagnosis of TB in patients with

respiratory symptoms. NTMs are often recovered in patients investigated for pulmonary TB in our setting.

#### OPP-471-01 Sputum AFB smear positivity in Singapore: pulmonary TB or NTM infection?

Y T Wang,<sup>1</sup> C Chee,<sup>1</sup> K M Kyi Win,<sup>1</sup> LKY Lim,<sup>1</sup> LH Sng,<sup>2</sup> R Jureen,<sup>3</sup> PL Ooi,<sup>4</sup> J Cutter.<sup>4</sup> <sup>1</sup>TB Control Unit, Tan Tock Seng Hospital, Singapore, <sup>2</sup>Central TB Laboratory, Singapore General Hospital, Singapore, <sup>3</sup>Microbiology, National University Hospital, Singapore, <sup>4</sup>Communicable Diseases Division, Ministry of Health, Singapore.  
e-mail: yee\_tang\_wang@ttsh.com.sg

The clinical and radiological presentation in Non-tuberculous mycobacterial (NTM) pulmonary infection may mimic that of pulmonary tuberculosis (PTB). In addition, sputum acid-fast bacillus (AFB) smears may be positive, prompting commencement of PTB treatment and notification to the public health authorities. TB notification is mandatory in Singapore. The national TB registry has access to all mycobacterial culture data nationally, and also captures all AFB smear data in the public hospitals. The aim of our study is to determine the proportion of sputum smear AFB positive cases which turn out to be NTM pulmonary infection instead of PTB and to compare the characteristics of these two groups using data extracted from the national TB registry. In Singapore, the annual incidence rate of TB is ~40/100,000. There were 2761 patients with positive sputum AFB smears and corresponding positive mycobacterial cultures in the three-year period 2009–2011. Of these, 2422 (88%) grew *Mycobacterium tuberculosis* Complex (MTC) and 339 (12%) grew NTM. Of the latter, 39 cases were deemed by the attending physician to have PTB despite no growth of MTC (the attending physicians did not withdraw the cases from the national registry and continued the TB treatment to completion). These 39 were excluded from the subsequent analysis. The remaining (n=2722) were categorised into Group A (n=2422) defined as cases notified to the national TB registry and whose sputum cultures grew MTC, and Group B (n=300) comprising cases whose sputum cultures grew only NTM. Speciation was done in 222 of the 300 NTM patients; 54.5% were rapidly growing mycobacteria (mainly *M. abscessus*), 21.2% were *M. kansasii*, and 19.8% *M. avium* complex. Group B were more likely than Group A cases to be above the age of 59 yrs (70% vs 32.2%,  $p<0.001$ ), and have a previous history of TB treatment (32% vs 7.7%,  $p<0.001$ ). In sputum AFB smear positive cases in Singapore, NTM pulmonary infection should be considered in the older patients and those who have had a previous episode of TB.

#### OPP-472-01 *Mycobacterium bovis* in urban Brazil: risk factors for infection in human cases

M Silva,<sup>1</sup> GN Souza,<sup>1</sup> FR Araujo,<sup>2</sup> AA Fonseca Junior,<sup>3</sup> LS Faria,<sup>1</sup> GD Sampedro.<sup>1</sup> <sup>1</sup>Embrapa Dairy Cattle, Brazilian Agricultural Research Corporation, Juiz de Fora, MG, <sup>2</sup>Embrapa Beef Cattle, Brazilian Agricultural Research Corporation, Campo Grande, MG, <sup>3</sup>LANAGRO, Ministry of Agriculture, Livestock and Food Supply, Pedro Leopoldo, MG, Brazil. e-mail: marcio-roberto.silva@embrapa.br

**Background:** The zoonotic tuberculosis (TB) caused by *Mycobacterium bovis* is a public health problem and the knowledge about the involvement of bovine tuberculosis (bTB) in human cases should be improved and made available for the effective control of the bTB. A previous study (sectional) conducted by the same team showed three (1.6%) co-infections *M. bovis* - *Mycobacterium tuberculosis* among 189 patients with TB in urban Brazil, which were published previously. The objective of this study was to evaluate risk factors for those cases of zoonotic TB, by means of a nested and matched case-control study.

**Design/Methods:** A case-control study was carried out nested in a cross-sectional study, which involved patients with TB from two health centers in urban Brazil, from March/2008 to February/2010. As cases were defined patients who presented co infections caused by *M. bovis*, and as controls those who showed only *M. tuberculosis*. We selected 14 controls for each case of co infection with *M. bovis*, matched for age ( $\pm 10$  years), sex and type of disease (both cases and controls had TB). The days of consumption of raw milk (RM) and cheese made with raw milk (CRM) were estimated by the time and the frequency lifetime of its consumptions by individual, considering as exposed those with days of consumption above the median. Zoonotic Exposure (ZE) was defined as both prior exposures to RM and CRM consumptions and involvement with occupations related to livestock or agro food industry of animal origin.

Factor	Expositions		OR MH**	p value ajusted (MH/Mid-P/ Fisher Exact)
	Cases	Controls		
Consumption of cheese made from raw milk above median levels (Yes)	3/3	19/42	3.58	0.055/<0.05*/0.09*
Zoonotic exposure (Yes)	3/3	14/42	5.71	<0.05/<0.05/<0.05
History of housing in rural areas	0/3	14/42	-	0.23/0.32/0.64
Clinical forms of TB (extrapulmonary)	2/3	5/42	12.5	<0.05/<0.05*/0.057
Consumption of raw milk above median levels (Yes)	0/3	19/40	-	0.11/0.16/0.33
HIV (Yes)	0/3	4/34	-	0.53/0.70/>0.99
BCG vaccine (Yes)	1/3	9/42	-	0.69/0.70/>0.99

\* 1-tail \*\* Odds ratio \*\*\* Mantel-Haenszel

**Results:** The three cases of TB that had co infections caused by *M. bovis* were 20, 33 and 50 years old. Of



these, one was diagnosed as pulmonary and two as extrapulmonary TB. Infections caused by *M. bovis* were associated ( $p \leq 0.05$ ) to exposures to consumption of CRM and ZE (Table 1). People exposed to consumption of CRM and ZE had 3.58 and 5.71 times more chances to have the co infection ( $p < 0.05$ ), respectively.

**Conclusion:** Possible sources of *M. bovis* to human beings were CRM and ZE. The potential risks to the health of zoonotic microorganisms carried by milk and dairy products, including *M. bovis*, should be emphasized. These results should be taken into consideration by the authorities of health and agriculture in Brazil, in order to prevent or control human cases of TB due to *M. bovis*. Table 1 – Stratified logistic regression for *M. bovis* co infections by means of a Matched case-control study

#### OPP-473-01 A cost-effective laboratory protocol for identification of *M. tuberculosis* by morphology, immunochromatographic assays and PCR assay

H Tu,<sup>1</sup> Y Lin,<sup>2</sup> M Tseng,<sup>1</sup> T Huang,<sup>1</sup> Y Chen.<sup>1</sup> <sup>1</sup>Infectious Disease and Laboratory Medicine, Kaohsiung Veterans General Hospital, Kaohsiung, <sup>2</sup>Human Resource and Knowledge Management, National Kaohsiung Normal University, Kaohsiung, Taiwan. Fax: (+886) 7605 1379. e-mail: easonlin@nknku.edu.tw

**Background:** Rapid diagnosis of tuberculosis by detecting and identifying *M. tuberculosis* complex (MTBC) from the clinical cultures can be achieved by combination of rapid tests. The objective of this study is to propose a cost effective laboratory protocol for MTBC identification.

**Design/Methods:** A total of 308 mycobacterial clinical cultures were tested using PCR restriction-enzyme analysis (PRA) as gold standard. The MTBC identification were performed and results were compared among microscopic morphology, two ICA methods (TibiliaTM and MeDiPro), and one Strand Displacement Amplification (SDA) method (BD ProbeTec ET).

**Results:** Microscopic morphology (cord serpentine-like) demonstrated a sensitivity of 95.5%, specificity of 96.5%, positive predictive value (PPV) of 96.7%, and negative predictive rate (NPV) of 95.1%. The overall sensitivity and specificity of the TibiliaTM assay were 98.2% and 98.6%, respectively, MeDiPro assay were 88.3% and 86.2%, and the ProbeTec ET assay were 98.8% and 97.9%. The PPV/NPV for the TibiliaTM, MeDiPro, ProbeTec ET were 98.8%/97.9%, 87.8%/86.8%, and 98.2%/98.6%, respectively. Cord serpentine-like microscopy is the least expensive and may be used for identification of MTBC. The ICA method offers a cost effective screening compared to SDA method. TibiliaTM has better performance than MeDiPro, and has a similar diagnostic value to SDA assay.

**Conclusion:** We recommend the combination of microscopic observation (serpentine cording morphology in smears) and TibiliaTM method which, in our study, further improve the specificity and NPV to 96.5% and 96.7% for less cost compared to SDA method.

#### OPP-474-01 Identification of non-tuberculous mycobacteria using matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry

I Marekovic,<sup>1,2</sup> V Katalinic-Jankovic,<sup>3</sup> Z Bocnjak,<sup>2</sup> A Budimir,<sup>1,2</sup> V Plecko.<sup>1,2</sup> <sup>1</sup>Medical Microbiology and Parasitology, University of Zagreb, School of Medicine, Zagreb, <sup>2</sup>Clinical and Molecular Microbiology, University Hospital Centre Zagreb, Zagreb, <sup>3</sup>Tuberculosis diagnostics, Croatian National Institute of Public Health, Zagreb, Croatia. Fax: (+385) 1 2367 373. e-mail: ivanamarekovic@yahoo.com

**Background:** Nontuberculous mycobacteria (NTM) are attracting growing attention, especially in countries where the incidence of tuberculosis is declining. Species identification of NTM isolates is of crucial importance because it can guide decisions about the necessity of antimicrobial treatment and can assist in selecting appropriate antimicrobials because of predictable susceptibility profiles in specific NTM species. A new tool for species identification of NTM is matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS). We have evaluated this method on 15 NTM clinical isolates.

**Design/Methods:** Fifteen NTM clinical isolates were cultivated on solid Lowenstein-Jensen (L-J) medium or in Mycobacterium Growth Indicator Tube (MGIT) culture bottles (Becton, Dickinson and Company, Sparks, USA). BD MGIT TBc Identification Test (Becton, Dickinson and Company, Sparks, USA) and niacin test were done on positive MGIT culture bottles and on cultures grown on L-J medium, respectively. When *Mycobacterium tuberculosis* was excluded, isolates were identified with MALDI-TOF MS. Extraction method with zirconia/silica beads was used. The extracts were analyzed with MALDI Biotyper 3.1 (Bruker Daltonik GmbH, Bremen, Germany) and the spectra were compared to Mycobacteria Library 1.0. NTM isolates with score value  $< 2.0$  were also identified by hybridization assay (Genotype Mycobacterium CM test, Hain Lifescience, Nehren, Germany).

**Results:** Fifteen NTM isolates were identified by MALDI-TOF MS as *M. fortuitum* ( $n=3$ ), *M. goodii* ( $n=2$ ), *M. avium* ( $n=2$ ), *M. xenopi* ( $n=2$ ), *M. abscessus* ( $n=3$ ) and *M. kansasii* ( $n=1$ ) (Figure 1.). For 2 NTM isolates MALDI-TOF MS showed no reliable identification. For 7 isolates MALDI-TOF MS achieved score value  $\geq 2.0$  corresponding to an identification at species level. For 6 NTM isolates with score value  $< 2.0$  the hybridization assay identified species corresponding to those identified with MALDI-TOF MS. Two NTM strains for which MALDI-TOF MS showed no reliable identification were identified by hybridization assay as *M. intracellulare* and *M. avium*.

**Conclusion:** MALDI-TOF MS is a promising new tool for fast and reliable identification of NTM species. In some cases NTM species identification with MALDI-TOF MS is correct despite score values indicating only probable genus identification. With improvement of extraction protocol higher score values could be regu-

larly achieved making this method one of the first choices for the identification of NTM species.

Table. Identification of NTM isolates by MALDI-TOF MS

	Organism (best match) (n=15)	Score value <sup>a</sup>
1	<i>Mycobacterium gordonae</i>	2.242
2	<i>Mycobacterium kansasii</i>	2.265
3	<i>Mycobacterium avium</i>	1.933
4	<i>Mycobacterium xenopi</i>	1.756
5	<i>Mycobacterium fortuitum</i>	1.889
6	<i>Mycobacterium abscessus</i>	2.208
7	<i>Mycobacterium abscessus</i>	2.270
8	<i>Mycobacterium abscessus</i>	1.958
9	<i>Mycobacterium fortuitum</i>	2.092
10	<i>Mycobacterium gordonae</i>	1.887
11	<i>Mycobacterium fortuitum</i>	2.308
12	<i>Mycobacterium avium</i>	2.009
13	not reliable identification	1.359
14	<i>Mycobacterium xenopi</i>	1.852
15	not reliable identification	1.669

<sup>a</sup>Meaning of score values: 0.000–1.699 not reliable identification, 1.700–1.999 probable genus identification, 2.000–2.299 secure genus identification, probable species identification, 2.300–3.000 highly probable species identification

#### OPP-475-01 Increasing trend of isolation of non-tuberculous mycobacteria from respiratory specimens in Serbia over five-year period: 2009–2013

I Zivanovic,<sup>1</sup> I Dakic,<sup>1</sup> D Vukovic,<sup>1</sup> G Stefanovic,<sup>2</sup>

LJ Tomic,<sup>2</sup> B Savic.<sup>1</sup> <sup>1</sup>Bacteriology, Institute of Microbiology and Immunology, Faculty of Medicine, University of Belgrade, Belgrade, <sup>2</sup>Clinical Mycobacteriology, Laboratory for Mycobacteria, Clinical Centre of Serbia, Belgrade, Serbia.

Fax: (+381) 11 364 3360. e-mail: branislava.savic@gmail.com

**Background:** Nontuberculous mycobacteria (NTM) are increasingly associated with pulmonary disease, which is partially due to the improvements in the laboratory techniques for identification of these bacteria. The molecular identification of NTM was introduced into the Serbian National Reference Laboratory for Tuberculosis (TB) in 2009. This study analyzed the isolation rates of NTM from respiratory specimens and prevalence of NTM pulmonary disease over the five-year period, 2009 through 2013, in Serbia. Method: Mycobacterial culture results of respiratory specimens obtained over the study period were retrieved from the national TB database and analysed retrospectively. In total, 548 cultures recovered from respiratory specimens were identified as NTM in Serbia over the study period. Species-level identification of the isolates was carried out by the GenoType Mycobacterium CM/AS (HAIN Lifescience) assays. The 548 NTM cultures were isolated from 449 patients. The laboratory record of each patient was reviewed, and the microbiological criteria of the American Thoracic Society NTM disease definition were used to identify cases of NTM pulmonary disease.

**Results:** The annual rates of NTM among patients with positive mycobacterial cultures recovered from respiratory specimens, one culture per patient was counted, were as follows: 4.4% in 2009; 5.5% in 2010; 10.2 in 2011; 8.9 in 2012; and 12.5 in 2013. Species-level identification was achieved in 382 (69.7%) cultures,

while the remaining 166 were identified as *Mycobacterium* sp., and considered contaminants. In total, 11 different species of NTM were recognized, with *M. xenopi* being the most common (n=129; 23.5%). Out of 449 patients, 61 met the ATS criteria for NTM pulmonary disease. The case rates per 100,000 population were as follows: 0.08 in 2009; 0.12 in 2010; 0.18 in 2011; 0.19 in 2012; and 0.26 in 2013. Most cases were due to *M. xenopi* (n=28; 45.9%), followed by *M. avium* (n=8; 13.1%) and *M. abscessus* (n=7; 11.5%).

**Conclusion:** The isolation rates of NTM from respiratory specimens as well as the case rates of pulmonary NTM disease are increasing in Serbia. This is obviously related to the improved laboratory detection of NTM. Nevertheless, the results may also reflect an actual increase in the incidence of NTM. As the incidence rate of TB declines in Serbia, namely from 37 in 2003 to 17 in 2012, an increase in the proportion of pulmonary disease caused by NTM may be expected.

#### OPP-476-01 Utility of Bact/ ALERT 3D System for mycobacteria isolates

M Martinez,<sup>1</sup> LM Mederos,<sup>1</sup> M Sardiña,<sup>1</sup> G Garcia Leon,<sup>1</sup>

R Díaz.<sup>1</sup> <sup>1</sup>National Reference Laboratory in Tuberculosis, Leprosy and others mycobacterias, Institute of Tropical Medicine "Pedro Kourí", Havana, Cuba.

e-mail: rosarys@ipk.sld.cu

**Background:** The rapid diagnosis of mycobacterial infections is essential to implement the adequate antimicrobial therapy. This study evaluates the performance of the Bact/ ALERT 3D system for isolates and identification of mycobacteria from clinical samples

**Design/Methods:** 1011 clinical specimens from non-sterile and sterile body sites were studied from August 2010 to December 2012 at the National Reference Laboratory of Tuberculosis, IPK, Cuba. The results obtained were compared with respect to time detection of mycobacteria and contamination rates, and were calculated the performance indicators of Bact/ ALERT 3D.

**Results:** The time detection of growth (TDG) for *Mycobacterium tuberculosis* (Mtb) and nontuberculous mycobacteria (NTM) by Bact/ ALERT 3D was 16,435 and 10,956, respectively; by LJ the TDG was 33,577 for Mtb and 35,952 for NTM. By culture method used the TDG for LJ was 33,577 and 6,435 by Bact/ ALERT 3D, this difference being statistically significant. The overall contamination rate (CR) for Bact ALERT 3D was 4.6% and 7.8% for LJ.

**Conclusion:** Bact/ ALERT 3D were a suitable method for recovering mycobacteria from clinical samples. It demonstrated a shorter time detection of mycobacteria growth; it was very useful to provide faster treatment and a better prognosis in patients AFB smear negative with HIV. The use of LJ culture and Bact/ ALERT 3D System was useful to assure a total mycobacterial recovery. We recommended carry out similar studies in the rest of the country for better management of patients with associated TB / HIV and contribute to the National Programme for Control of TB.

**OPP-477-01 Mycobactéries autres que *Mycobacterium tuberculosis* isolées au CHU Aristide Le Dantec à Dakar**

A Ba,<sup>1</sup> M Ndiaye,<sup>1</sup> GW Ossoga,<sup>1</sup> MY Fall Niang,<sup>1</sup> A Ndiaye Diawara,<sup>1</sup> A Gaye Diallo.<sup>1</sup> <sup>1</sup>Mycobacteriologie, Laboratoire de Bactériologie Virologie, Dakar, Senegal. Fax: (+221) 338 213825. e-mail: choux\_ba@yahoo.fr

**Background:** L'augmentation considérable des infections pulmonaires dues aux bacilles tuberculeux autre que ceux du complexe tuberculosis pose un réel problème de santé publique. Leur forte responsabilité dans divers pathologies humaines telles que les infections pulmonaires ressemblant à la tuberculose, les infections extrapulmonaires ou celles disséminées surtout chez les immunodéprimés mérite qu'on leur accorde une attention particulière.

**Design/Methods:** Nous avons réalisé une étude portant sur 1208 prélèvements collectés entre Janvier 2011 et Juin 2012. Les échantillons reçus ont été décontaminés par la méthode à la N acétyle Cystéine sodique puis ensemencés sur milieux liquides automatisés et sur Lowenstein Jensen. Une extraction ADN sur les cultures positives obtenues a été effectuée par la méthode au Chloroforme avant l'identification avec le kit Génotype Mycobacterium CM® et par spectrométrie de masse Maldi-TOF®.

**Results:** Notre population d'étude comprenait 59,7% d'hommes et 39,5% de femmes pour une tranche d'âge comprise entre 11 mois et 87 ans. Les nouveaux cas représentaient 93%, les cas de retraitement (4%), rechute (1%) et ils provenaient en majeure partie de services comme la Médecine Interne, la Pneumologie et la Pédiatrie. Les cultures positives aux mycobactéries atypiques représentaient 25,4% du total des cultures versus 74,5 % pour les Mycobactéries du complexe tuberculosis. *M. fortuitum* était l'espèce de mycobactéries atypiques la plus isolée (18,75%), suivi de *M. intracellulare* (12,5%). *M. gordonae* (5,6%) ; *M. abscessus* (3,7%) ; *M. intracellulare* (3,7%) et *M. malmoense* (1,8%). Cependant 39% des mycobactéries atypiques isolées n'ont pas pu être identifiées par le kit Genotype Mycobacterium CM® utilisé et par la spectrométrie de masse. *M. intracellulare* était isolée chez deux patients VIH, MDR et âgés de plus de 60 ans.

**Conclusion:** La diversité des souches de Mycobactéries isolées des patients hospitalisés constitue un véritable signe d'alerte quant à l'implication de ces bacilles dans certaines affections pulmonaires. Leur grande résistance aux antibiotiques à laquelle s'ajoute la complexité de leurs présentations cliniques constitue un frein à leur traitement et par conséquent à la prise en charge optimale des patients infectés par ces bacilles.

**OPP-478-01 Molecular identification of *Mycobacterium tuberculosis* complex and non-tuberculous mycobacterias: Peru, 2012–2013**

N Quispe,<sup>1</sup> E Valencia,<sup>1</sup> C Bartra,<sup>1</sup> L Asencios.<sup>1</sup> <sup>1</sup>Public Health, National Institute of Health, Lima, Peru. e-mail: nquispe@hotmail.com

**Background:** The etiologic agent of pulmonary tuberculosis is caused by the *Mycobacterium tuberculosis* complex (MTC); however, there are other species for the Mycobacterium gender called nontuberculous mycobacterias (MNT), which can cause pulmonary infections. These are widely spread in the environment and their infections usually go clinically unnoticed, therefore it is necessary a good etiological diagnosis. From the therapeutic point of view, the etiological diagnosis through accurate identification of the specie, results in a meaningful contribution because the clinical management of cases is different depending on the species involved. **Objective:** Identify the *Mycobacterium tuberculosis* complex and other MNT from f isolates, through the molecular test based on DNA-STRIP technology.

**Methods:** The identification was performed of mycobacterias isolates from respiratory origin samples of clinically suspected cases of multidrug-resistant tuberculosis collected during 2012 –2013. It was used the GenoType Mycobacterium CM/AS (Hain Lifescience, Germany) commercial kit, which uses two molecular DNA markers: insertion sequence IS6110, a feature of *M. tuberculosis* complex genomes, and the sequence of ribosomal 23s (ARNr23s) gene to identify the specie.

**Results:** There were obtained a total of 18317 isolates, from which 17921 (97.6%) were identified as MTC and 396 (2.2%) as MNT. The most frequent identified MNT species were *M. intracellulare* (35.6%, n = 141), *M. fortuitum* (13.9%, n = 55), *M. abscessus* (13.1%, n = 52), *M. avium* (10.6%, n = 42) *M. kansasii* (10.3%, n = 41), *Mycobacterium* sp. (7.1%, n = 28). Other identified species in fewer amounts were *M. scrofulaceum* (n = 9), *M. peregrinum* (n = 9), *M. gordonae* (n = 8), *M. szulgai* / *M. intermedium* (n = 5), *M. chelonae* (n = 3), *M. inerjectum* (n = 2), *M. simiae* (n = 1)

**Conclusion:** The infections caused by these MNT and their forecast will depend on several factors: the specie, drugs sensitivity, location, dissemination and comorbidities. Although detection of MNT in Peru is low (2.2%), it is indispensable the timely detection to stablish an adequate therapy. The molecular test is an importante tool for identifying the species of the *Mycobacterium* sp. gender.



### OPP-479-01 Expanding genotyping platform of *M. tuberculosis* for intraspecies of common mycobacteria on a base of microarray "Biochip"

S Popov,<sup>1</sup> A Kuzmin,<sup>1</sup> D Gryadunov,<sup>2</sup> S Lapa.<sup>2</sup> <sup>1</sup>MoH, RI Phthisiopulmonology IM Sechenov First State Medical University, Moscow, Russian Federation, <sup>2</sup>Russian Academy of Sciences, Engelhardt Institute of Molecular Biology, Moscow, Russian Federation. Fax: (+7) 495 681 5988. e-mail: popov\_s55@mail.ru

Steady increasing of HIV infection creates a good conditions for multidrug-resistant TB up-scaling and very high risk for mycobacteria infection. Mycobacteriosis are increasingly identified among various groups of patients. In 2013 in RIPP TB hospital was revealed 14% Mycobacteria spp. other then tuberculosis (MOTT). There are a few recommended methods for species identification of MOTT. Most of them have a good diagnostic parameters but can be supported by researchers or scientists only. We used hybridization platform Biochip with optical detection of product reaction. First time the idea was realized for DST of MTB and implemented in 15 laboratories in Russia, and gave a good results for MDR and Fq-resistance revealing. Technology for MOTT identification includes the PCR amplification of the gene *gyrB* fragment of the Mycobacterium DNA and hybridization fluorescently labeled PCR products with covalently immobilized species-specific oligonucleotides on the biochip® microarray. Analysis of pattern hybridization was performed in automatic mode on universal hardware-software ChipReader complex. The complex can recognize 17 species of Mycobacteria and give conclusion for lab technician. 74 mycobacterial clinical isolates from 49 patients and were examined in clinical bacteriological lab. Validation methods: direct microscopy of mycobacterial cultures for AFB, bacteriological study of mycobacterial cultures in accordance to WHO recommendations: the growth rate, abilities to grow at different temperatures and on different media, pigmentation, morphology of colonies, biochemical tests.

**Results:** All 74 isolated mycobacterial cultures and 2 museum strain (MTB H37Rv, *M. bovis* BCG) were determined by AFB, culture/biochemical methods and molecular-genetic method based on *gyrB* gene polymorphism. Clinical isolates were identified as: *M. tuberculosis* in 24 cases, *M. avium* –16, *M. smegmatis* –2, *M. xenopi* –3, *M. abscessus* –2, *M. fortuitum* –15, *M. kansasii* –2, *M. chelonae* –1, *M. gordonae* –6 and *M. simiae* –1.

**Results** of the analysis of museum strains coincided with the passport.

**Conclusion:** The species-specific sequences of the polymorphic locus *gyrB* using microarray MycoBiochip allowed to make a typing of clinical MOTT isolates as soon as possible and the results coincided with the traditional identification mycobacteria by means of bacteriological/biochemical methods. Discrimination of the method was enough for clinical purposes.

### 09. DRUG RESISTANCE AND DRUG-RESISTANCE SURVEYS

#### OPP-480-01 Mechanisms of fluoroquinolone resistance in clinical isolates of *Mycobacterium tuberculosis* from a tertiary centre of India

A Jain,<sup>1</sup> P Singh,<sup>1</sup> S Prakash,<sup>1</sup> P Dixit,<sup>1</sup> R Vangala.<sup>1</sup>

<sup>1</sup>Microbiology, King George's Medical University, Lucknow, India. e-mail: amita602002@yahoo.com

**Background:** Fluoroquinolones (FQs) play an increasingly important role in the treatment of multidrug resistant tuberculosis (MDR-TB). Rapid detection of FQ resistance (FQ-R) is becoming increasingly important for management of MDR and extensively drug resistant (XDR) TB cases. Rapid diagnostic techniques such as MTBDRsl assay offer lower sensitivity (86.2%) in detection of FQ-R may be due to incomplete understanding of mechanisms of FQ-R. Therefore, it is important to study the mechanisms causing FQ-R in *Mycobacterium tuberculosis* (MTB). We determined the prevalence of *gyrA* and *gyrB* gene mutations in quinolone resistance determining region (QRDR) region of FQ-R and FQ sensitive MTB clinical isolates from a tertiary centre in India and to assess the role of efflux pump in FQ-R.

**Design/Methods:** A total of 670 MTB isolates from MDR suspects were consecutively selected from TB laboratory, King George's Medical University, Lucknow, during Sep 2011-Aug 2012. Drug resistance pattern of five antitubercular drugs; streptomycin, isoniazid, rifampicin, ethambutol and ofloxacin were recorded. A total of 100 ofloxacin resistant (OFX-R) and 100 OFX sensitive (OFX-S) isolates of MTB were tested for minimal inhibitory concentration of OFX and QRDR of *gyrA* & *gyrB* genes were sequenced. A total of 50 MTB clinical isolates that included; 21 OFX-R isolates without mutations, 14 OFX-R isolate with mutations and 15 OFX-S isolates without mutations were studied to assess the effect of five efflux pump inhibitors.

**Results:** Among 670 isolates, 206 (31%) were MDR and 196 (29%) were OFX-R. Of 100 OFX-R isolates, 79% isolates had mutation in QRDR region of *gyrA* gene and 5% isolates had mutation in *gyrB* gene. All the isolates showing mutations in *gyrB* gene also had mutations in *gyrA* gene. No mutation was observed in QRDR region of *gyrA* and *gyrB* genes in OFX-S isolates, except the S95T mutation in *gyrA* gene. Most prevalent mutation was found at codon 94 in QRDR region of *gyrA* gene. Double mutations found in *gyrA* gene or in both *gyrA* & *gyrB* genes signifies higher levels of OFX-R. The effect of efflux pump inhibitors was observed in both OFX-S and OFX-R isolates.

**Conclusion:** The mutation (79%) found in QRDR region of *gyrA* gene, are associated with OFX-R. The effect of efflux pump inhibitors was observed in OFX-S as well as OFX-R isolates therefore, its role in FQ-R is still not clear. Further studies are required to study other mechanisms of FQ-R.

### OPP-481-01 Molecular detection of isoniazid resistance in a Canadian province with a low incidence of antibiotic resistant tuberculosis

S Christianson,<sup>1</sup> M Sharma,<sup>1,2</sup> D Long,<sup>3</sup> H Zhou,<sup>4</sup> Z Gao,<sup>3</sup> C Heffernan,<sup>3</sup> R Long,<sup>3</sup> J Wolfe.<sup>1</sup> <sup>1</sup>National Reference Centre for Mycobacteriology, Public Health Agency of Canada, Winnipeg, MB, <sup>2</sup>Faculty of Medicine, University of Manitoba, Winnipeg, MB, <sup>3</sup>Department of Medicine, University of Alberta, Edmonton, AB, <sup>4</sup>Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, AB, Canada.  
e-mail: sara\_christianson@phac-aspc.gc.ca

**Background:** Antibiotic resistance in *Mycobacterium tuberculosis* (MTB) has important implications in diagnosis, prophylaxis and treatment. Isoniazid (INH) resistance is of particular interest as it is the recommended antibiotic for prophylaxis. In 2012, Canada reported drug susceptibility results for 1404 MTB complex isolates. INH resistance was reported in 7.9% of cases and is the most prevalent antibiotic resistance in Canada. The purpose of this study was to investigate INH-resistant isolates from one major immigrant-receiving province of Canada and to determine the prevalence and distribution of INH-resistance associated genetic mutations in that population.

**Methods:** All adult (age >14 years) culture-positive, INH-resistant pulmonary cases of MTB in Alberta, Canada from 1991–2010, were selected for this study. In total, 97 INH-resistant strains and 45 susceptible strains were included. The 142 strains were tested for INH resistance at critical concentrations of 0.1 µg/mL and 0.4 µg/mL. Strains were also tested for mutations in the *katG*, *inhA* promoter region and the *oxyR*-*aphC* intergenic region. Phenotypic and genotypic results were correlated.

**Results:** A total of 45 strains were susceptible to both concentrations of INH tested, 21 strains were resistant to only the lower concentration of INH and 76 strains were resistant to the higher concentration of INH. Twenty of the sensitive strains had mutations in the *oxyR*-*aphC* intergenic region. No other mutations were seen in the sensitive strains. Of the strains with low level resistance, 15/21 (71%) had mutations in the *inhA* promoter region, but there were no mutations recorded in the *katG* gene. Two high-level resistant strains had *inhA* mutations and 62 strains had *katG* mutations. The *katG* gene did not amplify in 2 of the strains with high level resistance, indicating a likely mutation in the primer region. Ten strains (13%) resistant at the higher concentration of INH had no mutations. All *katG* and *inhA* mutations identified in this study have been previously reported as being associated with INH resistance.

**Conclusion:** Overall, mutations in the *katG* gene and *inhA* promoter region were able to detect 83% of INH-resistant cases. The *oxyR*-*aphC* intergenic region was not informative in predicting INH resistance. Mutation rates for genes associated with INH resistance in Alberta are consistent with those reported in the United States and elsewhere.

### OPP-482-01 Application of rapid colorimetric pyrazinamide resistance detection method to Korean *Mycobacterium tuberculosis* isolates

J Lee,<sup>1</sup> ES Son,<sup>1</sup> Jiim Lee,<sup>1</sup> EJ Eunjin,<sup>1</sup> CT Kim,<sup>2</sup> SN Cho,<sup>3</sup> SH Back.<sup>3</sup> <sup>1</sup>Microbiology, National Tuberculosis Research Center, Changwon, <sup>2</sup>Hospital, National Masan Hospital, Changwon, <sup>3</sup>Microbiology, Yonsei University, Medical school, Seoul, Republic of Korea. Fax: (+82) 552 461 162.  
e-mail: cosmosljs@gmail.com

**Aim:** Pyrazinamide (PZA) is an important drug for both of drug susceptible and drug resistant tuberculosis including multidrug resistant and extensively drug resistant tuberculosis. Current methods to determine PZA resistance takes weeks and reliability has been in question. We adapted a newly developed rapid colorimetric PZA resistance detection method and evaluated its efficacy on Korean *Mycobacterium tuberculosis* (Mtb) isolates.

**Methods:** 108 PZA resistant Mtb isolates and 12 susceptible isolates confirmed by Wayne method and MGIT method were applied. DNAs were extracted from each isolates, amplified the *pncA* gene including promoter region, and produced pyrazinamidase through in vitro transcription and translation, followed by colorimetric detection assay. Results were monitored by both of optical color changes and measure optical density (OD) at 460nm, and compared with currently used Wayne method and MGIT method

**Results:** Out of 108 PZA resistant isolates, 107 isolates have genetic alterations in *pncA*/promoter. Sequencing results of *pncA*/promoter showed 68 mutation types in 56 codons. Mutations were observed in either of *pncA* gene or its promoter region, but not in both. The overall test took 2 working days which was faster than Wayne method (average 7 days) or MGIT method (average 15 days); DNA extraction and amplification for the first day, overnight reaction of in vitro transcription and in vitro translation, and color detection for the second day. All the susceptible isolates except one isolate were clearly differentiated from resistant isolates by both of optical observation and OD measurement; OD measurement showed resistant isolates were 0.021 – 0.096 except one case, instead all the susceptible isolates were >0.177. One discrepant isolate showed susceptible in the rapid method (OD 0.226), but has mutation and resistant to PZA. The rapid method detected 87% (93/107) of PZA resistant isolates in 1<sup>st</sup> test, 90% (97/107) in second test, and 93.5% (100/107).

**Conclusions:** Korean Mtb isolates showed great diversity of mutations in *pncA*/promoter region than ever reported. Newly introduced method detected PZA resistance much faster than other methods. It is noteworthy that if the new method would be applied directly to clinical samples, the overall test duration will be dramatically reduced from at least 3–4 weeks to 2–3 days. However, the overall performance of new method should be improved which currently shown about 87% for the first examination.

### OPP-483-01 Resistance pattern for second-line Anti TB drugs among MDR-TB patients: experience from the national reference laboratory, Zaria, Nigeria

F Ajiboye,<sup>1</sup> N Ezati,<sup>2</sup> I Mosunmola,<sup>2</sup> I Ahmadu,<sup>1</sup> M Panwal,<sup>2</sup> S Labaran,<sup>1</sup> M Gidado.<sup>3</sup> <sup>1</sup>Laboratory, National Tuberculosis and Leprosy Training Center, Zaria, <sup>2</sup>Laboratory, Institute of Human Virology Nigeria, Abuja, <sup>3</sup>Country Director, KNCV, Abuja, Nigeria.  
e-mail: priscay2k2@yahoo.com

**Aim:** Nigeria is a high burden country for TB, MDR-TB and HIV. The TB prevalence stands at 322/100,000 population; HIV prevalence of 4.1%; TB/HIV co-infection of 27%; and MDR-TB prevalence of 2.9% among new cases and 14.3% among retreatment cases. With current scale-up of PMDT there is a need for capacity building and resources for routine SLD DST among MDR-TB cases. The aim of this paper is to describe the pattern of DST among MDR-TB patients on treatment.

**Methods:** From February 2013 to March 2014, all confirmed MDRs were subjected to SLD DST using Solid proportion method and Liquid MGIT 960 system. Total staff trained are 22. Any resistance with the aminoglycosides and fluoroquinolones were further tested with LPA (MTBDR sl). We started with kanamycin, levofloxacin, capreomycin and ethionamide and later added cycloserine and amikacin. Levofloxacin was done only on MGIT, cycloserine was only done on LJ. All the three methods are being validated. Forty-eight representative isolates were sent to the SRL, Milan for validation, awaiting results.

**Results:** Altogether SLD DSTs for 56 DR-TB patients were performed using both phenotypic methods. A total of 8(14.3%) were resistant to kanamycin, 13(23.2%) were resistant to Levofloxacin, 4(7.1%) were resistant to Capreomycin, 10(20.8%) were resistant to ethionamide, 3(37.5%) were resistant to cycloserine. A total of 48(85.7%) were sensitive to kanamycin, 43(76.8%) were sensitive to levofloxacin, 52(92.9%) were sensitive to capreomycin, 38(79.2%) were sensitive to ethionamide and 5(62.5%) were sensitive to cycloserine. Only one sample was resistant to capreomycin and ethionamide. No XDR has been found so far. However, one sample was totally resistant to all SLD and was later characterized to be an NTM. Most of the MGIT 960 and LJ DSTs agreed, 1 sample gave resistance to Kanamycin on LJ and sensitive on MGIT. Two of the 8 resistant to kanamycin and 3 of the 13 resistant to levofloxacin were retested using MTBDRsl.

**Conclusion:** With SNRL support in capacity building and mentoring; alternative power supply; and good laboratory network for sample collection and movement, SLD DST is feasible in developing countries. Mono resistance to the different SLDs was high, even though there is no XDR case reported

### OPP-484-01 Single tube two-colour analysis of all allelic variants of the pncA gene using LATE-PCR and allied technologies

J Rice,<sup>1</sup> W Wagh,<sup>1</sup> R M Warren,<sup>2</sup> M Whitfield,<sup>2</sup> S Marras,<sup>3</sup> B Kreiswirth.<sup>3</sup> <sup>1</sup>Reproduction Biology and Molecular Cytology, Brandeis University, Waltham, MA, USA; <sup>2</sup>Biomedical Sciences, Stellenbosch University, Tygerberg, South Africa; <sup>3</sup>Medicine, PHRI - Rutgers, Newark, NJ, USA.  
e-mail: kreiswba@njms.rutgers.edu

**Background:** Pyrazinamide (PZA) is a key antibiotic in the standard four drug regimen to treat tuberculosis, provided the patient is not PZA resistant. But, determining resistance to PZA phenotypically is difficult, and genotyping the vast array of mutations in the pncA gene is not practical. To circumvent these hurdles, we are developing a robust single-tube method that, at a minimum, can distinguish the wild type drug susceptible pncA gene sequence from all strains that have non-synonymous genetic alterations (including the variant of *M. bovis*) by coating them with fluorescent probes in three colors.

**Methods:** LATE-PCR has been used to amplify a 686 base long single-stranded amplicon encompassing the entire coding region of the pncA gene, including the upstream flanking sequence. This target is known to harbor at least 371 sites at which mutations correlate with drug resistance. The resulting amplicon is analyzed in a closed-tube assay by lowering the temperature at end-point, permitting 32 Lights-On/Lights-Off fluorescent probes labeled in three fluorescent colors to coat the single-stranded DNA product. The probes are then melted off the target and the resulting highly reproducible fluorescent signatures reveal the presence/absence of mutations.

**Results:** Version-1 of the assay has been tested against a blinded panel of 47 DNA samples with known pncA mutations. The first results showed that 27 of the 32 Lights-Ons/Lights-Off probes had 100% sensitivity and specificity in distinguishing the WT pncA sequence from the mutants. We are currently optimizing the sequence structure of the 5 failed probes to complete and test the assay against a robust panel of pncA mutants that span the entire gene.

**Conclusions:** A single closed-tube assay for amplification and detection of all pncA gene variants has been developed and is currently being optimized. Once completed this assay will distinguish drug-susceptible and drug-resistant variants of the pncA gene and its performance will be faster, less expensive, and more convenient than DNA sequencing.



### OPP-485-01 Increasing ethambutol resistance associated to high simultaneous isoniazid & ethambutol resistance in Lima, Peru

G Valle,<sup>1</sup> R Quispe,<sup>1</sup> T Caceres,<sup>1</sup> E Gotuzzo,<sup>1,2</sup> C Zamudio,<sup>1</sup> C Seas.<sup>1,2</sup> <sup>1</sup>Universidad Peruana Cayetano Heredia, Instituto de Medicina Tropical "Alexander von Humboldt", Lima, <sup>2</sup>Hospital Nacional Cayetano Heredia, Departamento de Enfermedades Infecciosas, Tropicales y Dermatológicas, Lima, Peru. e-mail: giancarlo.valle@upch.pe

**Background:** Surveillance systems based on routine drug susceptibility testing (DST) are encouraged by the World Health Organization (WHO). Nationwide surveys are desirable for programmatic reasons. However, tuberculosis (TB) prevalence, risk factors and resistance patterns can vary largely within a country. For instance, TB burden is concentrated in Peruvian capital city, Lima. Furthermore, scarce data exist about the drug resistance patterns in the areas with highest TB prevalence in Lima. This study reports drug resistance patterns in the most overcrowded district of Lima, San Juan de Lurigancho (SJL).

**Design/Methods:** Respiratory TB suspects from SJL were enrolled in parallel diagnostic trials during 2007-2011 and participated in the study. Patients with confirmed diagnosis of TB by positive Lowenstein Jensen (LJ) culture and positive Capilia test for *Mycobacterium tuberculosis* were included in the analysis. Proportion method in LJ medium was done to evaluate sensitivity of isolates to first-line drugs. The critic concentrations used were: INH 0.2 µg/mL, RIF 40 µg/mL, EMB 2 µg/mL, Streptomycin (SM) 4 µg/mL.

**Results** were categorized per previous TB history. Yearly trends for resistance prevalence to each drug were also evaluated.

**Results:** From 3054 TB suspects included in the study, 1088 (35.6%) had a positive culture for MTB, but 94.4% (1027/1088) had a complete DST result. Resistance patterns in overall study population were: INH 20.2%, RIF 11.6%, EMB 8.9%, and SM 23.4%. A statistically significant increasing trend was found for EMB resistance, from the period 2007-2008 to 2009-2011 in overall population (6.9% vs. 11.7%,  $p=0.008$ ), as well as in naïve TB patients (5.3% vs. 11%,  $p=0.003$ ). EMB was the only drug with significant annual increasing trend in new TB cases ( $p=0.0034$ ). Resistance to INH plus EMB was 7.5% in the overall population and showed a not statistically significant increase over time in both subgroups.

**Conclusion:** EMB – and simultaneous INH plus EMB – resistance in SJL are higher than latest Peruvian national report. EMB is showing an increasing trend, especially in new TB cases (primary resistance). Further evaluation should be done to closely evaluate the increasing rates of resistance patterns. Special concern for EMB resistance surveillance should be taken as inclusion of EMB is recommended to strength TB treatment especially in high INH resistance settings, like Peru.

### OPP-486-01 How the piloting of TB drug-resistance survey protocol can improve Ukraine's TB diagnostics system

A Barbova,<sup>1</sup> M Karnaukhova,<sup>2</sup> O Kheylo,<sup>2</sup> O Zhurilo.<sup>3</sup>

<sup>1</sup>National TB reference laboratory, National TB reference laboratory, Kyiv, <sup>2</sup>USAID| Strengthening Tuberculosis Control in Ukraine Project, USAID| Strengthening Tuberculosis Control in Ukraine Project, Kyiv, <sup>3</sup>Microbiology, National TB Institute, Kyiv, Ukraine. e-mail: mdolynska@stbcu.com.ua

**Background and challenges to implementation:** In preparing for the country-wide Drug Resistant Survey (DRS) in 2013, the USAID Strengthening TB Control in Ukraine Project piloted the WHO-recommended DRS protocol in two regions. The aim was to adopt the DRS protocol and to provide recommendations on TB diagnostics system improvement. Pilot regions included Kharkiv and Kherson oblasts with a population of over 2.7 million and 1.08 million, respectively. Four clusters with 31 primary and secondary health care and TB facilities with Level II and III laboratory network participated.

**Intervention:** Piloting steps: 1) national and international experts evaluated TB diagnostics system in two regions; 2) joint trainings of laboratory specialists and medical doctors were conducted; 3) during two months all medical facilities recruited new and re-treated TB patients, provided TB testing and registration in national and DRS databases; 4) data from regions was verified and analyzed during monitoring visits; 5) series of partners' meeting were conducted to develop recommendations on further study.

**Results and lessons learnt:** Main challenges: 1) lack of effective transport system and data flow, related to TB culture and drug resistance tests in different levels of TB laboratories; 2) absence of observed sputum collection in some facilities; 3) registration faults: about 50% of patients' records had mistakes mostly related to lack of correspondence between different registers and forms; 4) insufficient cooperation between different health care levels led to delays in referral and registration. The connections between different health care facilities were set up, TB focal-points were appointed in each facility, and system of clear feed-back from TB facilities was developed. This process was intensified all over Ukraine. Additional training opportunities were provided. Pilot regions became a reference-points to other regions of Ukraine on effective TB diagnostics system functioning. **Conclusion:** Due to partners' cooperation the DRS piloting became an entry point to systemic changes touching wide range of health system players, improving both cooperation between different levels of health care facilities, laboratory network and physicians, as well as county-wide implementation of reliable and cost-effective laboratory interventions.

### OPP-487-01 Next-generation sequencing of the *pncA* pyrazinamide resistance gene directly from sputum specimens collected and transported in PrimeStore MTM

LT Daum,<sup>1,2</sup> R Peters,<sup>3,4</sup> PB Fourie,<sup>4</sup> JD Rodriguez,<sup>1</sup> SA Worthy,<sup>1</sup> N Ismail,<sup>5</sup> G Fischer.<sup>1</sup> <sup>1</sup>Molecular Biology, Longhorn Vaccines & Diagnostics, San Antonio, TX, <sup>2</sup>Molecular Biology, University of Texas at San Antonio, San Antonio, TX, USA; <sup>3</sup>Molecular Medicine, Anova Health Institute, Johannesburg, <sup>4</sup>Department of Microbiology, University of Pretoria, Pretoria, <sup>5</sup>TB Reference Laboratory, National Institute for Communicable Diseases, Sandringham, South Africa. e-mail: longhorn-vandd@sbcglobal.net

**Background:** Antibiotic resistant *Mycobacterium tuberculosis* (MTB) is becoming increasingly common throughout the World, including in South Africa where in 2009 more than 10,000 cases of multidrug-resistant tuberculosis (MDR-TB) were reported (2.3% of the global burden). Since 2006, extensively drug resistant TB (XDR-TB) has further complicated the epidemic. However, little is known about pyrazinamide (PZA) resistance in this context. Pyrazinamide (PZA) is an important antibiotic in first and second line treatment of MTB.

**Aim/Methods:** The purpose of this study was to determine if the PZA resistance gene, *pncA*, could be sequenced directly from MTB sputum specimens collected in PrimeStore MTM® and shipped to a specialized laboratory for Ion Torrent next-generation sequencing (NGS). Sputum specimens were collected from patients with clinical symptoms of tuberculosis (TB) in the Limpopo region of South Africa. For transport, a flocced swab was swirled 5 times in the sputum specimen, placed in PrimeStore®, and transported at ambient temperature to a referral lab in South Africa and from there by air at ambient temperature to a molecular diagnostic laboratory in San Antonio, Texas. Original sputum specimens were sent for MGIT culture locally as per routine practice. The PrimeStore® specimens were extracted in San Antonio using PrimeXtract™ and analyzed by real-time PCR using PrimeMix® for MTB. Selected MTB-positive specimens were amplified and the *pncA* gene sequenced using Ion Torrent NGS.

**Results:** Of the 18 specimens selected for sequencing, the PrimeMix® MTB cycle threshold (CT) values ranged from 22–38. There were 13 specimens (72.2%) that provided NGS sequencing results. The full-length *pncA* gene plus promoter was sequenced directly from 10 of 13 specimens.

**Conclusion:** Specimens collected and shipped in PrimeStore® at ambient temperature from South Africa to the USA preserved high quality DNA for MTB real-time PCR detection and NGS. These data demonstrate that specimens in PrimeStore® can be efficiently transported from rural clinics to central labs for culturing or GenXpert processing and that NGS can simultaneously provide important and timely data on PZA drug resistance directly from specimens that are shown to be MTB-positive without the requirement for collecting an additional specimen. Specimen sequencing of the *pncA*

gene may be of value both in patient management and clinical TB drug development.

### OPP-497-01 Second National Drug Resistance Survey on tuberculosis in the Philippines 2012

N Macalalad.<sup>1</sup> <sup>1</sup>National TB Reference Laboratory, Department of Health, Manila, Philippines. Fax: (+630) 772 2063. e-mail: nmacalalad5000@yahoo.co.uk

**Background:** Tuberculosis (TB) strains resistant to rifampicin and isoniazid (multidrug resistant; MDR-TB) present a formidable public health challenge. Reliable estimates of the MDR-TB burden are crucial for planning. The Philippines, an Asian country with a high TB burden, conducted its second countrywide survey in 2011–2012 to derive a national MDR-TB estimate. In the countrywide survey of 2004, multidrug-resistant TB prevalence was 3.8% (95% Confidence Intervals 2.6–5.5) and 20.9% (13.0–32.0) for new and previously treated patients respectively.

**Design/Methods:** Cluster sampling of patients from public and private health care facilities was used. Patient sputum samples were tested for susceptibility to isoniazid, rifampicin, ethambutol, streptomycin, fluoroquinolones and second-line injectable drugs. Associations between MDR-TB and risk factors were expressed using adjusted odds ratios (aOR; 95% CI) from multivariable logistic regression.

**Results:** A total of 2692 eligible TB patients with drug-susceptibility test results – 2468 (91.7%) new and 194 (7.2%) previously treated – were enrolled. MDR-TB was detected in 49 new (2.0%; 95% CIs 1.4 %–2.7 %) and 42 retreated (21.4%; 95% CIs 15.6 %–28.7 %) cases. There were 6 cases (6.6%) with resistance to a second-line injectable drug but no cases had accompanying resistance to levofloxacin (extensive drug resistance; XDR-TB). For MDR-TB, only one variable, having/not having diabetes was significantly associated among new cases (OR=2.20, 95%CI: 1.03–4.67,  $p=0.041$ ) and 2.6 times (95%CI: 1.26–5.53,  $p=0.011$ ) among previously treated patients with diabetes.

**Conclusion:** The new estimates for MDR-TB in the Philippines show a 50% reduction in MDR-TB prevalence among new cases compared to the values measured in 2004. As compared to the countries in the Western Pacific Region with a prevalence of 4.7% (95% CI 3.3–6.1) for new and 22% (95% CI 18–27) for re-treatment, the estimate for new cases is significantly lower. The association with diabetes will be investigated further regarding its potential clinical and public health relevance.

## 10. TOBACCO, TB AND CANCER: TRIPLE THREAT

### OPP-488-01 Tuberculosis and tobacco: India attempts the new add-on evolved through best practice

M Aghi.<sup>1</sup> <sup>1</sup>Behavioral Science, Advocacy Forum for Tobacco Control (AFTC), New Delhi, India.  
e-mail: mirabaghi@gmail.com

**Background and challenges to implementation:** Although the association between tobacco smoking and tuberculosis (TB) has long been suspected, the scientific evidence for causal relationship between the two has emerged only in the last few years. The evidence is not only compelling but points out that active and passive tobacco smoking (called second-hand smoke, (SHS)) is related to a range of TB outcomes including infection, development of disease, treatment outcomes, relapse, as well as mortality. Additionally the association shows a strong dose-response relationship, which means the more the smoking, the worse the outcome for all indicators.

**Intervention** Indian TB control guidelines did not include any systematic patient education either on active smoking or exposure to second hand smoke (SHS). Not only that there has been a consistent rejection of any effort towards introducing it in the examination and treatment of TB. The revision of the TB guidelines accorded an opportunity to deal with this harmful gap.

**Results and lessons learnt:** A set of guidelines on tobacco intervention and cessation were written to add to the revised TB guidelines. The tobacco intervention guidelines (2010) are completely patient-driven based on an extensive research of information needs, entry skills, audience profiles, beliefs and perceptions, barriers and roadblocks encountered by the patients. The criteria for the guidelines were easy to understand, interesting, credible, practical and practicable. In addition they follow the principles of behavioral change arrived at by conducting in-depth formative research

#### Conclusions and key recommendations:

- Can be used in any health facility and by any health worker including a dot worker who has been specially selected because the patient's dwelling is far away from the health-center or sub center
- Used whenever a patient is encountered in a health service
- Has the advantage of protecting the patients from exposure to second hand smoke.
- Has the potential to reduce considerably the number of tobacco smokers

### OPP-489-01 Predictors of tobacco smoking abstinence among tuberculosis patients in South Africa

G Louwagie,<sup>1</sup> O Ayo-yusuf.<sup>2,3</sup> <sup>1</sup>Public Health Medicine, School of Health Systems and Public Health, University of Pretoria, Pretoria, <sup>2</sup>Oral Health Sciences (School), Faculty of Health Sciences, University of Limpopo (Medunsa campus), Tshwane, <sup>3</sup>School of Health Systems and Public Health, University of Pretoria, Pretoria, South Africa.  
e-mail: goedele.louwagie@up.ac.za

**Background:** Predictors of smoking abstinence have not been studied in tuberculosis patients with high HIV co-infection rates. This study examined predictors of smoking abstinence in TB patients enrolled in a randomised controlled trial at six primary care facilities in Tshwane, South Africa.

**Design/Methods:** Socio-economic, psychosocial and smoking-related information was collected at baseline through structured interviewer-administered questionnaires. Current smokers were randomised to either brief motivational interviewing (n=205) or a brief cessation message (control, n=204) and followed up at 3 time-points. We performed univariate and multivariate logistic regression with backward elimination to identify independent predictors of sustained 3- and 6-month abstinence and of 7-day point prevalence abstinence (PPA) at 1-month follow-up. Data were analysed by intention to treat. Predictors of making a quit attempt were also determined.

**Results:** After adjusting for the intervention, HIV-positive participants had a more than 3 times higher odds of sustained abstinence than their HIV-negative counterparts (OR 3.79, [95% CI 1.13; 12.75] and OR 3.37, [95% CI 1.00; 11.31] at 3- and 6-month follow-up respectively). A higher stress score at baseline was associated with a lower odds of sustained 6-month sustained abstinence (OR 0.92 [95% CI 0.85; 0.996]). At 1-month follow-up the intervention was only effective in smokers who were not nicotine dependent. Furthermore being HIV-positive (OR 3.58 [95% CI 1.31; 9.78] and higher self-efficacy predicted 7-day point PPA (OR 1.03 [95% CI 1.01; 1.06]).

**Conclusion:** A more intensive behavioural intervention may be needed to reduce stress and increase self-efficacy in smokers. Nicotine-dependent smokers may benefit from pharmacotherapy. Dual TB-HIV infection does not appear to pose an obstacle to smoking abstinence. Introducing smoking cessation services in TB services in South Africa is recommended.

### OPP-490-01 Smoking adversely affects treatment outcomes in tuberculosis

C-K Chan,<sup>1</sup> C C Leung,<sup>1</sup> C M Tam.<sup>1</sup> <sup>1</sup>Department of Health, Tuberculosis and Chest Service, Hong Kong SAR, China. Fax: (+852) 2374 3575. e-mail: chikuen\_chan@dh.gov.hk

**Background:** Smoking has been shown to be associated with tuberculosis. Relatively scanty data is available on its effect on outcomes of tuberculosis treatment. We aim to examine prospectively the association of smoking with



tuberculosis treatment outcomes and subsequent risk of relapse.

**Design/Methods:** Consecutive patients who underwent chemotherapy for tuberculosis at 18 government chest clinics from 1st January 2001 to 31st December 2003 were followed up prospectively for two years and then through linking with the territory-wide TB notification system for relapse till 31st December 2012. The proportions of patients who successfully completed treatment within 24 months were compared by baseline smoking status. For patients who successfully completed treatment, the effect of baseline smoking status on subsequent relapse of tuberculosis was assessed with the control of other baseline characteristics using appropriate statistical methods.

**Results:** Of 16345 patients included in the analysis, 13349 (81.7%) successfully completed treatment within two years. Four hundred and twenty-six patients had a relapse, of which 204 (47.8%) were bacteriologically confirmed. Current smokers and ex-smokers were less likely to have treatment success within two years compared to never-smokers (adjusted OR 0.72(0.64-0.82) and 0.73(0.65-0.82) respectively,  $P < 0.001$ ) on multivariate analysis. Among patients who successfully completed treatment, current smokers and ex-smokers were more likely to have a relapse compared to never-smokers (adjusted HR 1.63(1.29-2.06) and 1.33(1.04-1.71) respectively,  $P < 0.001$ ). Smoking contributed to 19.4(CI: 7.5–30.9)% of TB relapse among the successful treatment completers.

**Conclusion:** Smoking adversely affected outcomes of tuberculosis treatment and subsequent relapse after completion of therapy.

#### **OPP-491-01 The provision of smoking cessation interventions for hospitalised drug resistance tuberculosis patients: an opportunity for South Africa**

P Shangase.<sup>1</sup> <sup>1</sup>Public Health, University of KwaZulu-Natal, Durban, South Africa. e-mail: shangasep@ukzn.ac.za

**Background and challenges to implementation:** Studies have confirmed smoking as an associated risk factor that reduces the effectiveness of drug resistant tuberculosis (TB) treatment in patients. Additionally, drug resistant TB remains the leading cause of mortality and major cause of morbidity in South Africa. Despite this convergence between drug resistant TB treatment and smoking, there is still no evidence of availability of smoking cessation interventions in any health facility in South Africa. In this context, the association of smoking with resistance to second-line injectable drugs among drug resistance TB patients has also been reported in South Africa.

**Intervention or response:** An in-depth literature review of existing body of knowledge was applied with a view of making recommendations on how in-hospital smoking cessation interventions may be an effective quit strategy for drug resistance TB patients. The Cochrane Tobacco Addiction Group register was searched for studies of

interventions for smoking cessation in hospitalised patients in February 2014. Fifty studies met the inclusion criteria, comparison included 'inpatient', 'outpatient', 'cardiovascular disease', tuberculosis and 'smoking'.

**Results and lessons learnt:** Reviewed literature indicated that as hospital settings are enabling environments to sustain behavior, smoking cessation interventions contributed to significant improvements in the quality of patients' care without interrupting services, and within existing staff constraints. Furthermore, results showed that the advantage of institutions like hospitals is the availability of relevant resources that can be exploited in order to successfully implement smoking cessation interventions. Evidence from in-depth literature review clearly indicated that counselling and pharmacotherapy may be synergistic and that providing psychological support to quitting, counselling after discharge may also help increase quit rates by improving adherence to cessation medications that were started in the hospital. Additionally, health status was indicated to affect motivation for smoking cessation for patients diagnosed with smoking-related disease like drug-resistant TB.

**Conclusions and key recommendations:** Smoking cessation interventions increase quit rates when incorporated into the care of hospitalized patients who are smokers, and they can be an effective quit strategy for drug-resistant TB patients in South Africa.

#### **OPP-492-01 Excess deaths of cancer and respiratory diseases due to smoking among males in Tianjin, China**

GH Jiang,<sup>1,2</sup> ZL Xu,<sup>1</sup> W Li,<sup>1</sup> DZ Wang,<sup>1</sup> W Zheng,<sup>1</sup> H Zhang.<sup>1</sup> <sup>1</sup>Non-Communicable Diseases Control Institute, Tianjin Centers for Disease Control and Prevention, Tianjin, <sup>2</sup>School of Public Health, Tianjin Medical University, Tianjin, China. e-mail: jiangguohongtjcdc@126.com

**Background:** To assess smoking related cancer and respiratory diseases deaths among males from 2010 to 2012 in Tianjin, the third largest city of China.

**Design/Methods:** The mortality cases were collected from the Tianjin All Cause of Death Reporting System which covered the entire residential population over 10 million. Cause of death was classified according to the International Classification of Disease, 10<sup>th</sup> revision (ICD-10). Controls were men who had died of causes not associated with tobacco. A total of 18456 male death cases aged 18 to 69 years were recruited in current study. Case-control study was conducted to analysis the risk of smoking related specific disease death after adjusting age and education. The excess deaths were also calculated.

**Results:** The smoking rate were higher among cancers and respiratory diseases deaths than control group. From 2010 to 2012, 3526 (31.23%) cancer and 233 (15.88%) respiratory diseases deaths were caused by smoking. Among cancers, the association of lung cancer mortality risk and smoking was strongest (OR=3.10, 95%CI:2.80-3.44), then followed cancer of oral cavity and larynx (OR=2.36, 95%CI:1.84-3.03). The mortality risk of Chronic lower respiratory diseases was higher than

Other respiratory diseases (OR:1.83 vs 1.12). The mortality risks of all cancers and all respiratory diseases were 1.74 and 1.35 times higher than non-smokers.

**Conclusion:** 3526 (31.23%) cancer and 233 (15.88%) respiratory diseases deaths were caused by smoking, it is urgent for us to take effective methods to decrease tobacco use.

**Table 1 Mortality risk and excess deaths of all cancer and all respiratory diseases among men in Tianjin, China, 2010–2012**

Cause of death	N of deaths	N of smokers* (%)	OR# (95%CI)	N (%) of excess deaths due to smoking
Control	5701	2822 (49.5)	1.0	-
All cancers	11290	7491 (66.4)	1.74(1.62-1.87)	3526 (31.23)
Lung cancer	4317	3313 (76.7)	3.10(2.80-3.44)	2245 (52.01)
Cancer of oral cavity and larynx	328	233 (71.0)	2.36(1.84-3.03)	134 (40.95)
Cancer of digestive organs	5175	3112 (60.1)	1.46(1.34-1.59)	982 (18.97)
Other cancers	1470	833 (56.7)	1.25(1.11-1.41)	165 (11.22)
All respiratory diseases	1465	853 (58.2)	1.35(1.19-1.53)	233 (15.88)
Chronic lower respiratory diseases	636	404 (63.5)	1.83(1.53-2.20)	184 (28.86)
Other respiratory diseases	829	449 (54.2)	1.12(0.96-1.31)	49 ( 5.93)

\* smoker includes current smoker and former smoker # adjusting for age and education

#### OPP-493-01 National tuberculosis registry: a Kazakhstan case study

S Hermosilla,<sup>1</sup> A Terlikbayeva,<sup>2</sup> B Zhussupov,<sup>2</sup> A Aifah,<sup>3</sup> T Abildayev,<sup>4</sup> R Issayeva,<sup>5</sup> N Schluger,<sup>1</sup> S Galea.<sup>1</sup>

<sup>1</sup>Epidemiology, Columbia University, New York, NY, USA; <sup>2</sup>Global Health Research Center of Central Asia, Columbia University, Almaty, Kazakhstan; <sup>3</sup>School of Social Work, Columbia University, New York, NY, USA; <sup>4</sup>Directorate, National Center for Tuberculosis in Kazakhstan, Almaty, Kazakhstan; <sup>5</sup>Center for Life Sciences, Nazarbayev University, Astana, Kazakhstan. e-mail: sh2405@columbia.edu

**Background:** Despite recent declines in pulmonary tuberculosis (TB) morbidity and mortality globally, the potential for reservoirs of TB to threaten global public health warrants epidemiologic study. In Kazakhstan, a World Health Organization (WHO) high TB burden country, the development and transmission of TB is poorly understood. In 2010 86% of incident cases in the national TB registry had only the “unknown” category documented as a known TB risk factor.

**Design/Methods:** We studied the sensitivity and specificity of a low stigmatizing risk factor (smoking) reported in the Kazakhstan National TB registry managed by the

Kazakhstan National Tuberculosis Program (NTP) in a high multidrug-resistant TB burden province (Almaty oblast). Participants included 110 TB cases with newly detected pulmonary TB in 2012. Structured questionnaires, administered in Kazakh or Russian, measured known and hypothesized social and structural drivers of TB. Surveillance data were provided by the NTP.

**Results:** 110 (87%) of the 126 incident TB cases registered during the study period (June 2012-January 2013) met study inclusion criteria. 110 (100%) were interviewed and relevant data was extracted from their matched clinical record in the TB registry. Based on the study design, incident cases were identified through the TB registry, thus 110 (100%) of the TB cases were in the TB registry. 91 (83%) of cases have a risk factor listing in the clinical record as “unknown”. 41 (76%) of those who responded to the smoking item in the questionnaire reported that they had smoked a cigarette in the past six months. 0 (0%) of these smokers were categorized as smoking in the surveillance clinical record. 37 (90%) of the smokers have a risk factor of “unknown” as opposed to “smoking” in the clinical record.

**Conclusion:** The precise and timely reporting of TB cases to a national surveillance system can be a crucial tool in combating TB and MDR-TB. Additional work to improve the quality of documentation in these reporting systems is necessary to accurately document and address the growing MDR-TB epidemic.

#### OPP-494-01 Tobacco use and tuberculosis in India: implications in control of dual epidemics

K Sagili,<sup>1</sup> P Lal,<sup>2</sup> S Srinath,<sup>3</sup> R J Singh,<sup>2</sup> N Wilson,<sup>4</sup> S Chadha.<sup>3</sup> <sup>1</sup>Research, The Union, New Delhi, <sup>2</sup>Tobacco control, The Union, New Delhi, <sup>3</sup>Tuberculosis control, The Union, New Delhi, <sup>4</sup>Public Health, Independent Consultant, New Delhi, India. Fax: (+91) 011 4605 4430. e-mail: ksagili@theunion.org

**Background:** India is a high-burden country for tuberculosis and over a fourth of all TB globally is estimated to occur in the country – about 2 million patients annually. The Global Adult Tobacco Survey (2010) estimates that there are about 275 million adult (>15 years) tobacco users in the country. The increased risk for tuberculosis (infection, disease and death) have been well studied and the million death study (2008) in India showed that smoking men were three times more likely to die from TB than non-smokers.

**Design/Methods:** A cross-sectional community-based survey to assess knowledge, attitudes and practice with respect to TB was conducted in 30 districts across 15 states and responses recorded from 5300 adults from households within identified clusters. Of these, 4804 individuals were from the general population and 496 identified themselves as TB patients (patients who are currently undergoing treatment or had finished TB treatment in the past one year) (Table 1). A population proportionate to size (PPS) sampling method was used to determine the urban-rural dispersion. Pre-tested questionnaires were used to estimate the prevalence of tobacco use among the study population.

**Results:** Of the 4804 individuals from the general population, 1158 (24%) were tobacco users (Table 1). Among those who use tobacco, 405 (35%) smoke, 650 (56%) chew and about 103 (9%) are dual users. Of the 496 TB patients that were interviewed, 175 (35%) were tobacco users. Among those who use tobacco, 42 (24%) smoke, 63 (36%) smokeless, about 8 (5%) are dual users and a large section of them (35%) did not respond to this question.

**Conclusion:** Tobacco use (smokers, chewers and dual users) prevalence among TB patients is significantly high compared to the general population ( $p=0.0000001$ ). Of every 3 TB patients, one is a tobacco user and 1 tobacco user for every 4 in the general population. Tobacco use may be an important driver of the TB epidemic in India, whether in rural or urban settlements. Effective strategies for quitting tobacco use among TB patients must be implemented. Increasing the accessibility of cessation centres at village or ward level must be considered. This could have direct impact on TB treatment outcomes.

Table 1: Demographic profile and tobacco use among general population and TB patients from 30 districts in India

	General Population		TB Patients	
	Total N=4804		Total N=496	
	N	%	N	%
Rural	3360	70	369	74
Urban	1444	30	127	26
Male	2408	50	302	61
Female	2396	50	194	39
<b>Tobacco use</b>	<b>N=1158 (24%)</b>		<b>N=175 (35%)</b>	
Rural	835	72	127	73
Urban	323	28	48	27
Male	932	80	141	81
Female	226	20	34	19

### OPP-495-01 Could smoking change pulmonary tuberculosis feature?

S Ben Saad,<sup>1</sup> isla Mejri,<sup>1</sup> H Daghfous,<sup>1</sup> moun Ben Khelifa,<sup>1</sup> hela Cherif,<sup>1</sup> F Tritar.<sup>1</sup> <sup>1</sup> Respiratory Department (C), Abderahmen Mami Hospital, Ariana, Tunisia. Fax: (+216) 7182 1184. e-mail: hafaoua.daghfous@yahoo.fr

**Introduction:** Smoking reduces immunity and expose to multiple respiratory infections such as pulmonary tuberculosis (TB).

**Aim:** -Evaluate the socio-economical status of smokers with TB. Study the impact of smoking on the severity and the outcome of this disease.

**Methods:** Ninety six patients treated for Tb between 2011 and 2013O were enrolled in a retrospective and comparative study and subdivided in 2 groups: group 1 (G1): 48 smokers and group 2 (G2) 48 non-smokers. We compared their socio-economical status, clinical and radiological characteristics and their outcome.

**Results:** Mean age of patients was 40 years (G1: 44 years and G2: 40 years). According to risk factors of tuberculosis G1 was statically significant more likely to jobless (48% versus 8%), alcoholism (40 % vs 10%), drug addiction (8% vs 0%), history of incarceration (16% vs 0%) and diabetes mellitus (10% vs 2%) ( $p<$

0.001). Chronic respiratory diseases were statically more frequent in G1 12% versus (vs) 3% ( $p<0.01$ ). Non-smokers consulted earlier than smokers (63 days vs 95 days after first symptoms). G1 is more contagious than G2 ( $p<0.01$ ). Comparing radiologic lesions noted in 64% of cases in G1 vs 45% in G2, cavitations were significantly higher in G1 (69% vs 37%). During treatment, smokers were likely to develop medical side effects (60% vs 42%). In G1, sputum smear were positive in 33% of cases and 13% of cases in G2 after 2 months of treatment. Recovery was obtained in all cases after 6 months of treatment. Radiological sequels persisted in 36% (G1) and 15% (G2). There was no statistical significant difference in radiological outcome and smear and culture conversion in the 2 groups

**Conclusion:** Management of smokers with Tb needs particular attention. They are vulnerable because of their low socio-economic condition, alcohol and drug addiction. TB is severe due to late consultation.

### OPP-496-01 Effect of continuing to smoke in patients with lung cancer

R Roberts,<sup>1,2</sup> K Lewis.<sup>1,2,3</sup> <sup>1</sup>College of Medicine, Swansea University, Swansea, <sup>2</sup>R&D, Hywel Dda University Health Board, Llanelli, <sup>3</sup>Respiratory, Hywel Dda University Health Board, Llanelli, UK. e-mail: rachel.roberts3@wales.nhs.uk

**Background:** Studies suggest that continued smoking after a diagnosis of Lung Cancer (LC) independently worsens quality of life, and shortens life expectancy, but these were retrospective and smoking was not validated biochemically. We wanted to see if current smoking status independently affects prognosis in newly diagnosed LC.

**Design/Methods:** Early findings of our trial (NCT01192256) from 406 patients with newly diagnosed LC who were followed for at least 6 months. Smoking status was verified by exhaled carbon monoxide (eCO) on every clinical visit with anyone admitting to smoking within the last month or with eCO>10 ppm defined as current smokers.

**Results:** At the time of LC diagnosis 41% were current smokers, they were significantly younger yet had larger tumours and worse performance status. 73.6% of those who were smoking at the time of diagnosis were alive at 6 months, compared to 81.3% of ex- or never smokers. 51% of patients who smoked experienced treatment complications compared to only 41% of patients who did not smoke, however this was not significant ( $p=.143$ ). Of those patients who quit smoking within 1 month of diagnosis, 14% were deceased by 6 months compared to 22% of those who continued to smoke.

**Conclusion:** We have found that quitting smoking impacts survival in patients with Lung Cancer. Further data collection regarding histology, treatments and outcomes is ongoing. Results suggest smoking cessation treatments should be offered within LC MDTs and at all follow-up appointments.



## SYMPOSIA: SATURDAY 1 NOVEMBER 2014

### 38. PROGRESS AND LESSONS LEARNT FROM NATIONAL TB PREVALENCE SURVEYS

#### Results from the national TB prevalence survey of Indonesia

DB Lolong,<sup>1</sup> Iam Pangaribuan,<sup>1</sup> An Musadad,<sup>1</sup> MB Dwihardiani,<sup>2</sup> D Mustikawati.<sup>3</sup> <sup>1</sup>National Institute of Health Research and Development, Ministry of Health Republic Indonesia, Jakarta, <sup>2</sup>Tuberculosis, World Health Organization, Indonesia country office, Jakarta, <sup>3</sup>Communicable Disease Control, Ministry of Health Republic Indonesia, Jakarta, Indonesia.

**Background:** Indonesia has been applying the DOTS strategy since 1995. The 2005 Global target of treatment success of 85% has been achieved since the year 2000 and case detection rate reached 78% in 2010. However, the decrease of notification has not been observed. National TB Prevalence Survey is being conducted to monitor the TB epidemiological trends, the impact of TB control program, and clarify the non-declining notification.

**Method:** A cross sectional survey to determine the positive smear and bacteriological confirmed TB among those aged 15 or more in Indonesia was conducted from 14 April 2013 to 30 June 2014. Stratified cluster sampling based on region and rural urban division was applied. Eligible population was interviewed to find TB symptoms and screened with thorax x-ray. Sputum microscopy, Xpert MTB/Rif, and LJ culture were applied to those who were positively screened by interview or/and x-ray. Individual level analysis with multiple imputation and inverse probability weight was used to analyze the prevalence.

**Results:** There were 67,915 participants (89%) out of 76,528 eligible populations from 156 selected clusters. Preliminary analysis was conducted for 99 clusters (48,986 participants). Smear positive TB prevalence was 285.2 (95% CI: 222.6–347.8) and bacteriologically confirmed TB prevalence was 590.0 (95% CI: 505.5–674). Among TB cases, 55% presented with positive symptoms screening and 93% were with positive x-ray screening. Positive x-ray without positive symptoms screening contributed to 45% of cases. Only 5% of TB cases found admitted to be under treatment. Among participants who declared being under TB treatment, 54% took the treatment in public facilities (health center or hospital).

**Conclusion:** TB prevalence in Indonesia is still high. High proportion of TB cases had suggestive thorax x-ray results without positive symptoms. Very few TB cases were under treatment. Private facilities were highly

utilized for TB treatment. Strategies to increase case finding and notification should be widely implemented.

#### Overview, progress and the current standard design of national TB prevalence surveys

I Law. TB Monitoring and evaluation, Global TB Programme, World Health Organization, Geneva, Switzerland.

Surveys measuring the prevalence of tuberculosis (TB) disease have been ongoing for more than 50 years; most of which have been undertaken in Asia and Africa. In many countries with a high TB burden, national TB prevalence surveys are the only way to obtain a reliable and direct measure of the burden of TB disease and monitor trends. Given the global target to halve TB prevalence by 2015 compared with a baseline of 1990, there have been tremendous collaborative efforts for it to be accurately measured. From 1990 to 2014 there have been 32 TB nationwide prevalence surveys: 21 in 12 different countries in Asia (including repeat surveys), and in 11 different countries in Africa. The current survey methodology, developed by WHO in 2007 and revised in 2010, is primarily based on symptom and field chest X-ray screening, followed by sputum smear microscopy and culture for diagnostic confirmation. The use of new diagnostic technologies (e.g. GeneXpert) has been proven to work in such large-scale high-throughput surveys, and been of further use in defining and managing TB cases. Given the enormous efforts required to undertake a TB prevalence survey, often in poor-resourced countries, many stakeholders, donors and technical agencies are involved from initial protocol development, during field operations, data analysis through to the dissemination of final results and programmatic implications in order to ensure a high quality survey. It is clear that prevalence surveys have provided a wealth of information that not only fulfils the primary objective of determining the prevalence of pulmonary TB disease at the national level, but also assists national TB programmes with future policies and strategies to improve TB care and control.

#### Can we seek new and simpler methods for post-2015 surveys?

E Klinkenberg,<sup>1,2</sup> E Tiemersma,<sup>1,2</sup> N Kalisvaart,<sup>1</sup> E Mitchell.<sup>1,2</sup> <sup>1</sup>Research and Surveillance Unit, KNCV Tuberculosis Foundation, The Hague, <sup>2</sup>Global Health, Amsterdam Institute for Global Health and Development, Amsterdam, Netherlands.

The experience of recent surveys and new innovative technologies led to gains in efficiency and accuracy of the methodologies to estimate TB prevalence. The role of Xpert MTB/RIF has become critical to aid the diagnostic decision. Xpert has been used as confirmative test on smears with good results. The need for large numbers of cultures without affecting routine operations made for example Mozambique look for new innovative ways of measuring TB prevalence using Xpert as key diagnostic method. X-ray technology is rapidly developing; several

surveys used real-time quality assurance via transfer of images by internet/telephone. In addition, automatic X-ray reading systems are being explored to solve the shortage of radiology staff to read the large number of images involved. Data management has taken a flight evolving from fully paper-based surveys to surveys with fully integrated electronic data collection via PDA/tablet with barcodes linking all collected information (Zambia) as well as new web-based systems to be designed (Kenya). Integration of existing X-ray and laboratory systems for data processing may optimize data capturing. Increasingly, countries, especially in Africa, are integrating HIV testing for all presumptive TB cases (Rwanda, Tanzania) or for all participants (Zambia, Mozambique). Fear of the effect of stigma around HIV testing negatively affecting participation proved otherwise. Future surveys may consider adapted screening algorithms for HIV positive participants to minimize missing TB-HIV cases by optimizing the sensitivity of the screening methods deployed. Widening the symptom screening algorithm to include more symptoms, as done in Zambia, substantially increases the number of presumptive TB cases and thus laboratory workload. A two-tier algorithm could reduce the number of samples but at the same time increase sensitivity. Countries could explore combining HIV and TB prevalence survey to make efficiency gains in resources and promote joint TB-HIV operations exploring including CD4 and viral load. Testing for risk factors like diabetes could deliver much needed evidence. Another challenge to address is how best to capture the prevalence of the whole population, including children and the institutionalized population who are now excluded. New techniques to enhance sputum production may need to be explored. Nationwide prevalence surveys remain costly and time consuming and new methods to estimate the TB burden should be investigated.

### Results from the national TB prevalence survey of Malawi

R Banda,<sup>1</sup> J Mpunga,<sup>1</sup> A Munthali,<sup>2</sup> <sup>1</sup> Ministry of Health, National Tuberculosis Control Programme, Lilongwe, <sup>2</sup>University of Malawi, Chancellor College, Centre for Social Research, Zomba, Malawi.

**Background:** A nationwide tuberculosis prevalence survey was conducted in Malawi (2013- 2014) to determine the prevalence of pulmonary tuberculosis (PTB) among persons aged 15 years and older. The WHO estimated prevalence of TB was 278 per 100,000 in 2011.

**Methods:** A multistage cluster-sampled cross-sectional survey was implemented nationwide. All eligible persons aged at least 15 years were screened for TB symptoms (cough for two weeks or more) and by chest X-ray (CXR) in the field. Persons who screened positive were asked to submit spot and morning (2) sputum specimens for smear microscopy and culture. A bacteriologically-confirmed case was defined as an eligible participant with MTB confirmation by gene-Xpert or culture. Participants with

a smear-positive result of 4b or more were tested with gene-Xpert.

**Results:** Of 39,020 eligible individuals in 74 clusters, 31,579 (80%) participated in the survey. CXR was performed among 31,561 participants. A total of 1,989 (6.3%) participants were eligible for sputum examination. The provisional TB prevalence of bacteriologically-confirmed TB in those 15 years and above is estimated to be 301/100 000 (95%CI 246–368). Prevalence increased with age, was higher in men than in women, and higher in urban than rural areas. Most prevalent TB cases did not acknowledge that they were HIV-positive.

**Conclusion:** Although the estimated prevalence is slightly higher than the WHO estimate, this is a very conservative estimate because of the strict case definition. The provisional estimate is applicable to the adult population only. Nonetheless, there is need for the NTP to broadly strengthen TB control strategies that include improved case detection and with a specific focus on selected population groups.

### 39. ENGAGING COMMUNITIES OF SPECIAL RISK GROUPS IN CONFLICT AFFECTED COMMUNITIES

#### Challenges and opportunities of building tuberculosis control in a newly defined health system after over 20 years of civil war

C Minani,<sup>1</sup> R Ng'ielia,<sup>1</sup> S Natalina,<sup>1</sup> E Wasilwa,<sup>1</sup> E D'agostino,<sup>2</sup> H Lasu,<sup>3</sup> J Mogga.<sup>3</sup> <sup>1</sup>Health, Arkangelo Ali Association, Nairobi, Kenya; <sup>2</sup>Health, Comitato Collaborazione Medica (CCM), Juba, <sup>3</sup>Health, National TB, Leprosy and Buruli Ulcer Control Program (NTLBP), Juba, Republic of South Sudan

**Background:** South Sudan, the world's youngest nation, became independent in July 2011 after 28yrs civil war. The lingering effects of that war reflect a period of extensive social turmoil where basic services including healthcare and infrastructure were greatly disrupted, services in congregate setting are lacking and social and community networks affected resulting in inequitable distribution of resources limiting TB services to 25% coverage. On average, about 50-100km distances between health facilities is substantial for sick persons in a country where WHO in 2012 estimated TB burden at 257/100,000 and only 97/100,000 notified.

**Design/Methods:** Passive case finding, though economically viable, seems unsuitable to address the TB problem in South Sudan. Active case finding implemented April 2013-March 2014 in 5 states and 13 counties engaged local communities through Leaders, Community Health Workers, community radios and TB mobilizers to support door-to-door screening, referral and retrieval of treatment interrupters. TB screening targeted predefined congregate cosettings of prisons, army garrisons, IDP/ fishing/refugee/returnees/cattle camps, PLHIVs during monthly ART refills and hospital wards targeting individuals with chronic cough and malnourishment.

Satellite laboratories and TB clubs were initiated to minimize diagnostic delays and promote adherence.

**Results:** 75,407 were symptom-screened for TB; the highest yield was among chronic coughers at OPD/IPD services but with low confirmed cases ( $n=562$  SS+/B+) (0.8% or 130 individuals screened per case detected) compared to contact investigation of adult SS+/B+ index cases (2.7% or 38 screening per case detected). Direct activity yield was 862 SS+/B+ and 1520 all forms TB cases; a 20% and 33% increase respectively. 90% of the SS+/B+ and 94% of all forms TB initiated treatment within 48 hours of diagnosis with over 90% treatment success.

**Conclusion:** Community engagement increased case finding with minimal treatment interruptions. Down-shifting tasks linked to TB screening; facilitative on-job training, mentoring and coaching allowed increased coverage of TB services of sufficient quality in resource-constrained/conflict setting. We recommend budget-realistic funds for TB services in resource constrained/conflict settings and TBMUs expansion to increase access; and training on infection prevention control and sustained door-to-door screening of contacts to eliminate TB in the community.

### TB screening in the garments industry in Bangladesh during worker unrest and management reluctance

K Talukder,<sup>1</sup> MQK Talukder,<sup>1</sup> M Hasan,<sup>1</sup> R Islam,<sup>1</sup> I Jerin,<sup>1</sup> M Akter,<sup>1</sup> S Chowdhury,<sup>1</sup> A Rahman.<sup>2</sup> <sup>1</sup>Child Health, Centre for Woman and Child Health (CWCH), Ashulia, <sup>2</sup>Public Health and Informatics, Jahangirnagar University, Savar, Bangladesh.

The garments industry is arguably the leading contributor to the rapid transformation of Bangladesh from a low to a middle-income country. The country's garments workers are however vulnerable to tuberculosis because they are poor migrants working and living under crowded conditions. Two previous studies suggest TB in this population was 3–4 times the national estimates at the time. This led the Centre for Woman and Child Health (CWCH) in Bangladesh to design and implement a comprehensive garments TB screening and detection programme with TB Reach Wave 3 funding. Between April 2013 and September 2014 the CWCH had plans to screen approximately 500,000 garments workers working in 500 factories in Savar/Ashulia, Dhaka – the garments heartland of Bangladesh. This work is being carried out under NTP stewardship. The CWCH team of 15 screening personnel and one doctor enters a garments factory with a mobile chest x-ray bus in the morning. In the course of the day these 15 screening personnel walk down the production lines and ask each of about 1,500–2,000 workers about the following 11 features of TB: 1. Cough for more than 3 weeks; 2. Frequent fever; 3. Blood in sputum; 4. Cough not improving with antibiotics; 5. Weight loss; 6. Loss of appetite; 7. Night sweats; 8. Contact with TB patient; 9. TB not improving on treatment; 10. Swellings/lumps in the neck, armpits or

groin; 11. Swollen joints or limbs. If a worker answers positively to either Q1 or any three or more of the remaining questions, he/she is referred to the on-site CWCH team doctor who takes a more detailed history, examines the worker and orders a chest x-ray and/or sputum for AFB microscopy. The x-ray is done in the mobile x-ray bus and the sputum is collected at the factory and transported to the CWCH laboratory for AFB microscopy and Gene Xpert testing if necessary. The first 16 months of this programme between the 8<sup>th</sup> of April 2013 and the 12<sup>th</sup> of August 2014 has resulted in screening for TB in 275,029 garments workers, with detection and notification of 435 cases i.e. 158 all case detections per 100,000 workers. This rate of detection is lower than the “estimated” national incidence of 220 all cases per 100,000. The sputum positive detections were 176 cases among 275,029 workers – i.e. 64 per 100,000. The Bangladesh Nationwide Tuberculosis Disease-cum-infection Prevalence Survey from 2007-09 showed an overall adjusted prevalence of new smear-positive TB of 79 per 100,000 adult population.



### High prevalence of TB-HIV and rifampicin-resistant TB among military populations of Eastern Democratic Republic of Congo

E Andre,<sup>1</sup> J-P Chirambiza,<sup>2</sup> E Musafiri,<sup>2</sup> D Kalumuna,<sup>2</sup> D Bahati Rusumba,<sup>3</sup> D Kikobya,<sup>3</sup> J Creswell,<sup>4</sup> O Le Polain De Waroux.<sup>5</sup> <sup>1</sup>Pôle de Microbiologie, Université Catholique de Louvain, Institut de Recherche Expérimentale et Clinique, Brussels, Belgium; <sup>2</sup>Coordination Provinciale Lèpre et Tuberculose du Sud-Kivu, Programme National de Lutte contre la Tuberculose, Bukavu, <sup>3</sup>Médecine Interne, Hôpital Provincial FARDC, Bukavu, Democratic Republic of Congo; <sup>4</sup>TB Reach secretariat, Stop TB Partnership, Geneva, Switzerland; <sup>5</sup>Department of Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, UK.

**Background:** Although the prevalence of HIV and incidence of TB are known to be high among military communities in South Kivu (DRC), quantitative data are lacking. We here report the results from a TB screening programme conducted between 2012 – 2014 at the Provincial Military Hospital in Bukavu, South Kivu, using a rapid molecular test (Xpert MTB/RIF). Prior qualitative studies have shown this group is exposed to poverty, promiscuity, sexual behaviours at risk of HIV



and poor medical education. This project was supported by TB REACH.

**Design/Methods:** Patients clinically suspected of pulmonary TB with no prior history of TB treatment were included in this study. One sample per patient was tested after three negative smear results. We analysed 468 valid Xpert results and the HIV status of patients when available.

**Results:** 30 patients (6%) tested positive for TB, with a proportion decreasing from 16% (year 1) to 2.25% (year 3). Among TB-positive patients, 8 (27% (95%CI 14 – 46%)) were Rifampicin resistant. HIV test results were available for 25% (116/468) of the patients, with an HIV prevalence of 19% (95%CI 12 – 27%). Among the 102 TB negative patients with HIV results, HIV prevalence was much lower than among TB positive patients, in whom the prevalence was 71% (95%CI 40 – 90%)

**Conclusion:** Very high rates of TB, HIV and TB/HIV infections are prevalent among military communities. Xpert testing permitted the diagnosis of 6% of patients with TB symptoms but negative smear results. 27% rifampicin resistance was observed among these patients with no prior history of TB. This specific professional group and their families should urgently be targeted with specific active strategies in order to prevent dissemination of diseases both inside and outside their community.

### How could TB control be organised within an open conflict?

A Nasrat,<sup>1</sup> M Seddiq,<sup>2</sup> A Sanaie,<sup>1</sup> O Ramis.<sup>3</sup> <sup>1</sup>TB project, ACREOD, Kabul, <sup>2</sup>NTP, MoPH, Kabul, Afghanistan; <sup>3</sup>TB REACH Monitoring & Evaluation, HLSP and KIT, Barcelona, Spain.

**Aim:** The assessment aimed to explore the effects of open conflict and insecurity on TB control activities in Afghanistan.

**Methods:** The assessment targeted 47 Health Facilities (HFs) supported by TB REACH Wave-1 in 5 provinces (Nangarhar, Kunar, Kandahar, Paktia and Faryab). Methods of records and reports review and telephonic interviews were used for data collection to explore how the conflict increased vulnerability to TB, how conflict affected TB services and what were the responses of TB workforce to mitigate and reduce conflict effects. 47 HFs were sorted to areas with very good, good, fair, bad and very bad security conditions. Within 47 HFs, 3 major TB key indicators were assessed during 4 years (2010–2013)

**Results:** Conflict has given birth to poverty, displacement and obscured family income, which increase vulnerability to TB. The findings indicated that utilization of health services by respective population has been minimally affected by security as OPD attendants have remained constant in all areas during 2010 to 2013. In areas where security was a concern TB indicators were already below the line. However, deterioration of security during recent times has strongly affected TB services there as TB suspect identification among HF's OPD attendants was 3.6%, 3.2%, 2.6%, 2.3% and 1.8%; SS+ TB case detection among OPD attendants was 9.7%, 8.7%,

8.7%, 7.0% and 6.7% for areas with very good, good, fair, bad and very bad security conditions respectively. Conversely, the treatment success rate was relatively good in all areas though insecurity decreased quality of health services due to high turnover of staff, absence of qualified health staff and insufficient supervisory visits.

**Conclusion:** Conflict has increased the vulnerability to TB. Insecurity has been minimally affecting utilization of healthcare services in the area because the HFs are not continuously under open conflict. However, as the security situation deteriorates, the quality of TB services is greatly affected.

## 40. TUBERCULOSIS INFECTION CONTROL AND OCCUPATIONAL TB AMONG HEALTH CARE WORKERS: A TIME FOR ACTION

### Caring for the carers: occupational health in resource-limited settings

M Dlamini,<sup>1</sup> V Williams.<sup>1</sup> <sup>1</sup>Nursing, International Council of Nurses, Geneva, Switzerland.

Swaziland Wellness Centre Innovation The Swaziland Nurses Association established a nurse-managed wellness centre in the country in collaboration with the International Council of Nurses in 2006. The wellness centre provides confidential and comprehensive health service delivery to health care workers (HCWs) and their families from both the private and public sectors. The centre and its staff treat HCWs with respect and honor their right to receive high quality, confidential and compassionate care. Moreover, it plays a supportive role to the activities of Ministry of Health and Public Service HIV/AIDS Coordinating Committee (PSHAAC). HCWs are the most valuable asset for health care delivery and everything possible must be done to help them provide the highest quality of care. If HCWs are troubled by their own ill-health, or other stressful circumstances, then they will not be able to give their full attention to providing treatment and care to others. No hospital or clinic can function effectively if there is a high incidence of ill health among HCWs. There is a lack of data in the country on the impact of TB among HCWs although it is believed that the burden of TB among HCWs is high. In 2012 the Wellness Centre in collaboration with URC and the NTP conducted TB screening campaigns in hospitals and clinics across the country to screen HCWs for TB. The results indicate that screening HCWs for TB can be rolled out nationally with training and the incidence of TB among HCWs in Swaziland is estimated to be 1339/100,000.

### Surveillance of TB among HCWs in low-resource settings

S Verver,<sup>1</sup> M Meis,<sup>1</sup> S Kaminsa,<sup>2</sup> M Mwale,<sup>2</sup> C Mukwangole,<sup>2</sup> B Sichinga,<sup>2</sup> N Kapata,<sup>3</sup> MK Simpungwe.<sup>4</sup> <sup>1</sup>Unit Knowledge, Research and Policy, KNCV Tuberculosis Foundation, The Hague, Netherlands; <sup>2</sup>TB,

FHI360, Lusaka, <sup>3</sup>TB, Ministry of Community Development and MCH, Lusaka, <sup>4</sup>DMO, District Medical Office Ndola, Ndola, Zambia.

**Background:** Health care workers (HCW) are at higher risk of contracting TB. According to WHO/ILO guidelines they should get priority access to care for TB, and TB among HCW should be monitored. As an example we present a project to assess feasibility of a program on TB and HIV screening and monitoring among HCW in Zambia.

**Design/Methods:** 13 government supported clinics and 2 hospitals in 1 district (Ndola) participated in a larger project on TB infection control. HCW were screened in their own facility by an entrusted person. The agreed screening algorithm for HCW included annual symptom screening, with sputum smear, priority access to culture and chest x-ray performed for those suspected of TB. Only aggregated data were collected for surveillance to ensure confidentiality. Only priority diagnostics and data collection were funded, but not staff time, to encourage sustainability.

**Results:** A total of 1011 out of 1619 (62%) health care workers and 51% of 138 community volunteers were screened within 1 year. The 13 clinics reached a mean coverage (proportion screened) of 56%, the district hospital 76% and the children hospital 15%. 5% of those screened were presumptive TB cases. At least 5 HCW were diagnosed with TB during screening of whom 1 was already on treatment. The total number of cases among HCW in 2013 was 18 among 1757 HCW and volunteers together, showing a notified incidence among HCW of 1% (95% CI 0.6-1.6), similar in hospitals and clinics. After correction for age, this was similar to TB notification in the general population. One HCW died of TB.

**Conclusion:** It is feasible to conduct screening for TB and HIV among HCW in clinics and it facilitates monitoring of TB among HCW. Advocacy is needed to target managers and HCW on the protocol and the chosen screening algorithm. Resources should be allocated for ensuring priority access to diagnostics, logistics and confidential registration. Registration in regular surveillance system is possible using risk categories.

## 41. MOVING THE NEXT GENERATION OF TB DIAGNOSTICS FOR DRUG RESISTANCE CLOSER TO PATIENTS: DATA SHARING

### Population genomics of *Mycobacterium tuberculosis* complex

S Gagneux. Department of Parasitology & Infection Biology, Swiss Tropical and Public Health Institute, Basel, Switzerland.

The *Mycobacterium tuberculosis* complex (MTBC) adapted to humans currently comprises seven main phylogenetic lineages that are associated with different geographical regions and human populations. The evolutionary forces that shape the global diversity of

MTBC are not well understood. In particular, if and how these forces differ among the different human-associated lineages of MTBC is unknown. We have been using population genomic techniques and applied those to a global set of 419 whole-genome sequences of MTBC clinical isolates representative of all seven human-associated lineages. Our results show that these lineages differ both in the amount and the nature of within-lineage diversity, suggesting different forces driving the evolution of these lineages. Our findings also suggest a possible explanation for the global success of Lineage 4 of MTBC (also known as the Euro-American lineage).

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### A whole genome sequencing approach to investigate the evolution of drug resistance in South Africa

R Van Der Merwe,<sup>1</sup> S Sampson,<sup>1</sup> P Van Helden,<sup>1</sup> N Gey Van Pittius,<sup>1</sup> R M Warren,<sup>1</sup> A Abdallah,<sup>2</sup> P Arnab.<sup>2</sup> <sup>1</sup>DST/NRF Centre of Excellence for Biomedical Tuberculosis Research/MRC Centre for TB Research, Stellenbosch University, Cape Town, South Africa; <sup>2</sup>Pathogen Genomics Laboratory, King Abdullah University of Science and Technology, Thuwal-Jeddah, Saudi Arabia.

Despite significant advances in our understanding of the molecular basis of drug resistance in *Mycobacterium tuberculosis*, there are numerous gaps in our knowledge concerning the evolutionary processes preceding or following the selection of resistant mutants harbouring mutations in a known target gene. Recent reports have highlighted that the evolution of drug resistance is more complex than was previously thought. However, the role of such mutations (compensatory or mutatory) and their interactions through epistasis, remains unclear. This is problematic as current molecular diagnostics only detect a subset of the resistance markers and the impact of novel markers on treatment outcome remains largely unknown. This is especially true for isolates which are resistant to second-line anti-Tuberculosis drugs. In this study we used a bioinformatics approach to identify evolutionary events associated with the emergence of resistance to fluoroquinolones and aminoglycosides. We analysed the genome sequences of over 300 drug resistant isolates from the Western Cape of South Africa where the success rate for MDR-TB and XDR-TB treatment is 50% and 19%, respectively. Using this approach, previously uncharacterized variants associated with drug resistance were detected in several genes and intergenic regions. Strain classification, based on sequencing data, indicated that the Beijing strain type is the most prevalent, and that several other strains also circulate in the region. The detected variants were utilized in a phylogenetic investigation to determine the evolutionary relationship between strains from the Western Cape of South Africa and predominant international strains. This study indicates that drug resistance arises from a complex synergism of genomic variants and

provides a framework for building a complete spectrum of drug resistance conferring genomic variants for *M. tuberculosis* strains.

### Overview/intersection of advanced molecular methods and analyses

S Niemann.<sup>1,2</sup> <sup>1</sup>Molecular Mycobacteriology, Research Center Borstel, Borstel, <sup>2</sup>Borstel Site, German Center for Infection Research (DZIF), Borstel, Germany.

Drug resistant tuberculosis (TB) has become a global problem that is accelerated by the emergence of multidrug resistant (MDR) *Mycobacterium tuberculosis* complex (MTBC) strains. Key for the future successful control of the DR-TB epidemic is the rapid detection of resistances in clinical MTBC isolates that guides effective treatment regimens. Here, rapid molecular tests based on the detection of resistance determining variants (RDVs) such as the line probe assay MTBDRplus and the Xpert MTB/RIF assays have dramatically reduced the times to detection. However, their analytic capacity is limited as they detect a limited number of variations (mainly single nucleotide polymorphisms, SNPs) in few targets only. Furthermore, some genes such as *pncA* are not interrogated at all due to the diversity of resistance mutations. These limitations can potentially be overcome by new multi-analyte approaches e.g. based on array technologies or Next Generation Sequencing (NGS), however, the enormous amount of data generated requires new approaches for data analysis, data interpretation, and standardisation of analysis workflows. Current array technologies, targeted NGS or whole genome sequencing (WGS) analysis go far beyond conventional molecular tests by the detection of variants in a more complete set of genes or virtually all target genes involved in resistance development (resistome analysis). The latter, has become more realistic recently by the development of so-called bench top NGS systems, which can be integrated into a normal laboratory workflow, and allow for WGS of clinical isolates few days and at low costs. Rapid workflows are available for the analysis of clinical MTBC isolates using e.g. the Illumina MiSeq benchtop system in line with software pipelines usable in a small laboratory settings. Although such multi-analyte esp. NGS-based diagnostic approaches have a vast potential, their generalized use is still hampered by remaining challenges. Despite rapid cost decreases, advanced molecular analyses still remains too costly for many microbial/mycobacteriological laboratories. One major obstacle is the phenotypic interpretation of the genetic data: the genotype - phenotype challenge. Although some databasing tools are already available such as TBDRaMDB, more comprehensive and well-curated databases are needed in order to better and more quantitatively correlate genetic data with drug susceptibility phenotypes.

### Data standards for interoperability and sharing

A Starks. Division of Tuberculosis Elimination, Centers for Disease Control and Prevention, Atlanta, GA, USA.

**Background:** As molecular technologies improve, become increasingly cost-effective, and accessible to the global community, the understanding of the correlation of genotypic markers with phenotypic resistance to first- and second-line antituberculosis drugs, and ultimately patient outcomes, must keep pace.

**Design/Methods:** Whole genome sequencing is a powerful molecular technology that holds promise to advance our understanding of molecular determinants of resistance. However, this progression will require integration and analysis of laboratory data from multiple datasets and contributors into a single database. Laboratory data can be complicated by differences in genotypic and phenotypic testing methods and in formats used for results reporting. Assessment of data from disparate data sets necessitates adoption of common standards thereby enabling direct comparisons.

**Results:** The use of data standards has been shown to enable effective sharing, comparison, and integration of data from diverse sources to improve the research utility of data. This has importance for regulatory compliance should an aggregate database serve as a tool for development of new rapid diagnostics. Furthermore, development of a database could aid standards development for the capture of molecular data for global surveillance of drug resistance and reporting language for molecular diagnostics.

**Conclusion:** New Diagnostics Working Group, the Foundation for Innovative New Diagnostics, and the Critical Path to TB Drug Regimens jointly organized a meeting in February of 2014 to bring together a diverse group of subject matter experts to discuss systems to facilitate sharing of sequencing data. Continued collaborative efforts will include discussion and adoption of data standards for the purposes of an integrated database.

### Requirements for managing "big data": a global database of DR molecular sequence data

E Aviles. Data Standards, Management & Technology, Critical Path Institute, Tucson, AZ, USA.

The level of research activity focused on solving the challenges of drug resistant tuberculosis is rapidly increasing, with corresponding large increases in the amount of Mtb genotypic data, phenotypic data and data from clinical trials, surveillance studies and drug resistance studies. This presentation will provide an overview of a new database platform initiative that will integrate and store multiple types and sources of genotypic and phenotypic data intended to inform the development of rapid drug susceptibility tests and diagnostics for tuberculosis (TB). This work is being championed as part of the Critical Path to TB Drug Regimens initiative whose collaborators and partners include Critical Path Institute (C-Path), the Foundation for Innovative New Diagnostics (FIND), New Diagnos-



tics Working Group (NDWG), the Centers for Disease Control (CDC), and the National Institutes of Health (NIH). The Data Platform will house an investigational database where all data contributed to CPTR-RDST will reside. This investigational database will house curated, standardized TB bacteria genotypic and phenotypic data, human subject surveillance study data and human subject clinical trial data. Contributed data will be stored in its original form in an incoming data storage repository. The incoming data storage repository will be separated from the investigational database. This will preserve a copy of data "as received"; separate from the curated, standardized data stored in the investigational database. Data to be analyzed for specific projects will be extracted as analysis subsets from the investigational database, dependent on the specific task. In order to ensure quality and consistency of SNP reports generated for this effort, contributed TB full WGS data files (FASTQ files) will be processed through an RDST-defined unified pipeline under the guidance of TB subject matter experts to generate SNP reports that will be stored in the Data Platform. Within this Data Platform and where applicable, Clinical Data Interchange Standards Consortium (CDISC) data standards will be applied to ensure consistent representation of data throughout the system. The Data Platform architecture will be designed to allow for scalability, as it is anticipated that the amount of data, types of data, and rate of access to the data will increase rapidly as the work of the RDST project progresses.

### Genotype and phenotype analysis to understand pathogen success in mycobacterial strains

P Van Helden. Centre for TB Research, Stellenbosch University and MRC, Tygerberg, South Africa.

**Background:** Phenotype analysis of *M. tuberculosis* function can be complex and slow. Therefore much effort has been expended to assess whether genotype analysis can be done. However, before one can reasonably validate genotype results, studies to correlate genotype with phenotype are necessary. In this respect, genotype may be defined by simple methods such as SNP analysis, or RFLP, or more detailed analysis such as whole genome sequences. Each offers its own results and can be used to refine more rapid assays for translational work.

**Methods:** We explored a range of genotyping techniques to define *M. tuberculosis* strains, ranging from RFLP typing, SNP analysis and gene or genome sequencing. These were complemented with phenotyping, such as virulence in mice or antibiotic culture based susceptibility testing.

**Results:** Even within a family of strain types, defined by RFLP, there can be widely differing virulence in mice. At this stage, this is probably reflected in humans by population bias and the changing dynamics of strains. We have extensive data on antibiotic resistance, which is commonly explained by single nucleotide mutations. These range from the relatively simple (eg *rpoB*

mutations in a few codons of the gene confer rifampicin resistance) to the more complex, ie pyrazinamide resistance encoded in the *pncA* gene, or *inhA* mutations and their impact on isoniazid and ethionamide resistance and development of additional resistance. Furthermore, the use of second generation sequencing shows the underlying presence of resistant strains within "sensitive" patients. Our data shows that the epidemic of drug resistance in South Africa is primarily transmission driven.

**Conclusion:** Our data shows that genotype analysis provided it is used and interpreted correctly, holds enormous value for managing TB therapy. It illustrates the importance of early stage testing for antibiotic sensitivity and a clear interpretation of what the technology shows.

## 42. EMERGING PERSPECTIVES IN THE TREATMENT OF PAEDIATRIC MDR-TB

### The pharmacokinetics and toxicity of moxifloxacin in children with MDR-TB

S Thee,<sup>1,3</sup> A Garcia-Prats,<sup>1</sup> HR Draper,<sup>1</sup> H S Schaaf,<sup>1</sup> A Hesselning,<sup>1</sup> H McIlleron,<sup>2</sup> L Wiesner,<sup>2</sup> S Castel.<sup>2</sup>

<sup>1</sup>Paediatrics and Child Health, Faculty of Medicine and Health Sciences, Stellenbosch University, Desmond Tutu TB Centre, Tygerberg, <sup>2</sup>Medicine, University of Cape Town, Division of Clinical Pharmacology, Cape Town, South Africa; <sup>3</sup>Paediatric Pneumology and Immunology, Charité Universitätsmedizin Berlin, Berlin, Germany.

**Introduction:** Fluoroquinolones are often used in multi-drug-resistant tuberculosis (MDR-TB) and are being evaluated for their potential to shorten anti-TB treatment. Moxifloxacin is currently considered the most potent fluoroquinolone against *Mycobacterium tuberculosis*. There is little pharmacokinetic and safety data of moxifloxacin in childhood TB.

**Methods:** Children 7–15 years of age with MDR-TB receiving moxifloxacin (10mg/kg/day) as part of their MDR-TB treatment had intensive pharmacokinetic sampling done at steady state prior to, and at five time-points post-dose. Assays were performed using LC-MS/MS, and pharmacokinetic measures calculated using non-compartmental analysis. To monitor safety, children were followed up longitudinally; all adverse effects were graded using standard tables and attribution to moxifloxacin was assessed. 12-lead ECGs were performed 3 hours post-dose on PK sampling days.

**Results:** Twenty-three children were included (median age 11.1 years; interquartile range [IQR] 9.2 - 12.0); 6/23 (26.1%) were HIV-infected, of which three were underweight-for-age (UWA). In 3/23 children moxifloxacin tablets were crushed for administration. The median (IQR) C<sub>max</sub> [µg/ml], t<sub>max</sub> [h], half-life, and AUC(0–8) [µg×h/ml] for moxifloxacin were: 3.08 (2.85–3.82), 2.0 (1.0–8.0); 4.14 (IQR 3.45–6.11), and 17.24 (14.47–21.99), respectively. HIV infection (p=0.003) and UWA (p=0.045) were associated with low AUC0–8. T<sub>max</sub> was

shorter with crushed versus whole tablets ( $p=0.047$ ). Estimated pharmacodynamic indices were: median AUC<sub>0-24</sub>/MIC of 46.6 and a C<sub>max</sub>/MIC of 6.2. Children were followed for a median of 236 days (IQR 142–541). Main adverse effects were gastrointestinal ( $n=12$ ), headache ( $n=5$ ), elevated alanine-aminotransferase ( $n=4$ ) and arthralgia ( $n=4$ ). Except for one child with hepatotoxicity, all adverse effects were mild and non-persistent. No QT-prolongation >450ms occurred and mean corrected QT-time was 403ms (SD 30ms).

**Conclusion:** Children 7–15 years of age receiving moxifloxacin 10mg/kg/day as part of MDR-TB anti-TB treatment have low serum concentrations and pharmacodynamic indices compared with adults receiving 400mg moxifloxacin daily. Higher dosages may be required in children. Moxifloxacin was well tolerated in children treated for MDR-TB.

### Experiences in treating children with MDR-TB in India

S Sharma,<sup>1</sup> Vith Myneedu,<sup>2</sup> R Sarin.<sup>3</sup> <sup>1</sup> Pediatrics, <sup>2</sup> Microbiology, and <sup>3</sup> Direction, National Institute of Tuberculosis and Respiratory Diseases, New Delhi, India,

**Background:** Retrospective analysis of clinical profile, management and predictors of poor outcome for children with MDR TB was conducted in Delhi,

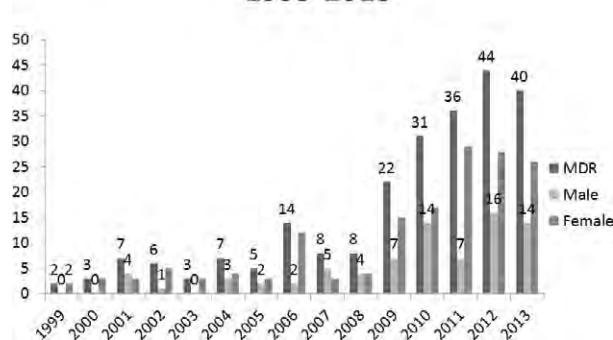
**Design/Methods:** We describe the results of 236 children < 15 years of age (January 1999 to December 2013) with MDR-TB diagnosed on BACTEC, MGIT, LPA, Gene-Xpert, solid based culture and drug sensitivity testing (DST) treated with STR or ITR and drugs given as mg/kg body weight.

**Results:** Significantly more girls (66.6%) than boys (33.4%) with median age  $12.09 \pm 2.28$  years (av- 12.75 yrs)(fig-1), mean symptom duration 18.6 months and mean duration of prior ATT 13.2 months. History of contact with TB and MDR TB was found in 17 and 7 cases. All patients except 2 had taken prior ATT and 33 had even taken reserve drugs. There were 181 and 55 PTB and EPTB cases respectively. All (100%) were malnourished and 59.2% anemic with hematocrit of  $28.27 \pm 5.08$ . HIV was negative in all 199 cases tested. Strains of Mtb were resistant to median of 3 drugs with XDR- 12 and TDR-3 respectively. Out of total 236 cases, MDR drug regimen could be started in 220 cases with DOTS-Plus in 47(21.3%) while community based self-administered STR in 106(48.1%) and ITR in 67(30.4%) cases. Only 12 patients had positive cultures at 6 months of treatment. There were 73(33%) patients still on treatment. Out of 147 cases, 108 (108/220; 49%) completed therapy with a successful outcome of 61(56%) cured and 47(44%) treatment completed or possibly cured, with no significant difference between DOTS-Plus and community based treatment. There were 11(5%) failures (with 9 diagnosed XDR), lost to follow-up 6(2.7%). There were total 33(14%) deaths, with 4 dying before diagnosis, 7 before start of treatment, while 22(10%) deaths during treatment. The major contributing cause of death was sepsis (15 children), pneumotho-

rax (6), massive hemoptysis (3), respiratory failure (5), aspiration (3) and suicide (1). Overall drug tolerance was good but only 8 cases of acute psychosis required modification of regimen for few days. All children where the treatment failed, relapsed or died had bilateral extensive pulmonary involvement. In a multiple Cox proportional- hazards regression model, predictors of poor outcome were low initial hematocrit, severe malnutrition and exclusion of pyrazinamide and ethambutol in the drug treatment regimen.

**Conclusion:** MDR TB in pediatric age group can be successfully treated even in resource poor countries. Enrollment has increased over the years due to availability of better rapid diagnostics and nationwide implementation of pediatric TB control programs. DOTS-Plus and Community based treatment have similar outcomes. Overall drugs tolerance is good with serious adverse events being rare.

Total Number of MDR Patient  
1999-2013



### Early experiences in the evaluation of a novel TB drug in children

J Hafkin. Otsuka Novel Products, Otsuka Pharmaceutical Development & Commercialization, Rockville, MD, USA.

Delamanid, a novel anti-tuberculosis agent with bactericidal activity, has demonstrated efficacy in previous clinical trials of multidrug resistant tuberculosis (MDR-TB) in adults. Limited data exists, however, with which to guide the treatment of MDR-TB in children. Moreover, until recently, no novel anti-TB agents have undergone clinical trials in pediatric populations. This presentation will provide an overview of some of the key experiences in the development of a delamanid for the treatment of MDR-TB in children. Specifically, the discussion will include aspects of the following: 1) An overview of the pediatric investigational plan which outlines the key goals to be achieved as well as the associated timelines; 2) Updates on the phase 1 and 2 clinical trials of delamanid in children including results achieved and lessons learned; 3) Finally, an overview of the development of the pediatric formulation as well as an update on the bioequivalence trial which will enable its appropriate usage in future pediatric trials.

### 43. MAGIC BULLET? DATA-DRIVEN INSIGHTS ON THE IMPACT OF COMMUNITY WORKERS ON CASE DETECTION AND TREATMENT OUTCOMES

#### Assessment of cost-effectiveness of community-based TB care in Namibia

K Vaughan,<sup>1</sup> V Remi.<sup>2</sup> <sup>1</sup>Health Area, Royal Tropical Institute (KIT), Amsterdam, <sup>2</sup>Verduin Public Health Consult, Verduin Public Health Consult, Oegstgeest, Netherlands.

**Background:** A variety of NGOs and CBOs contribute to community-based TB care (CBTBC) in Namibia using community volunteers called field promoters (FPs). Although all NGOs and CBOs use FPs to provide DOT, some NGOs are more aggressive with case finding and contract tracing, for example, or may provide patient treatment support through income generating activities or nutritional support. A recent assessment tried to assess both the cost-effectiveness of the NGOs as well as of the various elements of their CBTBC approaches.

**Design/Methods:** Seventeen of the country's 34 districts were sampled in the assessment, covering all 13 regions and including the major NGOs supporting CBTBC with FPs providing DOT in 54% of all health facilities. The assessment team collected data on case finding from NGO and district records. Data on NGO expenditures over a one year period was collected and expenditures were assigned to CBTBC activities based on FP activity records and information collected during interviews with NGO staff.

**Results:** The employed methodology made it possible to assess the cost-effectiveness of CBTBC NGOs in Namibia; at US\$266 to US\$4,292 (mean: US\$970; median: US\$644) per new smear positive TB patient successfully treated, all NGOs were deemed to be highly cost-effective according to WHO criteria. However, there were large differences in cost-effectiveness, corresponding to HIV prevalence rate among TB patients and presence of special populations although correlation could not be confirmed. Rurality, population density, HIV prevalence in the general population and case finding load had no apparent relationship with cost-effectiveness. The methodology did not allow for definitive conclusions about the cost-effectiveness of individual activities within the CBTBC approach. Challenges included assessing the effectiveness of individual FPs, changes in DOT location codes and isolating the community contribution to case finding and treatment outcome.

**Conclusions:** A different study design would be needed to allow for conclusions about the cost-effectiveness of individual activities within the CBTBC approach (for example, nutritional support). Additionally, techniques for assessing the effectiveness and cost-effectiveness of individual FPs and for isolating the community contribution to case finding and treatment outcomes are needed.

### 44. ZONOTIC TUBERCULOSIS: A GLOBAL SOCIO-ECONOMIC PROBLEM

#### The transmission, control and politics of bovine tuberculosis in Great Britain

E Brooks-Pollock. Veterinary Medicine, University of Cambridge, Cambridge, UK.

**Background:** Bovine tuberculosis (bTB), caused by *Mycobacterium bovis*, is one of the most complex, persistent and controversial problems facing the cattle industry in Great Britain. In 2012, over 35,000 cattle tested positive to the standard skin test: a 100-fold increase since the 1980s. Britain has operated an extensive national surveillance and control programme since the 1950s, which, coupled with now compulsory individual cattle tracing, has the potential to provide major insights into bTB epidemiology.

**Methods:** In this talk, I will discuss advances in understanding bTB infection and transmission from repurposing routinely collected data and discuss data and knowledge gaps yet to be filled. Cattle movement data can be used to quantify which animals were in contact and for how long, as well as the flow of animals between farms. Testing data indicates when infection was disclosed within the farm, although the infection status between tests is still unknown. As transmission is unobserved, we use mathematical models to infer transmission rates and mechanisms.

**Results:** Combining testing and movement data reveals the age-specific infection risks in cattle, within-farm persistence of infection, the role of wildlife reservoirs, mechanisms of between-farm transmission and highlights potential control options. Our analysis indicates that the age-specific infection risk follows a similar pattern to TB in humans, increasing by ~1% a year until 3–4 years, after which the risk plateaus. Young cattle under 12 months have the highest rates of visible lesions at slaughter, suggesting a different immune response to older animals. Using movements and spatial locations to model the transmission between farms reveals that movement of infected cattle is primarily responsible for spread into new areas, after which an environmental reservoir and poor sensitivity of the diagnostic test aids persistence. A small number of farms appear to be responsible for the majority of newly infected farms. Finally, we use models to evaluate a range of control options based on realistic behaviour and demonstrate that bTB can be controlled if drastic measures are taken.

**Conclusions:** Routinely-collected movement and testing data can be repurposed to investigate realistic control options for bTB. We show that bTB control in Great Britain requires a multi-stranded approach and that using a single control policy will not address the epidemiological complexity.



### Socio-economic impact of bovine tuberculosis in Ireland

J O'Keeffe. Runinant Animal Health, Department of Agriculture, Food and the Marine, Dublin, Ireland.

**Background:** The official bovine TB control program in Ireland commenced in 1958 when 20% of cows were infected with tuberculosis (TB). Currently the national herd comprises 6.5 million bovines, and there are 8.5 million skin tests carried out each a year. Ever animal slaughtered for human consumption inspected by an official veterinarian at the abattoir and every herd is tested at least once each year. Disease levels now are 2.4 positives per 1000 animals tested (15,680 test positives removed in 2013) with 4% of herds restricted each year. **Objectives:** The objectives of this presentation are to outline the costs of the various components of the national TB eradication program, the trading benefits associated with having the BTB program, and the current research evaluating the feasibility of replacing long-term culling of badgers with BCG vaccination. The bovine TB control program has a annual overall cost of €35M (million Euro) with a further €20M in administration costs, and results in TB levels in cattle that allow Irish produce to be traded, welcomed and valued on all the world's premium markets. A test and slaughter policy has operated nationally since 1958 based on the Single Intradermal Cervical Comparative Tuberculin Test (SICCT). The test and slaughter program led to rapid improvements in the early years of the program, but then TB levels remained at an unacceptable high plateau for the following decades (4.0 animals per 1000 animals tested). Research carried out in the 1980s lead to the realisation that a wildlife host, the Eurasian Badger (*Meles meles*) was involved in the epidemiology of tuberculosis in cattle. In 2014 a large scale field project began in 6 of the countries 26 counties that will evaluate if vaccination with BCG can be used as a substitute for a majority of the current culling program where 6,000 badgers are removed annually. Badgers are a protected species so the ideal outcome would be if vaccination of badgers can eventually result in fewer being culled.

**Conclusion:** The BTB program, while costly over the years, ensures that exported Irish agricultural produce (which is 90% of total agricultural produce) are accepted into the premium quality markets where the highest prices are offered and which yield the best returns for producers. Controlling a zoonotic disease that also has a wildlife reservoir with spill-over between bovines and badgers is complex, and more so when the wildlife species involved is a protected species.

### A one health approach to controlling zoonotic TB: the Michigan (USA) experience

J B Kaneene. Large Animal Clinical Sciences, Michigan State University, East Lansing, MI, USA.

One Health is generally defined as a science dealing with human health, animal health (domestic & wildlife), and ecosystem health in an integrated manor. This approach is particularly fit for dealing with infectious diseases such

tuberculosis, which have several species of animals serving as reservoirs. Tuberculosis caused by *Mycobacterium bovis* has been a major disease concern in the state of Michigan (USA) in cattle, white-tailed deer (free ranging and farmed), and humans since 1994. To effectively deal with this disease, a One Health Approach has been developed for the state of Michigan. The One Health Approach in Michigan has included the following elements: 1) Establishing a State Tuberculosis Advisory Committee, 2) Conducting integrated animal (domestic & wildlife) and human surveillance systems, 3) Sharing laboratory facilities and resources, 4) Sharing training of students and technologists, 5) Conducting research, and 6) Coordinating communication between government agencies. This presentation will demonstrate how the One Health Approach has improved the efficiency of TB surveillance, diagnosis, and control programs. In addition, lessons learned to date will be presented.

### Infection of great apes and a zoo keeper with the same *Mycobacterium tuberculosis* spoligotype

C Van Der Loo,<sup>1</sup> O Akkerman,<sup>2</sup> T Van Der Werf,<sup>2,4</sup> A Van Der Zanden.<sup>3</sup> <sup>1</sup>Department of Tuberculosis, Municipal Health Centre Gelre-IJssel, Apeldoorn, <sup>2</sup>Pulmonary Diseases and Tuberculosis, University Medical Center Groningen, Groningen, <sup>3</sup>Medical Molecular Microbiology, Laboratory for Medical Microbiology and Public Health, Hengelo, <sup>4</sup>Internal Medicine, University Medical Center Groningen, Groningen, Netherlands.

Infection of great apes and a zoo keeper with the same *Mycobacterium tuberculosis* spoligotype. A bi-annual screening for latent TB infection for employees of a zoo resulted in an animal keeper being diagnosed with active pulmonary tuberculosis. In the same period in this zoo, several bonobos were suffering from TB as well. Spoligotyping of the *M. tuberculosis* strains from both the animal keeper and the bonobos appeared identical. Evidence that the animals infected their keeper is provided.

### Prevalence of multidrug-resistant *Mycobacterium bovis* in bovines of eastern India: an emerging threat to human health

P Dandapat,<sup>1</sup> S.P. Singh,<sup>1</sup> A. Chakrabarty,<sup>1</sup> S. Bhattacharya,<sup>1</sup> S. Bandyopadhyay,<sup>1</sup> P.K. Nanda,<sup>1</sup> S. Bandyopadhyay.<sup>1</sup> <sup>1</sup>Eastern Regional Station, Indian Veterinary Research Institute, Kolkata, India.

**Background:** Limited information is available on drug resistance pattern of *Mycobacterium bovis*, which is an emerging threat to human health. We, therefore, identified and characterized *M. bovis* from bovines in eastern India to give an insight to determine the threat of its transmission in animal-human interface in tuberculosis burdened nation like India.

**Design/Methods:** Lung samples having tuberculous like nodules, collected from slaughter houses of eastern India, were tested for the presence of *M. bovis* to find out the pattern of drug resistance using proportional plate

method, multiple allele-specific PCR (MAS-PCR) assay, line-probe assay (GenoType MTBDR plus test) and gene sequencing.

**Results:** A total of nine *M. bovis* isolates were found to be multi-drug resistant (MDR) in respect to five first line drugs by proportional plate method, whereas only two isolates were identified as drug resistant by molecular methods like MAS-PCR assay, sequencing of respective genes and line-probe assay. This may be due to new mutations for MDR characteristics, although not frequently found in *M. tuberculosis*. Further, all the *M. bovis* isolates were found to be resistant to two important second line antituberculous drugs, D-cycloserine and ethionamide.

**Conclusion:** To address MDR in *M. bovis* in India, detailed longitudinal studies on the population structure of *M. bovis* both from humans and animals, their drug resistance profiling and identification of new mutated genes are urgently required.

### Diagnostics challenges of *Mycobacterium tuberculosis* complex in Cameroon

F Egbe,<sup>1,2,3</sup> Lucy Ndip,<sup>1,7</sup> M Sander,<sup>2</sup> A Asuquo,<sup>3</sup> R Kelly,<sup>4</sup> M Bronsvort,<sup>4</sup> K Morgan,<sup>5</sup> V Tanya.<sup>6</sup> <sup>1</sup>Laboratory for Emerging Infectious Diseases, University of Buea, Buea, <sup>2</sup>The Tuberculosis Reference Laboratory, Bamenda, Regional Hospital Bamenda, Bamenda, Cameroon; <sup>3</sup>Faculty of Allied Medical Sciences, University of Calabar, Calabar, Nigeria; <sup>4</sup>The Roslin Institute, University of Edinburgh, Edinburgh, UK; <sup>5</sup>University of Liverpool, University of Liverpool, Liverpool, UK; <sup>6</sup>The Institute for Research in Development, MINRESI, The Institute for Research in Development, MINRESI, Yaounde, <sup>7</sup>Faculty of Health Science, University of Buea, Buea, Cameroon.

**Background:** Bovine tuberculosis (bTB) is still an important cause of cattle production loss and it is still endemic in most sub-Saharan African countries. However, most policy makers still underestimate its burden, importance and zoonotic threat in Africa. We carried out a study to estimate the burden of bovine TB in slaughtered cattle, the proportion of human TB caused by *M. bovis* and investigate zoonotic evidence of *M. bovis* in Cameroon in 2012 and 2013.

**Design/Methods:** A total of 2,346 cattle were examined for the presence of suspected TB lesions during routine meat inspection at four slaughterhouses in Bamenda, Ngoundere, Garoua and Maroua covering the major cattle rearing regions of Cameroon. Up to 3 lesions per animal were collected and all lesions recorded as well as other basic data on age, breed, sex and potential origin of the animals. In addition, random retropharyngeal lymph nodes were collected from apparently healthy cattle. Samples were cultured for mycobacterial growth using the automated MGIT 960 and Lowenstein Jensen (supplemented with glycerol and pyruvate) systems. The recovered acid-fast bacilli were identified using the Hain's GenoType MTBC and CM/AS kits and characterize by spoligotyping and MIRU-VNTR assays. In addition, in the NW Region 157 AFB positive human

sputum samples screened by microscopy from new cases were cultured and typed to identify *M. bovis*.

**Results:** A total of 207 cattle (1 in 16 animals) had lesions representing lesions rates of 4% (45/1129), 11% (106/935), 24% (38/160) and 15% (18/122) in the four different abattoirs respectively. *M. bovis* confirmation rates from culture were 69%, 65%, 90% and 89% respectively. Interestingly, one *M. tuberculosis* and 3 *M. bovis* were recovered from apparently healthy animals. In addition 3 (2.1%) of the 150 culture positives from the human sputum samples were *M. bovis*. The spoligotyping pattern and MIRU-VNTR of one of these matches exactly with that of cattle suggesting zoonotic linkage while 2 had a far distinct pattern from cattle. A number of NTMs including *M. phlei* and *M. fortuitum* were also recovered from animals with visible lesions. **Conclusion** The burden of Btb and the prevalence of *M. bovis* seems to be high in these regions. This is important both due to the potential production losses and increased zoonotic risk from consumption of contaminated milk or meat particularly for people with HIV in Cameroon. This is reiterated in the zoonotic evidence of *M. bovis* in this study.

### Prevalence of bovine TB and milk handling practices of different cattle rearing populations in Cameroon: potential public health risks

R Kelly,<sup>1</sup> I Handel,<sup>1</sup> M Bronsvort,<sup>1</sup> V Tanya,<sup>2</sup> K Morgan,<sup>3</sup> Lucy Ndip,<sup>4,5</sup> F Egbe,<sup>5,7</sup> M Sander.<sup>6</sup> <sup>1</sup>Genetics and Genomics, The Roslin Institute, Royal (Dick) School of Veterinary Studies, University of Edinburgh, Edinburgh, UK; <sup>2</sup>Ministry of Scientific Research and Innovation, Yaounde, Cameroon; <sup>3</sup>Musculoskeletal Biology, Institute of Ageing and Chronic Disease School of Veterinary Science, University of Liverpool, Liverpool, UK; <sup>4</sup>Faculty of Health Science, University of Buea, Buea, <sup>5</sup>Emerging Infectious Disease Laboratory, University Buea, Buea, <sup>6</sup>Tuberculosis Reference Laboratory, Regional Hospital, Bamenda, Cameroon; <sup>7</sup>Microbiology and Parasitology Unit, Faculty of Allied Medical Science, University of Calabar, Calabar, Nigeria.

**Background:** Prevalence estimates and related risk factors of bovine tuberculosis (bTB) are still poorly quantified in much of sub-Saharan Africa in spite of Africa accounting for 20% of the global cattle population. Control of bTB in Africa is difficult due to poor monitoring of cattle movements and limited abattoir surveillance. It is reported that zoonotic TB accounts for 3% of human TB burden. Risk factors for zoonotic transmission include living in close contact with cattle and consumption of unpasteurised milk. Hence understanding the epidemiology of bTB in African cattle populations is important in regard to public health. This study aimed to: a) evaluating the level bTB awareness among cattle keepers and how these relate to husbandry practices within Cameroon and b) estimate bTB prevalence and its associated risk factors in these cattle populations **Study/Design:** Between 2012-13 a stratified clustered cross-sectional study of cattle herds from the North West Region, Vina Division and dairy cooperative in the NW Region was conducted and included 1448

cattle reared by 100 pastoralists and 60 cattle from 48 small holder dairy farmers. Individual animal data and herd-level management details were collected and animals were screened by both the single comparative intradermal skin test and gamma interferon test (Bovigam, Prionics).

**Results:** The prevalence of bTB in cattle was estimated between 4.1–11.4% depending on strata and test used. Clear differences in distribution were noted between the strata but in general herd prevalence was high. Fifty-nine percent of pastoralists were aware of bTB compared to 74% of dairy farmers. Ninety-two percent of herdsmen drank milk, however, only 23% were aware of the risks of milk borne zoonoses. Differences in husbandry and cultural practices of cattle keeper subgroups were observed. For example, 87.5% dairy farmers compared to only 30% pastoralists, sell milk to non-family members. Furthermore a multi-level multivariable risk factor model for animal-level test positivity was developed adjusting for animal and herd level confounders such as age.

**Conclusion:** This study demonstrates the widespread distribution of bTB within Cameroon. Identifying cattle risk factors and highlighting potential public health concerns within different cattle rearing communities.

## 45. PARTNERSHIPS: WORKING FOR COMMUNITY-DRIVEN IMPACT TO ENSURE QUALITY CARE FOR PERSONS AFFECTED BY TB

### Building better frameworks for community engagement: developing national strategies and guidelines in Central Asia

J Ismoilova,<sup>1</sup> S Okromeshko,<sup>2</sup> T Mohr.<sup>3</sup> <sup>1</sup>Tuberculosis, Project HOPE, Dushanbe, Tajikistan; <sup>2</sup>TB, PATH, Washington, DC, USA; <sup>3</sup>TB, Project HOPE, Almaty, Kazakhstan.

**Background:** Central Asia faces a growing TB epidemic, which has been intensified by dramatic increases in MDRTB in recent years. Factors contributing to the spread of MDRTB are poor case detection and poor patient compliance with treatment. Patients in Central Asia are unaccustomed to making demands of their health care systems, and may feel intimidated about asking for the testing or treatment that they need due to stigma and discrimination directed at TB infected individuals. Country level ACSM strategies seek to eliminate stigma and discrimination directed at TB-infected people, improve case detection and treatment and thereby reduce the spread of TB.

**Aim:** To assess the needs for a strategic approach to community involvement in the fight against TB.

**Design/Methods:** Project HOPE is working with national TB Programs in Central Asia to guide them through the process of developing and implementing ACSM strategies. In each country, Project HOPE experts provide technical assistance to working groups comprised of specialists from NTPs and civil society

organizations. The working groups were trained by Project HOPE and PATH experts on skills to develop ACSM strategies. Working group members then utilized these results to identify barriers patients face in completing their entire TB treatment. The NTP objectives were evaluated in light of the identified barriers and activities are designed to overcome those barriers and compile into a strategic plan.

**Results:** ACSM strategies have been endorsed by NTPs. The strategies were developed to guide and coordinate integrated, comprehensive activities addressing prioritized audiences for tuberculosis prevention and control. The National ACSM strategy will act as a living document, to be adapted in response to new research and circumstances. The strategies are used by NTPs and partners for the planning and evaluation of activities, to engage the community and civil society in the fight against TB, and are used for the development of new national programs and strategic plans.

**Conclusion:** A strategic approach to designing and implementing activities for community engagement, can contribute greatly to reaching the goals of the National TB Programs. Since the strategies were developed based on analysis and identification of existing barriers that hinder timely diagnosis and obtaining the full course of TB treatment, the implementation of the strategy can contribute to obtaining effective results and positively impact TB programs.

### Involving NGOs in community-based MDR-TB treatment support in Tajikistan

F Mirzoeva,<sup>1</sup> O Bobokhojaev,<sup>1</sup> J Ismoilova,<sup>2</sup> T Mohr.<sup>3</sup>

<sup>1</sup>Ministry of Health, National Tuberculosis Program Republic of Tajikistan, Dushanbe, <sup>2</sup>TB, Project HOPE, Dushanbe, Tajikistan; <sup>3</sup>TB, Project HOPE, Almaty, Kazakhstan.

**Aim:** To assess the influence of NGO involvement in improving outcomes of ambulatory treatment of MDR TB patients.

**Design/Methods:** The NTP of Tajikistan, together with partners actively involves NGOs and trained volunteers in social support of ambulatory MDR TB patients. The NTP is working to integrate best practices into the national program to improve patient outcomes. Best practices include using volunteers, religious leaders, Patients support groups, and other innovative methods to support ambulatory treatment. During the initial eight months of treatment, MDR TB patients visit PHC facilities daily to receive injectable medications. The following 16 months the NTP actively involves volunteers to provide DOT and has developed innovative ways to involve volunteers. The NTP also uses automated daily SMS messages for volunteers to confirm the daily status of DOT.

**Results:** Over the last 3 years more than 50% of MDR TB patients enrolled for SLD treatment are treated on an out-patient basis. The total number of MDR TB patients who are enrolled for SLD treatment for the last three years is 1584, and of these, approximately 800 patients have been treated on an outpatient basis. Overall cure



rates of MDR TB patients fluctuated between 61–64%. Countrywide, social workers and volunteers provide DOT for about 70% of ambulatory MDR TB patients. Of these patients, DOT is provided by social workers and volunteers at PHC facilities (60%) and at home (40%). In some cases, volunteers accompany MDR TB patients to PHC treatment centers on daily basis. If patients cannot visit PHC treatment center for any reason (e.g. distances, stigma, severe concurrent conditions) DOT is provided at home. Preliminary results for the first half of 2014 showed that smear conversion among MDRTB patients supported by NGOs was 79% compared to 64% among MDRTB patients that did not receive support from NGOs. The default rate is 7.5% and 14.8% respectively.

**Conclusion:** By working together with international partners, the NTP is adopting new methods to support TB patients who are on ambulatory treatment. These new methods are contributing to improved treatment outcomes in the country. As a result of this work the NTP of Tajikistan is adopting proven best practices from various innovations that have been piloted to be rolled out countrywide.

### **The keystone to improve TB control: involving community volunteers and community HIV support groups in Malawi**

R Nalikulungwi,<sup>1</sup> S Dalebout,<sup>2</sup> C Whalen,<sup>2</sup> A Trusov,<sup>2</sup> R Makombe,<sup>3</sup> R Matji,<sup>3</sup> J Mpunga,<sup>4</sup> L Kanyenda.<sup>4</sup> <sup>1</sup>Global Health, Project HOPE, Lilongwe, Malawi; <sup>2</sup>Global Health, Project HOPE, Millwood, VA, USA; <sup>3</sup>Regional Office, URC-CHS, Pretoria, South Africa; <sup>4</sup>TB Care II, URC-CHS, Lilongwe, Malawi.

**Background:** In Balaka, Machinga, Mangochi, Mulanje and Phalombe districts (population 3,745,623) in the Southern Region of Malawi, Central Africa, although the government provides free Tuberculosis (TB) screening and treatment services, case detection has been low due primarily to a passive approach of case finding and patients' difficulty accessing health facilities that provide TB screening. Consequently, patients suspecting TB often report late to health facilities, resulting in high TB transmission rate and high mortality among TB patients.

**Intervention:** From October 2012 to September 2013 USAID funded TB CARE II in partnership with Project HOPE and the Malawi NTP, led a comprehensive community approach to improve case finding through improving quality of sputum microscopy, establishing peripheral Sputum microscopy sites, training microscopists and community volunteers to conduct community TB health education, motivating people with presumptive TB to get examined, involving Community Based Organizations (CBOs) focusing on HIV, and establishing community sputum collection points for sputum collection and transportation to a nearest microscopy facility.

**Results:** Increasing community awareness, community involvement and empowering community volunteers in TB control activities increased acceptance of TB control services. 183 CSCPs and HIV Support Groups collected sputum for 62 peripheral microscopy sites. CSCPs

contributed 23% (4,585/20,242) of all patients with presumptive TB with an 18% (336/1,875) yield of new smear positive TB patients. 100% of patients with positive results started TB treatment. Adherence to treatment is increased by making access to TB treatment simple for patients through decentralized TB registration centers.

**Conclusion:** A community approach to TB control increased the number of people tested by 23% and contributed 18% of those diagnosed with TB. This approach, including CSCPs and CBOs, is making an important contribution to increasing the number of presumptive cases and new TB cases identified. Community approach, empowerment and involvement in mobilizing and supporting identification of presumptive TB patients and support to TB patients are effective approaches to improve TB control in rural areas. Providing peripheral sputum microscopy and TB registration services close to the people in the community supported by community sputum collection points enhance TB control.

### **46. INNOVATIVE SOLUTIONS IN SURVEILLANCE OF DRUG-RESISTANT TB: FROM PHENOTYPIC TO MOLECULAR TESTING**

#### **Xpert MTB/RIF as a screening tool in the national drug resistance survey of Pakistan**

A Van Deun,<sup>1</sup> M Zignol,<sup>2</sup> S Tahseen,<sup>3</sup> A Hussain,<sup>3</sup> FM Khanzada,<sup>3</sup> E Qadeer.<sup>4</sup> <sup>1</sup>Biomedical Sciences, Institute of Tropical Medicine, Antwerp, Belgium; <sup>2</sup>Global Tuberculosis Programme (GTB), World Health Organization, Geneva, Switzerland; <sup>3</sup>National TB Reference laboratory, National Tuberculosis Control Programme, Islamabad, <sup>4</sup>National Tuberculosis Control Programme, Islamabad, Pakistan.

**Background:** Pakistan First National TB drug resistance survey (DRS) was conducted in 2012-13. Xpert MTB/RIF assay was done in parallel with Phenotypic DST to study usefulness of Xpert MTB/RIF as a screening tool in the drug resistance survey

**Design/Methods:** Cross sectional study using weighted cluster sampling targeting all NEW smear-positive PTB patients. Sample size of 1600 smear +ve New cases divided in 40 randomly selected clusters. All sm +ve Retreatment cases registered during intake period of the new cases also included in study. Two specimens collected from patients, Xpert MTB/RIF used directly on sputum specimen in parallel with slow Drug susceptibility testing on Lowenstein Jensen (LJ DST). For QA all Rif resistant, equal number of rif susceptible and rif discordant results were tested at Supra National Reference laboratory (SRL) in Antwerp Belgium

**Results:** Total of 1984 patient were enrolled in DRS including 1695 (85.4%) new, 277 (14.0%) retreatment. 1906 (96.1%) patient sample were tested using both techniques. Valid rifampicin result were reported in 1805 (94.7%) on Xpert MTB/RIF. 1582 (83.0%) on LJ DST

and 1541 (80.8%) on both techniques. NO Rifampicin results were obtained on 14.7% (281) samples on LJ DST because of contamination or no growth. Additional DST results in 236 (12.4%) were obtained with use of Xpert. No rifampicin result were obtained in 101 (5.3%) patient samples on Xpert, for which LJ DST result were available in 41 (2.2%) cases. Agreement on Rifampicin results between two techniques was 97.9%, Rifampicin resistant was 118/1805 (6.7%) on Xpert MTB/RIF, 106/1582 (6.9%) on LJ DST. Discordance in Rifampicin results was reported in 32 cases. Out of discordant 17 were resistant on Xpert MTB/RIF and sensitive on LJ and in other group 15 were sensitive on Xpert MTB/RIF and resistant on LJ DST. Final conclusion was reached based on SRL DST and sequencing results. In the first group of discordance there was one false Resistant Xpert (5.9%) and six false susceptible DST (35.3%). In second group of discordance there were five false susceptible Xpert results (29.4%) and two false resistant DST (11.8%).

**Conclusion:** Xpert MTB Rif assay provided valid Rifampicin result on 94.7% versus LJ DST on 83.0%. Xpert MTB/RIF assay if used screening tool in DRS information on prevalence of resistance due to mutation outside rpoB gene will be missed.

Xpert MTB/RIF Assay result versus LJ Culture and DST results

		Xpert MTB/RIF result (SPUTUM)						Total #	Total %
		Rif-S	Rif-R	Neg	Fail, error	RIF ind			
LJ culture/DST	Rif-S	1420	17	6	23	10		1476	77.4%
	Rif-R	15	89	1	1			106	5.6%
	NTM	3		11				14	0.7%
	MIX								
	TB/NTM	24	1	3		1		29	1.5%
	Cont.	139	8	6		1		154	8.1%
	Neg.	86	3	37		1		127	6.7%
	Total #	1687	118	64	24	13		1906	
	Total (%)	88.5%	6.2%	3.4%	1.3%	0.7%			

### Performance of rapid rifampicin testing: experiences from multiple settings

A Van Deun.<sup>1,2</sup> <sup>1</sup> Institute of Tropical Medicine, Antwerp, Belgium; <sup>2</sup> International Union Against Tuberculosis and Lung Disease, Paris, France.

Sputum preserved in ethanol from the Tanzania national drug resistance survey (DRS) was tested by lineprobe assay (LPA). Of 321 samples tested by both conventional drug susceptibility testing (DST) and LPA, 269 yielded valid results for *M. tuberculosis* (MTB) in both tests. Culture/DST failed for 29 (9.1% of MTB), LPA failed for 49 (15%), mostly due to leaking tubes. MDR was 1.9% with both techniques, but only LPA detected 2 rifampicin mono-resistant confirmed by DNA sequencing. Alcohol-preserved sputa and sequencing of the rpoB gene was used for random samples from new cases registered in 5 sentinel clinics of Damien Foundation Bangladesh. Among 500 valid results from sputa preserved since

2005, 2 (0.4%) had a resistance-conferring mutation, and for samples dating from 2010, this was 11/522 or 2.1%. Two samples showed a silent mutation mixed with wildtype DNA, susceptible by LPA and Xpert MTB/RIF which did detect all resistance mutations tested. Over half of those belonged to the group with disputed importance and difficult to detect by (rapid) phenotypic DST. However, adverse treatment outcome was registered for 5/7 (71%) with disputed mutations. Molecular test failures were 5.8% of 1091, half compared to earlier DRS from the same clinics using conventional DST. Xpert directly from a second sputum specimen in parallel with conventional DST yielded 11% more valid rifampicin results in the Pakistan 2012 national DRS. Among 1541 samples with valid results for both, 32 with MTB isolated yielded discordant rifampicin results. Repeat DST and rpoB sequencing showed among 19 discordants from new cases only one false resistant result for Xpert (silent mutation) and one for DST, but 3 false susceptible Xpert and 4 DST; for 13 discordant retreatment cases there were respectively 0, 1, 3 and 2. Over half of the discordant were due to misidentification of specimens or heteroresistance between different specimens, since repeat Xpert from isolates confirmed the DST results, except for the 572 mutation not covered by the probes and for DST resistant with wildtype DNA. Rifampicin prevalence on DST was 3.5% among new and 28.0% among previously treated cases. Ignoring the misidentifications, specificity of Xpert among new cases was 99.9% and predictive value for resistance was 98%, equal to DST. Rifampicin DRS by DNA sequencing, LPA or Xpert is easier, more efficient and more accurate.

### Surveillance of drug resistance in Central Asia

M Jonevska,<sup>1</sup> H Hoffmann,<sup>2</sup> T Abildaev,<sup>3</sup> B Toksanbaeva,<sup>3</sup> M Abduloeva,<sup>4</sup> O Bobokhojaev,<sup>4</sup> G Kalmambetova.<sup>5</sup> <sup>1</sup>Europe/Eurasia, Project HOPE, Almaty, Kazakhstan; <sup>2</sup>WHO - Supranational Reference Laboratory of Tuberculosis, Institute of Microbiology and Laboratory Medicine, Gauting, Germany; <sup>3</sup>National Reference Laboratory, National TB Centre, Almaty, Kazakhstan; <sup>4</sup>National TB Program, Republican TB Centre, Dushabe, Tajikistan; <sup>5</sup>National reference Laboratory, National TB Centre, Bishkek, Kyrgyz Republic.

**Background** Anti TB drug resistance is significant health problem in all Central Asian Republics (CAR), identifying this region as one of the globally recognized hot spots for multidrug (MDR) and extensively drug resistance (XDR) TB.

**Objectives** To analyze MDR and XDR data, collected through representative Drug Resistance Surveys (DRS), identify the most common resistance patterns and risk factors, specific for the CAR region.

**Method** Drug resistance data were collected through nationwide surveys, following the WHO guidelines for conducting DRS in Tajikistan; Kyrgyzstan and Uzbekistan. Data from Kazakhstan, was provided from the established TB surveillance system. DST in all countries was performed by phenotypic methods. Molecular tests (MTBDR plus), were performed on a selected sample for

the purpose of quality control and further investigation of specific genetic mutation at respective SNL.

**Findings** High proportions of MDR in new cases were found in National DRSs, ranging from 12.5% (95CI: 9.9–15.6) in Tajikistan to 26.4% (95CI:22.7– 29.7) in Kyrgyzstan. Uzbekistan DRS found 23.2% (95CI: 17.8–29.5), while the routine surveillance system in Kazakhstan reported 22.9%. For previously treated cases, there were no significant differences between individual CAR countries (resistance between 51.6–55.0%), except for Uzbekistan, where the National DRS found 62% (95CI: 52.5–70.7). Mono resistance to Rifampicin was rare, found from 0.9 % in Uzbekistan to 2,2 % in Tajikistan, indicating that in this region Rifampicin resistance, can be used as a proxy for MDR TB. National surveys detected 19 XDR TB cases Tajikistan (7 were new case); 19 in Kyrgyzstan (11 with unknown treatment history) and 17 in Uzbekistan (8 in new cases). Resistance to fluoroquinolones or second line injectable drugs among MDR patients was also found in high proportions: 32.3% in Uzbekistan; 29.2% in Tajikistan and 30.5% in Kyrgyzstan. The surveys identified the most common risk factors associated MDR TB in the CAR region: previous TB treatment; age under 45; imprisonment history and labor migration.

**Conclusions** Data collected from the national surveys and continuous surveillance enabled the identification of common characteristics of MDR and XDR TB in Central Asian countries. Further strengthening of MDR TB surveillance systems and implementation of policies that will allow wider use of molecular tests for diagnosis and surveillance.

#### From facility to finding drug resistance mutations: drug resistance survey in Nigeria

V Sebastian,<sup>1,2</sup> I Uko,<sup>2</sup> T Abiola,<sup>2</sup> R Akpan,<sup>2</sup> S Ogiri,<sup>3</sup> N. Nwokoye,<sup>4</sup> C C Onubogu, Phd,<sup>4</sup> C Chukwuka.<sup>5</sup> <sup>1</sup>National DR TB Survey, NTBLCP, Abuja, <sup>2</sup>DGHA, US-CDC Nigeria, Abuja, <sup>3</sup>TUB, WHO Nigeria, Abuja, <sup>4</sup>TB Research Laboratory, Nigeria institute of Medical Research, Lagos, <sup>5</sup>Respiratory Medicine, University of Nigeria Teaching Hospital Enugu, Enugu, Nigeria

**Introduction:** Nigeria notifies about 100,000 SS+ TB cases annually and is listed among the 22 HTB countries.

**Objectives:** We determined the prevalence and pattern of resistance to anti-TB drugs (RIF and INH) using Line Probe assay (LPA) in-country and performed LPA(repeat) and culture DST at the SNRL on 10% of sensitive and all in-country resistant results for EQA and deriving thereby DR-TB (including M/XDR-TB) estimates.

**Survey methodology:** By modified cluster sampling we sampled 30 clusters of DOTS facilities proportionate to size (of new sputum smear positive (SS+) TB cases) and nationally representative. Consenting SS+ TB patients (>15yrs old) were consecutively enrolled at these facilities till a required national sample size of 1,723 respondents – new and treatment cases - were enrolled. Two most positive sputum samples per respondent were transported under cold-chain in triple layered-packaging to in-country TB RL for LPA (Genotype MTBDR plus)

testing and cultured (LJ slopes) to obtain isolates. Isolates of 10% of sensitive and of all resistant samples were transferred under cold chain to SNRL at CDC Atlanta and retested by LPA, solid and liquid culture DST to determine resistance to RIF and INH and other anti-TB drugs.

**Results:** Of 1,723 patients samples, 1449 were successfully subjected to LPA, 70 were found to be MDR-TB, giving a general prevalence of 4.8% (95% CI: 3.8 – 6.1 %), comprising a prevalence of 2.9% (weighted) among new TB cases (95% CI: 2.1 – 4.0%) and 14.3% (95% CI: 10.2–19.3%) among retreatment TB cases. We found resistance to other anti-TB drugs and the strongest predictor of MDR-TB was previous anti-TB treatment ( $p<0.000$ ). The results of LPA done directly on smear-positive sputum concurred highly with culture DST performed on isolates using MGIT 960. Sensitivity, specificity, positive and negative predictive values of Genotype MTBDR plus relative to conventional DST using MGIT 960 and agar proportion method for detection of resistance were 96.8, 92.1, 81.1 and 98.8 percent respectively for RIF and 73.8; 98.7;96.9 and 87.5 percent respectively for INH. No XDR-TB was found.

**Conclusions:** Genotype MTBDR plus assay/LPA was found to be feasible, rapid, sensitive and specific test for routine DST for diagnosis of RIF resistance. There is a notable prevalence of MDR-TB in Nigeria and potential for XDR, history of previous treatment a very strong predictor.

## 47. ENGAGING COMMUNITIES IN THE FIGHT AGAINST TB AND HIV

### Engaging policymakers and communities through north/south collaboration: MP delegation to Benin

F Belli,<sup>1</sup> A Zuinghedau,<sup>1</sup> N Adjibade,<sup>2</sup> P Bertrand.<sup>3</sup>

<sup>1</sup>International programs, AIDES, Pantin, France; <sup>2</sup>Advocacy, CERADIS, Cotonou, Benin; <sup>3</sup>Advocacy, Global Health Advocates France, Paris, France.

**Background:** 2013 was a crucial year for France and Benin's engagement in the fight against HIV and TB: France decided on the amount of its contribution to the Global Fund, Benin implemented universal medical coverage and the two countries drew up their priorities for the post 2015 agenda. Despite the engagement of French and Beninese governments, MPs do not appear to be mobilized, although they play a key role in budgets and policies.

**Method:** The NGOs AIDES, Advocates for Global Health and CeRadis organised a three-day field visit attended by six French and four Beninese MPs who were chosen for their responsibilities in international cooperation and health policies. The Health Minister, the Beninese member of the United Nations Panel for the post 2015 agenda, organisations involved in the HIV and TB responses, French and European diplomats all gathered together.



**Results:** The French MPs published a newspaper column, addressed several letters to the government and the President in support of the Global Fund and also organised a mission to the Global Fund's secretariat. The rapporteur for the Public Development Aid budget who attended the trip set up a hearing with the Executive Director of the Global Fund. The Health Minister got CeRADIS involved in the consultations to reform the Global Fund's country coordinating mechanisms. CeRADIS represented civil society during the French cooperation minister's visit and the Beninese MPs visited some projects taking place on the ground.

**Conclusion:** This fifth trip organised by AIDES and Advocates for Global Health has confirmed the relevance of parliamentary missions in strengthening the political stature of NGOs and reinforcing parliamentarians involvement, as those who took part in previous trips have remained committed and dedicated.

### Effective TB services for remote and hard-to-reach populations in Botswana

L Martindale,<sup>1</sup> O Maruping.<sup>1</sup> <sup>1</sup>Community Health, Kuru Family of Organisations, D'Kar, Botswana.

**Background:** Ghanzi District in Botswana has the highest TB notification rates in the country. The majority of the population consists of indigenous San minority groups. In remote areas, San experience challenges with access to health services. Language barriers, vast distances, poor infrastructure and lack of health workers' contextual understanding of cultural and socio-economic factors influencing health seeking behavior contribute to low uptake of existing services.

**Interventions:** Local non-governmental organization, Kuru Health facilitates TB-HIV prevention and care through indigenous health promoters. Kuru Health enables decentralized Community TB Care with promoters engaging in their own localities, using their own mother tongue languages to provide effective TB services with remote populations. Increasing access to TB treatment, improving contact tracing and case finding is done through supported community health programming.

**Results:** Indigenous community health promoters are transforming and strengthening the health care delivery system. Localized health communication tools designed and facilitated by community members have led to improved community understanding of HIV/AIDS and increased uptake of health services. Integrated monitoring and support of TB patients is most successful through linking community health promoters and civil society with the governmental health care system.

**Conclusion and Recommendations:** The demand for CTBC and community health initiatives in the remote areas is high. CTBC is necessary for TB and HIV services to be effective in hard to reach populations. Increased resource allocation to NGOs and partnership collaboration is required to capacitate remote area health systems and further increases access to health.

### The experience of the Small Grants Programme for NGOs in South Africa

K Mbengo,<sup>1</sup> E Mhlope,<sup>1</sup> L Mvusi,<sup>2</sup> N Sigwebela.<sup>3</sup> <sup>1</sup>USAID TB Project, University Research Company, Pretoria, <sup>2</sup>TB control and management, National Department of Health, Pretoria, <sup>3</sup>TB, University Research South Africa, Pretoria, South Africa.

**Background:** USAID TB Program South Africa, managed by URC, is a 5 year project implemented in South Africa. The project works with the national department of Health to strengthen TB and HIV management. As part of activities, the project implements a small grants program which provides limited funding to community based organizations. Since October 2009 to June 2014, 88 organizations. Activities provided by the funded organization ranged from TB and HIV prevention – ACSM, screening, testing, adherence support and basic research.

**Design/Methods:** Requests for proposals were sent out in phases over the 5 year period. In total 4 waves of awards were granted. Successful grantees were capacitated during Pre and post award workshops, on grant management processes as well as community management of TB. A reporting template with selected TB program indicators, in line with activities, was developed and used for reporting by the NGOs.

**Results:** Over the 5 year period, 85 organizations were funded as follows: Wave 1 (2009 – 2010): 16 grants; Wave 2 (2010 – 2012) 17: grants; Wave 3 (2012 – 2013): 18 grants; Wave 4 (2013 – 2014): 34 grants. In total more than 700 000 people were reached, more than 200 000 screened for TB and more than 4500 TB cases were diagnosed.

**Conclusion:** Involving communities in the management and control of TB improved TB treatment outcomes. Many grantees have pioneered innovative models of service delivery and community outreach, such as injection teams for MDR-TB patients and door-to-door TB and HIV screening, which can serve as models for other organizations working to combat TB and TB/HIV throughout the country, particularly among vulnerable and hard-to-reach populations.

### Involvement of workers' unions to augment TB control efforts in Swaziland

S Haumba,<sup>1</sup> M Calnan.<sup>1</sup> <sup>1</sup>Leadership and Strategic Management, University Research Co., LLC, Mbabane, Swaziland.

**Background:** The Swaziland Nurses Association (SNA) is a professional organization and a trade union for nurses that was formed to protect the rights and interests of its members including wages, benefits and working conditions. In Swaziland, TB and HIV are important factors affecting healthcare workforce capacity because of the high-prevalence rates. TB/HIV contributes to loss of valuable healthcare providers directly through death and absenteeism and indirectly affects family members, increasing work volume and decreasing performance. Two case studies are presented on involvement of

Workers' unions: i) a pilot of targeted TB screening among health care workers ii) unions engagement in the improvement of TB services at the national MDR-TB hospital. Involving the union aimed at stakeholder buy-in to augment TB control services for patients and among health care workers (HCWs).

**Methods:** The Wellness Centre board chaired by the President of SNA was engaged in establishing, a TB screening project implemented by the Wellness Centre, USAID ASSIST project, the national TB control Programme and the International Council of Nurses. Stakeholders were engaged in consultative planning meetings and joint implementation of a TB screening pilot in 14 wellness corners over 12 months. All HCWs were sensitized on TB screening and HIV testing and a mobile wellness corner was established to provide services for HCWs not comfortable accessing services within their health facility. The TB hospital in Manzini is responsible for MDR-TB management. The heads of departments engaged the workers union unit committee and worked together to improve infection control and MDR-TB services at the TB hospital after a series of industrial action in the preceding years. Training on infection control, quality improvement and standards of MDR-TB care were conducted and quality improvement projects for TB management established.

**Results:** Between October 2012 and September 2013, 2391 HCWs were screened, 746 had TB symptoms and 31 bacteriologically confirmed and initiated on TB treatment. Expansion to 26 health facilities has began. At the TB hospital no instances of industrial action were reported since the engagement of the union. Interim Culture conversion rates improved from 54% to 68%; ART uptake among MDR-TB/HIV co-infected patients increased from 54% to 97%.

**Conclusion:** Involvement of workers unions is critical in addressing the vulnerability of health care workers to tuberculosis.

### **Empowering communities in the clinical trial process: the TB Alliance model**

S Seidel. External Affairs, Global Alliance for TB Drug Development, New York, NY, USA.

**Background:** Having informed and engaged communities is a critical component of conducting successful and ethical clinical research. Through a Community Engagement (CE) program the TB Alliance works with individuals affected by tuberculosis (TB) around clinical trial sites to empower them with knowledge and skills, promoting open communication and participation in the TB drug research process.

**Methods:** Through a small grants program, TB Alliance supports the development and management of clinical research site-level strategies to engage local community stakeholders in the TB drug research and development process. Working with sites on an individual basis, TB Alliance provides funding, guidance, technical assistance and capacity building to site-level CE teams and Community Advisory Boards (CABs). Program initia-

tives prioritize research literacy and training to ensure CE staff and CABs are able to educate their community stakeholders about TB disease, treatment and TB drug research. Other initiatives of the program include cross-site engagement and learning to strengthen best practices and overcome common challenges, monitoring and evaluation of CE activities and advocacy for TB drug research and new regimens.

**Results:** Fourteen clinical trial sites in Kenya, South Africa, Tanzania and Zambia have initiated CE strategies around TB Alliance late stage Phase II and Phase III trials, since the program was initiated. A common model for CE programs across sites is the development of CABs and the placement of a dedicated member of the research team to act as CE Coordinator. Coordinators oversee their site's CE strategy and ensure an ongoing dialogue between the research team, the CAB and the wider community. CE teams and CAB members have participated in a research literacy training of trainers program and implement ongoing research literacy activities to raise the level of knowledge and understanding about TB drug trials amongst their community stakeholders.

**Conclusion:** The small grants model, and providing dedicated funds to research sites for CE has allowed more oversight of CE programs overall, and has empowered CE teams to take ownership of the planning and budgeting process for their activities. The grants process has also helped to build capacity of CE teams to seek additional sources of funding, and document and report on the progress and outcomes of their programs.

## **48. MULTI-FACETED REGIONAL RESPONSE TO TUBERCULOSIS IN THE MINING SECTOR IN SOUTHERN AFRICA**

### **Economic impact of a comprehensive TB intervention in mines, mining communities and labor sending areas**

O Okorafor. Health Nutrition & Population, The World Bank Group, Pretoria, South Africa.

This session presents the results of the cost and benefit implications of implementing a comprehensive intervention in South African mines comprising of annual universal testing of all mineworkers, and treatment of mineworkers diagnosed with tuberculosis (TB). Annual testing is considered using GeneXpert. Treatment of mineworkers is assumed to achieve the World Health Organization (WHO) standard of successfully treating 85 percent of those diagnosed with TB. The study was conducted using data for the gold and platinum group metal mines which employ more than 70 percent of all mineworkers in South Africa. The analysis employed a mathematical model that captures trans-boundary effects of exogenous TB infections due to the circular migration of mineworkers. The analysis forecasted the cost of maintaining status quo on TB testing and treatment versus a comprehensive approach, based on cost and treatment data from various mining companies and TB

programs in the four focus countries. Benefits of TB interventions are estimated from two separate but additional benefits. The first is the benefits from averted treatment costs from having fewer patients who progress to active and potentially drug-resistant TB. The second is the economic benefit of reduced mortality associated with TB. For the latter a value of statistical life approach is used. The results of the study indicate that the benefit of this intervention significantly outweighs the associated costs. For every US \$1 invested in this intervention, the benefits received are more US \$12. Benefits are higher in the gold mines than in platinum mines. The results also show that this intervention can significantly reduce the burden of TB in the South African mining sector. Due to the circular migration of mineworkers, the intervention will also reduce the burden of TB in labor sending countries, although the effects are relatively lower.

### Harmonisation of TB management in Southern Africa

I Manhiça,<sup>1</sup> M T Mbatha,<sup>2</sup> N Sigwebela.<sup>2</sup> <sup>1</sup>NTP, MISAU, Maputo, Mozambique; <sup>2</sup>TB, University Research South Africa, Pretoria, South Africa.

**Background:** The mining sector plays a significant role in the growth of southern Africa economies. Out of all neighbouring countries, the highest proportion of foreign mining labour to South African mines comes from Mozambique. The Southern provinces of Mozambique have high levels of cross-border migration, particularly to mines in South Africa. There are two primary diseases affecting the health of Mozambican mine workers: TB and HIV. These diseases affect current miners and ex-miners as well as communities surrounding from the three labour sending provinces in Mozambique: Maputo, Gaza and Inhambane.

**Methods:** Mozambique participated actively in the consultative process during the development of a regional framework for harmonized management of TB strengthen the continuum of care for Mozambican miners working in the South African mines. To support TB in the mines initiative, Mozambique government formed a committee with members from the National AIDS Council, Ministry of Health, Ministry of Labour, mine workers' representatives, the mining industry and intergovernmental organizations. Provision of health services to current miners, ex-miners and their communities is a key priority for the NTP in Mozambique. Mozambique conducted various mapping exercises to identify areas with the highest concentration of miners and ex-miners. Mozambique will be conducting will be consolidating all existing data to accurately identify geographical locations of miners, ex-miners and their families.

**Conclusion:** NTP is developing an innovative advocacy, communication and social mobilization strategy to advance the implementation of the harmonization intervention on TB management in the mines. NTP and its partners will be developing job aids and training

materials to support the implementation of the harmonized treatment protocol.

### Strategies for meeting service delivery needs of TB patients in Southern African communities

P L Osewe. Human Development, The World Bank Group, Pretoria, South Africa.

There are around 500,000 mineworkers in South Africa. Approximately 40 percent of these mineworkers are from Lesotho, Swaziland and Mozambique. It is estimated that there are up to 1.5 million ex-mineworkers in the four focus countries. These are high-risk groups contribute to the increased risk of contracting TB in the communities they reside. However, there are several factors that preclude effective TB management among these groups. (1) there is currently a lack of information on where most of the ex-mineworkers reside; (2) management of TB has historically been approached in silos, with various stakeholders (ministries of health, labor and mineral resources; and mining companies) addressing the TB challenge; (3) mining is private sector driven while TB is a public health challenge; (4) mineworkers regularly move across national and provincial boundaries, and for those infected with TB, there is no cross-boundary support to facilitate adherence to TB treatment; (4) mineworkers also face both social and occupational barriers to accessing TB services; (5) there is often a lack of information and awareness about TB and other occupational illnesses amongst many mineworkers and ex-mineworkers, although this varies by mining companies. A novel service delivery strategy has been developed to address this complex challenge of effectively addressing TB amongst mineworkers, ex-mineworkers and affected groups such as their families and communities. This is a regional approach that brings together different health systems and stakeholders to work together in addressing the challenge of TB in the mining sector in southern Africa. The various components of this approach include mapping of current mineworkers, ex-mineworkers and health services available to them; development of a database of mineworkers in region, design and implementation of a cross-boundary referral system for TB services, harmonization of TB management across countries and health systems, increasing the responsiveness of the health system to the needs of mineworkers through a science of service delivery approach, and improving geographic and financial access to occupational health services for mineworkers. This session will present key issues, challenges and lessons learnt from the what has been done up to date on the various components of this collaborative, regional and multi-sector strategy to addressing TB in southern Africa.



## Managing the cross-border challenges of TB in Southern African communities

T Dlamini. National TB Control Programme, Manzini, Swaziland.

South African mines source labor from various parts of South Africa and also from neighboring countries. Most of these mineworkers are migrant workers, travelling regularly between their home communities and the locations in which they work. For 40 percent of mineworkers who come from Lesotho, Mozambique and Swaziland, this involves crossing national borders. Mineworkers in South Africa have an elevated risk of contract tuberculosis and their circular migration increases the risk of cross-border transmission of TB. This session presents the challenges for managing cross-border TB patients from this migrant population, and the approaches adopted by this regional response to TB to address these challenges. Large mining companies usually provide TB treatment for their employees. However, when these actively infected mineworkers travel across national borders, there is no mechanism to ensure adherence to treatment. Similarly, there is no mechanism to ensure continuity of care for infected mineworkers who are dependent on their public health systems. Mineworkers seldom have information on where to seek appropriate TB care in their home countries, and the stigma associated with TB infection in home communities compounds the challenge of treatment adherence. In addition, there is no proper referral system between countries. This session will present strategies that have been developed to address these challenges, and the lessons learned from the implementation of these initiatives. These strategies include the development of a database of mineworkers and a cross-border referral system that connects the various health systems, mining companies and the relevant health facilities in these four countries.

## 50. ENHANCING TB CONTROL WITH STRUCTURAL INTERVENTIONS: FROM INCENTIVES AND ENABLERS TO SOCIAL PROTECTION

### The CRESIPT project: community feedback and practical challenges of conditional cash transfers for TB-affected families in Peru

T Wingfield,<sup>1,2,3,4</sup> M Tovar,<sup>1,4</sup> D Huff,<sup>1,5</sup> R Montoya,<sup>1,4</sup> D Boccia,<sup>1,6</sup> C Evans.<sup>1,2,4</sup> <sup>1</sup>Innovación Por la Salud Y Desarrollo (IPSYD), Asociación Benéfica PRISMA, Lima, Peru; <sup>2</sup>Infectious Diseases & Immunity and Imperial College Wellcome Centre for Global Health, Imperial College, London, UK; <sup>3</sup>The Monsall Infection Unit, North Manchester General Hospital, Manchester, UK, <sup>4</sup>Innovation For Health and Development, Laboratorio de Investigación y Desarrollo, Universidad Peruana Cayetano Heredia, Lima, Peru; <sup>5</sup>Global Health, University of Tulane, New Orleans, MS, USA; <sup>6</sup>Infectious

Diseases Epidemiology, London School of Hygiene & Tropical Medicine, London, UK.

**Background:** Cash transfers are identified as a key intervention in the World Health Organisation's post-2015 global TB policy. However, evidence for TB-specific cash transfers is limited. We implemented a socioeconomic intervention that included cash transfers to prevent TB in shantytowns in Lima, Peru: the ongoing CRESIPT pilot project. Aims of the pilot were to: i) adapt the intervention for maximum impact in the main CRESIPT study; and ii) evaluate the feasibility and community acceptance of the intervention.

**Methods:** Recruitment: from February 2014, all consecutive patients diagnosed with TB at National TB Program health posts were recruited, expanding from 2 to 32 health posts over 6 months. Randomization: consenting participants were randomized 1:1 by household to receive normal standard of care (comparison) or normal standard of care plus the socioeconomic intervention (supported). Socioeconomic intervention: Social dimension: household visits and participatory community meetings (educational workshops and TB Clubs) Economic dimension: assisting the patient to open a bank account and providing conditional cash transfers (Table). **Results (to August 11<sup>th</sup> 2014):** Recruitment: 96% (282/295) of patients diagnosed were recruited. 122 patients were randomized to the support arm. Social dimension: We held 22 participatory community meetings, attended by 254 participants. 90% (203/225) and 95% (213/225) rated the educational workshop and TB Club as good or excellent respectively; and 98% (220/225) would recommend other TB-affected families attend the meetings. Economic dimension: A total of 9,962 US dollars were provided in 433 cash transfers (Table). Banks were changed mid-pilot because account maintenance charges were introduced. Themes raised by participant feedback and field team focus group discussions included: Successes: implementation of TB-specific cash transfers generated novel practical evidence; multi-sectoral collaboration; and a patient-centred, empowering intervention Challenges: delay of cash transfers and hidden account charges eroded patient confidence; poor access to banking agents; perceived stigma in the banks; and difficulty meeting project conditions that required involvement of all household contacts (e.g. community meetings)

**Conclusion:** The CRESIPT pilot of a socioeconomic intervention provides evidence that TB-specific cash transfers are feasible in an impoverished, urban environment.

Table: Conditions and cash transfer incentives paid (number and US dollars)

Condition	Incentives paid				
	Number		\$USD		
	For optimal behaviour	For adequate behaviour	For optimal behaviour	For adequate behaviour	TOTAL*
Sputum sample provided	89	25	14	7	1421
Visited at home	96	4	18	9	1764
Attended community meeting	19	0	36	18	684
Household contacts screened for TB	69	2	54	27	3780
Adhere to treatment	128	1	18	9	2313
Completed therapy or chemoprophylaxis	N/A	N/A	36	18	N/A
<b>TOTAL</b>	<b>401</b>	<b>32</b>	<b>230**</b>	<b>115**</b>	<b>9962</b>

\*This column is the total incentives in US dollars paid during the pilot project for meeting each condition, calculated by: (Number of incentives paid for optimal behaviour + Incentives paid in US Dollars for optimal behaviour) + (Number of incentives paid for adequate behaviour + Incentives paid in US Dollars for adequate behaviour)

\*\*These figures are greater than the sum of their columns because incentives paid for treatment adherence were: monthly when TB treatment was prescribed and taken daily; and bimonthly when TB treatment was prescribed and taken 3 times per week. The figures shown in the Table correspond to a household in which there is a person with fully-sensitive TB being prescribed and taking 6 months of treatment. The figures for a person with HIV or MDR TB would be as follows: HIV-positive people with TB being prescribed and taking 9 months of treatment would receive 282 and 141 US dollars respectively; and people with MDR TB being prescribed and taking 24 months of treatment would receive 425 and 213 US dollars respectively.

N/A: The incentive paid for "Completed therapy or chemoprophylaxis" is not applicable because, at the time of writing, the first recruited pilot patient had not yet completed treatment

### Bangladesh experience in implementation of electronic tools and cell phones for PMDT program to improve adherence

P Daru,<sup>1</sup> M A Al-imran,<sup>1</sup> N Kak.<sup>1</sup> <sup>1</sup>TB CARE II, University Research Co. (URC), Dhaka, Bangladesh.

**Background:** Emergence of drug resistant TB has become a significant public health problem in Bangladesh. The country has adopted Community-Based Programmatic Management strategy for drug-resistant TB cases (cPMDT), which requires a strong system of follow up by community DR TB DOTs providers to ensure adherence for the full 20–24 months of treatment. Given the high percentage of mobile phone users, mHealth can play a vital role in ensuring drug adherence and monitoring of DOT services.

**Methods:** A web based smart phone application has been designed to support the provision of home-based DOT in cPMDT area. Each MDR TB DOT provider is provided a smartphone to assist in managing daily provision of DOT, and is able to routinely access each patient's tailored treatment regimen including drugs and dosing requirements. The Geo tagging mechanism allows program supervisors to verify when and where each DOT session was recorded. All information of this application is stored in a central database for monitoring centrally with the coordinate point of patients' residence tagged with the record.

**Result:** Currently, 305 MDR TB DOT providers are using the smart phone application covering 389 DR TB patients in 24 districts of Bangladesh. To date, drug compliance has increased in compared to the baseline through introduction of the Smartphone application. The regularity of the DOT providers' presence to the patients' house reached to 99%. Contact tracing through Smartphone application is contributing to active case finding.

**Conclusion:** Mobile phones have significant potential to facilitate case management of community-based MDR TB patients, particularly in rural areas in Bangladesh. Through active monitoring at the central level and with field level cooperation, mHealth can play an important role to ensure patient adherence to DOT and effective monitoring to reduce burden of TB in Bangladesh.

### Opioid substitution therapy and TB/MDR-TB: example of daily DOT, experience of integration and motivation

Z Islam,<sup>1</sup> O Smetanina,<sup>1</sup> S Filippovych,<sup>1</sup> A Shost.<sup>1</sup>

<sup>1</sup>Treatment, procurement and supply, International HIV/AIDS Alliance in Ukraine, Kyiv, Ukraine.

**Background:** As of July 2014, 8,279 PWID's received OST in all regions of Ukraine. OST sites operate based on drug treatment clinics, AIDS-Centers, TB clinics and general hospitals. Significant proportion of OST patients (42%) has HIV-infection or and TB (16%). Analysis of TB diagnosis and treatment were carried out at the integrated OST sites.

**Design/methods:** A structured survey of clients and staffs of OST sites were conducted using standard sociological methods (quantitative survey). Study regions were selected using representative principle (east, center, south, and west). Overall 500 OST clients were interviewed using semi-structured survey questionnaire, 8 focus group discussions were held with 64 OST clients; flexible interviews were conducted with 48 health care and social workers of OST sites.

**Results:** 2% of all respondents presented to OST program with verified diagnosis of tuberculosis. In 18% of respondents TB was discovered after they entered OST program. 100% of clients performed annual x-ray screenings and 68% were inspected using sputum smear microscopy. 93% of respondent's regularly undergone screening questionnaire concerning symptoms of tuberculosis; 72% of respondents with positive screening results received phthisiatrician consultation. 20% (101 persons) of all respondents have been diagnosed with tuberculosis, 91 persons were diagnosed after the start of OST. Nearly 10% of all respondents were receiving treatment. Two-thirds of them (35 persons) were being treated in an inpatient setting, third (19 persons) - as outpatients. The rest of the patients had completed their treatment programs (47 persons). No patient diagnosed with TB in this setting has reported an interrupted treatment program.

**Conclusions:** The study demonstrates an effective collaboration and coordination in regards to TB treatment in all OST sites. Effective implementation of using DOTS

for TB patients (early detection, immediate TB treatment initiation and DOT) at OST clinics especially at integrated care centers improves OST clients' treatment outcome and quality of life. These TB integration model must be further replicated to enhance patient centered service provision for the key population.

### Impact of social protection on TB incidence and treatment outcomes in Brazilian municipalities: implications for the national TB control programme

J Nery,<sup>1</sup> S Pereira,<sup>1</sup> D Rasella,<sup>1</sup> R Aquino,<sup>1</sup> M Barreto,<sup>1</sup> A Torrens,<sup>2</sup> D Barreira,<sup>2</sup> M Sanchez.<sup>3</sup> <sup>1</sup>Institute of Collective Health, Federal University of Bahia, SALVADOR, Bahia, Brazil, <sup>2</sup>National Tuberculosis Control Program, Ministry of Health of Brazil, Brasília, Distrito Federal, Brazil, <sup>3</sup>Faculty of Health Sciences - Collective Health Department, University of Brasília, Brasília, Distrito Federal, Brazil.

**Background:** Social determinants impact tuberculosis (TB) transmission and its progression to disease. Little is known about the role of public policies, as conditional cash transfer, like the Bolsa Família Program (BFP) in Brazil for contributing to reduction of poverty related diseases such as TB. The objective this study is evaluate the impact of BFP on TB incidence and treatment outcomes in Brazil.

**Design/Methods:** It was conducted a longitudinal ecological study with Brazilian municipalities between 2004 and 2013 and a historical cohort from TB cases diagnosed in 2010 in Brazil. In the ecological study data were obtained from national databases with information about socio - demographic and morbidity from TB. The main independent variable was the coverage of the BFP on the population of poor people and the outcome was incidence rate of TB. It was used fixed-effects negative binomial models for panel data, crude and adjusted for socio - demographic covariates. In the cohort study it was performed deterministic linkage between TB database and the Single Registry for Social Programs (CadÚnico) and BFP payroll. The intervention group was composed of individuals who received the cash transfer during the period of treatment and the group without intervention by individuals who underwent the intervention after end of treatment. It was used demographic, epidemiological, clinical, and socioeconomic data and amount and period of cash received. The measure of association used was the Risk Ratio.

**Results:** A total of 2,548 municipalities were classified as with quality of tuberculosis surveillance. Municipalities with higher BFP coverage has statistically significant reduction in the incidence rate of tuberculosis in crude models and adjusted for selected covariates (BFP coverage higher 70%; RR=0.90 95% CI = 0.87 - 0.93). Furthermore, out of the 71,660 new TB cases diagnosed in 2010, 13.1% was enrolled in BFP. The intervention group accounted with 79.4% (7,176) of the total beneficiaries and without intervention 20.6% (1,864). 76.4% of subjects in the intervention group received the benefit throughout period of treatment. Cure rate in the intervention group was 81.4%, whereas

in the non-intervention group it was 76.2% (RR=1.07, p < 0.01).

**Conclusion:** Preliminary results indicate a positive impact of BFP in TB incidence in the period 2004–2013 and in TB outcomes in 2010 cohort. These results can contribute to the discussion on the relationship between social policies and health conditions of the population.

### 51. COPD: DIAGNOSTIC AND THERAPEUTIC CHALLENGES IN DEVELOPING COUNTRIES

#### Choice of drugs for COPD patients

J-W Fitting. Respiratory Medicine, Lausanne University Hospital, Lausanne, Switzerland.

The burden of COPD is considerable on the individual and on society. The life of COPD patients is marred by disabling symptoms, exacerbations of disease, and premature death. The societal burden consists of direct costs due to maintenance therapy and mainly to hospital admissions for exacerbations, as well as of indirect costs due to loss of employment. Reducing symptoms and exacerbations is the objective of maintenance therapy in COPD. International guidelines recommend using inhaled bronchodilators in patients with respiratory symptoms, and the use of long-acting agents is now favoured: long-acting muscarinic antagonists (LAMAs) and long-acting  $\beta_2$ -agonists (LABAs). Among LAMAs, tiotropium and glycopyrronium are prescribed once daily, whereas aclidinium is prescribed twice daily. Among LABAs, formoterol and salmeterol are prescribed twice daily, whereas indacaterol, vilanterol, and olodaterol are prescribed once daily. As measured by FEV1, formoterol and salmeterol are approximately equipotent bronchodilators, and slightly less potent than indacaterol and tiotropium. Indacaterol, tiotropium, glycopyrronium, and aclidinium are approximately equipotent. This favourable effect, albeit small on FEV1, is more pronounced on lung volumes with a reduction of dynamic lung hyperinflation. This mechanism explains the beneficial effect on dyspnoea and exercise tolerance. In terms of symptoms and quality of life, indacaterol has a slightly better effect than formoterol, salmeterol, or tiotropium. Compared with placebo, long-acting bronchodilators reduce exacerbations by approximately 20%, with LAMAs showing a larger effect than LABAs. Given the distinct mechanisms of action of LAMAs and LABAs, combining these agents potentiates their effects without increasing adverse effects. A dual bronchodilator therapy yields a higher effect on FEV1, dyspnoea, and quality of life, albeit at a higher cost. Adding an inhaled corticosteroid (ICS), usually to a LABA, is recommended in patients presenting an Asthma-COPD Overlap Syndrome (ACOS), or in those with an FEV1 <60% predicted and frequent COPD exacerbations. In reality, ICS are largely overprescribed in COPD, leading to resource wasting and increased risk of side effects, in



particular pneumonia. Pharmacoeconomic analyses generally conclude that LAMAs and LABAs are cost-effective in COPD, but with variable results depending on methodological uncertainties and varying costs across health systems and countries.

### Despite a high disease burden and financial cost, why does COPD continue to be so neglected?

A El Sony,<sup>1</sup> H Elsadig,<sup>1</sup> S Hassanain.<sup>1</sup> <sup>1</sup>Lung Health, The Epidemiological Laboratory, Khartoum, Sudan.

COPD is a public health epidemic it is predicted to be the third cause of worldwide deaths by 2020. COPD should be under focus due to its high prevalence, morbidity and mortality, & profound effect on the quality of life that present challenges and cost for healthcare systems. COPD as a chronic progressive disease is not high on the agenda as enormous number of cases are under-recognized, under-diagnosed, and under treated. COPD is neglected by development partners, national, & international health and development plans at both programmatic and scientific evidence based level where few surveys were conducted to know the national prevalence. Having a coalition that compiles all efforts for evidence generation, cross fertilization, and for having a well-defined standardized programmatic prevention, management and control at the field level in a way that capitalize on leadership, governance as well as all health system building blocks is essential. Encompassing a unified definition for COPD, knowing the origins and the significance of COPD and its major role as major cause of death in LMICs is of utmost importance. We should all advocate for effort and capital' harmonization merely to utilize a strictly standardized rigorous and practical methods for estimating prevalence, risk factors, social and economic burden of COPD. Having COPD prominently featured requires strategic partnerships and much more investment from funding bodies and governments.

### Targeting smoking cessation in patients with chronic respiratory diseases

T S Bam,<sup>1</sup> C-Y Chiang.<sup>2</sup> <sup>1</sup>Tobacco Control, International Union Against Tuberculosis and Lung Disease (The Union), Singapore, Singapore; <sup>2</sup>Lung Health, The Union, Paris, France.

**Introduction:** The Union's Lung Health Scientific Section established a working group in December 2009 to research a simple, cost-effective approach to smoking cessation for TB patients. This group's efforts led to the development of the ABC approach outlined in The Union guide Smoking Cessation and Smokefree Environments for Tuberculosis Patients published in 2010. The ABC (A=ask, B=brief advice, C=cessation support) approach was initially piloted in Bangladesh, China, India and Indonesia.

**Objectives:** To share the outcomes and lessons learnt from implementing The Union's Guide Smoking cessa-

tion and smokefree environments for tuberculosis patients.

**Methods:** Key approaches are; establish TB services 100% tobacco-free, presents 'ABC for identifying TB patients who smoke, helping them quit, and promoting smokefree homes for patients and families. It is delivered systematically within routine programme and can be done within 5–7 minutes.

**Results:** The Union ABC approach has demonstrated encouraging smoking quit rates at the end of 6 month TB treatment. In Bangladesh, of the 615 current smokers, 75.4% reported they quitted smoking. In India, of the 1333 current tobacco users, 67.3% remained quitters. In China, of the 233 current smokers, 59.7% quitted smoking. In Indonesia, of the 582 current smokers, 66.8% quitted smoking successfully.

**Conclusion:** Brief advice of 5–10 minutes with minimum cessation support at every visit of TB patients resulted in high quit rates and higher awareness of health impacts of secondhand smoke exposure, which led patients to make smoke-free homes and health providers to make tobacco free health-care.

## 53. NON-COMMUNICABLE DISEASES AND TOBACCO CONTROL

### Tobacco control as a risk factor in NCD debate: approaches and consequences

E Efroymsen. NCDs, HealthBridge, Dhaka, Bangladesh.

Tobacco control has received significant attention in recent years and in some ways has made remarkable progress, especially in terms of the WHO Framework Convention on Tobacco Control. With tobacco use as one of the four main risk factors for NCDs, the question moving forward is whether it is possible to utilize the expertise gained from tobacco control to strengthen overall NCD prevention work and if so, how to make best use of that expertise. Given the scope of the NCD epidemic and limited resources devoted to health, an integrated approach to NCDs, incorporating tobacco use and other major risk factors, is probably inevitable. There are significant opportunities as well as threats to such an integrated approach. An integrated approach would require fewer resources, both human and material, than a vertical approach. It would facilitate application of lessons learned from tobacco control, in terms of reining in a powerful industry that profits from spreading disease, beyond tobacco to include the producers and promoters of alcohol, sugar-sweetened beverages, and other energy-dense foods. However, there is also the risk of tobacco control being diluted. While an integrated approach is probably inevitable, the specific details will be critical in ensuring both success in tackling other NCD risk factors and maintenance or strengthening of tobacco control worldwide. Important issues to consider include how to deal with the alcohol, beverage, and food industries and how to obtain funding. A carefully planned strategy for integration can strengthen

the ability of governments and NGOs to address tobacco control and increase effectiveness in preventing NCDs overall.

**Advertising, promotion and sponsorship of NCD risk factors in relation to the NCD Summit political statement and the Millennium Development Goals**

D Bettcher. Prevention of Noncommunicable Diseases, World Health Organization, Geneva, Switzerland.

Two thirds of NCD deaths are linked to four common risk factors: tobacco use, harmful use of alcohol, unhealthy diet, and physical inactivity. Through the 2011 UN Political Declaration on NCDs, the global leaders have recognized that multisectoral, cost-effective, population-wide interventions, such as banning advertising, promotion and sponsorship, are key to reduce these risk factors' impact. Either as best buy for reducing the use of tobacco and alcohol or as good buy for reducing an unhealthy diet, bans of advertising, promotion and sponsorship are key components of WHO recommended policies, strategies, tools to address NCDs and their risk factors. A comprehensive ban of tobacco advertising, promotion and sponsorship (TAPS) reduces population wide smoking levels by 4% to 9%. Each Party of the WHO FCTC is required to introduce a comprehensive ban of all TAPS within 5 years since becoming a Party. The WHO FCTC Article 13 guidelines provide clear guidance on how to implement such comprehensive ban. However, by 2012, only 10% of the world's population was covered by complete bans. The implementation of bans or comprehensive restrictions on alcohol advertising is also a best buy to reduce the alcohol-attributable burden, and some countries are already considering it, in line with the WHO Global Strategy to Reduce the Harmful Use of Alcohol. Most food and non-alcoholic beverages marketed are high in fats, sugar, and salt. There is ample evidence that marketing of such food and beverages to children influences their food choices, and consumption patterns. WHO developed a Set of Recommendations on the marketing of foods and non-alcoholic beverages to children, as well as an implementation framework, which aims to assist Member States in designing and implementing new policies, or strengthening existing ones, on food marketing communications to children. Currently implementation is slow, however there is an increasing commitment to accelerate in the next few years with support from WHO and partners. Through the 2011 Political Declaration on NCDs the world leaders acknowledged NCDs constitute one of the major challenges for development in the 21st century. In 2013 a High-level Panel of Eminent Persons on the Post-2015 Development Agenda recommended a target for priority NCDs and also the UN General Assembly called on Member States to consider including NCDs in the post-2015 development agenda. The Member States have now started to build business case for it.

## ABSTRACT PRESENTATIONS THURSDAY 30 OCTOBER 2014

### e-POSTER SESSIONS

#### 01. TOBACCO CONTROL LAWS: MAY THE FORCE BE WITH US!

##### EP-100-30 Capacity building training for the executive magistrates: a unique initiative to implement the tobacco control law in Bangladesh

MAU Ahsan,<sup>1</sup> SM Mahbus Sobhan,<sup>1</sup> H Syed Mahfuzul Huq,<sup>2</sup> Alam Md. Alamgir Sikder,<sup>1</sup> A-E- Sadat.<sup>3</sup> <sup>1</sup>Ministry of Health & Family Welfare, National Tobacco Control Cell, Dhaka, <sup>2</sup>Tobacco Control, World Health Organization, Dhaka, <sup>3</sup>Ministry of Health & Family Welfare, Ministry Of Health & Family Welfare, Dhaka, Bangladesh. Fax: (+880) 29580255. e-mail: ahsan5965@gmail.com

**Background and challenges to implementation:** Mobile court is the most useful tool for implementation of any law in Bangladesh. According to the government circular, executive magistrates conduct mobile courts on different laws. It punishes the law violator on the spot and it is also welcoming by the civil society. Moreover it can earn significant media coverage. Sensitize the executive magistrates to conduct mobile court exclusively on tobacco control law was really challenging. Executive magistrates remain very busy in maintaining law and order in the district and sub-district level. They worked under Ministry of Public Administration and apparently tobacco control law was not any priority to them. A few mobile court conducted occasionally but it is observed that magistrates working in the field are not equally aware and sensitize about tobacco control law, which sometimes discourages them in conducting court on tobacco control law. National Tobacco Control Cell came forward to train few executive magistrates on the tobacco control law exclusively. Although it was challenging to ensure magistrates participation from all over the country, but it became possible for active support from the Ministry of Public Administration and close follow up by the NTCC officials.

**Activities undertaken and response:** National Tobacco Control Cell (NTCC) organized day long training in Dhaka. This was the first ever training organized exclusively for the executive magistrates on Tobacco Control law in Bangladesh. Training module includes Global Tobacco Epidemic, Tobacco industries tactics and violations of the law. Till May 2014 NTCC has trained 81 executive magistrates from 64 districts of the country.

**Results:** It has been observed that lack of knowledge and information gap regarding this public health act is one of the main reasons of minimal implementation of the law.

After completion of the training, in one year 63 magistrates conducted 95 mobile courts at different public places and fined 247 persons and institutions for violation of the law. The magistrates conducted these mobile courts as a regular part of their job and however it costs nothing for the Ministry of Health or NTCC.

**Conclusion:** At the end of the training strong commitments achieved from the executive magistrates. It is also reported that trained magistrates are now more cooperative and interested to hold mobile courts on tobacco control than before.

##### EP-101-30 Creating tobacco-free industries through collaboration and mobilisation

M Sinha.<sup>1</sup> <sup>1</sup>Tobacco Control, Madhya Pradesh Voluntary Health Association, Indore, India. Fax: (+91) 7312877735. e-mail: sinhamukesh63@gmail.com

**Background and challenges to implementation:** Good employers are always concerned about employee's health as it increases productivity, reduces healthcare cost, create healthier workplace and work culture. Unfortunately large number of workers in industrial sector consume tobacco in one form or other. Workers are mostly governed with factory/labour laws. Indian Tobacco Control Act mandates smoke free workplace but do not emphasize on tobacco free workplace. However tobacco free workplace directly benefits the employers, employees and their families.

**Intervention or response:** A diamond cutting Industry of Dhar district of Madhya Pradesh having 1438 employees was selected and intervened. Top union leader of industry was oriented and motivated to take up issue before management, followed by a joint orientation of top management and union leaders. This created a path for making industry tobacco free. Series of orientations of workers, baseline survey, one to one contact with identified tobacco users, availability of educational materials were the part of the interventions.

**Results and lessons learnt:** Management took tobacco issue at the priority and formed tobacco control committee jointly with union leaders, displayed names and regular meeting started. Monitoring committee formed, checking started, signage's displayed at prominent places and fining mechanism is in place. 'Number of chewing tobacco users reduced to 68 and of smokers to 48 from a total of 300 tobacco users. Those who still use tobacco stopped using in factory premises and acute cases is being referred to cessation centres. Quitters started motivating other workers through peer education and case studies. Tobacco free industry mandate has become a part of the code of conduct of the company. Overall employees, users, non users, leaders and management all realized the importance and feel proud that their industry is heading in a right direction.

**Conclusions and key recommendations:** Planned and systematic advocacy and education, mutual agreement of employer and employees, union leaders and management play vital role in making Tobacco Free industry, which has direct impact on overall health status of the



employees and productivity. Tobacco free industry in a country like India has much more impact than a smoke free as plethora of chewing and non chewing tobacco products are being consumed.

### EP-102-30 Preventing tobacco industry interference in Myanmar: challenges and the way forward

A Tun,<sup>1</sup> T S Bam,<sup>2</sup> THU Zar Chittin,<sup>3</sup> T Sein,<sup>4</sup> Phyu T Han,<sup>1</sup> THUY Aung,<sup>1</sup> T Myint,<sup>3</sup> SU Mon Myat.<sup>3</sup> <sup>1</sup>Department of Community Health, University of Community Health, Magway, Myanmar; <sup>2</sup>Tobacco Control, The Union, Jakarta, Indonesia; <sup>3</sup>Department of Health, Public Health Division, Nay Pyi Taw, Myanmar <sup>4</sup>Tobacco Control, People's Health Foundation, Yangon, Myanmar. Fax: (+951) 573962. e-mail: aungtunmm@gmail.com

**Background and challenges to implementation:** Even though it ratified the WHO FCTC in 2004, Myanmar has failed to implement some of the WHO guidelines, including health warning on cigarette packs. Since the new government came into power in 2011, at least two cigarette companies have received approval to run businesses in Myanmar after decades of tight control over tobacco products. Due to weak enforcements of existing regulations, tobacco companies in Myanmar get about direct advertising bans through their corporate social responsibility arms sponsoring orphanages and entertainment events.

**Intervention or response:** Adoption of FCTC article 5.3 is being given priority to prevent tobacco industry interference in public health policy. Raising awareness and education campaign about Tobacco Industry Interference, Code of Conduct for civil servants, meeting/Interaction with Industry rules and Industry monitoring are main counter measures to tobacco industry interference in Myanmar. Collaboration between Civil society and Government are being strengthened in order to improve surveillance, reporting and enforcement mechanisms.

**Results and lessons learnt:** Over the past two years, Myanmar has strengthened the control cell within the Ministry of Health, worked with civil society to build support for tobacco control among the public, and partnered with related ministries and NGOs to prohibit all forms of direct and indirect advertising, promotion and sponsorship of tobacco. In 2012 Cigarette taxes in Myanmar are levied at 100% (commercial tax) of taxable turnover. Measures are underway to enforce regulations for the health warnings to be rotating, pictorial as well as textual and to be displayed taking at least 90% of the front of cigarette packages. According to Ministry of Health's strong rejection, the Myanmar Investment Commission has agreed that they will not permit new cigarette plants in Myanmar and Myanmar has also signed the Protocol to eliminate illicit trade in tobacco products, adopted at the fifth Conference of the Parties (COP5) in 2013.

**Conclusions and key recommendations:** In Myanmar the related ministries and sectors, NGOs and the community as a whole need to put the fight against tobacco industry

interference. The Government should develop regulations on interaction with the industry if and when such interaction is necessary and prohibit any interaction that may lead to undue influence and or interference.

### EP-103-30 The role of civil society in advancing tobacco tax revenue for health promotion in Indonesia

D Suhadi,<sup>1</sup> T S Bam,<sup>2</sup> B Nussarivera,<sup>3</sup> R Sinaga.<sup>3</sup> <sup>1</sup>Smoke Free Jakarta Alliance, Swisscontact Indonesia Foundation, Jakarta, <sup>2</sup>Tobacco Control, The International Union Against Tuberculosis and Lung Disease, Jakarta, <sup>3</sup>Smoke Free Jakarta Alliance, Sahabat Cipta Foundation, Jakarta, Indonesia. Fax: (+62) 21 79198691. e-mail: waty@swisscontact.or.id

The Regional Tax and Retribution Law No. 28/2009 defines financial resources for the sub-national government including sharing of tobacco tax revenue between national government and sub-national government. The tobacco tax provision states that tobacco tax revenue should be used among others for provision of smoking area. The Smoke Free Jakarta NGO Alliance challenged the provision in view of the fact that more than 120 sub-national governments in Indonesia have passed a local ordinance on Smoke-free Area. The activity included policy advocacy at national and regional level and technical assistance for the regional government. The primary target population is more than 22 million people in Greater Jakarta and the secondary target population is the people of Indonesia. The methods used: interviews with key informants who were involved in advocacy, drafting, and adoption of the tobacco tax local ordinance of Jakarta and other regions in Indonesia. A diary, relevant documents and press articles were investigated. Key substances of the first government draft are: 1) 50% of tobacco tax revenue for health services and law enforcement, 2) health services include among others provision of smoking area. The Alliance contributed to the improved final draft: 1) 70% of tobacco tax revenue to fund health promotion and law enforcement in tobacco control, 2) health promotion includes among others smoking cessation program through existing health system, mass media campaigns on the dangers of smoking, and public participation in tobacco control. The bill was passed by the regional parliament, however it failed certification by the national government on the basis that tobacco tax revenue should be used among others for provision of smoking area. Further advocacy was continuing at national level towards Ministry of Home Affairs and Ministry of Finance. The risk was identified: cancellation of the bill if the regional government did not accept the national government revision. The Alliance urged the regional government to reject the revision. Tobacco industry interference was observed at certain levels. In the end, the parties were successful in defending the bill. The result is expected to have an impact on policy change nation-wide. Future work: development of budgeting guideline for health promotion in tobacco control and monitoring of the implementation of the tobacco tax ordinance. Strong

leadership, building the belief of the risk of having wrong policies are key factor.

#### **EP-104-30 Media advocacy and high-level meetings increased compliance with tobacco control laws in educational institutions in Alwar district of Rajasthan**

B Pandya,<sup>1</sup> P Lal,<sup>2</sup> R Parmar.<sup>1</sup> <sup>1</sup>Operations, Population Services International (PSI), Jaipur (Rajasthan), <sup>2</sup>International Union Against Tuberculosis and Lung Disease (The Union), New Delhi, India. e-mail: bhaskar@psi.org.in

**Background:** In Rajasthan state, the average age of tobacco use initiation was found to be 17.3 years in the Global Adult Tobacco Survey (GATS-2010). The availability of tobacco products near primary and secondary schools is one factor that may increase rates of early tobacco initiation among youth. Implementation of the Cigarette and Other Tobacco Products Act (COTPA) is scarce, meaning education institutions often lack appropriate signage stating the prohibition of tobacco sales within 100 yards of a school.

**Intervention:** The District Tobacco Control Committee (DTCC) is a high-level committee formed under COTPA. Population Services International (PSI) is providing technical support for tobacco control interventions to the committee. The members include the District Collector, Police Superintendent, Chief Medical Officer, District Education Officer, PSI, and Food Safety Officer. PSI facilitated the formation of the DTCC and organized two high-level district meetings. The role of the DTCC is to monitor and enforce COTPA Act. PSI identified government primary and secondary schools where tobacco products were sold within 100 yards. PSI presented COTPA provisions and key compliance protocols in the meetings, with a combined audience of 90 officials. PSI took lead in sensitizing key journalists to the Act and violations. PSI launched a one month smoke free campaign for creating awareness on the harmful effects of tobacco and on the tobacco laws.

**Result:** The District Collector issued directives for enforcement of the tobacco control law and instructed the Alwar district education department to ensure that all educational institutions must display warning signs. Print media exposed schools violating the COTPA Act and published names, interviews and photographs. This created an opportunity for the government and civil society to start discussions about the harmful effects of tobacco on students' health. The Education department formed law enforcement squads to monitor the violations and to fine non-compliers. More than 90% of the government schools installed warning signs outside schools

**Conclusion:** High level meetings and highlighting major violations and compliances in the media sensitized all key stakeholders to comply with the COPTA provisions.

#### **EP-105-30 Compliance level monitoring of smokefree policies as one of MPOWER strategy to protect people from tobacco smoke**

BF Nusarrivera,<sup>1</sup> T S Bam,<sup>2</sup> D Suhadi,<sup>1,3</sup> R Sinaga.<sup>1</sup>

<sup>1</sup>Tobacco Control, Sahabat Cipta Foundation, Jakarta,

<sup>2</sup>Tobacco Control, International Union Against Tuberculosis and Lung Disease, Jakarta, <sup>3</sup>Tobacco Control, Swisscontact Indonesia Foundation, Jakarta, Indonesia. Fax: (+62) 2179198691. e-mail: fella\_fuschia@yahoo.com

**Background and challenges to implementation:** A public opinion poll that conducted in 2013 in Jakarta shows that 30% people exposed to secondhand smoke at home, 29% in public transportation, 25% exposed in work places, and 16% exposed at public places. Since there is no known safe level of secondhand smoke, the government have to protect people from exposure of secondhand smoke by adopting smoke free policies. Jakarta already have Governor Regulation No. 88/2010 and No. 50/2012 which ban smoking in all indoor public places. Information on the compliance level of the regulation is needed to regularly monitor implementation of the regulation

**Objective:** To examine compliance level of smoke free policies as one of MPOWER strategies to protect people from tobacco smoke.

**Methods:** Samples were randomly selected. Enumerators visited the place which had been randomized with the geographical mapping which is spread in five cities of Jakarta. A short training was conducted to enrich enumerator's knowledge to use compliance monitoring form as per Governor Regulation No. 50/2012. We tracked every detail in all phases.

**Results and lessons learnt:** 800 sample from 50.000 buildings in Jakarta were selected to be monitored. The 8 keys indicators were used by the inspector are referred to the Jakarta's Governor Regulation. The indicators are: a) the absence of people smoking, b) the availability of designated smoking rooms, c) no smoking signage availability, d) smell of cigarette smoke, e) ashtray availability, f) presence of cigarette butts, g) hotline service availability and h) supervisory team availability. From this study, it is found that overall compliance rate in 5 cities is 37% which shows decreasing trend from the previous monitoring.

**Conclusions and key recommendations:** In conclusion, compliance level data could become critical evidence-based finding to support the government to have stronger policies. At this stage, compliance level is not yet adequate and still needs to be improved by strengthening the capacity of inspectors and law enforcers, in order to have stronger tobacco control policies to achieve succeed in protect people from tobacco smoke.

### EP-106-30 How well we are performing in compliance towards smoke-free legislation? Monitoring results of 17 sub-national surveys in a state of India

S Goel,<sup>1</sup> R J Singh,<sup>2</sup> R Gupta.<sup>3</sup> <sup>1</sup>School of Public Health, Post Graduate Institute of Medical Education and Research, Chandigarh, <sup>2</sup>Tobacco Control, International Union Against Tuberculosis and Lung Disease, New Delhi, <sup>3</sup>State Tobacco Control Cell, Directorate of Health and Family Welfare, Government of Punjab, Chandigarh, India. Fax: (+91) 1722744993. e-mail: sonugoel007@yahoo.co.in

**Aim:** Compliance survey of smoke-free law is an effective means of measuring progress towards a smoke-free society. They also help policy makers to take appropriate action where strengthening measures are required. India has a comprehensive tobacco control law known as Cigarettes and Other Tobacco Products Act (COTPA 2003) which prohibits smoking in public places and requires display of 'No smoking' signage's with proper specifications at conspicuous points. However, its implementation and enforcement are still a matter of concern. The study was conducted to ascertain the level of compliance with smoke-free law in public places of state of Punjab in North India.

**Methodology:** Punjab is a state in northern part of India with estimated population of 27.7 million. It is divided into 22 administrative districts. A total of 4800 public places from 17 districts of Punjab were surveyed between November 2011 till December 2013 (26 months). The public places including hotels/restaurants/bars/shopping malls, government offices, educational institutions, healthcare facilities and transit stations were surveyed. The study tool was adapted from the guide on 'Assessing compliance with smoke-free law' developed jointly by the Campaign for Tobacco Free Kids, Johns Hopkins Bloomberg School of Public Health and International Union against Tuberculosis and Lung Disease.

**Results:** The overall compliance rate towards section 4 of COTPA was 84%. No active smoking was observed in 91% (81.4–97%) of the public places. In 86% (72–98%) of the public places 'No Smoking' signage were displayed as per COTPA. Health and educational institutions had maximum compliance with the smoke-free law while transit sites showed the least compliance.

**Conclusions:** Compliance to the smoke-free law was high in the study. The efforts should now be made to sustain the encouraging results.

### EP-107-30 Kerala voluntary health services' PIL and its state and national implications on tobacco control

S V Itty.<sup>1</sup> <sup>1</sup> Non Government Organization, Kerala Voluntary Health Services, Kottayam, India. Fax: (+91) 9847819080. e-mail: sajuitty@rediffmail.com

**Background:** The use of tobacco is one of the major risk factor of fatal disease in the state. As per the Global Adult Tobacco Survey Kerala has the 10<sup>th</sup> rank in terms of smoking prevalence. The secondhand smoke exposure rate is 18.7%. GATS says 48, 34,648 people annually

exposed to secondhand smoke. Article 19.1 of FCTC provides that "For the purpose of tobacco control, the Parties shall consider taking legislative action or promoting their existing laws, where necessary, to deal with criminal and civil liability, including compensation where appropriate." Based on the above context Kerala Voluntary Health Services(KVHS) started state level initiatives to control the use of tobacco in the state by using "MPOWER" package of WHO as a tool and Legal advocacy as a means to advance the mission.

**Method:** KVHS Filed a Public Interest Litigation in Hon. High Court alleges that the negligence and callous attitude of the law enforcing agencies have in effect flouted the provisions of Tobacco Control legislations and its allied rules. The petition was filed in 2010 with documentary evidence, scientific study reports and grass root level facts. After series of sitting the Hon Court finally delivered the judgment on 26<sup>th</sup> March 2012.

**Result:** The Hon. Kerala High Court judgment (WP(C) No.38513/2010) directed central and state Govts to enforce ban on TAPs in Cinema and Television programmes. It also strengthens the enforcement of section 6 (b) in the state. As per the direction the state government introduced a three tire systems for implementation and monitoring of section 6 of COTPA in Kerala by(GO (RT).No 1479/12/Home dated 17<sup>th</sup> May 2012. Therefore the strong monitoring mechanism is now institutionalized. It support ministry of health and family welfare to issued revised notification regarding TAPs in cinema and television programmes by(G.S.R.708(E).- Dated 21<sup>st</sup> September 2012. **Saju.V.Itty Executive Director Kerala Voluntary Health Services**

### EP-108-30 Ensuring political commitment in tobacco control

M Syed.<sup>1</sup> <sup>1</sup>Health Rights, Work for a Better Bangladesh (WBB) Trust, Dhaka, Bangladesh. e-mail: smalam@wbbtrust.org

**Background:** Lack of political commitment is one of the major challenges of Tobacco Control around the world. Tobacco Industry has continued work to influence and misguide policy maker about tobacco control inBangladesh. During passing the TC law and amendment process, industry had tried to delay the process in different way.Bangladesh tobacco control advocates work hard to motive policy makers to support favour of tobacco control law.

**Methodology:** During the TC law drafting process in the ministry, the advocates started work with parliament members to sensitize the importance of Tobacco Control and TC law. Through letter, personal meeting, TC briefing kit, inviting as the guest in program were the key tools to continue communication with them. Bangladesh Anti Tobacco Alliance (BATA) 's grass roots members met their each constituency MPs and sensitized them about tobacco control. BATA networks members involve local political leaders and intellectual in their delegation during the met with MPs. During the meeting with Ministers, TC advocates reviewed the relevant



ministry law and policy and prepared a brief statement, how TC contribute those ministry works. During the election TC advocates met with political parties leaders and request them to include tobacco control as an agenda in their election manifesto.

**Results:** Bangladesh Parliaments passed TC law 2005 and government enacted rules in 2006. During the law implementation process, many loopholes are indentified. Parliament amended tobacco control law in 2013. In the last parliament election in 2014, one of the political party include tobacco control issue in their election manifesto.

**Conclusion:** Bangladeshi TC advocates successfully motivate policy makers to enact law on smoke free public place, ads ban, pictorial packet warning, and ban tobacco sale to and by minor etc issue. But still the challenge remains in increasing tax on tobacco products, funding for tobacco control.

### EP-109-30 Establishing tobacco control in Indonesia

E Rahajeng,<sup>1</sup> T S Bam,<sup>2</sup> P Yosephine.<sup>1</sup> <sup>1</sup>Ministry of Health, Directorate of Noncommunicable Disease Control, Jakarta, <sup>2</sup>The Union, Tobacco control, Jakarta, Indonesia. e-mail: tsbam@theunion.org

**Background:** In Indonesia, smoking kills more than 200,000 people every year. About 80% of Indonesian households are exposed to SHS every day. Smoking prevalence in males was 67% and in females was 2.7%. Indonesia has not ratified the Framework Convention on Tobacco Control (FCTC) yet and also absence of a comprehensive tobacco control law at national level. however, government regulation on tobacco control was passed in 2012 which includes provision of smoke-free and pictorial health warning

**Objectives:** To explain the steps of establishing tobacco control in Indonesia

**Methods:** Policy development, capacity building, establishing tobacco control network, guidelines development, Mayors' and regents engagement in tobacco control, and surveillances are the key approached used.

**Results:** Approaches included amendment of Health Law 2009 with subsequent regulation and decrees passed. These policies include a smoke-free, a 40% pictorial health warning, identification of tobacco as an addictive substances. A national tobacco control roadmap adopted with key indicators of FCTC accession by 2014, and expansion of smoke-free. More than 25 provinces were trained on tobacco control, a mayors' alliance established to support program at sub-national level. Indonesian tobacco control network established with more than 100 members in place. Regular monitoring is conducted of tobacco use and prevention policies through basic health survey, GATS and GYTS.

**Conclusions:** MOH commitment resulted a significance improvement in tobacco control in Indonesia at national and sub-national level. A model of Mayors' alliance demonstrated ownership of the program at implementation level.

### EP-110-30 Tobacco industry interferences and additives ban in Brazil

M Pinho.<sup>1</sup> <sup>1</sup>Tobacco Control Area, Fundação do Câncer / Cancer Foundation, Rio de Janeiro, RJ, Brazil. Fax: (+55) 2121574630. e-mail: mariana.pinho@cancer.org.br

Brazil/2012, ANVISA published Resolution prohibiting additives in tobacco products and became pioneer in banning menthol. Measure is consistent with Partial Guidelines Art9-10 adopted by COP4. Brazil, 3rd largest tobacco producer and largest exporter, TI and front organizations have used strategies to interfere in FCTC measures. It was monitored TI strategies that interfered full adoption of banning additives-2010/2014. Strategies used by TI and their front organizations are constantly monitored by Brazilian government and civil society. Different communication channels, lawsuits, lobbying at legislative and executive were monitored. 2010-during the Public Hearings, proposals were placed on target of criticisms. Representatives of tobacco growers got support for suspend the ANVISA's PH by pushing different agencies in federal and states governments. Argument of these representations was the prohibition of additives in tobacco products, tobacco production would remove the burley type, affecting the employment of families of producers and consequential damage to retail. Congressman linked to tobacco sector presented Draft Legislative Decree, through Committee on Agriculture, aiming to suspend PH on prohibition of additives. Agriculture Committee also held PH on the subject. 2011-ANVISA has scheduled 2 PH to democratize debate and give opportunity for interested representations. Sinditabaco got injunction in court suspend them. 2011-ANVISA held audience in gymnasium in Brazilian capital. 2012-Federal Court of Brasilia granted injunction suspending Sinditabaco's injunction. At the same time, CNI has questioned Supreme Court of constitutionality of federal law that created ANVISA and constitutionality of Resolution. 2013-result of TI interference, measure failed to enforce and new decision ANVISA allowed 121 substances may be used on an exceptional basis and created a WG, which will decide whether they are essential to the process of manufacture of tobacco products. TI and front organization have directly and indirectly interfered in the adoption and implementation of TC measures in Brazil that was related to Art.9-10. The permission for use of additives, which improve palatability and reduce irritation caused by smoke, facilitates experimentation among youth. And the use of additives increases the ability to cause dependence and increase the toxicity of tobacco products, causing damage to smokers and those who are exposed to tobacco smoke.

## EP-111-30 Public Interest Litigation for advocacy on gutka ban

M Bhavna.<sup>1</sup> <sup>1</sup>Tobacco Control, Voluntary Health Association of India, Delhi, India. Fax: (+91) 11 26853708.  
e-mail: bhavna.alok@yahoo.co.in

**Background and challenges to implementation:** The Hon'ble Supreme Court in a petition *Ankur Gutkha Vs Indian Asthma Care Society & Ors.*, banned the use of plastics for packing Smokeless Tobacco such as gutkha, tobacco, pan masala and similar articles. The court also directed the Health Ministry to submit a report on the health harms of smokeless tobacco (gutka) usage. The Ministry of Health & Family Welfare constituted an Expert Committee and initiated collation of existing evidences to prove that consumption of gutka and pan masala are harmful to health. This provided a window of opportunity for civil society to intervene in the matter and ask for complete prohibition of these products based on the findings of the health report.

**Intervention or response:** In the petition *Ankur Gutkha Vs Indian Asthma Care Society & Ors.*, pending in Supreme Court of India, VHAI through its sister concern Health for Millions, became a party in the above case, praying for complete ban on the manufacture and sale of gutkha, tobacco, pan masala and similar articles and for implementation of the Food Safety and Standards Regulation 2.3.4., prohibiting sale of food products having tobacco and nicotine as its ingredients.

**Results and lessons learnt:** The Supreme Court directed the Central Government, State Governments and the Food Safety and Standards Authority to rigorously enforce the prohibition on the manufacture and sale of chewing tobacco (as such), gutkha and pan masala (having tobacco or nicotine) or any other products sold separately to constitute as gutka and pan masala in compliance of FSSAI Regulation 2.3.4 and take strict action against the defaulters. A total of 26 States and 6 Union Territories have banned the sale, manufacture and distribution of Gutka and pan masala (having tobacco or nicotine).

**Conclusions and key recommendations:** The judiciary has provided some path breaking judgments and case laws such as Smoke Free Law, Graphic Health Warnings, Point of Sale and Gutka ban Judgments, to the tobacco control movement. The support of Judiciary has been phenomenal to the movement both in terms of examining and interpreting the evidence related to tobacco consumption, its ill effects and the loopholes in the existing regulatory frame works.

## POSTER DISCUSSION SESSIONS

### 01. TB IN CHILDREN: LATENT TB AND IPT

#### PD-500-30 Safety and completion of a four-month course of difampin for latent tuberculosis infection in children

A Cruz,<sup>1</sup> J R Starke.<sup>1</sup> <sup>1</sup>Pediatrics, Baylor College of Medicine, Houston, TX, USA. Fax: (+1) 832 8251182.  
e-mail:acruz@bcm.edu

**Background:** Regimens for latent tuberculosis infection (LTBI) are efficacious, but long durations of therapy impact adherence and effectiveness. We evaluated completion rates and adverse events (AE) in children treated for LTBI.

**Design/Methods:** This was a retrospective cohort study of children diagnosed with LTBI by tuberculin skin test (TST) or interferon gamma release assay (IGRA) from 2010–2013. Isoniazid (9 months, 9H) or rifampin (4 month, 4R) was administered as self-administered, enhanced self-administered therapy (ESAT, where medication was delivered monthly with periodic calls), or as directly-observed preventive therapy (DOPT). Completion was defined as receipt of at least 6H or 4R.

**Results:** 404 children were treated: mean 7.3 years, 47% girls, 53% Hispanic, 29% Asian, 13% Black, 4% White. LTBI was diagnosed by TST (75%), IGRA (15%), or both (10%) ; 37% were identified during contact investigations. DOPT was used in 51%, self-administered therapy in 45%, and ESAT in 4%. 9H was started in 80% of cases. 81% completed therapy (Figure). Completion of 4RIF self-administered therapy were not statistically different than completion rates for children receiving 9INH administered as DOPT: 93% vs. 88% (OR: 0.6 [0.2-1.7]). AEs were rare: 20 (6%) in the 9H group (12 abdominal pain (2 with transaminitis), 4 each with rash and behavior changes) ; 2 (3%) in 4R group (1 abdominal pain, one myelosuppression). The most common reasons for default were family refusal (24/74, 32%) and moving (9%) ; reason for default was unknown in 43. There was no association between adverse events or completion rates by gender, race/ethnicity, country of origin, or diagnostic test used.

Regimen	All n (%)	Completed n (%)	Defaulted n (%)	OR [95% CI]
Total	404	326 (81%)	74 (19%)	-
9H Self-administered	125 (31%)	76 (62%)	46 (38%)	1
4R Self-administered	57 (14%)	52 (93%)	4 (7%)	7.9 [2.7–23]
9H DOPT	194 (48%)	171 (88%)	23 (12%)	4.5 [2.5–7.9]
4R DOPT	10 (2%)	10 (100%)	0	p=0.03
9H ESAT	5 (1%)	4 (80%)	1 (20%)	2.4 [0.3–22.3]
4R ESAT	13 (3%)	13 (100%)	0	p=0.01

**Conclusions:** Completion rates for 4R surpassed those of 9H for all methods of delivery, with completion rates for 4R given as self-administered therapy not being statisti-

cally different from rates achieved under 9H DOPT; the regimen was also well tolerated. The increased cost of 4R over 9H may be offset by the increased effectiveness, as gauged by completion rates.

### PD-501-30 IGRA testing in an international adoptee clinic

D Fisher,<sup>1</sup> L Delmar,<sup>1</sup> S Kuhn,<sup>1</sup> S Warner,<sup>1</sup> J Jarand,<sup>1</sup> M Lemay.<sup>1</sup> <sup>1</sup>Medicine, University of Calgary, Calgary, AB, Canada. Fax: (+1) 403 943 48 48.  
e-mail: dina.fisher@albertahealthservices.ca

**Background and challenges to implementation:** The majority of international adoptees (IA) come from countries in which tuberculosis (TB) is endemic. Infection with tuberculosis is particularly problematic in young children under the age of 5, who are at greater risk of severe forms of tuberculosis disease such as disseminated infection and TB meningitis. International guidelines recommend that all IA receive screening for latent tuberculosis infection (LTBI) in the form of tuberculin skin testing (TST) at first visit and at a 6 month visit. There are several concerns with this screening process in IA: sensitivity of TST in malnourished children; specificity of TST in children with recent BCG vaccination; multiple visits for LTBI assessment. For these reasons, the use of interferon release assays (IGRA) for LTBI assessment in IA was investigated in Calgary, Alberta, Canada.

**Intervention:** The use of IGRA testing, in addition to TST testing, for LTBI in IA was introduced at the international adoptee clinic (IAC) in Calgary in 2010. A retrospective chart review of all IA assessed at the clinic from 2010 to 2013 was performed to assess the following three questions: 1.) Feasibility of performing IGRA testing in IA 2.) Concordance of TST and IGRA in IA 3.) Determination of the most appropriate diagnostic test for LTBI in IA

**Results and lessons learnt:** 60 Children were assessed at the IAC in Calgary from 2010 to 2013 for LTBI. LTBI was diagnosed in 12% of IA utilizing TST testing compared to 15% of IA utilizing IGRA testing. There was a difference in LTBI incidence when assessing IA from different regions: 20% of IA from Africa had LTBI compared with 0% of IA from Asia (OR 0.11: 0.005 to 2.12). Concordance between IGRA and TST testing (utilizing a 10 mm cut-off) was 88 % (kappa statistic 0.56). IGRA testing performed better than TST with less rejected or missing results for IGRA versus TST (3 versus 7). IGRA testing also diagnosed more IA with LTBI infection (Table 1).

**Conclusions and key recommendations:** 1.) IGRA testing can be performed in IA to assess for LTBI 2.) Concordance between TST and IGRA is reasonable in IA 3.) IGRA had better performance characteristic than TST in IA with less rejected tests and improved diagnosis of LTBI 4.) Further assessment will be performed to determine the best LTBI assessment method for IA at the six month visit.

Table 1: Concordance of IGRA and TST (10 mm)

TST 10mm vs IGRA	Results
<b>N</b>	<b>60</b>
<b>Concordant</b>	<b>44</b>
QFT+ / TST+	5
QFT- / TST-	39
<b>Discordant</b>	<b>6</b>
QFT- / TST+	2
QFT+ / TST-	4
<b>Missing or invalid data</b>	<b>10</b>
<b>Percent Concordant</b>	<b>88.0%</b>
<b>Kappa Statistic</b>	<b>0.56</b>

### PD-502-30 Childhood TB management in Cambodia: improving pulmonary TB diagnosis and IPT management

K Seak,<sup>1</sup> T Bakkhim,<sup>1</sup> K Okada,<sup>1</sup> C Prum,<sup>2</sup> S Kim,<sup>2</sup> T E Mao.<sup>2</sup> <sup>1</sup>International Development Department, Japan Anti-Tuberculosis Association, Cambodia, Phnom Penh, <sup>2</sup>TB center, National Center for Tuberculosis and Leprosy Control, Phnom Penh, Cambodia. Fax: (+855) 23213347.  
e-mail: seakkunrath@yahoo.com

**Background and challenges to implementation:** Cambodia National Tuberculosis Program (NTP) developed a guideline for the management of childhood TB in 2008 which are aimed at strengthening case finding, diagnosis and treatment of childhood TB. The result reveals a remarkable detection number of childhood TB. However it is found that there was an over diagnosis for extra-pulmonary (cervical lymphadenitis) and less IPT implementation. The project is aimed at improving the skill of diagnosis for pulmonary TB and IPT screening.

**Intervention or response:** The implementation of childhood TB management activities by CENAT and JATA/TB CARE I/USAID started in late 2011 that covers 27 operational districts (OD). The main activities of the childhood TB are: developing algorithms for diagnosis, trainings on clinical management, chest x-ray reading, TST, workshops, supervision and on the job training, contact tracing by health centers and Community partners, referral of TB contacts to hospitals for further diagnosis. To improve the chest x-ray reading skill, supervision and on the job training on film reading have been provided at the fields for the TB physicians.

**Results and lessons learnt:** The childhood TB detected in 2012 was totally 4078 cases, mostly extra-pulmonary TB. Among these cases, pulmonary TB case is only 108 which are equal to 2.6%. After the intervention in 2013, there was an improvement of pulmonary TB detection. The report in 2013 reveals that among 3807 TB cases detected, there was an increase in pulmonary TB to 902 cases equal to 23.7%. Due to the less screening, only 220 TB contact children were eligible for IPT. With effort in



2013, the number of TB contact children who received IPT increased to 2050 cases.

**Conclusions and key recommendations:** Clear algorithms, clinical management trainings on diagnosis and chest x-ray reading play an important role in strengthening the pulmonary TB diagnosis and IPT screening. Regular supervision and on the job training at the fields on chest x-ray reading and IPT screening skills can improve the x-ray quality and skills of chest x-ray reading.

Childhood TB data in 2012

TB suspects		TB		S+	S-	EP
M	F	M	F			
15265	13600	2287	1791	28	81	3969
28865		4078		4078		
Pulmonary TB		2.6%				

Childhood TB data in 2013

TB suspects		TB		S+	S-	EP
M	F	M	F			
11683	10157	2211	1596	9	893	2905
21840		3807				
Pulmonary TB		23.7%				

IPT data in 2012 and 2013 ( will be update the outcome for 2013)

IPT	Completed	Developed	Defaulte	Died	Ongoing	Total
2012	213	1	6	0	0	220
2013	111	0	2	0	1937	2050

### PD-503-30 Access to HIV services by TB-HIV coinfectd children in Lagos, Nigeria: is co-location of services an important factor?

O Daniel,<sup>1</sup> O Adejumo,<sup>2</sup> H Abdur-razzaq,<sup>3</sup> J O Obasanya,<sup>4</sup> Ayo Awe.<sup>5</sup> <sup>1</sup>Tuberculosis control, World Health Organization, Lagos, <sup>2</sup>Community Health and Primary Health Care, Lagos State University Teaching Hospital, Lagos, <sup>3</sup>Tuberculosis and Leprosy control Programme, Lagos State Ministry of Health, Lagos, <sup>4</sup>Tuberculosis and Leprosy Control Programme, Federal Ministry of Health, Abuja, <sup>5</sup>Tuberculosis control, World Health organization, Abuja, Nigeria. e-mail: oluadejumo75@gmail.com

**Background:** HIV and TB are the leading causes of death from infectious disease worldwide. The World Health organization estimates that HIV prevalence among children with TB in countries with moderate to high prevalence ranges from 10 to 60% depending on the burden of TB, ART coverage and availability of equipments to diagnose both TB and HIV in children. This study is aimed at determining access to HIV services by TB/HIV co-infected children and the importance of co-location of services to uptake of ART services.

**Design/Methods:** A retrospective review of programme data submitted to the Lagos state TB and Leprosy control programme by TB treatment centres in the state. Information such as age, sex, HIV status, type of TB,

facility of referral etc of children diagnosed and treated for TB from January 1, 2012 to December 31, 2013 were extracted from the TB register. Polymerase Chain Reaction (PCR) and rapid test kits were used to diagnose HIV in children less than 2 years and older children respectively while confirmation was done at designated specialized laboratories in the state. Data was analysed by SPSS statistical package.

**Results:** A total of 1199 children aged between 0 –14 years were diagnosed with tuberculosis during the study period. Of these, HIV test was carried out in 1095 (91.3%) of children. Among those tested for HIV, 320 (29.2%) were HIV sero-positive with male:female ratio 1.3:1 which was higher than the national average of 4.4%. Of the 320 TB/HIV co-infected children, 57(17.8%) were less than one year old, 86 (26.9%) in the age group 1–4 years and 178 (55.6%) in the age group 5–14 years. Of the TB/HIV co-infected children 186 (58.1%) were commenced on CPT while 151 (47.2%) were on ART. ART and CPT uptake were significantly higher in facilities where TB/HIV services were co-located compared with those services were not co-located (P <0.001).

**Conclusion:** The prevalence of TB/HIV in children is high in Lagos state Nigeria while the uptake of CPT and ART were low. There is need to intensify effort at reducing HIV transmission in children. Increasing the number of ART treatment centres in the state will improve access of ART and CPT services to co-infected children.

### PD-504-30 Patient factors associated with acceptance and adherence of pediatric latent tuberculosis treatment in Rio de Janeiro

AP Silva,<sup>1,2</sup> P Hill,<sup>3</sup> R Menzies,<sup>4</sup> S Garcia Rabelo,<sup>2</sup> K Hornby,<sup>4</sup> C Valiquette,<sup>4</sup> M Belo,<sup>2</sup> A Trajman.<sup>1,2,4</sup>

<sup>1</sup>Internal Medicine Graduate Program, Federal University of Rio de Janeiro, Rio de Janeiro, RJ, <sup>2</sup>Students' Scientific League, Rio de Janeiro TB Scientific League, Rio de Janeiro, RJ, Brazil; <sup>3</sup>Centre for International Health, Otago University, Dunedin, New Zealand; <sup>4</sup>Montreal Chest Institute, McGill University, Montreal, QC, Canada. Fax: (+55) 21 253 21 661. e-mail: atrajman@gmail.com

**Background:** Treatment of latent tuberculosis infection in close contact children is highly recommended. Yet, in programmatic conditions, less than 50% of those who receive INH prescription complete treatment. Default usually occurs in the first two months. We evaluated patient-related factors associated with INH preventive therapy (IPT) acceptance and adherence as part of a study in public action to improve IPT in Brazil.

**Methods:** We interviewed 116 parents (or the adolescent if age >10). Children were pre-screened by a nurse; those eligible for IPT were offered to see the physician. Those who accepted were approached to participate in this study at same time that IPT was offered. A questionnaire gathering sociodemographic, belief and knowledge data was applied. Acceptance of IPT was considered if the child took at least 7 doses and adherence if at least 48 (80% of doses) were taken at day 60. Socioeconomic class was defined using Brazil Criterion (www.abep.org).

**Results:** Six (5%) children did not accept and 12 (11%) did not adhere to IPT. Factors associated with poor acceptance were drug use (OR=12.7; 95% CI: 2.2–73.7), not possessing a computer (OR=9.7; 1.1–81.3), belief that BCG protects against active TB (OR=8.4; 0.1–70.3), monthly income per capita <BRL 250 (US\$ 108, OR=7.0; 0.8–58.7), having to travel over 30 minutes to the health care unit and spending over BRL 10 (US\$ 4.3) on journey (OR=6.8; 0.8–56.7), and lower socioeconomic class (DE vs. ABC, OR=5.1; 0.9–27.3). Poor adherence was associated with income <BRL 250 (OR=31.2; 2.4–395) ; parents with a full-time non-flexible job (OR=12.1; 1.9–78.4), and time to reach the health care unit (OR=6.6; 1.0–41.2).

**Conclusions:** In this clinic, the rates of acceptance and adherence were high, possibly because screening pre-selected families. Socioeconomic factors, access to the health care system and misleading beliefs were associated with lower IPT adherence/acceptance. Actions to increase IPT completion might include monetary incentives, home visits and/or flexible opening hours of health units, and patient education. Treatment adherence, however, is only the tip of the iceberg. The evaluations of the barriers that precede treatment prescription (contact identification and testing) and of health care professionals knowledge, perceptions and beliefs, are ongoing. The impact of the public actions based on these evaluations will be assessed. **Funding:** FAPERJ (E-26/110.637/2012), CNPq (456901/2013-2 and 470344/2011-3)

### PD-505-30 Optimising latent tuberculosis infection screening in pediatric dialysis patients

A Cruz,<sup>1</sup> J Geer,<sup>1</sup> G Sarasak,<sup>1</sup> S Swartz.<sup>1</sup> <sup>1</sup>Pediatrics, Baylor College of Medicine, Houston, TX, USA. Fax: (+1) 832 8251182. e-mail:acruz@bcm.edu

**Background:** Dialysis patients may be at increased risk for progression from latent tuberculosis infection (LTBI) to disease. LTBI screening often occurs after children are immunosuppressed or relatively malnourished. Optimal LTBI testing strategies in pediatric dialysis patients are unknown.

**Design/Methods:** This was a prospective cohort study screening children in a low-TB-burden nation receiving hemodialysis (HD) or peritoneal dialysis (PD) for LTBI using the tuberculin skin test (TST), QuantiFERON (QFT) interferon gamma release assay (IGRA), and a risk factor questionnaire.

**Results:** 49 patients (31 HD, 18 PD): 29 Hispanic, 10 white, 8 Black, 40% female, mean age 15.6 years with the most common causes of ESRD to include nephrotic syndrome (10), glomerulonephritis (7), dysplasia (7), and obstructive uropathies (6) were included. 4 were immunosuppressed, receiving corticosteroids at time of LTBI screening. 25 had TB risk factors (14 had >1): parental foreign birth (23, 21 Latin America, 2 Asia) ; 11 child born abroad (11, all in Latin America) ; 3 contacts to incarcerated persons. 6 previously were treated for

LTBI: 5/6 were foreign-born (all BCG-recipients) and had foreign-born parents, but no other TB risk factors. All 6 had received 6–9 months of isoniazid; only 1/6 had a + QFT (Ag-nil: 5.16 IU/mL). 2 children previously TST-negative had + QFTs (Ag-nil ranged 0.36–1.02 IU/mL) ; both had failed renal transplants, were US-born, had no TB risk factors, 0mm TSTs (one was receiving corticosteroids), negative chest radiographs, and no signs or symptoms of TB disease. One child (with QFT 1.02 IU/mL) had a 2<sup>nd</sup> QFT that was negative (0.07) and a negative T-SPOT IGRA. The other child had a negative T-SPOT. Only 1 patient had an indeterminate QFT (failure of the positive control) ; her T-SPOT was negative. All children with negative QFTs had 0mm TSTs.

**Conclusions:** In this diverse community in a low incidence nation, many pediatric dialysis patients identified TB risk factors, most commonly parental foreign birth. However, these risk factors correlated poorly with QFT-positivity. Both children with QFT-positive tests were close to the cut-point and had repeat IGRAs that were negative. Future research should focus on the dynamics of IGRAs in dialysis patients. While they have the opportunity to increase diagnostic yield for LTBI, false positives or wobble around the cut-point could inadvertently result in unnecessary treatment for LTBI and delay in renal transplant.

### PD-506-30 Do we need to change our screening policy for children exposed to TB? Results from the UK-NIKS-study

B Kampmann,<sup>1</sup> B Williams,<sup>2</sup> S Welch,<sup>3</sup> Z Nademi,<sup>4</sup> J Paton,<sup>5</sup> J Bernatoniene,<sup>6</sup> S Patel,<sup>7</sup> A Riddell.<sup>8</sup>

<sup>1</sup>Paediatrics, Imperial College London, London, <sup>2</sup>Paediatrics, NWLH NHS Trust, London, UK, <sup>3</sup>Paediatrics, Heart of England, Birmingham, <sup>4</sup>Paediatrics, Newcastle upon Tyne Hospitals, Newcastle, <sup>5</sup>Paediatrics, Royal Hospital for Sick Children, Glasgow, <sup>6</sup>Paediatrics, Bristol Children's Hospital, Bristol, <sup>7</sup>Paediatrics, University Hospital Southampton, Southampton, <sup>8</sup>Paediatrics, Barts & The London Hospital, London, UK. Fax: (+44) 207 594 3894. e-mail: b.kampmann@imperial.ac.uk

**Background:** In many countries Interferon-gamma release assays (IGRA) have been introduced for screening for latent tuberculosis (TB) infection. Many algorithms only test children with IGRA who have been found to have a positive tuberculin skin test (TST), but this policy might miss some children eligible for treatment of LTBI due to discrepancies between TST and IGRA and late conversions.

**Methods:** As part of a study funded by the National Institute of Health Research (NIHR) into the diagnosis and management of TB in children in the UK, we undertook a large prospective study enrolling children with known exposure to a sputum smear/culture-positive household contact within 10 NHS Trusts in the UK. We conducted TST and IGRA simultaneously at the time of screening and again 6–8 weeks later in order to determine the discrepancies between TST and IGRA and rate of late conversions.

**Results:** Data from 403 participants are currently available for analysis. 81% of children were above 2 years of age and 49% were female. At baseline, 94 (23%) were TST and IGRA positive, 48 (12%) were TST+ve/IGRA-ve and 15 (3.7%) were TST-ve/IGRA+ve with 26% of this cohort remaining TST-ve at follow up. There was a 15% conversion rate for TST, compared with a 6.0% conversion rate for IGRA between the 2 screening episodes.

**Conclusion:** Our data suggest the step-wise approach to testing for LTBI advocated in UK and other national guidelines misses a proportion of children who require treatment for LTBI. Repeat screening with both IGRA and TST should be considered.

### **PD-507-30 Barriers and workable strategies for universal coverage of eligible children with isoniazid preventive therapy under the RNTCP**

S Samuel,<sup>1</sup> D Dharmaraj.<sup>1</sup> <sup>1</sup> Community Medicine, Acs Medical College And Hospital, Chennai, India. e-mail: susilajs\_1983@rediffmail.com

**Background and challenges to implementation:** Isoniazid Preventive Therapy (IPT), recommended under Revised National Tuberculosis Control Program (RNTCP) in India, can play a substantial role in eliminating the pool of latent infection among children who are in close contact with a sputum positive pulmonary tuberculosis patient. But its implementation continues to be suboptimal, IPT initiation rates ranging from 19% to 56% in studies in South India. Hence this study attempts to retrieve eligible children who are missed for initiation of IPT through an Interim evaluation strategy, identify barriers for IPT initiation among them and evolve workable strategies.

**Intervention or response:** There were 213 registered sputum positive patients in the study during July-September, 2013 in two Tuberculosis Units (TU) in Thiruvallur district, Tamilnadu. Their baseline details and valid phone numbers were noted. At the end of three months, the eligible child contacts who were missed during routine RNTCP were identified through structured telephonic calls to all sputum positive patients (mobile health strategy). Issue-based analysis of individual case studies was done to identify barriers and gaps in initiation of IPT.

**Results and lessons learnt:** Through the routine RNTCP programme in those TUs about 45 child contacts were identified. Interim evaluation retrieved 33 child contacts increasing the yield of cases by 42%. The various reasons for gaps in initiation of IPT include lack of proper guideline on definition of close contact under contact screening strategy, ignorance and misconceptions about the rationale for IPT, stigma, family conflicts and lack of clear consensus about IPT program among providers. Simple strategies like modification of the definition of "close contact" for the purpose of contact investigation of TB would increase the yield of cases by 34%.

**Conclusions and key recommendations:** There is scope for substantial increase in coverage of IPT by simple

operational guidelines especially on expanding the definition of close contacts. Ensuring collaborative involvement of patients and providers in program and external monitoring through m-health strategy is important to its success.

### **PD-508-30 Aspects of epidemiologic children with latent tuberculosis infection in hospital of reference**

A Mendonca,<sup>1</sup> A Kritski,<sup>1</sup> C Sant'anna.<sup>1</sup> <sup>1</sup>Department of Preventive Medicine, Federal University of Rio De Janeiro, Rio de Janeiro, RJ, Brazil. e-mail: angelamcm@uol.com.br

**Introduction:** It is estimated that 10 to 15% of tuberculosis (TB) cases affect under-15 year olds. Data on detection and treatment of latent tuberculosis infection (LTBI) as a preventive measure of TB disease in developing countries are scarce.

**Objectives:** To describe clinical and epidemiological features of all children and teenagers treated at Hospital Municipal Jesus, Rio de Janeiro Brazil, from 2002 to 2009, with a diagnosis of LTBI referred to isoniazid preventive therapy (IPT).

**Methods:** This is a descriptive, longitudinal and retrospective study.

**Results:** 286 cases with a diagnosis of LTBI referred to IPT were identified; in 135 cases (47.2%) the therapy had not been prescribed in the original Healthcare Unit. There was prevalence of: male (51.4%) ; age group 5-10 year-olds (46.6%) ; evident BCG vaccination (99.6%) ; reported contact with TB (92.3%) ; tuberculin skin test > 15 mm (51%). HIV infection was found in 18 (24.3%) of 74 tested cases. TB disease and past IPT was described respectively in 2.1% and 4.2% cases. Rates of dropout, adverse effect and evolution to TB disease were respectively 24.9%, 3.2% and 1.4% in those who had started IPT.

**Conclusion:** IPT prescription rates in children and teenagers treated in Healthcare Units are low. However, completion of IPT was relevant, and rates of adverse effects and evolution to TB disease were low. It is necessary to adopt strategies to increase compliance of the healthcare team to IPT prescription to this population.

### **PD-509-30 Acceptance of preventive treatment by immigrants when latent tuberculosis infection is diagnosed**

I Schreurs-Jonkeren.<sup>1</sup> <sup>1</sup>Tuberculosis, GGD Twente (Municipal Health Department), Enschede, Netherlands. Fax: (+31) 53 487 6742. e-mail: i.schreurs@ggdtwente.nl

**Background.** More than two third of the tuberculosis (TB) -patients in the Netherlands are persons from endemic countries. To further decrease the incidence of TB in the Netherlands in the future, immigrants from endemic countries diagnosed with latent tuberculosis infection (LTBI) should start and complete a preventive therapy (PT) so the chances of developing TB will be minimized. So 6 Municipal Health Departments screened



immigrants younger than 35 years, who needed their mandatory TB-test, also for LTBI. When LTBI was confirmed PT was offered. This study wanted to highlight the reasons why an immigrant would accept PT or not, based on the concepts of the Health Belief Model. Method Immigrants diagnosed with LTBI who were offered PT were studied in a cross-sectional study. This multi-centred study consisted of a self-administered questionnaire, with demographic questions and 20 statements. These statements were based on the concepts from the Health Belief Model: risk perception, perceived benefits and barriers, cues to action and self-efficacy.

**Results** Thirty eight immigrants (50%) out of 75 immigrants who were diagnosed with LTBI filled in a questionnaire. Twenty immigrants accepted PT. More than half of the respondents originated from Asia and a third from Africa. The majority came to the Netherlands because of family reunification (40%), followed by work (34%) and study (23%). The PT group was more concerned about getting TB ( $p=0,017$ ) and thought they had a great risk of developing TB if they would not take medication ( $p=0,010$ ). The non-PT group thought it was a problem to start on medication just after arrival in the Netherlands ( $p=0.034$ ). Also the non-PT group thought it was more difficult to take medication every day ( $p=0,033$ ).

**Conclusion** The PT group feels more susceptible to TB and is less worried about taking medication just after arrival in the Netherlands. Also they felt less worried about taking medication every day. The non-PT group is less worried about getting TB. Doctors, nurses and nurse practitioners should stay focussed on a possible lack of knowledge about (L) TBI. And they should pay special attention to taking medication, particularly after recent immigration and how this can be supported. More research is needed to better understand the underlying reasons why immigrants do or don't accept PT.

#### **PD-510-30 Status of chemoprophylaxis for children under six years of age exposed to active TB: a looming challenge in India**

K Sagili,<sup>1</sup> S Chadha.<sup>2</sup> <sup>1</sup>Research, and <sup>2</sup>Tuberculosis control unit, The Union, New Delhi, India. Fax: (+91) 011 4605 4430. e-mail: ksagili@theunion.org

**Background:** In 2013, 63,919 childhood TB cases were notified by the Revised National TB Control Program (RNTCP) in India. Globally, WHO reported about 530,000 childhood TB cases and 74000 of them died of TB. Under RNTCP, all children under 6 years of age are screened for TB and after active TB is ruled out children are initiated on Isoniazid chemoprophylaxis for 6 months. However, the adherence to this guideline has been sub-optimal and less than satisfactory till date. India being one of the high burden countries for TB with co-existent epidemics like HIV, Tobacco use and malnutrition poses severe threat to child survival.

**Design/Methods:** A community-based knowledge, attitude and practice survey was conducted in 30 districts covering 15 states. 496 TB patients (patients who were

currently undergoing treatment or had finished treatment in the past one year) (M: 302, F: 194; urban: 127, rural: 369) were identified using household listing process. Using a pre-tested questionnaire, TB patients were interviewed regarding their knowledge about TB, their diagnosis and treatment including family and household details.

**Results:** About 80% of the TB patients interviewed had children, with majority of them having more than 3 children (29%). About 38% (N=186) said they had children <6 years in their households. However, only 18% responded that the children were started on treatment. This leaves the remaining 82% at risk of developing TB. The proportion of patients from urban settlements with children <6 years was higher (41%, N=50) than the rural 37% (N=137), however there was no statistical association. Neither was any association with gender. About 37% of the patients who had children <6 years in their households also use tobacco. Most of the TB patients with children <6 years lived in joint or extended families (N=112, 60%), with more than four members in the house (89%) and mostly lived in one-two room house. 47% (N=87) of the patients with children <6 years in their households and 55% (N=18) of those who said the children were started on treatment were taking treatment from government centres.

**Conclusion:** Due to the various risk factors, Indian children exposed to active TB cases are at much higher risk of developing TB disease. The fact that only 18% TB patients said that the children <6 years in their houses were started on treatment; suggest that there is a serious neglect on prevention therapy among children exposed to active TB cases. Immediate efforts must be taken to rectify this problem and ensure protection for every child under 6 years.

#### **PD-511-30 Implementation of isoniazid preventive therapy (IPT) at a pediatric HIV clinic in Uganda**

F Kanyike,<sup>1</sup> S Kitaka,<sup>2</sup> B Nsangi,<sup>1,3</sup> M Sekadde,<sup>4</sup> F Baruga,<sup>1</sup> A Kekitiinwa.<sup>1,3</sup> <sup>1</sup>Pediatrics, Baylor College of Medicine Children's Foundation Uganda, Kampala, <sup>2</sup>Pediatrics, Makerere University School of Medicine, Kampala, Uganda; <sup>3</sup>Pediatrics, Baylor College of Medicine, Houston, TX, USA; <sup>4</sup>Pediatrics, National TB and Leprosy Program, Kampala, Uganda. e-mail: fkanyike@baylor-uganda.org

**Background:** Isoniazid Preventive Therapy (IPT) is recommended as part of the comprehensive HIV care package for children, adolescents, and adults living with HIV. However, national roll out in Uganda has not yet started. We examined the feasibility of IPT implementation and determined the occurrence of tuberculosis among HIV infected children and adolescents initiated on Isoniazid Preventive Therapy (IPT) at Baylor-Uganda.

**Design/Methods:** All new patients attending the Baylor-Uganda clinic were eligible for IPT. The roll out of IPT was incepted at the Baylor-Uganda clinic in 2012 as part of the routine HIV care. Symptomatic screening of all patients was done in addition to a Tuberculin Skin Test

(TST) that was offered to all new patients. Presumptive TB cases were then investigated for TB using clinical assessment, sputum analysis for ZN stain and/or gene Xpert, chest x-ray and histopathology when necessary. IPT was initiated according the WHO 2010 guidelines after ruling out active TB. We reviewed medical records of HIV infected children and adolescents aged 12 months to 19 years who received IPT. Records of those that had completed six months of IPT and had a follow up period of  $\geq 1$  year were identified. Information collected included age, history of TB contact, sex, TST induration size and history of ART. Data analysis was done using SPSS and proportions were determined.

**Results:** 444 children and adolescents had received IPT since its inception. 8/444 (1.8%) developed TB while still on IPT and 3/8 (37.5%) had smear positive TB. All these developed TB in the first 2 months of IPT. 253/444 (57%) had completed six months of IPT and had  $\geq 1$  year of follow up. 131/253 (51.8%) patients were female with a median age of 6.1 years (IQR 3.7 – 9.2) with 100 (39.5%), 133 (52.6%), and 20 (7.9%) patients aged  $< 5$  years, 5 -  $< 15$  years, and  $\geq 15 - 19$  years respectively. 5 of 253 (2%) patients reported a positive history of TB contact. 24 of 253 (9.5%) patients had a positive TST. 216/253 (85.4%) were on ART at the time of IPT initiation. We did not record any occurrence of TB among those that completed IPT and were followed up for  $\geq 1$  year post IPT.

**Conclusion:** IPT was successfully implemented in this clinic. TB development occurred in the first 2 months of therapy. IPT can be successfully implemented if there's a good screening program.

### PD-512-30 Decentralisation of ART care through option B+: an opportunity to improve IPT uptake for children?

J Firth,<sup>1</sup> C Lijinsky,<sup>2</sup> T Arscott-mills,<sup>3,4,5</sup> B Phelps,<sup>1</sup>

C Powell.<sup>6</sup> <sup>1</sup>Office of HIV/AIDS, United States Agency for International Development, Washington, DC, <sup>2</sup>Office of Sustainable Development, Bureau for Africa, United States Agency for International Development, Washington, DC, USA; <sup>3</sup>Pediatric TB Program, Botswana UPenn Partnership, Gaborone, Botswana; <sup>4</sup>Pediatrics, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA, <sup>5</sup>Pediatrics, Children's Hospital of Philadelphia, Philadelphia, PA, <sup>6</sup>Office of Health, Infectious Diseases, & Nutrition, United States Agency for International Development, Washington, DC, USA. Fax: (+1) 202 808-3742.

e-mail: drjacquiebup@gmail.com

**Background and challenges to implementation:** Isoniazid Preventive Therapy (IPT) has been shown to be effective in preventing TB disease progression in children exposed to adults with smear-positive TB. Unfortunately IPT programs in many countries have been hampered by the lack of programmatic emphasis on contact screening and confusion among providers about IPT recommendations. The roll-out of decentralized ART care through Option B+, which brings with it increased emphasis on TB screening in ANC clinics, has created a unique opportunity

to leverage two important programs to improve outcomes for children exposed to TB.

**Intervention or response:** We reviewed TB and HIV guidelines from the eleven countries in Sub-Saharan Africa with the highest co-infection rates of TB and HIV ( $>40\%$ ) to determine which countries currently have guidelines for IPT for children, and which have announced plans to roll-out Option B+. Furthermore, data collection forms were reviewed to determine if data was formally reported on numbers of persons screened as contacts and/or started on IPT.

**Results and lessons learnt:** Of the eleven countries whose TB and HIV guidelines were reviewed (Botswana, Lesotho, Malawi, Mozambique, Namibia, South Africa, Swaziland, Tanzania, Uganda, Zambia, Zimbabwe), all recommend isoniazid for children under five years who have been exposed to smear-positive TB. Four countries recommended older, inadequate dosing of isoniazid for children in their TB guidelines; all but one had the correct dosage in their HIV guidelines, which had been updated more recently. Only two countries collected data on numbers of persons started on IPT and/or screened as contacts. All but three countries have announced the adoption of Option B+.

**Conclusions and key recommendations:** Policies on IPT for children exist in all of the countries with co-infection rates  $>40\%$ , although updated HIV guidelines are more likely to recommend the correct dosage of isoniazid for children. Furthermore, data on numbers of contacts screened and persons started on IPT is not routinely being collected in most countries. Although several countries have begun to recognize and address the challenge of protecting children from developing active TB, combining forces with the ongoing roll-out of decentralized ART care may offer new opportunities for improving uptake of IPT for children. Disclaimer: The views expressed in this work do not necessarily reflect the views of USAID or the United States government.

Country	Co-infection Rate (WHO 2013)	IPT policy for children in guidelines? Dosage of INH? (older dose = 5mg/kg, new dose = 10mg/kg)	IPT and/or contact screening data collected?	Adopting Option B+?
Botswana	63%	Yes, in TB (2011), new dosage Yes, in HIV/ PMTCT (2012), no dosage given	Monthly report asks for contacts screened & children started on IPT	Considering
Lesotho	75%	Yes, in TB (2008), old dosage Yes, in HIV (2007), old dosage Yes, in PMTCT (2010), new dosage	No	At full scale

Malawi	59%	Yes, in TB (2007), old dosage Yes, in HIV (2011), new dosage	No	At full scale
Mozambique	58%	Yes, in TB (2008), no dosage given Yes, in HIV (2014), new dosage Not in PMTCT (2014)	(no forms in appendix to TB guidelines)	Phasing in
Namibia	47%	Yes, in TB (2011), new dosage Yes, in HIV (2010), new dosage	IPT patient card & quarterly IPT report	Preparing
South Africa	65%	Yes, in TB (2008), new dosage Not in HIV/ PMTCT (2010)	(no forms in appendix to TB guidelines)	Consider- ing
Swaziland	77%	Yes, in TB (2014), new dosage Yes, in Peds HIV (2006), new dosage	(no forms in appendix to TB guidelines)	Consider- ing
Tanzania	39%	Yes, in TB (2006), old dosage Yes, in HIV/ PMTCT (2009), old dosage	(no forms in appendix to TB guidelines)	Phasing in
Uganda	50%	Yes, in TB (2010), new dosage Not in HIV (2009)	No	At full scale
Zambia	54%	Yes, in TB (2008), old dosage Yes, in Peds HIV (2010), new dosage*	No	Preparing
Zimbabwe	70%	Yes, in TB (2010), new dosage Not in HIV (2010)	No	Preparing

\*Zambia Pediatric HIV guidelines instruct providers to ask about contact with someone with active TB at each visit

## 02. LUNG CANCER, OCCUPATIONAL EXPOSURE AND AIR POLLUTION

### PD-513-30 The analysis of factors associated with misdiagnosis of lung cancer in TB hospital

Z Laushkina.<sup>1</sup> <sup>1</sup>Pulmonary TB department, Novosibirsk Research TB Institute, Novosibirsk, Russian Federation. Fax: (+7) 3832038675. e-mail: zlaosh@list.ru

**Background:** Lung cancer is a common cancer disease. The delay diagnosis of lung cancer worsens results of treatment and prognosis of disease.

**Design/Methods:** Medical reports of 55 patients with lung cancer were analyzed. All patients have been hospitalized in TB hospital with wrong diagnosis “pulmonary TB”. Clinical presentations, radiological, laboratory data of all patients were collected. The chances for establishment of diagnosis and influencing factors were estimated. Odds ratios (OR) and nominal 95% confidence intervals were presented.

**Results:** Males 67 %, mean age  $59 \pm 11$  yrs. 62 % of patients – smokers. The period from the disease manifestation up to making a hospital diagnosis was  $126 \pm 70$  days. 44 % of patients were previously treated of an assumed pneumonia before hospitalization in TB hospital. In 5.5 % of all cases a few acid-fast bacilli were found in sputum by luminescent microscopy. Factors associated with increase of diagnostic delay: acute disease beginning (OR 0.36,  $p=0.005$ ), fever (OR 0.35,  $p=0.01$ ), detection of AFB (OR 0.20,  $p=0.000$ ), nonspecific microbial growth in sputum (OR 0.08,  $p=0.003$ ), absence of hematological changes (OR 0.30,  $p=0.001$ ), cavitory pattern on chest X-ray (OR 0.52,  $p=0.037$ ), misinterpretation of chest radiogram (OR 0.11,  $p=0.002$ ). Factors, associated with decrease of a diagnostic delay – old age (OR 4.87,  $p=0.000$ ), low body weight (OR 4.45,  $p=0.000$ ), lost of appetite (OR 8.93,  $p=0.000$ ), dyspnea (OR 3.66,  $p=0.000$ ), leukocytosis (OR 2.82,  $p=0.001$ ), ESR acceleration (OR 3.52,  $p=0.000$ ), lymphopenia (OR 2.84,  $p=0.003$ ), spherical opacity patterns on chest X-ray (OR 4.79,  $p=0.000$ ), presence of atypical cells in sputum (OR 88.03,  $p=0.000$ ), biopsy performed (OR 4.54,  $p=0.000$ ).

**Conclusion:** Chest X-ray raising no suspicion of cancer was an important reason for misdiagnosis. Other important reasons for misdiagnosis: non-typical symptoms, false-positive result of detection of AFB. Diagnosis requires histological confirmation.

### PD-514-30 Education in lung cancer patients: advocacy project by Indian Cancer NGO

S Pramod.<sup>1</sup> <sup>1</sup> Community Medicine, Health Promotion Society of India [NGO], Meerut, India. e-mail: hpsiindia99@gmail.com

**Introduction:** The essence of Lung cancer patient's education is in providing specific knowledge about disease and anticancer treatment, and in educating family on home based care. Informed and educated patients are able to save self-esteem, to establish good relationship with social environment and to achieve better social participation. The aim of this study was to investigate the impact of the education on patient's self-image and the impact of the education on lung cancer patient-social environment relationship. Especially lung cancer sufferers who return to villages in rural parts of India after taking chemotherapy/surgery in city hospitals need this assistance. Community NGO's can play key role in providing cancer care including patient & family education.

**Patients and methods:** 42 lung cancer patients (38 men & 4 women, age 50–60 yrs) included in Our analysis and



control group (n=30), all matched regarding age and educational level. Both groups answered questionnaire specifically designed to assess self-image of Lung cancer patients and relationship with social environment, family support & community centers. Cancer educational efforts must be devised suitable to local communities. Due to lack of resources, this issue of role of education in lung cancer care has been neglected for last decade.

**Result:** The education significantly improved self-image in lung cancer sufferers group when compared to control group ( $P<0,03$ ). There was no significant difference after education between these group with regard to social relationship ( $P>0,03$ ). Due to resource constraints we limited sample size & evaluation parameters. But Our cancer NGO is seeking multi-institutional-collaborations to conduct more-scientific pilot project on this unexplored issue in lung-cancer-patients community

**Conclusions:** Our cancer NGO has taken initiative on this front of cancer patients education as supportive care. The education has important contribution in establishing self management approach in which patients assume responsibility for their behavior, for changing their environment, and for planning their future. For successful Lung cancer patients' psychosocial adaptation and social participation, it is necessary that the whole society provides more resources for psychosocial support. This is low cost approach to improve care outcomes in resource constrained settings. This issue is fertile ground for further studies.

#### PD-515-30 Effects of biomass fuel on child acute respiratory infections in Cameroon and Gabon

P Loty.<sup>1</sup> <sup>1</sup>Local Research Group, CARE-IFA, Yaoundé, Cameroon. e-mail: danieloty@yahoo.com

**Background:** Use of biomass fuel for cooking is a risk factor linked to Acute Respiratory Infections (ARI), a leading cause of morbidity and mortality among children in developing countries. Currently in the ECCAS (Economic Community of Central African States), the role of biomass fuel on child ARI remains understudied due to the expensiveness of tools needed to measure indoor air pollution. Therefore, the research question of this study is: what is the relationship between biomass fuel and ARI in Cameroon and Gabon? The study's purpose was to investigate the link between biomass cooking fuel and ARI, a link already evidenced in countries of Southern and Eastern Africa. Specifically, this study estimates levels of biomass-fuel-related exposure to ARI among children in each country. The study also provides a comparative analysis aiming to identify in both countries the regions where children are mostly affected.

**Design/Methods:** The analysis was based on a two-stage cluster sample of 11 732 children in Cameroon (resp. 6 067 in Gabon). Data were collected during the standard Demographic and Health Surveys conducted in Cameroon (2011) and in Gabon (2012). Data collection procedures were pre-tested and training was provided

for the field staff in Cameroon (resp. Gabon) over a 3-week period (resp. 6-week period) in October 2009 (resp. November 2011 – January 2012). Cameroon 2011 DHS Report and Gabon 2012 DHS Report provide all details concerning survey design, management and data quality. Logistic regression helped to estimate the risk of suffering from ARI among children living in biomass-fuel-using homes compared to children living in homes using cleaner fuels (gas, electricity) after controlling for potential confounders.

**Results:** In both countries, children in households using biomass fuel did not suffer higher risks of ARI. However, analysis of interactions between "region" and "biomass fuel" revealed that children from biomass-fuel using homes living in specific regions could be 8 times more exposed to ARI than children from households using gas in other regions. This suggests the effect of biomass fuel was blurred by the variable region.

**Conclusion:** The findings show that the impact of biomass fuel on ARI among children less than five years vary across regions of the same country. This strongly calls for targeted efforts to curb child ARI in areas at risk. Moreover, funding direct measurements of indoor air pollution is needed to fine tune these findings.

#### PD-516-30 Prognosis of Mycobacterium tuberculosis infection in patients with non-curable gastric cancer

S-F Huang,<sup>1</sup> Y Chao,<sup>2</sup> C-P Li,<sup>3</sup> C-Y Kuo,<sup>3</sup> W-J Su.<sup>4</sup> <sup>1</sup>Division of Infectious Disease, Department of Internal Medicine, <sup>2</sup>Cancer Center, <sup>3</sup>Division of Gastroenterology, Department of Medicine, and <sup>4</sup>Department of Chest Medicine, Taipei Veterans General Hospital, Taipei, Taiwan. e-mail: sfhuang.dr@gmail.com

**Background:** Gastrectomy and chemotherapy in patients with gastric cancer had been demonstrated as a risk factor in developing of active tuberculosis. However, mycobacterium infection might have prognosis benefit in some solid organ malignancies. The aim of the study was to investigate the prognosis effect of active TB in patients with gastric cancer receiving anti-cancer therapy.

**Design/Methods:** A retrospective case-control cohort study was conducted by retrieving from a 7-years (2000–2006) database with at least 5 years of follow-up in a tertiary medical center in Taiwan. A total of 48 patients with newly diagnosed active TB after 2 months of gastric cancer diagnosis were identified and 161 age-sex matched patients without developing active TB were randomly sampled from the database as control group. Clinical factors and overall survival were analyzed between groups, and patients who received curable or non-curable treatment were identified. Thirteen patients with gastric cancer and concurrent active TB were also retrieved from the database for comparison.

**Results:** More patients received surgical treatment with/without chemotherapy for gastric cancer with newly diagnosed active TB than control groups (77.5% vs. 50.3%), and fewer patients receive chemotherapy alone than in control groups (6.3% vs. 21.7%,  $p<0.05$ ). The five-year mortality were similar between patients with

newly diagnosed TB and control groups (60.4% vs. 65%,  $p>0.05$ ), but with more median survival time 51.5 (95%CI: 27–76) and 16.7 (95%CI: 9.1–24.2) months, respectively. Patients with gastric cancer concurrent with TB infection had worst prognosis (5 year mortality 100%) with median survival time 2.65 ( $p<0.05$ ) months. Subgroup analysis showed the proportion of curable gastric cancer were similar among patients with newly diagnosed TB (36.8%) and control groups (31.3%,  $p>0.05$ ). In patients who received non-curable treatment, the overall mortalities were lower in patients with newly diagnosed TB than in control groups (53.6% vs. 67.8%) but a better 5-year survival ( $p<0.05$ ).

**Conclusion:** In summary, patients with gastric cancer concurrent with active TB had worst prognosis. Among patients with curable gastric cancer, patients who develop newly diagnosed TB had no significant increased risk for mortality. However, in patients receiving non-curable treatment for gastric cancer, infection with tuberculosis might have survival benefit in prognosis of gastric cancer. Further investigation is warranted to investigate the molecular evidence of immune modulator theory during tuberculosis infection in prognosis of solid organ malignancies.

#### PD-517-30 The effect of exposure to wood smoke on treatment outcomes for childhood pneumonia in Botswana

M Kelly,<sup>1,2</sup> K Wirth,<sup>3</sup> T Arscott-Mills,<sup>2,4,5</sup> J Madrigano,<sup>6</sup> M Smieja,<sup>7</sup> C Cunningham,<sup>1</sup> K Feemster,<sup>4,5,8</sup> A Steenhoff.<sup>2,4,5,8</sup> <sup>1</sup>Pediatric Infectious Diseases, Duke University Medical Center, Durham, NC, USA;

<sup>2</sup>Botswana-UPenn Partnership, Gaborone, Botswana;

<sup>3</sup>Epidemiology, Harvard School of Public Health, Boston, MA,

<sup>4</sup>Global Health, Children's Hospital of Philadelphia, Philadelphia, PA, <sup>5</sup>Pediatrics, Perelman School of Medicine, Philadelphia, PA, <sup>6</sup>Department of Environmental and Occupational Health, Rutgers School of Public Health, Piscataway, NJ, USA, <sup>7</sup>Pathology and Molecular Medicine, McMaster University, Hamilton, ON, Canada; <sup>8</sup>Pediatric Infectious Diseases, Children's Hospital of Philadelphia, Philadelphia, PA, USA. e-mail: mskelly7@gmail.com

**Background:** Nearly half of the world's population uses wood and other unprocessed solid fuels for cooking and heating. Exposure to smoke from these fuels increases pneumonia risk among children, but it is unclear whether it also worsens pneumonia outcomes.

**Design/Methods:** We conducted a hospital-based, prospective cohort study involving 195 HIV-negative children aged 1–23 months with pneumonia. Children were recruited within six hours of presentation to a tertiary hospital in Botswana. Household use of wood as a cooking fuel (yes/no) was assessed during a face-to-face questionnaire with caregivers. The primary outcome, treatment failure, was assessed at 48 hours and defined as persistent lower chest wall indrawing, new danger signs, oxygen saturation  $<80\%$ , requirement for positive airway pressure or mechanical ventilation, or death. A nasopharyngeal swab was obtained for detection of respiratory syncytial virus (RSV) by polymerase chain

reaction. We used Cox proportional hazards regression to directly estimate crude and adjusted risk ratios (RR) and 95% confidence intervals (CI) for treatment failure. We examined effect modification by age (1–5 vs. 6–23 months), birth weight ( $<2500$  vs.  $\geq 2500$  grams), and detection of RSV (yes vs. no).

**Results:** Median age was 6.1 months, and 25 (13%) children had moderate or severe malnutrition. RSV was detected in 75 (38%) children. Sixty (31%) children failed treatment at 48 hours and 11 (6%) children died. In crude analyses, household use of wood as a cooking fuel was associated with treatment failure at 48 hours (RR: 1.85; 95% CI: 1.23–2.78;  $P=0.003$ ). After adjustment for known and hypothesized confounders, the effect attenuated slightly, but remained statistically significant (RR: 1.69; 95% CI: 1.05–2.71;  $P=0.03$ ). We observed significant heterogeneity in the effect of household use of wood as a cooking fuel according to low birth weight ( $P=0.02$ ); the effect was stronger among children with birth weight  $\geq 2500$  grams (RR: 2.16; 95% CI: 1.31–3.57). We found no evidence for effect modification by age ( $P=0.23$ ) or RSV status ( $P=0.10$ ).

**Conclusions:** Exposure to wood smoke is associated with worse outcomes from childhood pneumonia. The role of birth weight in moderating this relationship requires further study as the number of low birth weight children in the current study was small. Efforts to prevent exposure to smoke from solid fuels may improve pneumonia-related outcomes among children in resource-limited settings.

#### PD-518-30 Health seeking behaviour of the miners: a case from Pakhar mines, Lohardarga district, Jharkhand

S Gadala,<sup>1</sup> S Diwakar,<sup>1</sup> M Krithika,<sup>1</sup> T Thomas,<sup>1</sup> P Banuru Muralidhara.<sup>2</sup> <sup>1</sup>Project Axshya, Catholic Health Association of India, Hyderabad, <sup>2</sup>Project Axshya, Union Against Tuberculosis & Lung Diseases, New Delhi, India. Fax: (+91) 40–27811982. e-mail: srinivasa-rao@chai-india.org

**Background:** Jharkhand is one of India's poorest states, with more than 40% of the population in poverty. Mining is major economic generation activity of the people. Livelihood of these miners easily succumbs to diseases like tuberculosis (TB) and other lung diseases pertaining to the occupation. As per the Mines Act 1952, more focus has been given to the accidents in the mines and the diseases are kept as a secondary issue. This study documents the health seeking behavior of miners in areas of "Pakhar mines", particularly to those associated with Tuberculosis symptoms.

**Method:** Structured questionnaire interview was conducted in March 2014 among 200 workers in two mines of Lohardarga on their health seeking behavior.

**Result:** Out of 200 workers interviewed, 89% stated difficulties in visiting the PHC of which 61% stated long distance as a barrier in visiting. Among other difficulties, 18% informed timing of OPD hours as a difficulty while 12% stated that the PHC staffs asked for repeated visits.

It was also observed that 11% preferred to get medicines from the private facilities including the less-than-fully-qualified professionals.

**Conclusion and recommendations:** With increasing mechanization, mining equipment has grown larger and more powerful resulting in increase in the number of laborers and poor health of the miners. Distance of the health care facilities from the working area makes it difficult for the miners to get adequate medical treatment and health becomes a secondary factor. Establishment of clinics and DMCs near the working areas is recommended.

### PD-519-30 Lung health of coal mining workers and their health seeking behaviour in Dakra, Ranchi district, India

S Gadala,<sup>1</sup> Rout Sanchita,<sup>1</sup> M Krithika,<sup>1</sup> T Thomas,<sup>1</sup> P Banuru Muralidhara.<sup>2</sup> <sup>1</sup>Project Axshya, Catholic Health Association of India, Hyderabad, <sup>2</sup>Project Axshya, International Union Against Tuberculosis & Lung Diseases, New Delhi, India. Fax: (+91) 40-27811982. e-mail: srinivasa-rao@chai-india.org

**Background:** Due to the exposure to the coal mine dust, coal miners and the inhabitants of the vicinity of these areas are often subjected to a number of lung diseases and disorders. The growth of open-cast coal mining operations in Jharkhand's Northern Karanpura Valley poses a foremost threat to the region's population and local environment. Purnadih mine project, which is running for 30 years, is owned by Central Coalfields Limited (CCL), a subsidiary of the state-owned company Coal India Limited (CIL). The families of 200 villages located in the vicinity of mining areas are also affected. This paper analyses the issues and the health seeking behavior of the population residing nearby opencast mines area of Dakra, Jharkhand.

**Method:** Awareness about TB and lung diseases, health seeking behavior and issues faced by the community were captured through one-to-one interview guided by a structured questionnaire. Using simple random technique, about 100 coal mine workers and families residing nearby open cast mining of Purunadih, Dakra coal field were interviewed.

**Results:** From 100 workers interviewed, 50% were unaware of the safety measures of underground mining as well as occupational hazard involved with mining. More than 50% of them were illiterate and 18% of them suffered from Bronchial Asthma. 5 % of families in close radius who had lived for 20 years had suffered from pneumoconiosis. At the time of illness most of them (>50%) depend on local private providers and other travel long distance to avail basic facilities. With little knowledge about illness, 80% of them preferred over-the-counter drugs instead of travelling.

**Conclusion:** Coal mining is predominant economic generation activity of the region. Workers in these areas, lack awareness about safety measures, poor healthcare facilities etc. Community engagement activities among these workers were conducted and informed about TB. District TB forum members were sensitized about the

issue and are in constant consultation with policy makers for ensuring safety of miners.

### PD-520-30 Lung cancer among patients at Tikur Anbessa Specialised Hospital (TASH), Addis Ababa, Ethiopia

M Parekh,<sup>1</sup> F Oumer,<sup>2</sup> J Schneider,<sup>2</sup> A Binegdie Bekele,<sup>2</sup> T Bayisa,<sup>2</sup> O Braendli,<sup>3</sup> C Sherman,<sup>4</sup> N Schluger.<sup>1,5</sup>

<sup>1</sup>Division of Pulmonary and Critical Care Medicine, Columbia University Medical Center, New York, NY, USA; <sup>2</sup>Division of Pulmonary and Critical Care Medicine, Addis Ababa University, Addis Ababa, Ethiopia; <sup>3</sup>East African Training Initiative, Swiss Lung Foundation, Lausanne, Switzerland; <sup>4</sup>Division of Pulmonary and Critical Care Medicine, Brown University, Providence, RI, <sup>5</sup>East African Training Initiative, World Lung Foundation, New York, NY, USA. e-mail: madhavi.j.parekh@gmail.com

**Introduction:** Few lung cancer data are available in sub-Saharan Africa, including Ethiopia. While lung cancer is the leading cause of cancer-related death worldwide, it ranks only 5<sup>th</sup> among men in cancer incidence and outside of the top-ten causes of cancer for women in Africa (American Cancer Society, 2011). However, no systematic studies have been performed to confirm these estimates, and it is unclear if lung cancer is adequately in many regions of Africa. The purpose of this study is to examine the types of and risk factors for lung cancer among patients at a tertiary care hospital in Ethiopia.

**Methods:** A retrospective cross-sectional chart review of patients who underwent fiberoptic bronchoscopy from January-December 2013 at Tikur Anbessa Specialized Hospital (TASH) was performed. Patient demographics, pathologic diagnoses, staging, and management were included in the analysis.

**Results:** During the study period, 76 patients underwent bronchoscopy for workup of lung mass or suspected malignancy; 41 had a malignant pathologic diagnosis made. The mean age was 47; 80% of patients were under the age of 65. Only 20% were ever-smokers, all of whom were men. Squamous cell (25%), adenocarcinoma (20%), and carcinoid (15%) were the most common diagnoses. Women comprised 28%, and predominantly had a diagnosis of adenocarcinoma (7 of 11 women). All 16 patients for whom staging was available were stage IV at diagnosis. Six patients underwent surgery (5 pneumonectomies, 1 lobectomy), 13 received chemotherapy and/or radiotherapy, and the remainder received no treatment (10), were lost to follow up (7) without treatment, or died soon after diagnosis (5).

**Conclusions:** Several features of this study cohort are striking. Patients were diagnosed at a remarkably young age overall (average age under 50), as compared to a much older average age of diagnosis in the US—70 years. Moreover, a relatively small number (20%) smoked cigarettes, all of which were men, as compared to an estimated 85% smoking rate among lung cancer patients in the US (American Cancer Society, 2014). Most patients were stage IV at diagnosis, and many received only palliative therapy. This study suggests the profile of lung cancer in Ethiopia is different overall than in the



developed world; it is likely that other exposures (eg. indoor and outdoor air pollution) are contributors. Future study will be prospective and will include those captured beyond bronchoscopy alone.

### PD-521-30 Utility of fiberoptic bronchoscopy at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia

F Oumer,<sup>1</sup> M Parekh,<sup>2</sup> J Schneider,<sup>1</sup> A Binegdie Bekele,<sup>1</sup> T Bayisa,<sup>1</sup> O Braendli,<sup>3</sup> C Sherman,<sup>4</sup> N Schluger.<sup>2,5</sup>

<sup>1</sup>Division of Pulmonary and Critical Care Medicine, Addis Ababa University, Addis Ababa, Ethiopia; <sup>2</sup>Division of Pulmonary and Critical Care Medicine, Columbia University Medical Center, New York, NY, USA; <sup>3</sup>East African Training Initiative, Swiss Lung Foundation, Lausanne, Switzerland; <sup>4</sup>Division of Pulmonary and Critical Care Medicine, Brown University, Providence, I, <sup>5</sup>East African Training Initiative, World Lung Foundation, New York, NY, USA.  
e-mail: madhavi.j.parekh@gmail.com

**Background:** Fiberoptic bronchoscopy (FOB) aids in the diagnosis of various pulmonary conditions. However, reported data regarding bronchoscopy is largely from developed countries; little is known regarding the clinical profile of patients referred for and the diagnostic yield of bronchoscopy in Ethiopia. The purpose of this study is to assess characteristics of patients who underwent FOB, indications, and diagnostic yield of bronchoscopy, a recently adopted procedure at Tikur Anbessa Specialized Hospital (TASH), Addis Ababa, Ethiopia.

**Methods:** A retrospective cross-sectional chart review of patients who underwent FOB from January-December 2013 at TASH was performed. Patient demographics, indications for bronchoscopy, procedural findings, histopathology, cytology, culture data and management of patients were included in the analysis.

**Results:** During the study period, 142 patients underwent FOB, approximately 74% of which were outpatients. The mean age was 42 years and 90 (63%) were men. Among those whose smoking status was known, 15% of patients were smokers. The most common indication was lung mass (presumed malignant) in 76 (52%) of the patients followed by tuberculosis in 18 (13%) of the patients. Twelve patients had a confirmed diagnosis of HIV at the time of bronchoscopy (8%). The most common endoscopic finding was endobronchial lesion in 32%. Biopsies were performed in 75 patients (53%), 59 (79%) of which were endobronchial, and 16 (21%) were transbronchial. Sixty-five of the 75 cases biopsied yielded specimens; 31 (48%) had a positive diagnosis. Twenty-one patients (68%) had histopathology consistent with a malignant process, squamous cell carcinoma being the most common (48%) followed by adenocarcinoma (19%). Nineteen patients who underwent BAL had positive cytology or culture, among which 7 (36%) were positive for *Mycobacterium tuberculosis*, and 6 (32%) were positive for bacterial infection.

**Conclusions:** Patients who underwent bronchoscopy during the study period were predominantly middle-aged men, for evaluation of lung mass. The yield of FOB in making a histopathologic diagnosis was overall 48%.

The most common diagnosis encountered by biopsy was squamous cell carcinoma. Bronchoscopy was introduced to TASH at the beginning of the study period; yield may improve with experience. Future study will include a prospective observation of patients who undergo FOB with identification of risk factors, yield of bronchoscopy and clinical outcomes.

### PD-522-30 Tuberculosis and chronic kidney disease: a systematic review

K Al-efraij,<sup>1</sup> L Mota,<sup>1,2</sup> V Cook,<sup>1,2</sup> J Johnston.<sup>1,2</sup>

<sup>1</sup>Medicine, University of British Columbia, Vancouver, BC, <sup>2</sup>Tuberculosis Control, British Columbia Centre for Disease Control, Vancouver, BC, Canada.  
e-mail: lorena.mota@bccdc.ca

**Background:** Chronic kidney disease (CKD) is a health problem with a global prevalence of 8–16%. CKD is associated with impaired cell-mediated immunity and is often associated with medical immunosuppression. Furthermore, CKD is common in patients with diabetes mellitus and HIV, two major drivers of global TB incidence. The relationship between CKD and active TB risk is not well described. We conducted a systematic review of the CKD-TB literature to better characterize TB risk in CKD populations.

**Methods:** We searched Ovid Medline, EMBASE, Cochrane databases, and relevant journals. We included studies if they were peer-reviewed cohorts, case-control, or cross-sectional studies that reported or allowed computation of quantitative effect estimate of the relationship between CKD and active TB and controlled for at least one demographic variable. We excluded studies if they were case studies, reviews, paediatric studies, studies that did not provide or allowed for the computation of effect estimates in odds ratios, rate ratios, or risk ratios; studies that did not adjust for demographic variables; studies that employed different methods for assessing TB among individuals with and without CKD or for assessing CKD among TB patients and controls; single centre studies; anonymous reports; and duplicate reports.

**Results:** We identified and screened 3406 articles. Of these, we excluded 3221 because they did not measure active TB risk, were paediatric studies, reported clinical manifestations or prognosis of active TB, were case reports, reviews, letters, or studies on latent TB. Of the remaining 185 articles, 150 were excluded because they were single center studies; studies on clinical manifestation of TB in CKD, studies of extra-pulmonary TB only, were abstracts or were untraceable. After exclusion of articles that did not control for demographic factors, we identified 5 eligible articles. Studies reported TB risk in CKD patients undergoing dialysis; four were cohort studies and one was a case-control study. CKD patients consistently had an increased risk of active TB, with the adjusted effect estimate ranging from 2.3 to 25.3 when compared with non-CKD patients. No studies were identified that examined TB risk in pre-dialysis CKD populations.

**Conclusions:** People with CKD may be important targets for active case finding, latent TB screening and preventative therapy. Further research on other CKD populations such as pre-dialysis and post kidney transplant are needed.

### PD-523-30 Relationship between paint thinner exposure with impaired lung function to painting workers in one of automotive industry in Jakarta, Indonesia

R Haryanti,<sup>1</sup> N Prihartono.<sup>2</sup> <sup>1</sup>Epidemiology, Alumni Faculty of Public Health Universitas Indonesia, Depok, <sup>2</sup>Epidemiology, Faculty of Public Health University of Indonesia, Depok, Indonesia. e-mail: rizki.sri11@alumni.ui.ac.id

**Background:** Most of auto industry still use paint thinner containing VOCs ( consisting of benzene, toluene, xylene, etc ) in performing automotive painting. This study aims to determine the relationship between paint thinner exposure with impaired lung function after controlled confounding variables on workers painting section in the automotive industry company in Jakarta.

**Design/Methods:** The methods of research is an observational study with cross-sectional design. The study determined the relationship of paint thinner exposure to lung function by using causality models. The independent variable of this study is exposure to paint thinner in which respondents categorized by job title and job description. Workers are categorized into 4 categories: no exposure, middle-exposed, exposed a little thinner and other chemicals and full exposed. Workers with no exposure work in the office, UBS, sealer, and Dojo ; workers with middle exposure work in the Touch -up ; workers exposed a little thinner and other chemicals work in the PTC - ED and workers with full exposure work in Top Coat and mixing. The dependent variable is lung function. Lung function are categorized as impaired (restrictive, obstructive or mix ) and normal lung function. In addition, clients are also asked to answer questions about smoking behavior, age, the use of mask, BMI, and duration of exposure per week. The research location was in an automotive industry company in Jakarta, painting department. Number of respondents in this study were 195 people who were taken by simple random sampling. Data were analyzed using modification of proportional hazard with Cox regression analysis.

**Results:** Research shows amount 5 % of workers experienced a pulmonary obstructive disorder, amount 12 % of workers had impaired pulmonary restriction and 8 % had restriction and obstruction ( mix ). After controlled with the use of mask, smoking behavior and exposure a little paint thinner and other chemicals known that workers exposed to the middle portion of thinner had PR to impaired lung function amount 1.87 ( 95 % CI = 0.74 to 4.71 ). In workers exposed to full thinner had PR for impaired lung function amount 3.23 ( 95 % CI = 1.36 to 7.59).

**Conclusion:** The greater exposure to paint thinner had higher risk for impaired lung function. Based on these results it is recommended that the company conduct

health promotion efforts to minimize the risk of impaired lung function to painting workers.

**Table 1 Thinner Exposure Relationship with Impaired Lung Function**

Variable	PR	95% CI	
		Lower	Upper
Paint thinner exposure			
No exposure	1		
Middle exposure	1,87	0,74	4,71
Full exposure	3,23	1,36	7,69
Exposure a little paint thinner and other chemicals	3,94	1,47	10,56
Masker using			
Always	1		
Often	1,13	0,45	2,79
Seldom	1,33	0,55	3,18
Never	1,78	0,69	4,62
Smoking habit			
Never	1		
mild	0,87	0,36	2,12
middle	1,01	0,46	2,22
Past smoker	1,31	0,62	2,76

### PD-524-30 Non-TB respiratory comorbidity among patients attending primary care practices in India

S Pati,<sup>1</sup> S Swain,<sup>1</sup> C Salisbury.<sup>2</sup> <sup>1</sup>Indian Institute of Public Health, Public Health Foundation of India (PHFI), Bhubaneswar, Odisha, India; <sup>2</sup>Centre for Academic Primary Care, University of Bristol, Bristol, UK. Fax: (+91) 6746655614. e-mail: drsanghamitra12@gmail.com

**Background:** Multimorbidity, the coexistence of two or more chronic diseases in a single individual, has been identified as a major challenge to primary care in developed countries and associated with poorer outcomes and increased healthcare costs. However, little is known about the magnitude of respiratory multimorbidity in developing countries. The present study attempted to explore the prevalence and pattern of respiratory morbidity among patients attending primary care practices in India and examined their health care utilization (HCU) and health related quality of life (HRQL).

**Design/Methods:** A total of 1649 adult patients attending 20 public and 20 private primary care facilities were interviewed during April - September 2013. A pre-designed validated questionnaire was used to elicit detailed information on self-reported respiratory morbidities. Data was analyzed to estimate the prevalence, identify comorbidities, and measure HCU and HRQL. TB was not included in the analysis.

**Results:** The overall prevalence of any respiratory morbidity (excluding TB) was 3% and the mean was 52 years [95% CI: 47.57-56.42]. Among these, more than half were females. Nearly 52% of them visited government hospital for treatment. All the patients had been prescribed medicine/drugs by their physicians but 76% of them are continuing it. Major reasons for discontinuation were cited to be financial problem and

ignorance towards it. Of total patients with respiratory diseases 17.02% were using alternative system of medicine (Ayurvedic). From all the patients with respiratory diseases 64% had one or more and 37% had two or more chronic conditions. Acid-peptic disease (40%), hypertension (29%), arthritis (17%) and visual problem (15%) were found to be leading comorbidities. Tuberculosis was seen among 9% of the patient population. Both the physical and mental component score were seen to be low among the patients with mean score of 43.50 [95% CI: 42.22–44.97] and 43.70 [95% CI: 41.70–45.69] respectively, which worsen with presence of other chronic conditions.

**Conclusion:** This study is the first to explore the extent of respiratory comorbidity in primary care settings in India. The findings suggest the need to re-design health services to focus more on managing the burden of respiratory disease which is likely to increase further in future.

### 03. TB IN CHILDREN: DIAGNOSIS

#### PD-525-30 Validation of the "Keith Edwards" TB score chart among suspected paediatric TB cases in a West African setting with low-HIV prevalence

T Togun,<sup>1</sup> U Egere,<sup>1</sup> A Sillah,<sup>1</sup> J Otu,<sup>1</sup> M Antonio,<sup>1</sup> J Sutherland,<sup>1</sup> P Hill,<sup>2</sup> B Kampmann.<sup>1,3</sup> <sup>1</sup>Vaccinology (Childhood TB Research Group), Medical Research Council (MRC) Unit - The Gambia, Banjul, Gambia; <sup>2</sup>Preventive & Social Medicine, University of Otago School of Medicine, Dunedin, New Zealand; <sup>3</sup>Paediatrics (Academic), Imperial College London, St. Mary's Campus, London, UK. Fax: (+220) 4495919. e-mail: ttogun@mrc.gm

**Background:** Childhood tuberculosis (TB) is diagnosed in resource limited settings mostly by symptom-based diagnostic approaches that were not prospectively validated. We evaluated the diagnostic utility of the Keith Edwards Paediatric TB Score Chart (PTSC) used by the TB Control Programme in The Gambia.

**Methods:** All children aged <15 years presumed to have TB attending the MRC Gambia TB clinic from February 2012 to April 2013 were prospectively enrolled and investigated including assessment of their nutritional status, chest x-ray and induced sputum for smear microscopy, liquid culture and GeneXpert. Each child was also assessed with the PTSC and an overall score of  $\geq 7$  is deemed highly suggestive of TB in children by convention; these results were compared to the case definition for TB proposed by the W.H.O incorporating bacteriologically confirmed and clinically diagnosed TB cases as reference standard.

**Results:** 396/410 (97%) of children enrolled were included in the analysis. The median age was 6 years (IQR 3–10 years), 203 (51.3%) were females, 27.5% were malnourished and none was HIV infected. 35/396 (8.8%) children were diagnosed with TB and started on treatment comprising 10 bacteriologically confirmed and 25 clinically diagnosed TB cases. The overall sensitivity,

specificity, positive and negative predictive values of the PTSC were 88.6% (95% CI, 73.3–96.8%), 72.6% (95%CI, 67.7–77.1%), 23.9% (95%CI, 16.8–32.1%) and 98.5% (95%CI, 96.2–99.6%) respectively. The sensitivity, specificity and predictive values did not vary with age when assessed separately among children <5 years of age and those aged  $\geq 5$  years (Table 1). The prevalence of malnutrition among children with false positive PTSC results (i.e. score  $\geq 7$  with no TB) that were aged <5yrs (weight-for-height z-score < -1 standard deviation of reference) and  $\geq 5$ yrs (BMI-for-age z-score < -1 standard deviation of reference) were 50% and 80%, respectively.

**Conclusion:** As a diagnostic tool, the PTSC was sensitive and had a high negative predictive value in our setting but with a reduced precision, which was attributed to malnutrition. Therefore, it is important to modify this scoring system for use in contexts with a high prevalence of malnutrition and to consider its use for screening – rather than diagnosis – to identify children that will be referred for further evaluation for TB. Otherwise, the use of the PTSC as it is will result in over-diagnosis and unnecessary treatment of children for TB.

Table 1 Performances of the PTSC by age group

Estimates	<5 years	$\geq 5$ years
Sensitivity (95% CI)	87.5% (61.7–98.5%)	89.5% (66.9–98.7%)
Specificity (95% CI)	72.1% (63.5–79.6%)	72.8% (66.6–78.5%)
Positive Predictive Value (95% CI)	28.0% (16.2–42.5%)	21.3% (12.9–31.8%)
Negative Predictive Value (95% CI)	97.9% (92.6–99.7%)	98.8% (95.8–99.9%)

#### PD-526-30 Comparison of MGIT and MODS mycobacterial culture methods for diagnosis of childhood pulmonary tuberculosis in Kenya

A Brent,<sup>1,2,3</sup> H Twahir,<sup>4</sup> V Bandika,<sup>4</sup> D Mugo,<sup>2</sup> R Musyimi,<sup>2</sup> S Morpeth,<sup>2</sup> M Levin,<sup>3</sup> JAG Scott.<sup>2,5</sup> <sup>1</sup>Medical Sciences Division, University of Oxford, Oxford, UK; <sup>2</sup>Department of Epidemiology & Demography, KEMRI-Wellcome Trust Research Programme, Kilifi, Kenya; <sup>3</sup>Dept Paediatrics & Wellcome Trust Centre for Clinical Tropical Medicine, Imperial College London, London, UK; <sup>4</sup>Department of Paediatrics, Coast Provincial General Hospital, Mombasa, Kenya; <sup>5</sup>Department of Infectious Disease Epidemiology, London School of Hygiene & Tropical Medicine, London, UK. e-mail: dr.a.brent@gmail.com

**Introduction:** Childhood TB is paucibacillary, so bacteriological diagnosis relies on mycobacterial culture. Commercial liquid culture methods like the BACTEC MGIT 960 system are more rapid and sensitive than traditional solid media. However barriers to uptake include cost and a lack of trained personnel and biosafety level 3 facilities. Potential advantages of the Microscopic Observation Drug Susceptibility (MODS) culture technique include higher sensitivity; more rapid results that include drug susceptibility testing; lower cost; and less stringent biosafety requirements. However only limited data exist for children. We compared MGIT with MODS for diagnosis of childhood TB in Kenya.



**Methods:** Between March 2010 and December 2011 we obtained spontaneous or induced sputum samples from 1461 children who presented to hospital in Kenya with features of suspected TB. Equal aliquots were cultured by MGIT and MODS and a positive culture defined as isolation of *M. tuberculosis* by either method.

**Results:** 98/1825 (5%) sputum specimens were *M. tuberculosis* culture positive. Culture yield was higher for MGIT than MODS overall (MGIT sensitivity 89.9%, MODS sensitivity 75.3%, McNemar's  $\chi^2$  test  $p=0.020$ ) with a similar trend among induced sputum samples (MGIT 85.9%, MODS 71.9%,  $p=0.083$ ). Time to detection was slightly longer for MGIT than MODS (12 versus 11 days,  $p=0.007$ ).

**Conclusion:** MGIT is more sensitive and almost as rapid as MODS for diagnosis of childhood pulmonary TB.

### PD-527-30 Childhood tuberculosis: retrospective review of samples received at a microbiology laboratory in KwaZulu Natal

M Khan Mbchb,<sup>1</sup> P Mahabeer,<sup>2</sup> K Mlisana.<sup>2</sup> <sup>1</sup>Enhancing Care Foundation, Faculty of Health Sciences, Durban University of Technology, Durban, <sup>2</sup>Medical Microbiology, University of KwaZulu Natal & National Health Laboratory Service, Durban, South Africa. e-mail: mlisana@ukzn.ac.za

**Background:** Childhood tuberculosis (TB) remains a worldwide problem. Approximately half a million new paediatric cases are diagnosed annually and in 2012, 74 000 deaths occurred in HIV uninfected children from TB. Diagnosis of TB in the newborn and early childhood period however remains a challenge and diagnostic tests of high sensitivity and specificity are essential to early diagnosis and appropriate management. A retrospective descriptive review of samples received for the investigation of TB in children ( $\leq 12$  yrs) was conducted.

**Design/Methods:** Laboratory data of all paediatric samples (including sputum, gastric lavages, etc) submitted for TB diagnosis over a 6 month period were collated. Auramine smears were performed on all samples before being cultured into the Bactec MGIT960 system. Positive cultures were confirmed with Ziehl-Neelsen (ZN) staining and MTBDR plus assay (Hain-Life Science) was performed on those ZN positive with cording.

**Results** are presented in 2 broad categories on the basis of hospital admission: neonates who were delivered at the hospital and admitted to the nursery as well as admissions into the paediatric wards.

**Results:** A total of 751 samples were received over the six month period comprising of 159 (21%) from neonatal nursery and 592 samples from the paediatric wards. The samples originated from 81 neonates and 343 paediatric patients. There were only 2 neonates who were culture positive for TB. From the 343 paediatric admissions, 15 (4.4%) were acid fast bacilli positive; forty (11.7%) were MGIT960 culture positive, 4(10%) of which turned out to be nontuberculous mycobacteria (NTM). Of the thirty six (10.5%) paediatric admissions who were MTBDR<sup>+</sup> (line probe assay) positive, five (13.9%) were multidrug

resistant (MDR) -TB and 2 (5.6%) had rifampicin monoresistance.

**Conclusion:** TB diagnosis in children remains a challenge especially in neonates. The low sensitivity of TB microscopy underscores the advantages of the South Africa's recent roll-out of GeneXpert (Cepheid) to improve patient management. MDR-TB in children is worrisome and warrants urgent attention.

### PD-528-30 TB Incidence during follow-up of children contacts of smear-positive cases according initial levels of TST induration and IFN- $\gamma$ production

M N Altet Gomez,<sup>1</sup> MA De Souza-galvao,<sup>1</sup> J Dominguez,<sup>2</sup> MA Jiménez,<sup>1</sup> T Soriano,<sup>1</sup> J Solsona,<sup>1</sup> & Orcau Palau,<sup>3</sup> JA Caylà.<sup>3</sup> <sup>1</sup>de Tuberculosis Vall d'Hebrón-Drassanes, Hospital Universitario Valle de Hebrón, Barcelona, <sup>2</sup>Servei de Microbiologia, Institut d'Investigació Germans Trias i Pujol, Badalona, <sup>3</sup>Agència Salut Pública de Barcelona, Agència Salut Pública de Barcelona, Barcelona, Spain. e-mail: jadomb@gmail.com

**Objectives:** There is a positive association between the reactivity of the tuberculin skin test (TST) and the development of TB: the risk is greater when the diameter of the induration is greater. The aim of this study is to verify if this happens with IFN- $\gamma$  production.

**Patients and methods:** 457 children ( $<15$  old), contacts of TB bacillary cases with 48 months of follow-up. TB infection was diagnosed using TST and QuantiFERON-GIT (QFN.GIT); their initial data were stratified. There were 32 co-prevalent cases (diagnosed during 1–12 weeks after the Index Case diagnosis): these cases had been excluded from the follow-up analysis.

**Results:** We present the results of 299 contacts of bacillary Index-Cases, those who are at increased risk of TB. During follow up 7 TB cases were developed, all in the first 2 years. In the table you can see the TB incidence rate (I.R) during follow-up: it's greater as the basal concentration of IFN- $\gamma$  increases, this also happens with the TST, just like with the positive predictive value (PPV).

		N	TB cases	I.R/1000p.a	V.P.P
IFN- $\gamma$ initial (UI/ml)	0.0– 0.34	178	0	0	Reference
	0.35 – 5	52	1	4.8	2 (–2 – 6)
	5.01 – 9.9	27	2	18.5	7 (–2 – 17)
	$\geq 10$	42	4	23.8	10(1– 8)
TST initial (mm)	0–4	119	0	0	Reference
	5–9	25	0	0	0 (0-0)
	10–14	81	2	6.2	2 (–1 –6)
	$\geq 15$	74	5	16.9	7 (1–12)

**Conclusions:** These data have a great significance in clinical practice. The production of IFN- $\gamma$  levels  $\geq 5$  IU/ml is a good “biomarker” of the risk of developing TB disease: in contacts of TB cases, if the QFN.GIT (+) is necessary to recommend TITL especially if the observed baseline level is over 5 IU/ml or TST  $\geq 10$ mm, specially if QFN.GIT  $\geq 10$ UI/ml or TST  $\geq 15$ mm. When it is not possible, the first two years after infection are at high risk of developing tuberculosis.

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### PD-529-30 Diaskintest® - screening method in mass examination of the child population for tuberculosis in Russia

V Aksenova,<sup>1</sup> N.I. Klevno.<sup>1</sup> <sup>1</sup>Research Institute of Phthisiopulmonology, I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation.  
e-mail: axellex@yandex.ru

In Russia there is a new effective way to identify initial presentation of tuberculosis - Diaskintest® ( DST ), which is a combination of two antigens (ESAT / CFP) presented in virulent strains of *Mycobacterium tuberculosis* and absent in the vaccine strain BCG and non-tuberculous mycobacteria. As opposed to QuantiFERON TB and T- SPOT widely used in other countries, DST injected intradermally and causes specific cutireaction of delayed hyperresponsiveness in people with TB infection. Individuals vaccinated with BCG and noninfected by *Mycobacterium tuberculosis* have no reaction to DST. The aim of the investigation is to study effectiveness of this test alternatively to skin test with PPD (Mantoux test with 2TE) in conditions of mass screening for tuberculosis. The investigation included healthy children (7–14 years) and adolescents (15–17 years). Over 44% of them had positive reactions to tuberculin. All children (n = 1238) were examined by the DST. Positive reactions were noted only in 4%. After X-ray examination 7 patients revealed local tuberculous changes. Thus, as a result of examination all school children and teenagers by the DST, identifying of local tuberculosis was 0.56%. **Conclusion.** DST has a high specificity using the secretory proteins ESAT-6 and CFP-10. Introduction into medical practice of new method of tuberculosis diagnosis as a screening method of children examination will allows sharply improve the quality of tuberculosis infection diagnosis, reduce material costs for tuberculosis detection in children and improve the epidemiological situation of tuberculosis in general.

### PD-530-30 Interferon-gamma release assay positivity is associated with time since BCG vaccination in infants in rural Malawi

P Khan,<sup>1,2</sup> T Mzembe,<sup>2</sup> D Mulawa,<sup>2</sup> F Simukonda,<sup>2</sup> A Crampin,<sup>1,2</sup> J Glynn,<sup>1</sup> P Fine.<sup>1</sup> <sup>1</sup>Infectious disease epidemiology, LSHTM, London, UK; <sup>2</sup>Chilumba site, Karonga Prevention Study/MEIRU, Karonga, Malawi.  
e-mail: palwasha.khan@lshtm.ac.uk

**Background** Despite a plethora of publications on interferon gamma release assays (IGRAs), there are few data on infants, especially in high-burden settings. One of the advantages of IGRAs over tuberculin skin tests (TST) is their increased specificity for the diagnosis of *M. tuberculosis* infection, particularly in BCG-vaccinated individuals. By only including antigens unique to *M. tuberculosis*, there should not be any cross-reactivity with BCG.

**Methods** Study hypothesis: TST but not IGRA positivity will vary as a function of time since BCG Setting: Demographic surveillance site, northern Malawi with high BCG coverage Dates: January 2012 to March 2014 Design and procedures: Cross-sectional study nested within a cohort study investigating incident *M. tuberculosis* infection. A 2-stage testing strategy was undertaken using TST (2-TU dose of purified protein derivative RT23) followed by QuantiFERON-TB Gold in-tube (QFT-GIT) if TST ≥ 10mm.

**Results** 1009 infants were eligible for the study, of whom 879(87.1%) were enrolled. Of these infants, 870(98.9%) had TST placed and read within 48-72hrs. 156(17.8%) infants had a TST ≥ 10mm and 46(5.3%) had a TST ≥ 15mm. BCG vaccination date was available for 803(92.3%). 4 infants had BCG vaccination after TST and were excluded. 34/799(4.3%) of infants were HIV-exposed and 154(19.3%) had unknown HIV exposure status. The odds of TST positivity (defined as TST ≥ 10mm) decreased by 26% with every 6-week increase in time since BCG vaccination (AOR 0.74, 95%CI 0.59-0.95). Of the 156 infants with TST ≥ 10mm, 148(94.9%) had blood taken. 10 infants were over 1 year by time of blood draw and were excluded. Of the 138 infants under-one with QFT-GIT results: 10(7.3%) were indeterminate; 104 were negative and 19(14.5%) were positive. Infants with indeterminate results were excluded from further analysis. BCG vaccination date was available for 124/128. The odds of having a positive IGRA decreased by 53% for every 6-week increase in time since BCG vaccination (AOR 0.47, 95%CI 0.25-0.87).

**Conclusion** IGRA positivity was strongly associated with time since BCG vaccination in our study and this warrants further investigation. A potential limitation is that TST (which includes *M. tuberculosis* antigens) was administered prior to blood draw. This study adds to the evidence base for not using IGRAs in infants and highlights the limitation of a 2-stage testing strategy (TST preceding IGRA) recommended by a number of guidelines.

Table. Characteristics associated with QFT-GIT positivity: univariable and adjusted analysis (n=124)

	QFT-GIT positive	Crude OR (95% CI)	p-value <sup>a</sup>	Adjusted OR* (95% CI)	p-value <sup>a</sup>
Time since BCG (weeks)	n/N (row %)				
<15	2/4 (50.0)	0.82 (0.60-1.13)	0.22	0.47 (0.25-0.87)	0.034
15-20	4/18 (22.2)				
21-26	4/24 (16.7)				
27-32	2/30 (6.7)				
33-38	5/23 (21.7)				
39-44	2/14 (14.9)				
≥45	1/11 (9.1)				
Age at QFT-GIT (months)	n/N (row %)	0.96 (0.62-1.50)	0.87	2.60 (1.03-6.55)	0.042
<4.0	1/4 (25.0)				
4.0-5.9	3/25 (12.0)				
6.0-7.9	7/43 (16.3)				
8.0-9.9	7/31 (22.6)				
≥10.0	2/21 (9.5)				
Total	20/124				

\*Adjusted for age and time since BCG

<sup>a</sup>Likelihood ratio test for trend

### PD-531-30 Bacteriologically confirmed pulmonary tuberculosis among children with presumptive tuberculosis at the National Referral Hospital in Uganda

M Sekadde,<sup>1</sup> E Wobudeya,<sup>2</sup> W Ssengooba,<sup>3</sup> M Joloba,<sup>3</sup> H Kisémba,<sup>4</sup> S Kitaka,<sup>5</sup> P Musoke.<sup>5</sup> <sup>1</sup>National Tuberculosis and Leprosy Program, Ministry of Health, Kampala, <sup>2</sup>Paediatrics and Child Health, Mulago National Referral Hospital, Kampala, <sup>3</sup>Microbiology, Makerere University College of Health Sciences, Kampala, <sup>4</sup>Radiology, Mulago National Referral Hospital, Kampala, <sup>5</sup>Paediatrics and Child Health, Makerere University College of Health Sciences, Kampala, Uganda. e-mail: moorine.sekadde@gmail.com

**Background:** The occurrence of bacteriologically confirmed TB among children in resource limited settings is largely not described. We describe the magnitude and factors associated with bacteriologically confirmed pulmonary tuberculosis among children with presumptive TB in Uganda.

**Design/Methods:** We report data collected between January 2011 and January 2012 for 250 children aged 2 months – 12 years that met the WHO definition for presumptive TB at the Mulago National Referral Hospital in Uganda. Enrolled children were subjected to detailed clinical history, physical examination, Tuberculin Skin Test, HIV testing, chest radiography, sputum smear microscopy, Xpert MTB/RIF and sputum culture. Bacteriologically confirmed TB was defined as having a positive sputum culture or Xpert MTB/RIF test. Continuous and categorical data were described using medians (IQR) and proportions respectively. Factors associated with bacteriologically confirmed TB were assessed for using logistic regression analysis.

**Results:** The median age was 36 months (IQR 15.7–72 months). Majority of the children were male (53.6%) and 134 (46.4%) were HIV-infected. A positive history of TB contact 86/250 (34.3%), BCG scar 76/250 (30.4%), positive TST 169/250 (67.6%), history of prior TB treatment 28/250 (7.2%), and severe wasting 68/250 (27.2%) were recorded. 42/250 (17%) children had bacteriologically confirmed TB. The factors independently associated with bacteriologically confirmed TB were: Age > 5 years (OR 2.7 (95% CI 1.3–5.7) p value <0.01), severe wasting (OR 2.7 (95% CI 1.2–6.1) p value 0.02), positive TST (OR 4.1 (95% CI 1.9–9.0) p value <0.01), and a positive history of TB contact (OR 2.2 (95% CI 1.2–6.1) p value 0.04). HIV infection was not associated with bacteriologically confirmed TB.

**Conclusion:** A diagnosis of TB was bacteriologically confirmed in less than a quarter of the children with presumptive TB. Age > 5 years, a positive TST, severe wasting, a positive history of TB contact in a child with presumptive TB were more likely to be associated with bacteriologically confirmed TB. Bacteriological confirmation of TB in children presents a major challenge to the management of TB in children. There is need for further research to strengthen clinical diagnosis of TB in children.

### PD-532-30 Use of the QuantiFERON®-TB Gold in-tube test in paediatric patients with a "Borderline Positive" tuberculin skin test does not improve compliance

L Perkins,<sup>1</sup> J Lewis,<sup>2</sup> W Wang,<sup>3</sup> WG Hunt.<sup>1,4</sup> <sup>1</sup>Pediatric Infectious Diseases, Nationwide Children's Hospital, Columbus, OH, <sup>2</sup>Quality Improvement Services, Nationwide Children's Hospital, Columbus, OH, <sup>3</sup>Biostatistics Core, The Research Institute at Nationwide Children's Hospital, Columbus, OH, <sup>4</sup>Pediatrics, The Ohio State University College of Medicine, Columbus, OH, USA. e-mail: w.garrett.hunt@nationwidechildrens.org

**Background:** The guidelines for using interferon- $\gamma$  release assays to detect latent *Mycobacterium tuberculosis* infection (LTBI) published by the CDC in 2010 advocated a tuberculin skin test (TST) and an IGRA when needed to encourage compliance. Also, recipients of the Bacille Calmette-Guérin (BCG) vaccine not at risk for a poor outcome and with a TST  $\geq 10$  mm but <15 mm could have this "borderline positive" result discounted with a negative IGRA. In late 2009, our Pediatric TB Clinic began using QuantiFERON®-TB Gold In-Tube (QFT-GIT, Cellestis Inc.) in patients 5–15 years old with a TST of 10–15 mm and negative chest x-ray, PA and lateral. The same nurse practitioner took care of all patients. Those with a positive (+) QFT-GIT were offered 270 doses of daily isoniazid to be completed in 1 year; those with a negative QFT-GIT were considered uninfected and were not treated. The objectives of this retrospective cohort study were: 1) to determine if the rates of initiation of therapy ( $\geq 23$  pills in 60 days) and completion of therapy were greater with TST/QFT-GIT compared to TST only, and 2) to determine if initiation of therapy predicted successful completion of therapy for either group.

**Design/Methods:** Data were collected as a part of routine clinical care and then queried later in the local database, from 11/1/08–10/31/09 for the TST only group and from 12/18/09–12/17/10 for the TST/QFT-GIT group.

**Results:** In the TST only group, 99/263 patients met age and TST criteria. In the TST/QFT-GIT group, 112/245 patients met criteria, and 14/112 (12.5%) had a + QFT-GIT. Demographic data (see table) were not significantly different between the two groups (P values not shown). In the TST only group, 75/99 (76%) initiated therapy; in the TST/QFT-GIT group, 12/14 (86%) initiated therapy (not significant [Fisher's exact test (FET), P=0.52, OR 1.92, 0.401–9.195]). For the same two groups, the percentage of completion also was not significantly different (TST only, 70 of 99 (71%) vs. TST/QFT-GIT, 8 of 14 (71%), [FET P=0.36, OR 0.55, 0.176–1.734]). In the TST only group, initiation of therapy predicted completion [Chi-Square, LR 43.1, P<0.0001], but there was no correlation in the TST/QFT-GIT group.

**Conclusion:** The use of QFT-GIT for children and adolescents with a "borderline positive" TST was not associated with improved initiation or completion of therapy, and initiation did not predict completion of therapy. However, 87.5% of patients tested by QFT-GIT had a negative result, thereby avoiding unneeded



treatment. It remains important to find other methods to improve compliance with LTBI therapy.

#### Patient Demographics

	TST only (%)	QFT-GIT/TST (%)
Male	56/99 (56.5%)	5/14 (35.7%)
Female	43/99 (43.4%)	9/14 (64.2%)
Median age (years)	10	13
BCG placed at birth	79/99 (79.7%)	11/14 (78%)
Country of Birth		
- Mexico/Central and South America	6/99 (6%)	1/14 (7%)
- Sub Saharan Africa	82/99 (82%)	9/14 (64%)
- Northern Africa and Middle East	13/99 (13%)	1/14 (7%)
- Eastern Europe	2/99 (2%)	0/14 (0%)
- USA	10/99 (10%)	1/14 (7%)
- Asia	11/99 (11%)	4/14 (28%)

#### PD-533-30 Tuberculosis bacteremia not detected in febrile children in western Kenya

P Pavlinac,<sup>1</sup> J Naulikha,<sup>2</sup> F Onchiri,<sup>1</sup> B Singa,<sup>3</sup> L Cranmer,<sup>2</sup> E Lokken,<sup>1</sup> G John-Stewart,<sup>1,2,4,5</sup> Judd Walson.<sup>1,2,4,5</sup>

<sup>1</sup>Epidemiology, University of Washington, Seattle, WA, USA; <sup>2</sup>Pediatrics, University of Washington, Seattle, WA, USA; <sup>3</sup>Centre for Clinical Research, Kenya Medical Research Institute, Nairobi, Kenya; <sup>4</sup>Global Health, University of Washington, Seattle, WA, USA; <sup>5</sup>Medicine, University of Washington, Seattle, WA, USA.  
e-mail: ppav@u.washington.edu

**Background:** While *Mycobacterium tuberculosis* (MTB) frequently manifests as isolated pulmonary disease in immune-competent adults, MTB commonly disseminates in children, leading to non-specific signs and symptoms including fever. We determined the prevalence of MTB bacteremia among febrile children living in the Nyanza province of Kenya, a region with high HIV prevalence.

**Design/Methods:** Between March 2013 and February 2014, we enrolled children aged 6 months to 5 years presenting with fever (axillary temperature  $\geq 37.5^\circ\text{C}$ ) to two Nyanza district hospitals. Blood samples (1–5 mL) were inoculated in Bactec<sup>TM</sup> Myco/F lytic culture vials, shipped within 24 hours to a microbiology lab (CDC/KEMRI, Kisumu, Kenya), incubated in the BD 9120 system for 60 days, and positive bottles subcultured using standard methods. Demographic and clinical data were collected and child HIV-status ascertained by antibody testing or PCR if  $<18$  months. The HIV status of the accompanying caregiver was determined by self-report or by antibody testing if unknown. The prevalence of MTB bacteremia was determined and 95% confidence intervals (CI) constructed using a binomial distribution.

**Results:** Among 157 children enrolled, median age was 39 months (interquartile range: 22–49 months), 15.5% were stunted (height-for-age z-score  $< -2$ ), and 18.2% wasted (weight-for-height z-score  $< -2$ ). Most children (98.7%) had evidence of a BCG vaccination scar. Few children reported night sweats or a cough of  $\geq 2$  weeks duration (6.3% and 9.2%, respectively) and only 1.6% had a fever  $> 1$  week. Although 15.6% of children were

accompanied to the hospital by an HIV-infected adult, only 1.3% were HIV-infected. Nine children (6.9%) were living in a household with one or more members who had been diagnosed with active TB, but none had received isoniazid preventive therapy. No MTB or other mycobacterial species were identified in the bloodstream (0%, 95% CI: 0–2.3%).

**Conclusion:** MTB bloodstream infection was not detected in this pediatric cohort, a finding consistent with other pediatric studies. Despite an increased risk of disseminated tuberculosis in children, detection of MTB bacteremia may be rare.

#### PD-534-30 Determining the capability of sputum collection through induction for the diagnosis of tuberculosis in children in Kenya

J Oliwa,<sup>1</sup> R Oberhelman,<sup>2</sup> D Wamalwa,<sup>3</sup> P Ayieko,<sup>1</sup> D Marangu,<sup>3</sup> J Oyugi,<sup>4</sup> E Obimbo.<sup>3</sup> <sup>1</sup>Public Health Research, Health Services Unit, KEMRI-Wellcome Trust Research Programme, Nairobi, Kenya; <sup>2</sup>Tropical Medicine, Tulane University, New Orleans, LA, USA; <sup>3</sup>Paediatrics and Child Health, University of Nairobi, Nairobi, Kenya; <sup>4</sup>Microbiology, University of Nairobi, Nairobi, Kenya.  
e-mail: narotso04@gmail.com

**Background:** The diagnosis of pulmonary tuberculosis (PTB) in children is challenging. Clinical diagnostic specimens are rarely obtained due to failure to collect good quality sputum. Induced sputum has been recently suggested to aid diagnosis. The procedure is not widely adopted in Kenya due to concerns for infection control and limited experience. Our main aim was to pilot and describe sputum collection by induction among children in our facilities, documenting quality of samples, safety and tolerability of the procedure.

**Design/Methods:** Children aged 2mths to 14yrs with suspected TB at Kenyatta National Hospital (tertiary level) and Mbagathi District Hospital (secondary level) whose parents consented were enrolled between March to December 2013. Children on current or recent ant-TB treatment were excluded, as well as those with severe respiratory distress unable to tolerate the procedure. Pretreatment was with nebulised salbutamol followed by hypertonic saline; thereafter sputum was removed by nasopharyngeal catheter aspiration into a mucous trap or coughed out into a sputum container. A second sputum sample was obtained within four hours.

**Results:** Median age of the 79 children enrolled was 2.2 yrs (IQR 0.9–6.3), 70.9% were  $\leq 5$  yrs; 48 (60.8%) were female; median Weight-for-Height Z (WHZ) score was  $-2.1$  SD (IQR  $-2.9$  to  $-0.6$  SD). The most common clinical presentation was fever in 58 (73.4%). A first sputum sample was successfully obtained in all 79 children, and a second sputum sample in 57 (total 136 samples), of which 20 (14.7%) were self expectorated and 95 induced sputum (69.9%) samples. Children who successfully self-expectorated without induction were older than 4.3 yrs. Of the 79 first sputum samples 70 (88.6%) were of good quality and were successfully cultured with an additional four successful cultures obtained after second sample collection yielding an

overall success rate in 74 out of 79 (93.8%) children. Reasons for poor quality samples included presence of food particles (n=2); presence of blood (n=3); or insufficient quantity (n=1). No major complications occurred during sputum induction. Minor events reported included slight nasal bleeding and coughing.

**Conclusion:** Sputum induction was feasible, safe and well tolerated among children in this high volume resource-limited public hospital setting, and provides a valuable approach to sputum collection to enhance confirmation of pulmonary tuberculosis even in young children.

#### PD-535-30 Utility of microscopic observation-direct susceptibility (MODS) sputum culture & PCR (Xpert®MTB/RIF) in detection of *M. tuberculosis* in Kenyan children

E Obimbo,<sup>1</sup> D Marangu,<sup>1</sup> P Ayieko,<sup>2</sup> J Oyugi,<sup>3</sup> J Oliwa,<sup>2</sup> D Wamalwa,<sup>1</sup> R Oberhelman.<sup>4</sup> <sup>1</sup>Paediatrics & Child Health, University of Nairobi, Nairobi, <sup>2</sup>Wellcome Trust, Kenya Medical Research Institute, Nairobi, <sup>3</sup>Medical Microbiology, University of Nairobi, Nairobi, Kenya; <sup>4</sup>Tropical Medicine, Tulane University, New Orleans, LA, USA. Fax: (+254) 20 2731970. e-mail: eobimbo@yahoo.com

**Background:** Timely diagnosis of tuberculosis (TB) in children is challenging due to similarity in clinical presentation to common childhood illnesses, and paucibacillary disease with low sensitivity of sputum microscopy and slow current *Mycobacterium tuberculosis* (MTb) culture methods. Two tests that provide rapid antigenic confirmation as well as drug susceptibility characteristics of MTb have recently been endorsed by the WHO - TB polymerase chain reaction assay (Xpert®MTB/RIF Cepheid SAS) (Xpert) and the Microscope Observation-Direct Susceptibility (MODS) culture assay, however there is minimal experience of these in African children. We piloted the use of Xpert and MODS and compared their diagnostic yield in children with suspected pulmonary TB (PTB) at two public hospitals in Nairobi.

**Methods:** Children age 2mth to 14yr with suspected PTB whose parents consented were eligible. Children on current or recent anti-TB treatment, or with severe illness (oxygen saturation <90%) unable to tolerate sputum induction were excluded. Children were assessed for contact history, suggestive TB symptoms and signs, tuberculin test, chest radiograph, and 2 sputa specimens were collected ≥4 hr apart by induction or self-expectoration (older children). Samples were evaluated using MODS Xpert, & acid-fast bacilli (AFB) microscopy.

**Results:** We enrolled 79 children, 60.8% were female, of median age 2.2 years [IQR 0.9-6.3], and 13.9% were HIV positive. All 79 children gave a 1st sputum sample, and 57 a 2nd sample. 1st sample results: 2 AFB positive (+), 5 MODS+, and 6 Xpert+; 2nd sputum revealed 2 AFB+, 2 MODS+ and 4 Xpert+. Combining all 136 sample there were 4 (2.9%) AFB+, 7 (5.1%) MODS+, and 10 (7.3%) Xpert+, with overall confirmed TB in 6 (7.5%) children. MTb growth was detected in 5 positive

MODS cultures on day 5 (n=3), day 10 (n=1) and day 11 (n=1), giving median time to detection of 5 days, and all were rifampicin & isoniazid susceptible; all Xpert+ samples were rifampicin susceptible. Overall agreement between MODS and Xpert was 96.3% (95% CI 91.6–98.8). Sensitivity and specificity of Xpert was 85.7% (42.1–99.6) and 96.9% (92.3–99.1) respectively using MODS as gold standard (table 1).

**Conclusions:** Xpert compared favorably to MODS in detection of MTb in child sputum, both provided drug susceptibility profile, and culture time to detection was short. Both assays are a valuable rapid diagnostic option for PTB confirmation in children in the African setting.

Table 1: Sputum MODS culture and TB PCR (Xpert®MTB/RIF) Results Kenyan Children

	Xpert Positive No. Children	Xpert Negative No. Children	
MODS Positive	6	1	7
MODS Negative	4	125	129
	10	126	139

#### 04. XPERT MTB/RIF: DIAGNOSIS OF PULMONARY AND EXTRAPULMONARY TB

##### PD-536-30 Results of RT-PCR examinations in the diagnosis of pulmonary and extra-pulmonary tuberculosis

T Pyanzova,<sup>1</sup> M Primkulova,<sup>1</sup> N Luzina.<sup>2</sup> <sup>1</sup>Department of Phthisiology, Kemerovo State Medical Academy, Kemerovo, <sup>2</sup>Clinical TB department, Kemerovo Regional Clinical TB dispensary, Kemerovo, Russian Federation. Fax: (+7) 3582 586925. e-mail: tatyana\_vezhnina@mail.ru

**Background:** To study the results of PCR molecular-genetic methods for detection of MBT DNA aimed at diagnostics of pulmonary and extrapulmonary TB at the level of the regional dispensary.

**Design/Methods:** The study included 656 TB patients. Isolation of MBT DNA was performed using the method of PCR diagnostics - GeneXpert MTB/RIF and TB-Biochip. In addition, pathological specimens were examined three times by fluorescent microscopy, as well as by cultures on solid media followed by the DST (absolute concentration method). Diagnostic material: sputum – 92.8%; bronchial washings – 1.6%; spinal fluid – 3.8%; urine – 0.9%; pleural, ascitic, pericardial fluids – 1.4 %; fistulous drainage – 0.4%.

**Results:** Sputum and bronchial washings were the most informative environment for identification of MBT DNA. MBT DNA was detected in 407 cases, of them positive results of bacterioscopy were reported in 264 cases (64.8%) (p<0.05) and MBT growth in media was observed in 317 cases (77.8%) (p<0.05). PCR tests allowed detection of MBT DNA in 77.4% of patients with positive cultures and in 24.2% patients with negative bacterioscopy results. In patients with negative cultures MBT DNA was detected in 18% cases (17

patients). Twenty nine PCR tests of spinal fluids by TB-Biochip method had positive results in 34.48%. PCR by GeneXpert method used for 14 patients detected DNA in 35.71% cases. At the same time, positive microscopy results of spinal fluid was reported in 1 case out of 38 (2.6%), positive MBT culture of spinal fluid was observed in 21 patients out of 33 (63.6%). Median time from the moment of MBT DNA identification by PCR to the time when the solid culture results became available was 42.7 days for positive cultures and 76.2 days for negative cultures.

**Conclusion:** The use of PCR for the diagnosis of pulmonary and especially extrapulmonary TB at the level of the regional TB dispensary allows the reduction of time needed for the verification of a diagnosis which is especially important for cases with negative smears and TB meningitis. Considering the difficulties of establishing the origin of meningitis, especially with HIV associated TB, multiple examinations of spinal fluids are required using PCR for identification of MBT DNA.

#### **PD-537-30 Culture results of presumptive drug resistant pulmonary TB patients with *Mycobacterium tuberculosis* not detected result on Xpert MTB/RIF®**

P Dave,<sup>1</sup> P Patel,<sup>2</sup> B Vadera,<sup>3</sup> B Modi,<sup>4</sup> K Rade,<sup>3</sup> S Bharaswadkar,<sup>3</sup> M Ghedia,<sup>3</sup> A Amar Shah.<sup>3</sup> <sup>1</sup>Health and Family Welfare, State TB Cell, Gandhinagar, <sup>2</sup>Health and Family Welfare, Intermediate Reference Laboratory, Ahmedabad, <sup>3</sup>RNTCP Technical Support Network, World Health Organization Country Office for India, New Delhi, <sup>4</sup>Health and Family Welfare, GMERS Medical College, Gandhinagar, India. e-mail: dpranavpatel09@gmail.com

**Background:** Xpert MTB/RIF® has been introduced in India under Revised National TB Control Programme since 2012. Currently, it is largely used for diagnosis of Drug Resistant TB (DR-TB) and offered to presumptive DR-TB patients. One major concern however remains is a result 'MTB not detected' on Xpert MTB/RIF® among these patients who are already being diagnosed as pulmonary TB either based on smear microscopy or chest X-ray and clinically. In present study, we assessed the result of culture examination of such presumptive DR-TB patients and generate scientific evidence within the programme at this early stage of implementation of the assay.

**Methods:** Under RNTCP, all presumptive DR-TB patients with MTB not detected result on Xpert MTB/RIF® are re-tested for drug susceptibility with different method. A retrospective cohort study included patients tested at four GeneXpert laboratories from August 2012 to December 2013 in state of Gujarat in India. All samples with results reported as MTB not detected on Xpert MTB/RIF assay were subjected to Liquid culture after smear microscopy. All positive culture growth underwent speciation test to differentiate MTB and Non tuberculosis Mycobacteria. Data were collected from different sources of records in a pre-structured data collection proforma. Univariate analysis was done to describe the demographic details, smear results and

culture results among Xpert MTB/RIF negative presumptive DR-TB patients.

**Results:** A total of 404 presumptive DR-TB patients declared as MTB not detected result on Xpert MTB/RIF from August 2012 to December 2013. Mean age of the study patients was 40 years with 90% patients were between age of 15–64 years. Male to female ratio was 3:1. Out of 404 patients, 94 (24%) patients had smear positive results and 104 (25.7%) patients had a positive growth on culture. Total 35 (8.7%) patients had growth of MTB complex and another 69 (17.1%) patients were detected with non-tuberculosis mycobacteria (NTM). Among smear positive patients, 21.3% (20) were detected with MTB complex and 4.8% (15) smear negative patients were detected with MTB complex on culture.

**Conclusions:** The findings of the study revealed that it is worth to re-examine smear positive Xpert negative patients for drug susceptibility with different method. Another option of re-testing of these patients again with Xpert MTB/RIF assay can be explored in decreasing delay and avoiding sending samples to another laboratory.

#### **PD-538-30 Detection of *Mycobacterium tuberculosis* from faeces sample by Xpert MTB/RIF**

S. Yoshimatsu,<sup>1</sup> H Kokutou,<sup>2</sup> Lina Yi,<sup>2,3</sup> K Mizuno,<sup>4</sup> Y Sasaki,<sup>2</sup> S Mitarai,<sup>3,5</sup> <sup>1</sup>Epidemiology & Clinical Research, Research Institute of Tuberculosis, Tokyo, <sup>2</sup>Respiratory Medicine, Fukuji Hospital, Tokyo, <sup>3</sup>Basic Mycobacteriology, Graduate School of Biomedical Science, Nagasaki University, Tokyo, <sup>4</sup>Clinical Microbiology, Fukuji Hospital, Tokyo, <sup>5</sup>Mycobacterium Reference and Research, Research Institute of Tuberculosis, Tokyo, Japan. e-mail: yoshioji@jata.or.jp

**Background:** Detection of *Mycobacterium tuberculosis* (MTB) is essential for the definite diagnosis of tuberculosis (TB), and it generally requires sputum specimen. It, however, is not easy to obtain the specimen from suspects who cannot expectorate sputum such as children, elderly and seriously ill cases. In such case, the faeces specimen occasionally helps the bacteriological diagnosis of TB. In this study, we tested Xpert MTB/RIF (Cepheid) for the detection of MTB using faeces specimen.

**Method:** This is a proof of concept study. We collected faeces specimens from the patients of definite pulmonary TB and non-TB diseases at the respiratory department of Fukuji Hospital from September 2013 to April 2014. Approximately 10 mL of distilled water was added to 2 cm<sup>3</sup> of faeces specimen, and it was homogenised by vortex mixing. The supernatant was collected after leaving 15 minutes at room temperature, and was centrifuged by 3000 × g for 20 minutes. The sediment was digested/decontaminated by adding 10mL of 3% NALC-NaOH solution. After 15 minutes at room temperature, 40 mL of phosphate buffer (PB; pH 6.8) was added, then centrifuged by 3000 × g for 20 minutes. The sediment was recovered and resuspended in 3 mL of PB. Xpert MTB/RIF was performed according to the manufacturer's instruction (for sputum specimen). Brief-



ly, 1 mL of the suspension was mixed with 2 mL of sample reagent, then incubated for 15 minutes. This mixture was transferred into a Xpert MTB/RIF cartridge, and loaded into the GeneXpert.

**Result:** We obtained 46 faeces specimens from 38 active TB cases (including 33 smear-positive and 5 smear-negative) and 8 non-TB cases including 3 *M. avium* complex infections. Thirty (78.9%) out of 38 TB cases, and 29 (87.9%) out of 33 sputum smear and culture (and/or PCR) positive cases were Xpert MTB/RIF positive from faeces specimen. One out of 5 smear-negative and culture (and/or PCR) positive cases was detected by Xpert MTB/RIF. All of non-TB cases were Xpert MTB/RIF negative. We had 4 multi-drug resistant (MDR) cases and 2 of them (50%) were detected rifampicin resistant even by Xpert MTB/RIF with faeces. Besides this, we had 3 indeterminate results for rifampicin resistance by Xpert MTB/RIF.

**Conclusion:** Xpert MTB/RIF with faeces could show high sensitivity and 100% specificity to detect pulmonary TB. We may be able to utilise faeces specimen with Xpert MTB/RIF for TB suspects from whom the sputum specimen is not readily available.

#### PD-539-30 Utility of string test and stool for diagnosing pulmonary tuberculosis using geneXpert MTB/RIF

A Dinardo,<sup>1</sup> A Hahn,<sup>1</sup> J Leyden,<sup>2</sup> E Graviss,<sup>3</sup> C Stager,<sup>4</sup> E Baron,<sup>5</sup> A Mandalakas,<sup>6</sup> E Guy.<sup>1</sup> <sup>1</sup>Internal Medicine, Baylor College of Medicine, Houston, TX, <sup>2</sup>Biotechnology, Rice University, Houston, TX, <sup>3</sup>Pathology, Houston Methodist, Houston, TX, <sup>4</sup>Pathology, Baylor College of Medicine, Houston, TX, <sup>5</sup>Pathology, Stanford Medical School, Palo Alto, CA, <sup>6</sup>Pediatrics, Baylor College of Medicine, Houston, TX, USA. e-mail: andrew.dinardo@bcm.edu

**Background:** Until recently, diagnosis of pulmonary tuberculosis (pTB), has relied on smear microscopy and culture, however microscopy is only 40–80% sensitive and diagnosis via liquid culture requires at best 7–14 days. While Xpert® MTB/RIF has significantly advanced the field of TB diagnostics, it fails to yield a diagnosis in one-third of adult and 45% of pediatric smear-negative cases. Therefore, in cases in which respiratory samples are challenging to obtain or in cases of paucibacillary disease, complementary means of obtaining specimens are needed. We therefore studied the utility and feasibility of using stool and string test with Xpert® MTB/RIF as an alternative means of diagnosis.

**Design/Methods:** From August 2013 to March 2014, we enrolled 13 adult patients with suspected pTB having received <72 hours of anti-tuberculosis therapy (ATT). String test was performed as previously described: the capsule was swallowed and the trailing end taped to the cheek until it was removed 4 hours later by gentle traction. Stool was processed by two low-technology (not requiring centrifugation) methods, one using sugar flotation and the other using TB MicroSense Beads® (Microsense Medtech, London, UK).

**Results:** Thirteen patients with suspected pTB were enrolled with 8 having microbiologically-confirmed

pTB including 2 with smear-negative pTB. The string test was well tolerated with a median, and mean, Wong Baker score of 2. The Xpert® MTB/RIF from the string test was positive in all 8 cases of microbiologically confirmed pTB including both cases smear-negative pTB. Stool was collected in 10 of 13 participants before 72 hours of ATT. Using both stool methods, Xpert® MTB/RIF detected 7 of 7 cases, however 30% of stool specimens were read as invalid. The sugar method detected 3 of 7 cases of pTB compared to 5 of 7 by MicroSense beads. Specificity of Xpert® MTB/RIF was 100% for both the string test and both stool methods including 2 cases of Non-tuberculous Mycobacteria.

**Conclusion:** This pilot study highlights the potential utility of Xpert® MTB/RIF on specimens obtained from string test and stool. The string test had 100% concordance with sputum microbiologically confirmed pTB and does not require electricity or a trained respiratory therapist, making it an attractive means of obtaining respiratory specimens in resource-limited settings. With improved methods to remove the fibrous material from stool, this also has the potential to be a non-invasive means of pTB diagnosis.

Sputum Smear Status	Sputum Culture	Sputum Xpert®	String Xpert®	Micro-Sense Bead Xpert®	Sugar Xpert®	Wong Baker Face
<b>Mtb CULTURE POSITIVE, SMEAR POSITIVE</b>						
2–4+	Mtb	Positive	Positive	Positive	Positive	1
4+	Mtb	Positive	Positive	Positive	Invalid	6
1+	Mtb	Positive	Positive	Negative	Positive	2
3+	Mtb	Positive	Positive	Positive	Invalid	2
3+	Mtb	Positive	Positive	Positive	Positive	2
1+	Mtb	Positive	Positive	Positive	Positive	2
<b>Mtb CULTURE POSITIVE, SMEAR NEGATIVE</b>						
Negative	Mtb	Positive	Positive	Unable to produce		4
Negative	Mtb	Positive	Positive	Positive	Invalid	0
<b>MTB CULTURE NEGATIVE</b>						
1+	<i>M. avium</i>	Negative	Negative	Negative	Invalid	1
3+	<i>M. kansasii</i>	Negative	Negative	Negative	Negative	2
Negative	Negative	Unable to produce	Negative	Unable to produce		2
Negative	Negative	Negative	Negative	Unable to produce		0
Negative	Negative	Negative	Negative	Invalid	Invalid	2

#### PD-540-30 The role of loop-mediated isothermal amplification (TB-LAMP) and Xpert MTB/RIF for the diagnosis of pleural tuberculosis

Mulu Getahun,<sup>1</sup> Y Fisiha,<sup>1</sup> A Kebede,<sup>1</sup> T Gebeyehu,<sup>1</sup> Z Dagne,<sup>1</sup> A Abebe,<sup>1</sup> S Mitarai,<sup>2</sup> E Lemma.<sup>1</sup> <sup>1</sup>TB, Ethiopian Public Health Institute, Addis Ababa, Ethiopia; <sup>2</sup>Bacteriology, Research Institute of Tuberculosis, Tokyo, Japan. e-mail: mimishaget@yahoo.com

**Background:** TB pleurisy remains a diagnostic challenge. Diagnosis of TB pleurisy is usually accomplished with several laboratory methods. Most high TB incidence regions have limited financial resources and lack the infrastructure needed for sensitive detection methods. Thus, cost-effective diagnostic approach is important.

**Design/Methods:** A cross sectional study was conducted in TB pleurisy suspects referred to six health facilities. On the collected samples detection of *M. tuberculosis* using iLED microscopy, TB-LAMP, Xpert MTB/Rif, white cells and differential count, protein and cholesterol measurement was performed. Mycobacteria culture was done for reference using MGIT and L-J. Sensitivity and specificity was determined for smear and molecular detection methods.

**Results and Discussion:** Among 124 suspects, 26 were culture positive. Of this 25 were by MGIT whereas 8 were by L-J. There was no smear positive. Sensitivity and Specificity of TB-LAMP and Xpert MTB/Rif were compared to MGIT and L-J. Sensitivity and Specificity of TB-LAMP compared to MGIT was 52% and 81.6%, while 50 % and 76.5% when compared to L-J. The sensitivity TB-LAMP is higher than in previous study. The variation may be due to the reference method difference. Whereas, the specificity of TB-LAMP was lower than previous study. This could be due to cross contamination, reading bias or patient was on treatment. Sensitivity and Specificity of Xpert MTB/Rif compared to MGIT were 12.5% and 97.9%, while 25% and 97.3% when compared to L-J. We found that LJ more sensitive but less specific compare MGIT in molecular detection. This was due to sensitivity of MGIT. Seventeen cases were isolated using MGIT only.

**Conclusion:** TB-LAMP and Xpert MTB/Rif improved the sensitivity as compare to iLED. Xpert MTB/Rif were better in specificity.

#### **PD-541-30 Use of a connectivity solution (GxAlert) in GeneXpert machines improves DR-TB data collection and patient management in Nigeria**

K Jimoh,<sup>1,2,3</sup> J Takle,<sup>1,2</sup> L Ekblad,<sup>1,2</sup> J O Obasanya,<sup>3</sup> C Macek,<sup>4</sup> O Adeleke.<sup>1,2</sup> <sup>1</sup>International Health Division, Abt Associates, FCT Abuja, Nigeria; <sup>2</sup>International Health Division, Abt Associates, Cambridge, MA, USA; <sup>3</sup>Public Health, National TB and Leprosy Training Centre, FCT Abuja, Nigeria; <sup>4</sup>Client Technology, SystemOne, Cambridge, MA, USA. e-mail: kehindeagbaiyero@yahoo.com

**Background and Challenges** The WHO ranks Nigeria 10<sup>th</sup> among 22 high TB burden counties in the world. Nigerian Tuberculosis and Leprosy Control Program (NTBLCP) pursued the use of cost-effective technologies to improve healthcare responses to DR-TB management. The project focused initially in 8 GeneXpert laboratories and eventually scaled national to all 49 GeneXpert sites across the country. Due to its success in improving data system and patient management, NTP decided to scale up to all facilities in the country.

**Intervention:** Abt Associates-led, initiated and developed a highly innovative mobile-based solution across 8 pilot laboratories in Nigeria. GxAlert is configured on GeneXpert systems by installing a modem from a telecom that gives access to internet and encrypting the data sent to the GxAlert database. The system sends GeneXpert MTB/RIF diagnostic results in real time to a secure web-based database, shortening a reporting period from

months to mere seconds and enabling better data quality and faster recruitment of patients into appropriate care.

**Results and Lesson Learnt:** In Federal Capital Territory, the proportion of DR-Tb patients enrolled for treatment jumped to 80% in January 2014 from 35% in March 2012. Real-time data are uploaded automatically from GeneXpert systems to improve national level policy-making. SMS alerts are sent to Facility Manager, LGA supervisor and State program manager upon MTB+ Rif+ case to speed recruitment, and patient management. Weekly reports of all new TB+ cases are emailed to local health officials to ensure better connection between diagnosis and treatment. Faster, better quality data on MDR-TB portion of total TB indicators are now reported with very minimal error or effort.

**Conclusions and Key Recommendations:** The use of GxAlert in genexpert machines has a Model for Sustainability - training and installation is done locally in-country. The technology is kept simple as local telecom modems which are readily available and affordable for GxAlert connectivity. GxAlert eliminated the need for human error in data entry, reduced the lag time, and helped pinpoint patients that should be place on care. The GxAlert strengthened surveillance of DR-TB, TB in children and TB in the HIV infected, speeding response and improving programmatic decision making for enrollment and placement of DR-TB patient on treatment. Based on the experience from the result, a national rollout of the approach is recommended.

#### **PD-542-30 Assessment of bacterial load quantitation by Xpert®MTB/RIF to predict the smear microscopy grade of TB patients: a rural lab network in Swaziland**

G Obregon Boltan,<sup>1</sup> B Kerschberger,<sup>1</sup> A Antierens,<sup>1</sup> R Dela Tour.<sup>1</sup> <sup>1</sup>Operational Centre, Médecins Sans Frontières, Geneva, Switzerland. e-mail: flankan.damagon@gmail.com

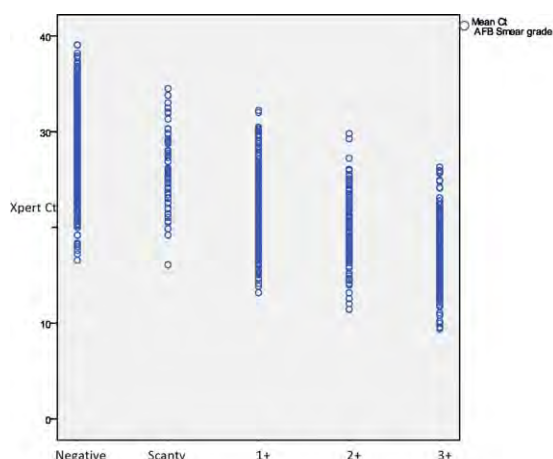
**Background:** *Mycobacterium tuberculosis* load in a biological specimen has been used to determine disease severity and disease transmission risk. In Swaziland, the Xpert®MTB/RIF replaced the smear microscopy in accordance with the recommendation of the World Health Organization. We calculated the threshold-cycle (Ct) -provided by Xpert®MTB/RIF- that best predicted smear-positive status.

**Design/Methods:** 1,072 sputum samples were processed by fluorescent smear microscopy, Xpert®MTB/RIF and culture in routine laboratory conditions at 3 health facilities in the rural Shiselweni region (Swaziland), from August 2011 to December 2012. An internal control real-time polymerase chain reaction was evaluated for Xpert®MTB/RIF results. Correlation between Ct and smear microscopy grade was determined by Spearman rank correlation coefficient. A received operating curve (ROC) was generated. Sensitivity and specificity of a Ct cutoff was computed to define smear positivity for the range of possible Ct values.

**Results:** 6.3% (n=67) of *Mycobacterium tuberculosis* tests with an internal control greater than 34 were

excluded. An inverse relationship between decreasing Ct and smear microscopy grade ( $r_s = -0.75$ ) was detected. The Ct cutoff of 29.4 predicted smear-positive status with 98% sensitivity and 46.3% specificity.

**Conclusion:** Mycobacterial quantitation of Xpert®MTB/RIF offers a standardized approach to measuring *Mycobacterium tuberculosis* load in the sputum of the patients with tuberculosis. Ct cutoff level permits to correctly predict smear-positive status. This may help clinicians to assess transmission risk in the community.



**Figure.** Xpert® quantitation compared with smear microscopy grade. Only tests with an internal control Ct less than 34 are included. Inverse relationship between increasing smear microscopy grade and Ct value is found ( $r_s = -0.75$ )

#### PD-543-30 Remote calibration: experience from GeneXpert implementation in Malawi

A Omer,<sup>1</sup> S Dalebout,<sup>2</sup> Stev Neri,<sup>3</sup> B Gadama,<sup>1</sup> M Mkata,<sup>1</sup> A Mwanyimbo,<sup>1</sup> R Nalikulungwi,<sup>1</sup> A Trusov.<sup>2</sup> <sup>1</sup>TB, Project HOPE Malawi, Blantyre, Malawi; <sup>2</sup>Global Health, Project HOPE, Millwood, VA, USA; <sup>3</sup>Regional HQ, Project HOPE Namibia, Windhoek, Namibia. Fax: (+265) 1466247. e-mail: aomer@projecthope.org

**Background and challenges to implementation:** Project HOPE in collaboration with NTP implemented the TB REACH project in Malawi to improve TB case detection using the GeneXpert platform.

**Intervention or response:** During Q4 2011, 8 Xpert machines (4 modules) were installed in 8 sites in 6 districts. The first remote calibration was performed on all machines in April 2013, the second calibration one year later. Both used Cepheid's remote calibration kits. With a \$450 cost for each remote calibration kit and \$14,400 for module replacement, the project spent for the two calibration rounds a total of \$21,600 which is \$6,300 less than what would have been spent if calibration was done using the swapping method (at the end of one year, Cepheid, the manufacturer, ships replacement modules to customers and the customer does the replacement of the used module with the new one and ships back the used modules). The failure rate was much higher than the manufacturer's expected 5–10%. In the first year we considered different factors for failure

including delays in the calibration process itself, frequent power interruption, high lab room temperatures and high volume of tests. Although some of these issues were addressed, the failure rate was higher in year 2. When excluding the site with the 6 failures in the calculations, the overall performance improved from 64.7% for year 1 to 75% in year 2, but remained below the target.

**Results and lessons learnt:** In the first year of calibration, 8 abnormal modules were excluded and 24 modules were calibrated, of which 15 (62.5%) passed and 9 (37.5%) failed. These failed modules were re-calibrated, of which one passed. In year 2 calibration, 6 were excluded (3 abnormal and 3 recent replacements) and 26 modules were calibrated, of which 15 (57.7%) passed and 11 (42.3%) failed. Six of these failed modules came from one site with two machines. All failed modules were also re-calibrated, of which none passed. In the first year 17 modules (8 abnormal and 9 failures) were replaced, for a total of \$8,100. In the second year 13 modules (2 abnormal and 11 failures) were replaced for a total of \$6,300.

**Conclusions and key recommendations:** Despite our relative high calibration failure rate, remote calibration was a less expensive approach compared with the swapping method, although the issue of failure needs to be addressed. Re-trying calibration on failed modules does not add to the success and may lead to shortages of XpertCal cartridges.

#### PD-544-30 Evaluation of cost-effectiveness of MODS vs GeneXpert MTB/RIF for the diagnosis of pulmonary TB in an African setting

P Wikman Jorgensen,<sup>1</sup> J Llenas-Garcia,<sup>2</sup> T Perez-Porcuna,<sup>1</sup> A Morales-Cartagena,<sup>3</sup> M Hobbins,<sup>4</sup> R Abellana,<sup>1</sup> A Mussa,<sup>5</sup> C Ascaso.<sup>1</sup> <sup>1</sup>Salut Pública, Universitat de Barcelona, Barcelona, Spain; <sup>2</sup>SMART, SolidarMed Mozambique, Ancuabe, Mozambique; <sup>3</sup>Internal Medicine, Hospital 12 de Octubre, Madrid, Spain; <sup>4</sup>SolidarMed Switzerland, SolidarMed, Luzerne, Switzerland; <sup>5</sup>Operational Research Nucleus of Pemba, Provincial Health Directorate, Pemba, Mozambique. Fax: (+34) 622038430. e-mail: wikman.philip@gmail.com

**Background:** Globally, only 66% of the estimated TB cases are diagnosed, mainly due to poor diagnostic means in low income countries (LIC) based on smear microscopy. Microscopic Observation Drug Susceptibility Assay (MODS) could be a valuable technique for the diagnosis of TB, using microscopic observation of TB micro-colonies in liquid culture media with concomitant drug susceptibility testing. WHO has recommended the roll-out of GeneXpert MTB/rif. Nevertheless, other techniques like MODS could also be considered an alternative for LIC. We aimed to compare cost-effectiveness of MODS and GeneXpert for the diagnosis of TB in a rural district of a LIC.

**Methods:** A health provider perspective was used for the evaluation. Cost estimates were obtained using a micro-costing approach. Effectiveness was evaluated using a life-table method and the Hazard Ratio of each techniques was calculated through a simplified model of the disease. Input parameters were obtained from the



literature. A yearly 3% discount rate was used. One way sensitivity analysis was carried out for key parameters, as well as a probabilistic sensitivity analysis using a Monte-Carlo simulation. The evaluation period considered was over a life-time of 90 years.

**Results:** We found that MODS would have the potential to save a total of 10,076.49 life-years at a cost of 2,119,328.98 2013 USD (210.32 USD per life-year gained, LYG). The installation of a GeneXpert module would have the potential to save a total of 8,345.10 life-years at a cost of 1,767,638.43 2013 USD (211.81 USD per LYG). According to this input data and assumptions GeneXpert would have an ICER of 104.47 when compared to the base case of smear microscopy. MODS would have an ICER of 203.12 compared to GeneXpert. When the probabilistic sensitivity analysis was carried out the overlap of the ICER clouds was big.

**Conclusion:** Both MODS and GeneXpert are cost-effective techniques when compared to the base case of smear microscopy. With the assumptions made in this evaluation and with the data introduced, we would conclude that although GeneXpert seemed to be more cost-effective, we were not able to conclude that any technique dominated the other. Thus, both techniques could be considered for implementation in LIC.

#### PD-545-30 A pragmatic randomised trial to assess impact of LPA versus Xpert MTB/RIF versus MGIT in Brazil

A Kritski,<sup>1</sup> M De Oliveira,<sup>2</sup> D Ramalho,<sup>1</sup> I Langley,<sup>3</sup> P Philips,<sup>4</sup> A Detjen,<sup>5</sup> P Fujiwara,<sup>6</sup> S Squire.<sup>3</sup> <sup>1</sup>Academic Tuberculosis Program, Medical School, Universidade Federal do Rio de Janeiro, Rio de Janeiro, RJ, <sup>2</sup>Innovation Coordination Area, Brazilian Tuberculosis Research Network - Rede TB, Rio de Janeiro, RJ, Brazil; <sup>3</sup>Centre for Applied Health Research & Delivery (CAHRD), Liverpool School of Tropical Medicine, Liverpool, <sup>4</sup>Institute of Clinical Trials & Methodology, MRC Clinical Trials Unit at UCL, London, UK; <sup>5</sup>The Union North America Office, International Union Against Tuberculosis, New York, NY, USA; <sup>6</sup>Department of Aids, International Union Against Tuberculosis and Lung Disease, Paris, France. e-mail: kritskia@gmail.com

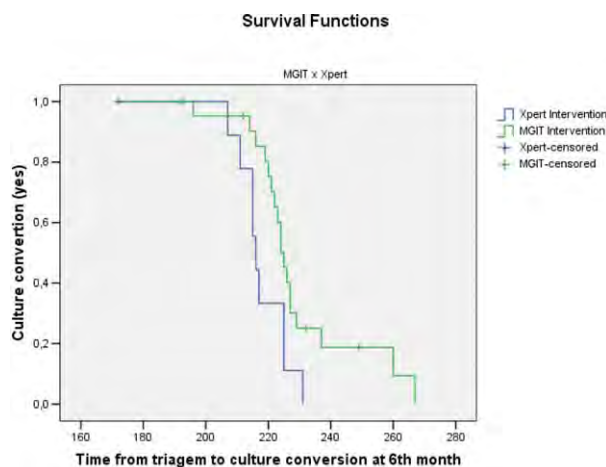
**Background.** MGIT960 (MGIT), MTBDRplus assay (LPA) and Xpert MTB/RIF (Xpert) have been recommended by the WHO for use as the initial diagnostic test in MDR-TB suspects. However, there are few evaluations of the effectiveness of these tests on clinical outcomes.

**Methods:** A pragmatic, cluster-randomised, cross-over trial was carried out in 5 sites across Brazil. Participants in the trial were 18 years of age or older and were drug resistant TB (DR-TB) suspects. The trial consisted of Arm 1 (Xpert vs MGIT) and Arm 2 (LPA vs MGIT) for the laboratory diagnosis of DR/MDR-TB. **Outcomes:** a) the time to initiation of appropriate DR/MDR therapy and, b) culture conversion for DR/MDR patients at 2 and 6 months after 1st evaluation at reference center (RC).

**Results:** Between Feb 2011 to May 2013, 1535 DR-TB suspects were referred by primary and secondary health centers (HCs). Drug susceptibility tests were performed in 808 (52.3%). Among them, 161 (19.9%) were

confirmed as DR-TB and enrolled in the study (Arm 1: MGIT-44 vs Xpert-20, and Arm 2: MGIT-57 vs LPA-40). At triage, in both arms, specialists adopted TB treatment in ~90% of cases at the first evaluation before the MGIT results, and 44% and 61% before Xpert and LPA results respectively. Patients started appropriate TB treatment more rapidly when Xpert was used compared to MGIT [15 days (4.5–38.5) vs 40.5 days (31.5–68.5);  $p=0.02$ ]. No statistically significant difference was detected between LPA and MGIT groups [36 days (18.3–97.0) vs 55 days (8.5–79.50);  $p=0.87$ ]. Culture conversion at 2nd month was similar in both arms; Arm 1 (Xpert – 9 (64%)/14 and MGIT – 12 (43%)/28;  $p=0.30$ ) and Arm 2 (LPA – 27 (48%)/56 and MGIT – 14 (44%)/32;  $p=0.15$ ). At 6<sup>th</sup> month, higher culture conversion was observed in Arm 1, with Xpert (9/10) compared to MGIT (18/23) ( $p=0.03$ ). No difference was found in Arm 2 (LPA 24/30 and with MGIT 19/23,  $p=0.119$ ). No other important differences were observed in other outcomes.

**Conclusion –** At Triage, specialists tend to wait for the molecular test results before starting any DR-TB treatment more often than for MGIT. Despite this, the time to appropriate DR/MDR TB treatment initiation was significantly shorter for Xpert compared to MGIT but no significant difference was detected for LPA compared to MGIT. Culture conversion at 6<sup>th</sup> months was significantly higher for Xpert compared to MGIT but no significant difference was detected in the comparison of LPA and MGIT.



#### PD-546-30 Confirmation of Xpert-detected rifampicin resistance adds unnecessary complexity to treatment decisions

N Lorent,<sup>1,2</sup> C Kong,<sup>2</sup> T Kim,<sup>3</sup> W De Rijk,<sup>4</sup> S Thai,<sup>2</sup> L Rigouts.<sup>4</sup> <sup>1</sup>Clinical Sciences, Institute of Tropical Medicine, Antwerp, Belgium; <sup>2</sup>Infectious Diseases, Sihanouk Hospital Center of HOPE, Phnom Penh, <sup>3</sup>Mycobacteriology laboratory, Sihanouk Hospital Center of HOPE, Phnom Penh, Cambodia; <sup>4</sup>Mycobacteriology Unit, Institute of Tropical Medicine, Antwerp, Belgium. e-mail: natalielorent@yahoo.com

**Background:** Until recently WHO recommended, in settings with low MDR-TB prevalence, confirmation of rifampicin (RMP) resistance by an alternative – ideally

rapid – drug susceptibility test (DST). Besides Xpert MTB-RIF, the line probe assay (LPA) is the only other rapid WHO-endorsed DST. We report the field experience on LPA-confirmation of RMP-resistance detected by Xpert among MDR-TB suspects in Cambodia.

Table 1. Overview of the diagnostic test results (Xpert MTB/RIF assay, line probe assay MTBDR<sub>plus</sub>, phenotypic drug susceptibility testing, DNA sequencing of *rpoB* gene) for detection of rifampicin resistance among multidrug-resistant tuberculosis suspects, and subsequent referral for second-line tuberculosis treatment.

	Phenotypic DST	<i>rpoB</i> -gene sequencing	Second- line TB treat- ment referral, n
<b>MDR-TB</b>			
suspects, n	293		
Xpert MTB+/RIF+, n	40		39 <sup>c</sup>
<b>MTBDR<sub>plus</sub></b>			
done	36		
Concordant LPA (RIF+)	26		26
	RMP-resistance	18 <i>rpoB</i> -mutation <sup>a</sup>	15
		pending	3
	no RMP-resistance	2 511Pro-&508Ser	1
		pending	1
	pending not done (cult negative)	1 -	
		5 -	
Discordant LPA (RIF-)	6		6 <sup>d</sup>
	RMP-resistance not done (cult negative)	3 <i>rpoB</i> -mutation <sup>b</sup>	3
		3 -	
Invalid LPA	4		3 <sup>e</sup>
	RMP-resistance	1 531Leu	1
	no RMP-resistance	1 wild type	1
	not done (cult negative)	2 -	
<b>MTBDR<sub>plus</sub></b>			
not done	4		4
	RMP-resistance	1 pending	1
	pending	2 pending	1
		526Tyr	1
	not done	1 -	

DST denotes drug susceptibility testing, MDR-TB: multidrug-resistant tuberculosis, RMP: rifampicin.

<sup>a</sup> *rpoB*-sequencing revealed the following mutations: 531Leu (n=6), 516Tyr (n=4), 526Tyr (n=3), 531Gln (n=1), 516Tyr&511Arg (n=1)

<sup>b</sup> *rpoB*-sequencing revealed the following mutations: 526Arg (n=1), 526Leu (n=1), 533Pro&562Ala (n=1)

<sup>c</sup> All but one patient were referred for second line TB regimen (SLD). Four patients, on whom we did no longer perform LPA because it was no longer valid in our setting, were referred based on Xpert results and clinical assessment.

<sup>d</sup> One patient refused referral to an MDR-TB treatment centre.

<sup>e</sup> We withheld SLDs in one patient with discordant Xpert/LPA result for she was clinically considered low risk. Following the *rpoB*-sequencing results, we discontinued SLDs in one patient with a wild type *Mycobacterium tuberculosis* strain. Repeat Xpert in this case was also negative.

**Methods:** Prospective data collection between 2/2012 –3/2014 at tertiary level. MDR-TB suspects – defined as

retreatments, smear non-converters at month 2/3, known MDR-TB contacts or new TB/HIV-infected – were screened with Xpert. If Xpert detected RMP-resistance, a confirmatory LPA MTBDR<sub>plus</sub> (v2) test was performed on sputum. All patients had a single phenotypic culture (Löwenstein-Jensen) and - if growth -DST (proportion method) performed. Treatment decision was based on clinical risk assessment and rapid molecular results while pending phenotypic DST. Second-line (SLD) TB treatment (at least 18 months) was standardised. For all Xpert(RIF+), sequencing of the *rpoB* gene was performed.

**Results:** Xpert detected RMP-resistance in 40/293 (13,7%) MDR-TB suspects (26 retreatments, 6 non-converters, 5 HIV-infected, 3 MDR-TB contacts). The MTBDR<sub>plus</sub> assay, done on 36/40, confirmed RMP-resistance in 26/36 (72,2%), but did not detect any *rpoB*-mutation in 6/36 (16,7%) and was invalid in 4/36 (11,1%). All but one patient with RMP-resistance detected by Xpert was referred for SLD, regardless of LPA results, and within a similar time frame: median of 6 and 7 days for cases with con/discordant RMP-results. Subsequent phenotypic DST confirmed RMP-resistance in 3/6 patients with discordant Xpert(RIF+) /LPA(RIF) results and 1/4 patients with Xpert (RIF+) /LPA (invalid). Among the latter, *rpoB*-sequencing also revealed one wild type M.TB strain. Overall, the positive predictive value (PPV) of Xpert was 92,6% (25/27), whereas the PPV of MTBDR<sub>plus</sub> was 73,1% (19/26) when considering RMP-resistance on either phenotypic DST or *rpoB*-sequencing as the gold standard.

**Conclusion:** Our findings confirm previous reports that LPA for rapid confirmation of RMP-resistance is no longer a valid option. In high risk patients, all Xpert (RIF+) cases should be referred for SLD, pending DST.

### PD-547-30 Contribution of Xpert® MTB/RIF real-time PCR in the diagnosis extrapulmonary tuberculosis

F Doucet-Populaire,<sup>1</sup> C Guillet Caruba,<sup>1</sup>

N. Bourgeois-Nicolaos,<sup>1</sup> A. Vessieres,<sup>2</sup> F. Jaureguy,<sup>2</sup>

C. Theis,<sup>1</sup> B. Picard.<sup>2</sup> <sup>1</sup>Service de Bactériologie-Hygiène, APHP Hôpital Beclere, Université Paris SUD, Clamart,

<sup>2</sup>Service de Bactériologie-Virologie-Hygiène, APHP hôpital Avicenne, Bobigny, France.

e-mail: florence.doucet-populaire@abc.aphp.fr

**Background:** Diagnosis of extrapulmonary tuberculosis (EPTB) can be baffling, with a high index of clinical suspicion but a paucibacillary load in specimens. Xpert®MTB/RIF (Cepheid) is a real-time PCR assay which simultaneously detects within 2 hours the presence of *M. tuberculosis* and rifampicin resistance. We performed a prospective study in 2 university hospitals located near Paris to assess the performance of the XpertMTB/RIF in diagnosing EPTB in a low incidence setting.

**Design/Methods:** 132 Consecutive patients with high suspicion of EPTB were included. The results of the XpertMTB/RIF were correlated with those of the

mycobacterial culture in the same specimen and in other clinical specimens from the same patient. Samples deemed non sterile were decontaminated with standard NALC NaOH procedure then were inoculated into MGIT liquid medium (BACTEC) and Lowenstein-Jensen medium and used for the PCR assay.

**Results:** Among the 132 extrapulmonary specimens: 33 (25 %) grew with *M. tuberculosis* on solid or liquid medium taking a median time of 24 days. Of these, 33 (100%) were identified as positive by Xpert MTB/RIF. AFB smear results were negative in 14 cases (42 %). One specimen grew with *M. intracellulare* and was negative by the Xpert MTB/RIF assay. For the 98 culture-negative samples, the Xpert MTB/RIF yielded 4 positive-PCR results. *M. tuberculosis* was identified in other specimens for these 4 patients. The 37 positive-PCR specimens included 14 biopsies (12 lymph nodes, 2 lungs), 7 purulent exudates, 12 gastric aspirates, 1 urine, 1 bone marrow, 1 articular fluid and 1 pleural fluid. Sensitivity and specificity were 100 % and 96 % respectively using mycobacterial culture of the same sample as a gold standard. However, the positive predictive value and the negative predictive value were 100 % using the detection of *M. tuberculosis* by culture in other specimens from the same patient. Two rifampicin-resistant strains were detected; the results of the Xpert MTB/RIF were confirmed by the MTBDRplus (Hain) assay and the VersaTREK susceptibility testing.

**Conclusion:** Although the role of culture remains central in the microbiological diagnosis of EPTB, the sensitivity of Xpert MTB/RIF assay in rapidly diagnosing the disease makes it a much better choice compared to smear microscopy. In our prospective study, the Xpert<sup>®</sup> MTB/RIF assay allows to confirm or invalidate 100% of the diagnosis of EPTB.

## 05. GENE POLYMORPHISMS AND IMMUNOLOGY

### PD-548-30 Vitamin D receptor (FOK I) gene polymorphism in pulmonary tuberculosis patients at Mulago hospital

E Acen,<sup>1</sup> J Erume,<sup>2</sup> W O Worodria.<sup>3</sup> <sup>1</sup> Physiology, Makerere University, Kampala, <sup>2</sup> Bio molecular Resources and Bio laboratory Sciences, Makerere University, Kampala, <sup>3</sup> Internal Medicine, Mulago Hospital, Kampala, Uganda.  
e-mail: mulamester@yahoo.com

**Background:** *Mycobacterium tuberculosis* (TB) still presents as a serious problem globally especially in Africa. However only 1 in 10 individuals infected with the disease may become sick with active TB possibly due to host-genetic and environmental factors. The vitamin D metabolic pathway has important genetic variations which may affect its bioavailability yet according to studies there is a link between vitamin D status and TB. Although several studies have extensively examined *fok I* VDR and susceptibility to TB in different populations' findings have been inconclusive. This study investigated

the relationship between VDR *fok I* gene polymorphism and susceptibility to pulmonary TB. State study objectives, study question or a description of the challenge addressed by the research.

**Design/Methods:** An analytical cross sectional study was done in 41 newly diagnosed smear positive TB patients and 41 non TB healthy workers at the hospital who were enrolled by consecutive sampling between April and June 2013 at Mulago National Referral Hospital with a 1500 bed capacity located north Kampala, Uganda. Genotyping was by Polymerase chain Reaction (PCR) - direct sequencing method using the ABI sequencer. Categorical variables were summarized into frequencies and percentages. Pearson's Chi squared test was used to determine potential deviation from Hardy Weinberg equilibrium and alpha of  $p < 0.05$  was considered significant. State the setting, methods, desired outcomes, procedures and techniques used to collect and analyse information. Include a description of participants, procedures, measures and appropriate statistical analyses.

**Results:** The frequency distribution of *fok I* genotype in TB patients was 87.8% homozygous-dominant (FF)  $n = 36$ , 7.3% (Ff) heterozygous  $n = 3$  and 4.8% (ff) homozygous recessive  $n = 2$  (and normal healthy subjects, (FF) 38 (92.6%), (Ff) 1 (2.4%) and (ff) 2 (4.8%). No significant difference was observed in the genotype and allele distribution of *fok I* among TB patients and normal healthy subjects. A significant difference was observed in the *fok I* genotype among gender  $p$  value 0.02. No significant difference observed in ethnicity,  $p$  value 0.30. Present specific findings to date.

**Conclusion:** The frequency distribution of *fok I* gene in the Ugandan TB HIV and non HIV patients is not significantly different from that in normal healthy subjects. There is no association between vitamin D receptor *fok I* gene polymorphism and susceptibility to TB disease in the Ugandan population. Studies need to examine other vitamin D receptor polymorphic variants and susceptibility to TB. State the implications of the results and key recommendations. Present specific findings on how the research addressed the study, question and challenge. Highlight opportunities for future research as well as implications for further research or TB prevention and control programmes.

### PD-549-30 Influence of gene polymorphism (IL-2 and IL-4) and cytokines in patients with recurrent pulmonary tuberculosis on standard chemotherapy

D Butov,<sup>1</sup> M Kuzhko,<sup>2</sup> A Stepanenko,<sup>1</sup> T Butova.<sup>3</sup>  
<sup>1</sup> Phthisiatry and Pulmonology, Kharkiv National Medical University, Kharkiv, <sup>2</sup> Phthisiopulmonology, National Institute of Phthisiology and Pulmonology "F.G. Yanovskyi NAMS" of Ukraine, Kharkiv, <sup>3</sup> Internal medicine, Kharkiv National Medical University, Kharkiv, Ukraine.  
e-mail: dddimad@yandex.ru

**Background and objective:** To study the influence of gene polymorphism (IL-2 and IL-4) and cytokines in patients with recurrent pulmonary tuberculosis (RPTB) on standard chemotherapy.



**Methods:** The study comprised 130 individuals in Kharkiv region of Ukraine including 100 patients RPTB (group 1) and 30 healthy donors (group 2). Serum levels of cytokines IL-2 and IL-4 were evaluated by ELISA. Measurements on serum samples of patients were conducted prior or during first days after admission to the hospital and after 2 months on standard anti-mycobacterial therapy. Investigations of gene polymorphisms of these cytokines were performed using restriction analysis of the amplification products of specific regions of the genome. Two polymorphic variants were examined: T-330G region of IL-2 gene and promoter region C-589T of IL-4. All patients received standard TB drugs: Isoniazid (0.3 g) ; Rifampicin (0.6 g) ; Pyrazinamide (2 g) ; Ethambutol (1.2 g) and/or Streptomycin (1 g).

**Results:** In the 1<sup>st</sup> group the levels of IL-4 and IL-2 were  $9.55 \pm 0.24$  pg/L and  $39.44 \pm 0.71$  pg/L, while in 2<sup>nd</sup> group these values were  $29.99 \pm 1.27$  pg/L and  $21.60 \pm 0.80$  pg/L respectively ( $p < 0.05$ ). Among patients with RPTB the heterozygous genotype was most prevalent; 74% (N=74) for IL-2 and 61% (N=61) for IL-4. The homozygous genotype was accordingly less common: 26% (N=26) and 39% (N=39), of which 18% (N=18) and 21% (N=21) of patients had mutation and remaining had normal homozygote genotype, i.e., 8% (N=8) and 18% (N=18) for IL-2 and IL-4 respectively. In contrast, most of healthy donors had normal homozygous genotype with 60% (N=18) and 56.66% (N=17) with low frequency of mutations; 16.66% (N=5) and 23.34% (N=7) and heterozygous genotype 23.34% (N=7) and 20% (N=6) for IL-2 and IL-4 genes respectively. Following a 2 month treatment, there was a significant reduction of cytokine levels in the IL2 ( $29.59 \pm 0.55$ ) pg/L and increased in the IL4 ( $16.68 \pm 0.44$ ) pg/L, when compared to the beginning of therapy and after 2 months ( $p < 0.001$ ).

**Conclusion:** Compared to healthy controls patients with RPTB had significantly lower levels of serum IL-4 and high - IL-2. This coincided with greater frequency of heterozygous polymorphism C-589T and T-330G genes of IL-4 and IL-2. Further studies are warranted whether higher rate of recurrent TB has a causal immunogenetic relationship to allelic polymorphism of genes encoding for IL-2 and IL-4. Standard 2-month TB therapy results in reversal of inflammation characterized by decrease in IL-2 and increase of IL-4 to the levels comparable to healthy donors. IL-4 and IL-2 are immune correlates of treatment outcome and can help to identify better strategy for TB management. TB chemotherapy may have immunomodulatory effect of anti-inflammatory nature.

### PD-550-30 Associations between human leukocyte antigen class I variants and the *Mycobacterium tuberculosis* subtypes causing disease

M Salie,<sup>1</sup> L Van Der Merwe,<sup>2</sup> M Moller,<sup>1</sup> P Van Helden,<sup>1</sup> X Gao,<sup>3</sup> R M Warren,<sup>1</sup> M Carrington,<sup>3</sup> E Hoal Phd.<sup>1</sup> <sup>1</sup>MRC Centre for Tuberculosis Research and the DST/NRF Centre of Excellence for Biomedical TB Research, Division of Molecular Biology and Human Genetics, Stellenbosch University, Tygerberg, <sup>2</sup>Department of Statistics, University of Western Cape, Bellville, South Africa; <sup>3</sup>Cancer and Inflammation Program, Frederick National Laboratory for Cancer Research, Frederick, MD, USA. e-mail: egvh@sun.ac.za

**Background:** Interactions between the human host and the genotype of the infecting bacterial strain can influence disease outcome. Some studies have indicated the adaptation of *M. tuberculosis* strains to specific human populations, in terms of geographical occurrence. We investigate the role of the human leukocyte antigen (HLA) class I genes in the response to infection.

**Design/Methods:** Direct sequencing was used to type 300 South African tuberculosis patients for their HLA class I alleles. The genotype of the infecting *Mycobacterium tuberculosis* strain was determined by IS6110 restriction fragment length polymorphism genotyping and spoligo-typing.

**Results:** The HLA-B27 allele lowered the odds of having an additional episode of TB (odds ratio, 0.21;  $P = 0.006$ ). In individuals with multiple disease episodes, it was the Beijing strain that occurred more frequently ( $P < 0.001$ ). Associations were also identified for specific HLA types and disease caused by the Beijing, LAM, LCC, and Quebec strains. Specific HLA types were also associated with disease caused by strains from the Euro-American or East Asian lineages, and the frequencies of these alleles in their sympatric human populations identified potential coevolutionary events between host and pathogen.

**Conclusion:** We have demonstrated the association of human HLA types and *M. tuberculosis* strain genotype. This has implications for vaccine development and use in different populations, and illustrates the frequently overlooked point that both host and pathogen genetics need to be taken into consideration when studying tuberculosis disease development.

### PD-551-30 Racial differences in neutrophil counts and reported neutropenia in two international TB treatment trials, rifapentine-rifampicin, TBTC Studies29-29x

R Moro,<sup>1,2</sup> A Borisov,<sup>1</sup> J L Johnson,<sup>3,4</sup> C C Leung,<sup>5</sup> K-C Chang,<sup>5</sup> N Martinson,<sup>6</sup> S Goldberg.<sup>1</sup> <sup>1</sup>Division of Tuberculosis Elimination, Centers for Disease Control and Prevention, Atlanta, GA, <sup>2</sup>Research Collaboration, CDC Foundation, Atlanta, GA, USA, <sup>3</sup>Research Collaboration, Uganda-Case Western Reserve University, Kampala, Uganda; <sup>4</sup>Research, Case Western Reserve University School of Medicine, Cleveland, OH, USA; <sup>5</sup>Health, Tuberculosis and Chest Service, Hong Kong, China; <sup>6</sup>Research, University of the Witwatersrand and Baragwanath, Soweto, South Africa. Fax: (+1) 404 639-8961. e-mail: rmoro@cdc.gov

**Background:** Variation in absolute neutrophil count (ANC) between Africans and other populations has been reported. Neutropenia has been associated with rifamycin use. The National Institute of Health Common Terminology Criteria (CTC) and the Division of AIDS (DAIDS) toxicity tables are commonly used to assign severity grades to laboratory values in clinical trials (CT), but have not been validated in different populations. Definitions and clinical manifestations of neutropenia might differ between populations. Different scales might affect results reported from CT.

**Design/Methods:** The Tuberculosis Trials Consortium recently completed two international phase 2 randomized CT in adults using rifapentine (RPT) in place of rifampicin (RIF) during the first two months of otherwise standard TB treatment. 337 participants received RIF (10mg/kg), and three groups of 361, 81, and 81 received RPT in 10, 15, and 20mg/kg, respectively. ANC and clinical manifestations were evaluated at baseline, and at 2,4,6,8, and 12 weeks. A non-parametric test was used to compare median ANC at baseline, and Fisher's exact test was used to evaluate the rate of neutropenia events, defined as at least grade 3 based on the CTCv2.0 ( $>500$ – $<1000$ /mm<sup>3</sup>) or the DAIDS (500–749/mm<sup>3</sup>) between black and non-black populations.

**Results:** 860 participants received at least 1 dose of study drugs, 590(69%) were male. 32(3.7%) neutropenia events were reported, all of them in black participants, of which 6 were infected with HIV. One subject developed fever. All improved and none required interruption of treatment. Neutropenia event rates did not differ by treatment arm or dose, Study29: RIF10mg (8/254[3.1%]), RPT10mg (10/275[3.6%]), Study29x: RIF10mg (2/83[2.4%]), RPT10mg (5/86[5.8%]), RPT15mg (4/81[4.9%]), RPT20mg (3/81[3.7%]). Among black participants, those living in Africa had lower baseline median ANC but similar neutropenia event rates. Among participants living outside Africa, blacks had similar baseline median ANC but more neutropenia events (see table). If DAIDS criteria were applied, only 13 neutropenia events would have been reported due to lower ANC cutoff.

**Conclusion:** Compared with non-black participants, black participants had lower baseline ANC values and a higher frequency of Grade 3 or higher neutropenic events using the CTC scoring system. Consideration of

the participant population and the clinical implications of neutropenia might be helpful in optimizing neutropenia reporting definitions for TB CT.

Comparison of baseline Absolute Neutrophil Count (ANC) median, range, and rates of neutropenia between black and non-black participants living in African and non-African countries who took at least one study dose in Studies 29 and 29x (N = 860)

	Black (n=513)	Non-black (N=347)	p-value
Median ANC/mm <sup>3</sup> (range)	4960 (1310–29640)	5800 (1205–15566)	< 0.001*
Neutropenia event†	32 (6.2%)	0	< 0.0001‡
	Black African** N=435	Black, Not African** N=78	
Median ANC/mm <sup>3</sup> (range)	4840 (1310–29640)	5743 (1420–22616)	0.004*
Neutropenia event†	28 (6.4%)	4 (5.1%)	0.89‡
	Black, Not African** N=78	Non-black, Not African** N=344	
Median ANC/mm <sup>3</sup> (range)	5743 (1420–22616)	5821 (1205–15566)	0.077*
Neutropenia event†	4 (5.1%)	0	0.0004‡

\*Kolmogorov-Smirnov (Asymptotic) non-parametric test

†Based on the Common Terminology Criteria v2.0

‡Fischer's exact test, 0.5 was added to the cells when the number in at least 1 cell was <5

\*\*African: living in an African country at enrollment

Neutropenia was not reported in the 3 non-black participants living in African countries (not shown in the table)

### PD-552-30 Laboratory indices in the patients with pulmonary tuberculosis according to CYP2E1 genotype

P Antonenko,<sup>1</sup> V. Kresyun,<sup>1</sup> V. Filuk,<sup>2</sup> K Antonenko,<sup>1</sup> N. Gerasimova,<sup>2</sup> Yu Danilenko,<sup>2</sup> G Mozolevich.<sup>2</sup>

<sup>1</sup>Department of General and Clinical Pharmacology, Odessa National Medical University, Odessa, <sup>2</sup>Pulmonary tuberculosis, Odessa Regional Antituberculosis Dispensary, Odessa, Ukraine. e-mail: peterantonenko@yandex.ru

It is known that efficiency of treatment of many diseases, their course and outcome, largely depend on the genetic features of a patient, in particular from polymorphism of genes of detoxication of xenobiotics. Among the last is and gene of cytochrome P-450 2E1 (CYP2E1) – that is an enzyme taking part in metabolism of the most effective antituberculosis preparation isoniazid. The aim of present work was to detect the peculiarities of pulmonary tuberculosis (TB) according on cellular content of cells count and biochemical markers in the blood depending on cytochrome P-450 2E1 (CYP2E1) genotype in Odessa regional antituberculous dispensary in 2012 year. At the end of in-patient treatment it was studied medical cards of 84 patients that according to polymorphism of intron 6 of CYP2E1 were divided into 73 patients with CC genotype and 9 patients with CD, DD genotype. At the beginning as well as at the end of hospital phase treatment patients with CC genotype had higher level of biochemical indices like alanine aminotransferase, aspartate aminotransferase and gamma glutathione transferase than patients with CD, DD genotypes. In the moment of completion of in-patient treatment there was a certain decline of general bilirubin in both groups of patients, but unreliable character had this process. Also the amount of patients with the genotype of CC, which had a hyperbilirubinemia, diminished in 2,4 times ( $R<0,05$ ;  $\chi^2=4,17$ ), however such cases were absented among patients with the genotypes of CD, DD. The indexes of thymol test had a tendency to growth for the carriers of CC genotype and tendency to the decline for

patients with the genotypes of CD, DD ( $P > 0,05$ ). During in-patient treatment the indexes of alanine aminotransferase (ALT) grew on 18,4% ( $P = 0,009$ ;  $CI = -7,58...1,12$ ) for the individuals with CC genotype and on 30,9% ( $P = 0,018$ ;  $CI = -7,98...-0,86$ ) for patients with the genotype of CD, DD. Also the amount of patients with CC genotype and overactivity of ALT grew almost in 2 times ( $R < 0,05$ ;  $\chi^2 = 4,01$ ). At the end of in-patient treatment the level of aspartate aminotransferase (AST) for the carriers with CC genotype grew on 10,2% ( $P > 0,05$ ), for the patients with CD, DD grew on 16,9% ( $P = 0,036$ ;  $CI = -6,59...-0,25$ ). The level of gamma glutamine transferase (GGT) in plasma of blood for the carriers of CC genotype increased on 6,9% ( $P > 0,05$ ), for patients with CD, DD genotypes – on 31,4% ( $P = 0,016$ ;  $CI = -12,46...-1,48$ ). At the end of in-patient stage treatment for the patients with CC genotype the level of AST and ALT was higher than for patients with the genotypes of CD, DD on 49,5% ( $P < 0,001$ ;  $CI = 9,37.21,95$ ) and on 23,9% ( $P = 0,003$ ;  $CI = 3,21.15,41$ ) correspondently. Also among patients with the genotypes of CD, DD in general were absent patients with the increased activity of ALT and AST, at the same time for individuals with the genotype of CC there were 32,8% ( $P < 0,05$ ;  $\chi^2 = 4,13$ ) and 31,1% ( $P < 0,05$ ;  $\chi^2 = 3,85$ ) correspondently of such patients. That also correlates with higher concentration of dyene conjugates and lower activity of catalase in patients with CC genotype relatively to patients with CD, DD genotype. The obtained data proved that tuberculosis patients with CC genotype have higher risk of hepatotoxicity development that carriers of CD, DD genotype.

#### PD-553-30 Expression of membrane-bound receptors to tumor necrosis factor alpha in active pulmonary tuberculosis

A Alshevskaya,<sup>1</sup> Z Laushkina,<sup>2</sup> F Kireev,<sup>1</sup> J Lopatnikova,<sup>1</sup> S Sennikov.<sup>1</sup> <sup>1</sup>Laboratory of Molecular Immunology, Federal State Budgetary Institution ((Research Institute of Clinical Immunology)) under the Russian Academy of Medical Sciences Siberian Branch, Novosibirsk, <sup>2</sup>Clinical Department, Federal State Budgetary Institution ((Novosibirsk Research Institute of Tuberculosis)) under the Ministry of Health of Russian Federation, Novosibirsk, Russian Federation. e-mail: alkkina@yandex.ru

**Background:** Tumor necrosis factor alpha (TNF) plays a central role in antituberculous immunity. TNF have two types of membrane-bound receptors (TNFR1 and TNFR2) which modulate the efficacy of cytokine not only in different percent of positive cells in subsets but also in number of receptors themselves. Thereby the complex study of these parameters is necessary for better understanding of TNF-mediated processes in tuberculosis.

**Design/Methods:** Peripheral blood samples were collected from 45 patients with active pulmonary tuberculosis and 22 healthy individuals. Peripheral blood mononuclear cells were isolated from the whole blood by ficoll gradient centrifugation method. The percent of T cells, B cells and monocytes bearing TNFR1 and TNFR2 was

estimated by flow cytometry using phycoerythrine (PE) labelled antibodies to TNFRs (eBioscience, USA), and the number of TNFRs per cell using QuantiBRITE PE calibration beads (BD Biosciences, USA). Comparison between groups was performed by Mann-Whitney test using Statistica 6.0 program.

**Results:** Among tuberculosis patients subsets T-lymphocytes demonstrated the highest percent of TNFR2+ cell but had the lowest number of both receptors type 1 and 2 on cells while among healthy donors subsets monocytes had the highest percent and density of receptors types 1 and 2 expression. The percent of TNFR2+ monocytes and TNFR2+ B-lymphocytes were significantly lower in tuberculosis patients than in healthy individuals. Number of TNF receptors type 2 on monocytes and T-lymphocytes was lower in tuberculosis patients compared with health. In all studied individuals in T-, B-lymphocytes and monocytes percent of TNFR2+ cell was higher than percent of TNFR1+ cells, but only B-lymphocytes had significantly differences between receptors types expression density and number of TNFR1 on them was higher than number of TNFR2.

**Conclusion:** Received data show that expression of membrane TNF receptors types 1 and 2 differ in immunocompetent cells subsets and between patients with active pulmonary tuberculosis and healthy individuals and changes in the percentage of positive cells and the number of receptors are not necessarily unidirectional. Lower number of TNF receptors on cells are shown altered mechanisms of cytokine regulation in pathological process of pulmonary tuberculosis.

#### PD-554-30 DEFB1 gene polymorphisms and tuberculosis in a north-eastern Brazilian population

H Da Cruz,<sup>1,2</sup> R Celerino Da Silva,<sup>2</sup> L Segat,<sup>3</sup> L.A. Cavalcanti Brandão,<sup>2</sup> R Lima Guimarães,<sup>2</sup> L.M. Lapa Montenegro,<sup>4</sup> H Charifker Schindler,<sup>4</sup> S Crovella.<sup>2,3</sup> <sup>1</sup>Department of Genetics, Federal University of Pernambuco, Recife, Pernambuco, <sup>2</sup>Laboratory of Immunopathology Keizo Asami (LIKA), Federal University of Pernambuco (UFPE), Recife, Pernambuco, Brazil; <sup>3</sup>Genetic Service, Institute for Maternal and Child Health- IRCCS "Burlo Garofolo", Trieste, Italy; <sup>4</sup>Department of Immunology, Aggeu Magalhães Research Center (CPqAM/FIOCRUZ), Recife, Pernambuco, Brazil. e-mail: heidi.alves@gmail.com

**Background:** Remarkably, 90–95% of the estimated two billion people infected with *Mycobacterium tuberculosis* worldwide never develop active tuberculosis. Thus in the majority of the population, cell-mediated immunity is sufficient for containing *M. tuberculosis* infection and preventing disease. However, the factors that predispose 5–10% of infected people to developing disease are unknown in the majority of cases. Defensins are low molecular weight antimicrobial and immunomodulatory peptides. Their participation against *M. tuberculosis* infection has been scarcely studied. Beta-defensin-1 antimicrobial peptide, encoded by the DEFB1 gene, is constitutively expressed in airway epithelia and plays an important role in lung mucosal immunity. Three single



nucleotide polymorphisms (SNPs), located at -52 (G>A), -44 (C>G) and -20 (G>A) position in the 5' untranslated region (UTR) of the DEFB1 gene have been reported to promote functional alteration of hBD-1 expression in different cell models.

**Design/Methods:** In our study we analyzed, by direct sequencing, this three DEFB1 polymorphisms in a group of 92 TB patients and 286 healthy controls in order to evaluate their eventual association with tuberculosis.

**Results:** Allele, genotype, and haplotype frequencies were calculated using contingency tables as appropriate. DEFB1 SNPs allele and genotype frequencies were similar in TB patients and healthy controls and no significant difference has been found ( $p>0.05$ ), also when TB patients were stratified according to the pulmonary and extrapulmonary form of disease. We computed the haplotypes and observed that the three SNPs in the 5'UTR of DEFB1 are in strong linkage disequilibrium ( $D'>0.9$ ), forming four haplotypes. However, no significant differences were found when comparing TB patients and healthy controls. The post hoc analysis of the study through the G\*power software, indicate the following power for three SNPs: 0.30 (-52G>A), 0.5 (-44C>G) and 0.16 (-20G>A).

**Conclusion:** Even if our results seem to exclude an association between DEFB1 polymorphisms and TB development in Northeast Brazilian population, however since DEFB1 could be a potential candidate gene for susceptibility to TB and only very few studies have addressed this topic achieving controversial results, we think that further studies on a larger number of patients and in other populations are needed to disclose the role of DEFB1 variations in tuberculosis development.

#### PD-555-30 Evaluation of the association of single nucleotide polymorphisms of genes of TNF $\alpha$ and IL-10 with susceptibility to pulmonary tuberculosis

L Montenegro,<sup>1</sup> A Nascimento,<sup>1</sup> F Santos,<sup>1</sup> A Peixoto,<sup>1</sup> M Cardoso,<sup>2</sup> H Da Cruz,<sup>1</sup> C Morais,<sup>1</sup> H Charifker Schindler.<sup>1</sup> <sup>1</sup>Imunology, Centro de Pesquisas Aggeu Magalhães, Fiocruz, Recife, Pernambuco, <sup>2</sup>Genetic, Universidade Federal de Pernambuco, Recife, Pernambuco, Brazil. e-mail: lilian@cpqam.fiocruz.br

**Background:** Single nucleotide polymorphisms (SNPs) in the genes promoter regions of the cytokines TNF- $\alpha$  and IL-10 influence of the immune response and may be involved in resistance or susceptibility to tuberculosis. This study aimed to evaluate the association between SNPs of genes functional cytokine TNF- $\alpha$  (-308G/A) and IL-10 (-1082A/G) with resistance or susceptibility to active pulmonary tuberculosis in patients from the state of Pernambuco, Brazil.

**Design/Methods:** Participated 282 individuals, divided into study groups according to clinical, radiological and laboratory tests. The case group consisted of 71 patients with active pulmonary tuberculosis, control 1: 53 patients with respiratory symptoms and latent tuberculosis, control 2: 57 patients with respiratory symptoms bearers of nonspecific lung infections and control 3 of

101 clinically healthy individuals, from of public health services. Were collected 5-10mL of sputum and 4.5 mL of peripheral blood, performed genomic DNA extraction and determination of genetic polymorphism using Real-time PCR.

**Results:** Analysis polymorphic comparative study groups showed that the mutant allele-1082G [ $p<0.0001$ , OR = 3.90 [2:45-6:59] and genotypes-1082GA [ $p<0.0001$ , OR = 2.90 [1:42-5.95] e-1082GG [ $p<0.0001$ , OR = 15:50 [5:18-1.62] was associated with the risk of developing pulmonary tuberculosis when the case group was compared with control 3. The genotype -308AG [ $p=0.005$ , OR = 0.374 [0.17-0.76] showed a statistically significant association between the case group and control 3. There was no statistically significant difference in the association analysis of SNPs-308G/A and-1082A/G in the comparison between the case group and controls 1 and 2.

**Conclusion:** Thus, mutant allele-1082G carriers, equivalent to increased protein levels of IL-10 may influence the immune response against *M. tuberculosis*. However, carriers of the-308GA genotype showed a protective factor for disease development. The study demonstrated that the SNPs has an important role in susceptibility or resistance to pulmonary tuberculosis in the Pernambuco/ Brazil population studied.

## 06. IMMUNE RESPONSES IN TB

#### PD-556-30 Impaired immune response of peripheral blood mononuclear cells from non-human immuno-deficiency virus infected patients with MAC-LD

C-C Shu,<sup>1,2</sup> C-J Yu,<sup>3</sup> J-Y Wang,<sup>3</sup> L-N Lee.<sup>4</sup> <sup>1</sup>Graduate Institute of Clinical Medicine, College of Medicine, National Taiwan University, Taipei, <sup>2</sup>Traumatology, National Taiwan University Hospital, Taipei, <sup>3</sup>Internal Medicine, National Taiwan University Hospital, Taipei, <sup>4</sup>Laboratory Medicine, National Taiwan University Hospital, Taipei, Taiwan. e-mail: stree139@yahoo.com.tw

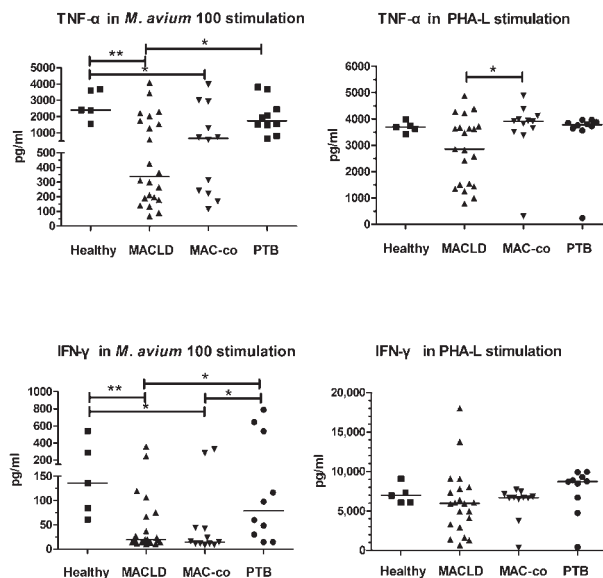
**Background:** *Mycobacterium avium* complex-lung disease (MAC-LD) became important but the diagnosis is still difficult and doesn't include host immune response which is unclear at present.

**Methods:** This prospective study was conducted in a tertiary referral center in northern Taiwan and enrolled 50 participants including 23 patients with MAC-LD, 12 with MAC contamination, 10 with pulmonary pulmonary tuberculosis (PTB), and 5 healthy controls. The responses were measured and compared by cytokines production from peripheral blood mononuclear cells (PBMC), which were stimulated by MAC antigen.

**Results:** Comparing with different groups, the responses of tumor necrosis factor (TNF) - $\alpha$ , interleukin-1 $\beta$ , interleukin-10 and interferon- $\gamma$  in MAC stimulation assay were higher in PTB and healthy controls than that in MAC-LD patients as well as MAC contamination (Figure). Within MAC-LD patients, those with high

interferon- $\gamma$  ( $\geq 60$  pg/ml) response was young and abnormally thin and had short symptoms duration. The ratio of interferon- $\gamma$ /interleukin-10 was higher in patients with MAC-LD than healthy controls. TNF- $\alpha$  production in mitogen stimulation was higher in MAC contamination than MAC-LD patients.

**Conclusions:** Weak cellular immune in MAC-LD patients might be associated with disease development, especially in patients with old age. Patients with MAC contamination also had weak PBMC response. High TNF- $\alpha$  production in mitogen stimulation may prefer contamination rather than disease and high IFN- $\gamma$ /IL-10 ratio could be considered as an potential indicator for disease.



### PD-557-30 The diagnostic role of inflammatory and anti-inflammatory cytokines and effector molecules of cytotoxic T lymphocytes in tuberculous pleural effusion

C-C Shu,<sup>1,2</sup> C-J Yu,<sup>3</sup> J-Y Wang,<sup>3</sup> L-N Lee.<sup>4</sup> <sup>1</sup>Graduate Institute of Clinical Medicine, College of Medicine, National Taiwan University, Taipei, <sup>2</sup>Traumatology, National Taiwan University Hospital, Taipei, <sup>3</sup>Internal Medicine, National Taiwan University Hospital, Taipei, <sup>4</sup>Laboratory Medicine, National Taiwan University Hospital, Taipei, Taiwan. e-mail: stree139@yahoo.com.tw

**Background:** Early diagnosis of tuberculous pleural effusion (TPE) remains difficult. While some inflammatory markers in pleural effusion (PE) are helpful in diagnosis, the roles of anti-inflammatory cytokines and effector molecules of cytotoxic T lymphocytes have never been investigated.

**Methods:** Lymphocyte-predominant exudative PE samples were assayed for inflammatory and anti-inflammatory cytokines and effector molecules of cytotoxic T lymphocyte. Logistic regression analysis was applied to identify factors independently associated with TPE and to predict the probability of TPE. Receiver operating

characteristic (ROC) curve analysis was applied to determine the optimal cut-off value for the predicted probability.

**Results:** Of 95 patients enrolled, 35 had TPE, 46 malignant PE, and 14 had PE due to other etiologies. Interferon- $\gamma$ , adenosine deaminase (ADA), Decoy receptor (DcR) 3, monocyte chemo-attractant protein (MCP) -1, interferon-induced protein (IP) -10, granzyme A, and perforin were higher in TPE than other PEs. By logistic regression analysis, interferon- $\gamma \geq 75$  pg/ml, ADA  $\geq 40$  IU/ml, DcR3  $\geq 9.3$  ng/ml and soluble tumor necrosis factor receptor 1 (TNF-sR1)  $\geq 3.2$  ng/ml were independent factors associated with TPE. The predicted probability based on the four predictors had an area under ROC curve of 0.920, with 82.9% sensitivity and 86.7% specificity under the cut-off value of 0.303. In the TPE group, patients with positive PE/pleura culture for *Mycobacterium tuberculosis* had higher pleural interferon- $\gamma$ , MCP-1, IP-10, and perforin than those with positive sputum but negative PE culture.

**Conclusions:** While pleural interferon- $\gamma$  and ADA are conventional markers for diagnosing TPE, simultaneously measuring DcR3 and TNF-sR1 can improve diagnostic efficacy.

### PD-558-30 Interferon-gamma responses to ESAT-6/CFP-10 and PPD are comparable between children of all age groups in the Gambia

T Togun,<sup>1</sup> M.P Gomez,<sup>1</sup> U Egere,<sup>1</sup> M Daramy,<sup>1</sup> A Sillah,<sup>1</sup> L Tientcheu,<sup>1</sup> J Sutherland,<sup>1</sup> B Kampmann.<sup>1,2</sup>

<sup>1</sup>Vaccinology (Childhood TB Research Group), Medical Research Council (MRC) Unit - The Gambia, P.O.Box 273 Banjul, Gambia; <sup>2</sup>Paediatrics (Academic), Imperial College London, St. Mary's Campus, London, UK. Fax: (+220) 4495919. e-mail: ttogun@mrc.gm

**Background:** Despite concerns about the sensitivity of interferon-gamma release assays (IGRAs) especially in children aged  $<5$  years, there is paucity of age-related data on paediatric T-cell based assays. We investigated age-related interferon-gamma (IFN- $\gamma$ ) responses in children aged  $<15$  years diagnosed with either active TB or "other lung infections but not TB" (OD) in The Gambia. **Methods:** Undiluted whole blood from children aged  $<15$  years were incubated overnight with *M. tuberculosis* antigens ESAT-6/CFP-10 (EC) and purified protein derivative (PPD) and the concentration of IFN- $\gamma$  was measured in the supernatants using a validated in-house IFN- $\gamma$  ELISA. We compared IFN- $\gamma$  responses in children aged  $<5$  years with those aged  $\geq 5$  years diagnosed with either active TB or TST+ OD using Mann Whitney non-parametric test.

**Results:** High levels of IFN- $\gamma$  were seen following both EC and PPD stimulations in children with TB and TST+ OD and we found no significant difference in the IFN- $\gamma$  levels between the two groups (Table 1). There was no significant difference in the median (IQR) IFN- $\gamma$  levels between children diagnosed with active TB aged  $<5$  years (N=13) compared to those aged  $\geq 5$  years (N=15) following stimulations with EC [2265 (1335 – 4231) pg/

ml vs. 2291 (301 – 4586) pg/ml] and PPD [4169 (1618 – 4552) pg/ml vs. 1833 (260 – 4220) pg/ml]. Similarly, we found no difference in the median (IQR) IFN- $\gamma$  levels between children with TST+ OD aged <5 years (N=6) compared to those  $\geq$  5 years (N=19) following stimulation with EC [4416 (1930 – 4966) pg/ml vs. 3914 (1536 – 4803) pg/ml] and PPD [4870 (3970 – 4956) pg/ml vs. 4406 (2234 – 4919) pg/ml].

**Conclusion:** In line with previously published studies, we found no significant difference in the IFN- $\gamma$  production between children diagnosed with TB and TST+ OD. However, IFN- $\gamma$  responses to EC and PPD among children <5 years of age with TB or TST+ OD in our setting is comparable to that of older children. This could reflect a high rate of ongoing sensitisation through repeated Mtb exposures from very young age. These preliminary results hold promise for the development of diagnostic tests based on host biomarkers that will be applicable for use in all age groups of paediatric subjects, however it also reinforces the need for a complementary biomarker or host biosignatures (with or without IFN- $\gamma$ ) that could reliably distinguish childhood TB from other lung diseases and LTBI in a TB endemic setting with a high rate of transmission and infection.

**Table 1.** In vitro IFN- $\gamma$  responses following EC and PPD stimulation

	TB (n=28)	TST+ OD (n=25)	TST- OD (n=30)	p-values*
Antigen IFN- $\gamma$ , median; (IQR) pg/ml	IFN- $\gamma$ , median; (IQR) pg/ml	IFN- $\gamma$ , median; (IQR) pg/ml		
EC	2278; 1034–4413	4062; 1729–808	186.4; 43.7–72.4	a = ns b < 0.0001 c < 0.0001
PPD	4195; 3277–4474	4770; 2408–4920	209.6; 128.5–34.4	a = ns b < 0.0001 c < 0.0001

\*a=TB vs. TST+ OD; b=TB vs. TST- OD; c=TST+ OD vs. TST- OD; ns= not significant

### PD-559-30 Mycobacterial antigens disappear from host tissue during latent *Mycobacterium tuberculosis* infection

T Mustafa,<sup>1,2</sup> H Wiker,<sup>3</sup> M Harboe,<sup>4</sup> G Bjune.<sup>5</sup> <sup>1</sup>Global Public Health & Primary Care, University of Bergen, Bergen, <sup>2</sup>Thoracic Medicine, Haukeland University Hospital, Bergen, <sup>3</sup>Clinical Science, University of Bergen, Bergen, <sup>4</sup>Immunology, University of Oslo, Oslo, <sup>5</sup>Health and Society, University of Oslo, Oslo, Norway. e-mail: tehmina.mustafa@cih.uib.no

**Background:** Little is known comparing the in situ expression of *M. tuberculosis* antigens during various clinical manifestations of tuberculous infection.

**Design/Methods:** B6D2F1 mice were inoculated with different doses of *M. tuberculosis* H37Rv to develop models for latent and active disease. Immunohistochemistry was used to investigate the in situ distribution of major mycobacterial secreted (antigen 85 complex, MPT64) and somatic antigens (lipoarabinomannan (LAM) and cell wall components detected by polyvalent anti-BCG) by using rabbit polyclonal antibodies in

murine pulmonary tissues during latent infection (n=8) and active tuberculosis (n=10), and human disseminated pulmonary (n=3) tuberculous lesions.

**Results:** Latently infected mice remained healthy throughout their lifespan (~2 years), no focal cellular infiltrates were detectable in the lungs, while bacilli could be isolated by culture. At week 24 after infection, few (<2%) of lung parenchyma cells showed antigen 85 and other BCG antigens. At week 70, even lower number of cells stained for these two antigens, and at week 113 none of these antigens were detectable. MPT64 and LAM were not detectable throughout the course of latent infection. Mice with active disease developed focal inflammatory infiltrates, and all four antigens were detectable within the macrophages in the infiltrates. BCG and LAM were more abundant (10–25% cells) as compared to the antigen 85 and MPT64 (2–9% cells). As the mice became sicker, and the infiltrates expanded, more mycobacterial proteins were detectable except antigen 85. Lung biopsies from the uninfected sentinel control mice (n=4) were negative for all antigens. The human lung biopsies showed pneumonic infiltrates without typical TB granulomas. All the four mycobacterial antigens were expressed abundantly in these infiltrates.

**Conclusion:** During latent infection mycobacterial antigens gradually disappear from the murine pulmonary tissue, implying that *M. tuberculosis* changes metabolically during the course of infection and healthy hosts with the passage of time might be able to clear away the latent infection. During disseminated pulmonary disease abundantly expressed mycobacterial antigens depict replicating bacilli. These findings are supported by recently published paper on the waning of latency in human tuberculosis (Wiker et al. BMC Infect Dis. 23;10:37), which showed that the risk of reactivation of latent infection decreases with age which may reflect the rate at which latent tuberculosis is eliminated from a population with minimal transmission of tubercle bacilli. This suggests that the total population harbouring live tubercle bacilli and consequently the future projection for increased incidence of tuberculosis in the world is probably overestimated. Preventative measures against transmission of tuberculosis will be the most effective tool for tuberculosis control.

### PD-560-30 Antigen-induced perforin production by populations of cytotoxic (CD8+) T-cells in children and adolescents with tuberculosis infection

LI Mordovskaya,<sup>1</sup> M Vladimirovsky,<sup>2</sup> V Aksenova.<sup>2</sup> <sup>1</sup>Immunological Laboratory, Research & Practice Center for Tuberculosis, Yakutsk, <sup>2</sup>Research Institute of Phthysipulmonology, I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation. e-mail: limordovskaya@mail.ru

**Background:** T-cells are capable of producing molecules exerting a direct effect on mycobacteria: bactericidal activity of granulysin- and perforin-synthetizing CD8+ T-cells against *M. tuberculosis* (MTB) has been shown in an



in vitro test system. Antimicrobial effect of granulysin can be achieved owing to perforin activity, by enhancing macrophage endocytosis or forming pores in the membranes of mycobacteria-containing macrophages.

**Design/Methods:** Aim was to study antigen-induced perforin production by cytotoxic (CD8<sup>+</sup>) T-cells during latent and active tuberculosis (TB) infection in children and adolescents. Study included 11 patients known to have MTB infection for <2 years without radiologic signs of localized primary TB, and 10 patients with newly identified pulmonary TB (PTB). 12 male and 9 female patients aged 3 to 16 were examined. Prior to antibacterial therapy, we assessed peripheral lymphocyte populations (CD3<sup>+</sup>, CD3<sup>+</sup>perforin<sup>+</sup>, CD3<sup>+</sup>CD8<sup>+</sup>, CD8<sup>+</sup>perforin<sup>+</sup>) induced by tuberculin PPD and ESAT-6 after short-term incubation, using direct immunofluorescence test and monoclonal antibodies (Becton Dickinson, USA).

**Results:** Total T-cell percentages (CD3<sup>+</sup>) in patients with active PTB were reliably lower than in patients with latent infection (69,6±0,9% and 63,5±2,0% respectively, p<0,05). Proportions of perforin-producing T-cells (CD3<sup>+</sup>Per<sup>+</sup>) did not differ significantly between patients with latent infection (1,68±0,52%) or active PTB (2,21±1,1%). In both groups, proportions of perforin-producing T-cells were higher in samples incubated in presence of PPD and ESAT-6, compared to controls without antigen stimulation, although differences were statistically significant only for ESAT-6. After stimulation with PPD and ESAT-6, samples of patients with active PTB showed significantly higher proportions of perforin-producing cytotoxic CD8<sup>+</sup> T-cells (4,13±0,62% and 5,06±0,78% respectively), than those from patients with latent infection (1,69±0,74% and 2,29±0,63% respectively), p<0,01.

**Conclusion:** Our findings show that it is possible to differentiate latent infection and active PTB by analyzing the antigen-induced perforin-producing T-cell population content.

### PD-561-30 Biomarker candidates for LTBI treatment efficacy: an exploratory study

M Lisboa Bastos,<sup>1,2</sup> J Lima,<sup>3</sup> M Siqueira,<sup>3</sup>

S Garcia Rabelo,<sup>2</sup> T Pedro,<sup>3</sup> C Ponte,<sup>3</sup> P Antas,<sup>3</sup>

A Trajman.<sup>2,4,5</sup> <sup>1</sup>Infectious Diseases, Federal University of Rio de Janeiro, Rio de Janeiro, RJ, <sup>2</sup>Medicine, Tuberculosis Scientific League, Rio de Janeiro, RJ, <sup>3</sup>Laboratório de Imunologia Clínica, Oswaldo Cruz Institute, Rio de Janeiro, RJ, Brazil; <sup>4</sup>Respiratory Epidemiology and Clinical Research Unit, McGill University, Montreal, QC, Canada; <sup>5</sup>Internal Medicine Graduate Program, Federal University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil.

e-mail: mayara\_bastos@yahoo.com.br

**Background:** There are no biomarkers to evaluate the efficacy of latent tuberculosis infection (LTBI) treatment. TST rarely reverses, and IFN-γ release assays spontaneously convert and revert, regardless either re-exposure or treatment. We tested different serum biomarker candidates before and after LTBI treatment

**Design/Methods:** 15 adherent (at least 80% of doses taken) and 6 non-adherent participants in a randomized trial comparing 9 INH with 4 RIF performed QuantiFERON®-TB Gold-in-Tube (QFT-GIT). Multiple cytokines were also detected in supernatants of TB and Nil tubes using the Bio-Plex protein multiarray system® (Bio-Rad, Hercules, CA, EUA). TB minus nil levels before and after treatment were compared, regardless of study drug

**Results:** Although not statistically significant, IFN-γ, TNF-α and IL-17 had the most relevant changes after treatment (table). Among adherent patients, the levels of IL-10 decreased among those who took 4 RIF (median difference= 0 pg/ml; IQR=-60.25;0) pg/mL), and increased among those who took 9 INH (median difference=0 pg/mL; IQR=0; 70.4 p=0.027).

**Conclusion:** In this small sample, we identified three other promising biomarker candidates besides IFN-γ. These cytokines will be further explored in a larger cohort and analysed by study drug. Table-Difference of biomarker levels (TB stimulated minus unstimulated) from after to before treatment

Cytokines (pg/mL)	TB-NIL		p-value
	Completed treatment (N=15)	Did not complete treatment (N=6)	
IL1b	0 (-7.6;164.6)	70.6 (-67.9;714.2)	0.910
IL2	10.2 (-13.5;58.6)	-49.7 (-154.1;12.0)	0.392
IL4	0 (-1.5;0.6)	-0.4 (-11.1;7.0)	0.754
IL5	0 (-0.15;0.05)	-0.5 (-0.1;0)	0.937
IL6	-549.6 (-1271.8; 704.9)	-1350.4 (-3097.7;0)	0.302
IL7	0 (0; 84.4)	0 (0;41)	0.733
IL10	0 (0;0)	0 (0;0)	1.0
IL12	0 (-0.3;0.3)	0.2 (-0.4;0.6)	0.622
IL13*	0 (14.7;0)	0 (0;0)	0.242
IL17	50.6 (-73.9;328.8)	-59.6 (-227.7;0)	0.161
MCP1	0 (-9.9;0)	-1692.1 (-8772.6;44.7)	0.519
MIP1	2204.09 (0;4446.15)	25.4 (-4121.2; 4629.4)	0.507
GCSF	0 (-6.2;12.3)	0 (-80.2;18)	0.694
GMCSF*	0 (0;0)	0 (0;0)	0.359
IFNY	-695.6 (-798.5;0)	0 (-495; 163.6)	0.329
TNFα	0 (-61.1;57.2)	-37.0 (-114.4;0)	0.172
MMP9*	0 (0;0)	0 (0;0)	1.0
IL27	-12.0 (-86.0;88.5)	55.5 (-1062;504)	0.640
QFT-GIT†	-0.4 (-2.03;11.0)	0.02 (0.0;0.92)	0.161

\* Levels for all patients that did not complete treatment.

† QFT-GIT- QuantiFERON® Gold-in-Tube. For QFT-GIT unit is IU/ml

### PD-562-30 Latency-associated antigens: interferon-gamma immunoreactivity evaluation in close contacts recently exposed to *Mycobacterium tuberculosis*

L Araujo,<sup>1</sup> N Da Silva,<sup>1</sup> R Da Silva,<sup>1</sup> JA Leung,<sup>2</sup> F Mello,<sup>2</sup> TH Ottenhoff,<sup>3</sup> MH Saad.<sup>1</sup> <sup>1</sup>IOC, Fundação Oswaldo Cruz, Rio de Janeiro, RJ, <sup>2</sup>Clementino Fraga Filho Hospital, Federal University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil; <sup>3</sup>Leiden University Medical Centre, Leiden University, Leiden, Netherlands. e-mail: araujo.s.leonardo@gmail.com

**Background:** Latent tuberculosis (TB) infection (LTBI) diagnoses and treatment are required for TB control and

eradication. Nowadays, the LTBI diagnoses rely on the tuberculin skin test (TST) and the interferon-gamma release assay (IGRA) using RD1 (ESAT6/CFP10) stimulation. Both have limitations as false-negative results, the TST cross-reactivity with non-tuberculous mycobacterias and the IGRA-RD1 inability to differentiate between latent and active TB. An alternative is to look for other mycobacterial antigens (Ags) that are up regulated at LTBI and may have immunogenic potential. The goal of the present study was to investigate the potential of a set of five Ags that are up regulated during Mtb latency mimesis, of which two not yet studied, as LTBI marker in high endemic area for TB.

**Methods:** We used the ELISA for measuring immunogenicity by IFN- $\gamma$  released after PBMC 5-day stimulation using the DosR Rv2029c, Rv2031c and Rv2628, and the unpublished Rv2034 and Rv3353. We enrolled 64 recent close contacts (rCt) and 07 pulmonary TB subjects. Blood was collected at enrolment and 12 months after or at active TB progression/TST+ conversion. The rCt were stratified by TST and IGRA-RD1 results. To all rCt with a TST+ the isoniazid preventative treatment (IPT) was offered.

**Results:** All selected Ags demonstrated significantly higher mean IFN- $\gamma$  response at LTBI versus non-infected rCt, with the only exception of Rv3353c. Despite the active TB group had shown higher mean reactivity than uninfected rCt, there was no statistical difference. While all demonstrated higher IFN- $\gamma$  reactivity at LTBI than at active TB groups, but significance was only achieved for the Rv2031c and Rv2034. In the follow up analysis, a reversion for latency-Ags IFN- $\gamma$  positivity rate varying between 60% - 100% was observed at LTBI group after the IPT. While TST conversion resulted in a notable increase on mean IFN- $\gamma$  response to Rv2029c, Rv2034 and Rv2628. The rCt with primary progression to active pulmonary TB only demonstrated positive IFN- $\gamma$  response to Rv2029c that increased after the disease.

**Conclusion:** For the first time we described the immunogenicity of Rv2034, which was significantly more recognized by PBMCs of LTBI than to active pulmonary TB subjects, as well as the DosR Rv2029c and Rv2031c. Our data suggest that these three Ags have a good potential to compose an IGRA for LTBI/primary TB progression detection, however further studies with a larger population are needed to validate it.

#### PD-563-30 Tuberculosis IFN- $\gamma$ : responses in breastmilk of HIV-infected mothers

L Cranmer,<sup>1,2,3</sup> M Kanyugo,<sup>3</sup> B Lohman-payne,<sup>3,4,5</sup> K Tapia,<sup>4</sup> G John-stewart.<sup>1,4,5,6</sup> <sup>1</sup>Pediatrics, University of Washington, Seattle, WA, <sup>2</sup>Pediatrics, Seattle Children's Hospital, Seattle, WA, USA; <sup>3</sup>Paediatrics, University of Nairobi, Nairobi, Kenya; <sup>4</sup>Global Health, University of Washington, Seattle, WA, <sup>5</sup>Medicine, University of Washington, Seattle, WA, <sup>6</sup>Epidemiology, University of Washington, Seattle, WA, USA. e-mail: lcranmer@uw.edu

**Background:** Infant TB vaccine strategies typically rely on stimulating infant immune responses to prevent TB. TB-specific cells in breastmilk could potentially contrib-

ute to infant immune responses either passively in the respiratory mucosa or by enhancing development of infant TB immunity. Prior studies have demonstrated cellular responses to purified protein derivative (PPD) in maternal breastmilk, but TB-specific immune responses in breastmilk have not been described.

**Design/Methods:** In a historical perinatal HIV cohort, TB IFN- $\gamma$  responses were measured in cryopreserved maternal breastmilk cells (BMCs) and peripheral blood mononuclear cells (PBMCs) at 1 month post-partum using the T-SPOT.TB ELISPOT assay. Median IFN- $\gamma$  SFCs in response to ESAT-6 and CFP-10 above nil in BMCs and PBMCs were compared using Wilcoxon signed-rank tests. Data were log-transformed and Spearman's correlation of BMC and PBMC IFN- $\gamma$  responses to ESAT-6 and CFP-10 were assessed.

**Results:** Of 11 paired maternal BMC and PBMC assays, 8 BMC and 10 maternal PBMC assays were valid. Of valid assays, TB IFN- $\gamma$  responses to either ESAT-6 or CFP-10 were present in 6 (75%) BMCs and 4 (40%) maternal PBMCs. For positive BMC assays, median response to ESAT-6 was 221 SFCs (IQR 68-493) and CFP-10 was 112 SFCs (IQR 12-280). Among positive maternal PBMC assays, median IFN- $\gamma$  response to ESAT-6 was 48 SFCs (IQR 38-71) and CFP-10 was 31 SFCs (IQR 21-204). Median positive IFN- $\gamma$  response to ESAT-6 and CFP-10 were higher in BMCs than PBMCs ( $p=0.02$  for both antigens). Maternal BMC and PBMC TB IFN- $\gamma$  SFCs were highly correlated (ESAT-6  $r=0.91$ ,  $p=0.004$  and CFP-10  $r=0.86$ ,  $p=0.01$ ).

**Conclusion:** TB IFN- $\gamma$  responses were present in breastmilk of HIV-infected mothers. In comparison to PBMCs, TB IFN- $\gamma$  responses were more prevalent in BMCs and of significantly higher magnitude. Further studies to determine whether and how breastmilk TB cellular immunity influences infant immunity and susceptibility to TB will be important, and may inform complementary maternal vaccine strategies that potentially enhance protection of infants via breastmilk.

#### PD-564-30 Cytokine levels during TB treatment in a paediatric cohort

L Hasper,<sup>1</sup> M Chachage,<sup>2</sup> N Elias,<sup>2</sup> A Rachow,<sup>1,3</sup> A Bauer,<sup>1</sup> M Hoelscher,<sup>1,3</sup> C Geldmacher,<sup>1,3</sup> I Kroidl.<sup>1</sup> <sup>1</sup>Division of Infectious Diseases and Tropical Medicine, Medical Center of the University of Munich (LMU), Munich, Germany; <sup>2</sup>Mbeya Medical Research Centre, National Institute for Medical Research, Mbeya, United Republic of Tanzania; <sup>3</sup>Partner site Munich, German Center for Infection Research (DZIF), Munich, Germany. Fax: (+255) 25 2503134. e-mail: pclowes@mmrp.org

**Background:** For diagnostic purposes, the potential of *M. tuberculosis* (MTB) to induce a powerful immune response is used by different commercially available test, such as Interferon-gamma (IFN) -Release Assays. However, the role of IFN-gamma and other cytokines for TB-treatment monitoring has not been evaluated yet.

**Design/Methods:** Paediatric TB suspects were enrolled into a prospective cohort study, conducted in Mbeya, Tanzania. At day 0, 14, 28, 168 and 336 whole blood

was stimulated with RD-1 antigens for 24 hours, using the Quantiferon-TB-Gold test (QFT). For 31 children aged 6 months to 14 years of age, who had a positive response to the QFT at baseline, the supernatants were tested for additional cytokines. Twenty-three of the children were treated against TB, 11 of them being co-infected with HIV. Additional 8 children improved without receiving TB treatment, leading to the classification of "latent" MTB infection. The QFT-supernatants were tested for Interleukin-1 Receptor antagonist (IL-1RA), IL-2, IFN- $\gamma$ , IL-10, IL-13 and IL-17 using the cytometric bead array method.

**Results:** Participants with "latent" MTB infection showed a trend to higher production of the cytokines IL-10, IL-17, IL-13 and IL-1RA at baseline, compared to children with active TB. These cytokines did not change over the period of one year. IFN- $\gamma$  and IL-2 did not differ between participants with active or latent disease. In the sub-group of children with active TB infection and ART-naïve HIV co-infection a decline was noted during TB treatment. This was not seen in participants with either "latent" MTB infection or HIV negative participants with TB disease.

**Conclusion:** Testing the supernatant of the QFT for more cytokines is not a useful method for differentiating between "latent" MTB infection and active TB disease, as the trends which were seen for IL-10, IL-13, IL-17 and IL-1RA were too small and did not adequately differentiate between the clinical groups. However, we saw a decline over time for IL-2 and IFN- $\gamma$  in the subgroup of HIV/TB co-infected ART naïve children. This decline might have the potential to be used for monitoring of treatment and needs to be further investigated.

#### PD-565-30 Immunological parameters in children with tuberculosis and LTBI

A Starshinova,<sup>1</sup> I. Dovgaluk,<sup>1</sup> N Korneva,<sup>1</sup> Yu Ovchinnikova,<sup>1</sup> O. Yakunova,<sup>1</sup> S. Ananiev.<sup>1</sup>

<sup>1</sup>Phthiopulmonology, St. Petersburg Research Institute of Phthiopulmonology, St. Petersburg, Russian Federation. Fax: (+812) 5915788. e-mail: starshinova\_777@mail.ru

**Background: Objective:** Identify immunological criteria in diagnosis of LTBI and active TB in children.

**Design/Methods:** 202 patients from 3 to 14 years old were examined at children's phthiopulmonology department during 2011–2013. Diagnostic complex included: computed tomography (CT), DST, QFT. All children were divided in 3 groups: I group (76) - healthy children (negative results of DST and QFT), II group (29) - LTBI (positive results of DST and QFT), III group (126) - TB (positive results of DST and QFT). The results of serological tests for definition titers of anti-TB antibodies, assessment of leucocytes' subsets (CD3<sup>+</sup>, CD4<sup>+</sup>, CD8<sup>+</sup>, CD16<sup>+</sup>, CD20<sup>+</sup>, CD25<sup>+</sup>, CD95<sup>+</sup>, HLAII), cytokines (TNF- $\alpha$ , IL-2, IL-4, INF- $\gamma$ ), the phagocytic function of neutrophils (phagocytic number, phagocytic index, phagocytic completeness) were compared between groups.

**Results:** Titers anti-TB antibodies in III group were higher than in I and II groups for all serological tests. Statistically significant differences were established only in complement fixation test ( $15.34 \pm 5.86$  (III group) vs.  $9.72 \pm 5.3$ ,  $p=0.002$  (I) and  $9.75 \pm 4.6$  (II),  $p=0.04$ ). Leucocytes' subsets: level of CD8<sup>+</sup> ( $p=0.0026$ ) was increased in I group, CD25<sup>+</sup> ( $p=0.009$ ) - in II group, CD3<sup>+</sup> ( $p=0.003$ ) and CD4<sup>+</sup> ( $p=0.02$ ) - in III group. Induced cytokine level of IL-2 were statistically higher in II group than I group ( $323 \pm 244.9$  vs  $181.6 \pm 132.74$ ,  $p=0.04$ ); there were a trend of increasing levels of all cytokines in II group vs III group: IL-2 ( $323 \pm 244.9$  vs  $274.5 \pm 203.6$ ); IL-4 ( $2.30 \pm 1.05$  vs  $1.65 \pm 1.02$ ); IFN- $\gamma$  ( $22856 \pm 10800$  vs.  $20800 \pm 11055$ ); TNF- $\alpha$  ( $1111 \pm 681.5$  vs.  $954.9 \pm 732.1$ ). The number of stimulated neutrophils ( $71.1 \pm 3.05$  vs.  $66.88 \pm 3.36$  and  $64.12 \pm 4.17$ ) and phagocytic index ( $7.34 \pm 1.23$  vs  $4.85 \pm 0.49$  and  $3.51 \pm 0.87$ ) were higher in III group vs I and II. Completeness of phagocytosis was comparable in all groups ( $1.03 \pm 0.14$  (I) vs.  $0.92 \pm 0.14$  (II) and  $0.94 \pm 0.06$  (III)).

**Conclusion:** LTBI is associated with increase of cytokines' levels (TNF- $\alpha$ , IL-2, INF- $\gamma$ ) and activation. Active TB associated with activation of the humoral response and function of neutrophils. The distinction latent from active disease remains a challenge and needs research into novel immunological biomarkers.

#### PD-566-30 Evidence of lipid antigen presentation by CD1d pathway in murine alveolar epithelial cells against *Mycobacterium bovis* (BCG) infection

Z Rizvi,<sup>1</sup> Niti Puri,<sup>1</sup> R K Saxena.<sup>2</sup> <sup>1</sup>School of Life Sciences, Jawaharlal Nehru University, New Delhi, <sup>2</sup>Faculty of Life Sciences and Biotechnology, South Asian University, New Delhi, India. e-mail: zaigham.abbas15@gmail.com

**Background:** CD1 antigen presentation defines an evolutionary conserved pathway of lipid antigen presentation that is known to elicit rapid yet efficient cytotoxic response against fast mutating pathogens. CD1d pathway, the only isoform of CD1 family present in mouse, has been shown to recognise important component of the Mycobacterium cell wall like phosphatidylinositol mannosides. The expression of CD1d molecule has been studied so far only in professional antigen presenting cells (APCs) like B cells, dendritic cells, etc. In the present study we explored the possibility of lipid antigen presentation via the CD1d antigen presentation pathway by alveolar epithelial cells (AECs). The anatomical location of the AECs makes them the most prone to the onslaught of pathogens entering from the nasal cavity like *Mycobacterium tuberculosis* (Mtb). Although the physiological role of these AECs is well described in literature, the role of these cells in the adaptive immune response especially in terms of the CD1d pathway has never been researched.

**Design/Methods:** The expression of CD1d on LA4 (mouse AECs) cell lines, and also on AECs both in vivo and in situ, by flow cytometry and immuno-histochem-



istry respectively. The next objective was to study the response of these AECs against Mtb infection, for this we established live infection of *Mycobacterium bovis* BCG (which is an avirulent strain used as Mtb model) in mouse and did mRNA expression profiling by qRT-PCR for few of the crucial molecules involved in CD1d pathway. Finally we performed a functional CD1d presentation assay, on AECs from murine, by exploiting an already established protocol of  $\alpha$ -GalactosylCeramide ( $\alpha$ -GalCer) (a lipid antigen) presentation by CD1d pathway.

**Results:** The important novel finding of our study is that AECs do express CD1d molecule and in presence of a pathogenic challenge like BCG infection the whole machinery of CD1d molecule assembly, the pathogen uptake, processing and presentation is significantly upregulated. Also we provide direct evidence for the first time that a non-professional antigen presenting cell like AECs is capable of actual lipid antigen presentation by CD1d pathway.

**Conclusion:** Our findings suggest that lipid antigen presentation may be an important component of immunological role of AECs as thus contributing to the immune defenses against *Mycobacterium tuberculosis* infection.

#### PD-567-30 A cohort study of duration and changes in BCG effectiveness against tuberculosis with time since vaccination in Norway

P Nguipdop-djomo,<sup>1</sup> P Mangtani,<sup>1</sup> L Rodrigues,<sup>1</sup> K Rønning,<sup>2</sup> I Cappelen,<sup>2</sup> E Haldal,<sup>2</sup> I Abubakar.<sup>3</sup>

<sup>1</sup>Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, UK; <sup>2</sup>Infectious Disease Surveillance, Norwegian Institute of Public Health, Oslo, Norway; <sup>3</sup>Institute of Epidemiology and Health, University College London, London, UK.

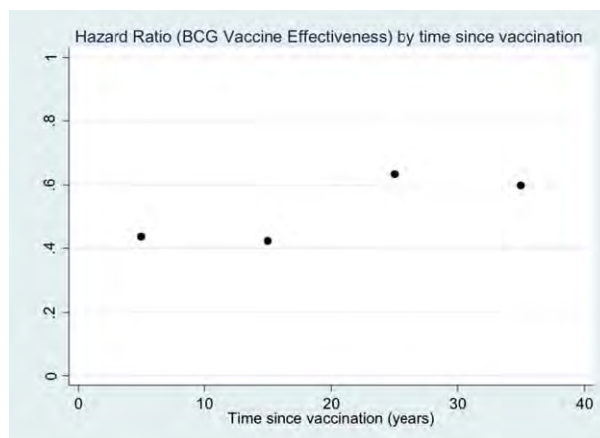
e-mail: patrick.nguipdop-djomo@lshtm.ac.uk

**Background:** BCG vaccines remain the sole licensed prophylactic vaccines against tuberculosis (TB) to date. Evidence regarding their duration of protection and how this change with time since vaccination is sparse; several studies suggest the vaccines are effective up to at least 10–15 years after vaccination, but not much is known beyond this point. The information could be useful to revise the cost-effectiveness of various BCG vaccination strategies, as well as in the development, field-testing and scheduling of new TB vaccine candidates, notably BCG boosters. Objective: Measure BCG vaccine effectiveness (VE) against tuberculosis up to 40 years after vaccination when given to tuberculin-negative subjects.

**Design/Methods:** Cohort study using the Norwegian-born population screened for active and latent TB and offered BCG as part of a national program from 1962–1975, and followed up to 2011. We used a Cox regression model to compare TB rates between vaccinated and unvaccinated subjects in successive 10-year time intervals since vaccination, while controlling for confounding.

**Results:** 326,242 BCG vaccinated and 84,408 unvaccinated tuberculin-negative subjects aged 13 to 50 years were followed from 1962 up till 2011. Overall there was respectively 108 TB cases among unvaccinated over 3,234,105 person-years (crude rate 3.3 per 100,000 person-years), compared to 159 cases in BCG vaccinated in 12,761,037 person-years (crude rate 1.2 per 100,000 person-years), for an average VE of 50% (95%CI: 28% to 65%) over 40 years. The VE was roughly 60% over the first 20 years after vaccination (respectively 56% [19% to 76%] 0–9 years, and 58% [27% to 76%] 10–19 years after BCG), seemingly decreasing to about 35% 20 to 40 years after vaccination (respectively 37% [-35% to 70%] 20–29 years, and 40% [-26% to 72%] 30–40 years after BCG). The results were similar when restricted to pulmonary TB.

**Conclusion:** These results support the hypothesis of long lasting BCG-derived protection up to at least 40 years, and suggest that BCG vaccine effectiveness wanes with time since vaccination, with apparent drop in protection after 20 years. Our findings are comparable to data from North America, which reported persistent BCG efficacy up to 50–60 years after vaccination in American Indians and Alaska Natives.



## 07. MOLECULAR DETECTION OF TB AND DRUG RESISTANCE - I

#### PD-568-30 Cost-effectiveness of XDR-TB diagnostics: GCDD results

E Groessl,<sup>1</sup> N Hillery,<sup>1</sup> A Trollip,<sup>2</sup> L Jackson,<sup>3</sup> R Garfein,<sup>3</sup> T Rodwell,<sup>3</sup> T Ganiats,<sup>1</sup> A Catanzaro.<sup>3</sup> <sup>1</sup>Family and Preventive Medicine, University of California San Diego, La Jolla, CA, USA; <sup>2</sup>Department of Biomedical Sciences, Stellenbosch University, Port Elizabeth, South Africa; <sup>3</sup>Medicine, University of California San Diego, La Jolla, CA, USA. Fax: (+011) 8585524321. e-mail: egroessl@ucsd.edu

**Background:** MGIT drug susceptibility testing (DST) is the reference standard for diagnosing drug-resistant tuberculosis, but time to results is typically >3 weeks. New diagnostic tests can reduce the time to result from

>3 weeks to <7 days, but usually sacrifice some level of accuracy in comparison to MGIT. In addition to the time to result and the accuracy of the test, it is important to also consider the cost of each diagnostic test in relation to these other factors. Our study examines the cost-effectiveness XDR-TB diagnostics in three unique settings.

**Design/Methods:** 1128 subjects with confirmed TB were enrolled from TB clinics in Mumbai, India; Chisinau, Moldova; and Port Elizabeth, South Africa. Subject sputum samples underwent DST for 7 drugs (rifampin, isoniazid, ofloxacin, amikacin, kanamycin, capreomycin, moxifloxacin) using 2 growth-based (MGIT, MODS) and 2 molecular (Pyrosequencing [PSQ], line-probe assays [LPA]) assays. Time to result was the primary measure of effectiveness. Sensitivity and specificity were also evaluated. Cost to perform each test was recorded by site. Costs included test-specific materials, personnel, and equipment costs. Overhead costs were estimated. Incremental cost-effectiveness ratios were calculated in terms of \$/day saved to DST result. Sensitivity analyses examine the impact of batch size and personnel costs.

**Results:** Data presented previously indicate that the mean time to DST results was 26.9 days, 14.5 days, 5.0 days, and 3.1 days for MGIT, MODS, LPA, and PSQ, respectively. When diagnosing MDR-TB, MODS was most accurate in comparison to MGIT, with PSQ and LPA producing similar results. For diagnosing XDR-TB, MODS was the most accurate, followed by PSQ, and then LPA. For a standard batch size, mean cost per sample without equipment or overhead was \$23, \$28, \$33, and \$41 for the MODS, MGIT, PSQ, and LPA, respectively. For incremental cost-effectiveness, MODS was both quicker and less costly than MGIT. The PSQ and LPA cost more but were considerably faster than MODS. PSQ was 1.9 days faster than LPA, and also cost less under most scenarios. Batch size and personnel costs were the main drivers of cost variation.

**Conclusion:** When diagnosing XDR-TB, the benefit of faster time to result in comparison to the MGIT must be weighed against reduced accuracy, and for some tests, increased costs. If diagnosing MDR-TB, there are multiple tests that produce faster results with a high degree of accuracy, and a similar or even lower cost.

#### **PD-569-30 Isolation and identification of nontuberculous mycobacterium by polymerase chain reaction: restriction enzyme - a simple and robust method**

A K Verma,<sup>1</sup> G Kumar,<sup>1</sup> J Arora,<sup>1</sup> M Bhalla,<sup>1</sup> S Panchal,<sup>1</sup> V Myneedu,<sup>1</sup> R Sarin.<sup>1</sup> <sup>1</sup>Microbiology, National Institute of TB and Respiratory Diseases, Delhi, India.  
e-mail: akv\_680@yahoo.co.in

**Background:** The species identification of NTMs is important as it determines the line of treatment and management of the disease. The routine conventional procedure for identification is time consuming, lengthy and sometimes fails to identify species of non-

tuberculous mycobacterium. Therefore, we have standardized an in-house polymerase chain reaction – restriction enzyme analysis (PRA) method to identify the mycobacterial species within a short span of 72 hours.

**Design/Methods:** For identification of mycobacterium species, a total of 45 confirmed nontuberculous mycobacterial specimens were placed for PRA and biochemical test simultaneously. In PRA test the DNA were extracted from positive solid and liquid cultures which were amplified by using Hsp-65 target gene followed by restriction enzyme digestion with endonuclease enzyme Bst E 11 and Hae 111 enzyme. The digested product was subjected to Gel electrophoresis on a 3% agarose gel and the results were compared with the standard pattern to identify the species. Using conventional method, 16 different biochemicals were used to identify mycobacterial species

**Results:** In the PRA test, initial amplification was seen with all 45 mycobacterial strains which produced 439bp of amplification band. Out of 45 NTMs, 42 were identified to species level when digested with BstE 11 and Hae 111 restriction enzyme and 03 isolates were not identified to species level. In PRA test, altogether 12 types of NTMs were identified, whereas in biochemical test 8 categories were acknowledged. Common species identified were *Mycobacterium chelonae* (18) among the rapid growing NTM(26) and *Mycobacterium avium* complexes (8) amongst the slow growing NTMs (16). PRA and biochemical identification showed 93% (42/45) concordant results.

**Conclusion:** PRA is a valid alternative for identification of NTM in a routine laboratory. It is fast, cheap and accurate for identification of potentially pathogenic NTM..

#### **PD-570-30 Rapid molecular detection of *Mycobacterium tuberculosis* and drug-resistance to isoniazid, rifampicin, fluoroquinolones and injectable drug from sputum**

N Sung,<sup>1</sup> N Lee,<sup>1</sup> JH Jung,<sup>1</sup> J Choi,<sup>2</sup> H Ahn,<sup>1</sup> CT Kim,<sup>1</sup> H Kang.<sup>1</sup> <sup>1</sup>Clinical Research Center, National Masan Hospital, Changwon, <sup>2</sup>Research and Development Center, Seegene Institute of Life Sciences, Seoul, Republic of Korea, e-mail: paratb@gmail.com

**Background:** We comparatively evaluated multiplex Real-Time PCR based Anyplex™ II MTB/MDR/XDR Detection kit (hereinafter AnyplexII, Seegene Inc., Rep. of Korea) and line probe based detection systems (GenoType MTBDRplus and MTBDRsl (Hain life-science, Germany) ) for detecting *M. tuberculosis* (Mtb), drug resistance to isoniazid (INH), rifampicin (RIF), fluoroquinolones and injectable drugs from sputum samples of tuberculosis patients.

**Methods:** Sputum samples (N=265) banked in Tuberculosis Specimen BioBank established in Masan National Hospital were randomly selected. Selected sputa were applied to smear examination, DNA extraction and Mtb

isolation. Then extracted DNAs were applied to three molecular methods, AnyplexII, GenoType MTBDRplus, and GenoType MTBDRsl to detect Mtb and mutations in genes of *inhA*, *katG*, *rpoB*, *gyrA*, *rrs*, and *eis*. Mtb isolates were applied for conventional culture based DST (proportion method) which was considered as the gold standard. Sensitivity and specificity of the 3 molecular methods to detect the drug resistant associated mutations from sputum were comparatively analyzed.

**Results:** Among 265 sputum samples, 180 were culture positive and were employed in this study; 85 samples were culture negative or contamination thus excluded. Mtb detection rates from sputum were 98.3, 100, and 87.2% using AnyplexII, MTBDRplus, and MTBDRsl, respectively. With DNAs extracted from the sputum (N=180), Sensitivity and specificity for INH resistance using AnyplexII were 83.3 and 96.7%, respectively, while MTBDRplus were 87.1 and 76.6%, respectively. For RIF resistance, AnyplexII showed 91.8 and 95.4% of sensitivity and specificity, respectively, while MTBDRplus 87.6 and 83.6%, respectively. For sensitivities to detect resistance for moxifloxacin, levofloxacin, kanamycin, and amikacin, AnyplexII showed 88.7, 92.3, 68.4, and 85.2%, respectively, while MTBDRsl 86.2, 90.2, 60.0, and 80.8%, respectively. Specificities for moxifloxacin, levofloxacin, kanamycin, and amikacin using AnyplexII were 91.7, 96.2, 100, 97.2%, respectively, but using MTBDRsl 91.9, 96.9, 86.9, and 87.8%, respectively.

**Conclusions:** AnyplexII showed excellent diagnostic performance to simultaneously detect Mtb, INH, RIF, and FQ from sputum of pulmonary TB patients. However, the molecular method should be improved to detect kanamycin resistance from sputum, when considering low sensitivity.

#### PD-571-30 Detecting resistance to nine anti-tuberculosis drugs in a single reaction tube

M De Vos,<sup>1</sup> J Rice,<sup>2</sup> L Rice,<sup>2</sup> B Kreiswirth,<sup>3</sup> E Streicher,<sup>1</sup> P Van Helden,<sup>1</sup> R M Warren,<sup>1</sup> W Wangh.<sup>2</sup> <sup>1</sup>Biomedical Sciences, Stellenbosch University, Cape Town, South Africa; <sup>2</sup>Biology, Brandeis University, Waltham, MA, <sup>3</sup>Public Health Research Institute Center, New Jersey Medical School, New Jersey, NY, USA. e-mail: margab@sun.ac.za

**Background:** In 2012, WHO estimated that approximately 684,000 (5.7%) of the 12 million TB cases had multiple drug resistant (MDR) -TB. Less than 20% of MDR cases were correctly diagnosed and even fewer were treated according to WHO standards. The WHO Stop TB Department has emphasized the need to strengthen diagnostic services and highlighted the need to develop rapid diagnostics. The GenoType® MTBDRplus line probe assay and the Xpert® MTB/RIF only provide evidence for resistance to isoniazid and/or rifampicin, which is insufficient to ensure optimal treatment of MDR-TB. A critical need remains for a more comprehensive convenient diagnostic technology. The highly multiplexed LATE-PCR assay for M(X) DR-TB described here was designed to meet that need. Our goal was to establish a highly multiplexed LATE-PCR

single closed-tube assay that can simultaneously detect and distinguish multiple mutations in multiple gene targets known to confer resistance to isoniazid, rifampicin, ethambutol, ofloxacin, moxifloxacin, amikacin, kanamycin, capreomycin and ethionamide.

**Design/Methods:** DNA from *M. tuberculosis* clinical isolates harbouring all the known mutation types in *rpoB*, *katG*, *embB*, *inhA* promoter, *gyrB*, *gyrA* and *rrs* were selected from a DNA bank housed at Stellenbosch University. This comprises a total of 49 possible allelic variants in a multitude of possible combinations. Each DNA sample was amplified and the seven singled-stranded products were scanned for mutations at end-point using 20 Lights-On/Lights-Off Probes. The resulting fluorescent signatures distributed over four fluorescent colours were compared to that of H37Rv, a pan-susceptible "wildtype" strain.

**Results:** Analysis of 85 drug resistant isolates generated a library of signatures reflecting all of the known mutations in *rpoB*, *katG*, *gyrA*, *rrs*, *embB*, *inhA* promoter and *gyrB*. Each unique mutation had its own, highly reproducible fluorescent signature which was distinct from that of H37Rv, as well as all other isolates with different mutations at the same or different codons.

**Conclusion:** This study demonstrates that this single tube multiplexed assay can simultaneously distinguish the different mutations that confer resistance to rifampicin, isoniazid, ethambutol, ofloxacin, moxifloxacin, amikacin, kanamycin, capreomycin and ethionamide in less than three hours. Automation of this methodology will enable clinicians to optimise treatment of drug resistant TB thereby ensuring improved outcomes.

#### PD-572-30 MDR-TB management in a low-income country: GeneXpert™ versus Hain Lifescience™ assays for TB

Z Kashongwe Munogolo,<sup>1</sup> B Bisimwa,<sup>1</sup> S Callens,<sup>2</sup> E Andre.<sup>3</sup> <sup>1</sup>Kivu, ISTM Bukavu, Bukavu, Democratic Republic of Congo; <sup>2</sup>Gent University, Gent, <sup>3</sup>Université Catholique de Louvain, Bruxelles, Belgium. e-mail: zkashongwe@yahoo.fr

**Background:** South Kivu is a post conflict area in the East part of DR Congo. Effective TB control is challenged by the weak socioeconomic status of the country and the concomitant HIV epidemic.

**Opportunity:** In 2013, a screening network MDR TB was initiated under the governance of WHO TB Reach initiative and the Flemish VLIR\_UOS project. Ten GeneXpert® Kits were distributed in different health districts all over the Province and a molecular biology laboratory using Hain Lifescience® assays for TB was installed in the main city Bukavu

**Methods:** 82 sputum specimens were collected from high risk groups (military, police, PLHIV, minors, retreatment cases) from september2013 to march2014; Then 20 rifampicin resistant on GeneXpert underwent screening for rifampicin and INH resistance by Hain MTB plus assay.

**Results:** 14 (70%) specimens showed resistance to Rifampicin and INH, 5 (25 %) were Rifampicin



resistance only and 1(5%) was identified as atypical mycobacterium.

**Conclusion:** GeneXpert is an efficient mean for Rifampicin resistance detection and suspicion of MDR\_TB, but it needs complementary tests to confirm MDR\_TB

### PD-573-30 Impact of a newly-certified LPA laboratory as the only testing facility for the diagnosis of MDR-TB under PPM mode in a State of India

M Mawlong,<sup>1</sup> M Kunnemuriyil,<sup>2</sup> M Puthenchirayil,<sup>3</sup> P Varghese,<sup>3</sup> T Rangad,<sup>4</sup> G Singh,<sup>3</sup> S Rynthathiang,<sup>4</sup> K Ranee.<sup>1</sup> <sup>1</sup>Clinical Microbiology & Mycobacteriology, Nazareth Hospital, Shillong, <sup>2</sup>Nazareth Hospital, Shillong, <sup>3</sup>Catholic Bishops' Conference of India Coalition for AIDS and Related Diseases, Catholic Bishops Conference of India, New Delhi, <sup>4</sup>State TB Office, Reid Provincial Chest Hospital, Shillong, India. e-mail: michael.mawlong@gmail.com

**Background and challenges to implementation:** Susceptibility testing for isoniazid and rifampicin is pivotal for the diagnosis of MDR TB. Subsequent management of the case as per the Programmatic Management of Drug Resistant TB (PMDT) programme of India is dependent on a reliable laboratory diagnosis. We assessed the effect on the state PMDT programme after the introduction of the only certified Line Probe Assay (LPA) laboratory in the state of Meghalaya in India under the Public Private Mix (PPM) mode.

**Intervention or response:** Data for a period of one year (pre and post introduction of the LPA laboratory) were analysed to assess the impact of the PPM model. A pre tested questionnaire was used to interview State and District Tuberculosis Officers (STO, DTO) to document their views on the PPM.

**Results and lessons learnt:** For the period April 2012 to March 2013, samples could be sent only after consultation with the testing laboratory in an adjoining state. However after March 2013, samples could be sent at any time. The average time taken to receive a report, previously 10 days (range 4–13 days), was subsequently reduced to 5 days (range 3–10 days). The expense incurred in sending samples to the testing laboratory for four of the seven districts was higher than compared to that when sending to the new LPA laboratory. The total number of samples tested previously was 203 (out of 283) as compared to 310 (out of 375) tested subsequently, as 80 & 60 samples respectively were smear negative and could not be processed for LPA. The total number of Multi Drug Resistant (MDR) patients was 121 of 203 (59.61%) and 118 of 310 (38.06%) samples respectively. Rifampicin and isoniazid mono-resistance stood at 22, 16 (10.84%, 7.88%) & 13, 25 (4.19%, 8.06%) respectively for the two periods. It was found that all the respondents suggested that the LPA laboratory also start follow up cultures to reduce delays in intervention during treatment.

**Conclusions and key recommendations:** The entire testing load of the state in the PMDT programme can be borne by the LPA laboratory from the NGO/Private sector without compromising on the quality of the result.

The turnaround time from sample collection to issue of report was found to be shorter. If the LPA laboratory could introduce follow up cultures, it perhaps would have a greater impact on the overall success of the programme in the state.

### PD-574-30 Performance of MLPA assay in tuberculosis resistance detection

PF Santos,<sup>1</sup> Elis Dalla Costa,<sup>2</sup> M C Lourenco,<sup>3</sup> S Sengstake,<sup>4</sup> I Bergval,<sup>4</sup> R Anthony,<sup>4</sup> A Kritski,<sup>1</sup> M De Oliveira.<sup>1</sup> <sup>1</sup>Center for Tuberculosis Research, Rio de Janeiro Federal University, Rio de Janeiro, RJ, <sup>2</sup>Centre for Scientific and Technological Development, State Foundation for Health Research and Production, Porto Alegre, RS, <sup>3</sup>Laboratory of Bacteriology and Bioassays, Oswaldo Cruz Foundation, Rio de Janeiro, RJ, Brazil; <sup>4</sup>KIT Biomedical Research, Royal Tropical Institute, Amsterdam, Netherlands. e-mail: paula.gonsantos@gmail.com

**Background** Rapid diagnosis of mono, multi and extensive drug-resistant tuberculosis (DR/MDR/XDR-TB) is essential for early adoption of appropriate antimicrobial treatment, and preventing the spread of resistant strains. Molecular tests for rapid detection of MDR-TB (for rifampin and isoniazid) were recommended by WHO, but lower sensitivity for isoniazid resistance (INH<sup>R</sup>) detection have been described, as other genes involved to INH<sup>R</sup> were not included in those commercial tests. MLPA is a molecular method that adopts simultaneous multiplexed identification of multiple SNPs in *M. tuberculosis* by amplification of sequence-specific MLPA probes. Additionally, MLPA allows the inclusion or removal of probes according to the local prevalence of different drug resistant TB pattern. To evaluate the performance of MLPA to detect mutations in *rpoB*, *katG*, and *inhA* genes in isolates of *M. tuberculosis* and to compare its accuracy with Genotype<sup>®</sup> MTBDRplus for DR/MDR-TB diagnosis.

**Design/Methods:** Retrospective study with *M. tuberculosis* isolates obtained from TB cases with presumed drug resistant TB attended at four referral TB hospitals and one Secondary Health Unit in the Rio de Janeiro city, Brazil, from January 2004 and July 2006. Isolates from DR-TB suspects were evaluated by drug susceptibility testing (DST) using Proportion Method, MLPA with Luminex, MTBDRplus assay and DNA sequencing.

**Results:** 97 isolates were evaluated, according to DST and DNA sequencing, respectively, overall DR was observed in 16 (16.5%) and 17 (17.5%), and MDR-TB in 08 (8.2%) and 06 (6.2%) cases. The agreement between the results of the sequencing and MTBDRplus assay for the assessment of Rifampicin resistance (RIF<sup>R</sup>) and INH<sup>R</sup> was 96.9% and 92.7% respectively. The agreement of MLPA and sequencing for RIF<sup>R</sup> and INH<sup>R</sup> was 96.8% and 96.9%, respectively. Assuming DNA sequencing as a standard pattern, the specificity of MLPA and MTBDRplus for detection of RIF<sup>R</sup> and INH<sup>R</sup> was higher than 95%. MLPA had a lower sensitivity for detection of RIF<sup>R</sup> (60% vs 80%) and but higher for detection of INH<sup>R</sup> (84.6% vs 76.9%).

**Conclusion:** The promising results of both molecular tests indicate that MLPA Luminex and GenoType®MTBDRplus can be used in the detection of drug-resistant TB in culture isolates of *M. tuberculosis*.

### PD-575-30 Comparison of two molecular assays with phenotypic rifampicin DST and rpoB gene sequencing

B Magazi,<sup>1</sup> P Jotam,<sup>2</sup> N Maningi,<sup>1</sup> F Ismail,<sup>1</sup> N Mbelle,<sup>1</sup> T Gumbo.<sup>2</sup> <sup>1</sup>Medical Microbiology, University of Pretoria, Pretoria, South Africa; <sup>2</sup>Medicine, UT Southwestern Medical Centre, Dallas, TX, USA. e-mail: beki.magazi@nhls.ac.za

**Background:** Rifampicin resistance is used as a surrogate marker for the detection of multiple-drug resistance tuberculosis (MDR-TB). We sought to evaluate the performance of two commonly used molecular assays against phenotypic rifampicin DST and rpoB gene sequencing in a clinical laboratory in South Africa, during routine pulmonary TB clinical care

**Design/Methods:** We sequenced a 496bp region of the rpoB gene, including the RRDR, in 40 patients suspected to have RIF resistance. Two molecular assays (GenoType®MTBDRplus, HainLifesciences, and GeneXpert/MTBRIF, Cepheid) were also performed on culture sediments from each sputum sample and then compared with DST performed in the BD Bactec™MGIT™ 960 system. Agreement between the molecular assays was determined using both % and  $\kappa$ -statistic, after adjusting for MGIT and sequencing results.

**Results:** Excluding two patients with mixed infections for whom the rpoB sequences were not available (Table), the sensitivity and specificity for the GeneXpert were, 0.96 (95% CI 0.80-1.00) and 1.00 (95% CI 0.75-1.00), respectively. Similarly, estimates for GenoType®MTBDRplus were 0.72(95% CI 0.53-0.87) and 0.67 (95% CI 0.30-0.93). These findings are in agreement with published literature. On the other hand, 5/18 (28%) patients with known mutations were sensitive on MGIT, compared to 11/13 (85%) without mutations, suggesting that the RIF critical concentration of 1 $\mu$ g/ML might be high. Despite the high rpoB mutations prevalence (60%), the positive predictive value with the MGIT was only 0.15 (0.02-0.45). Overall, % agreement between the molecular assays was 75%, and  $\kappa$ -statistic was minimal but significantly varied 0.38 $\pm$ 0.15. Nonetheless, among the 14 patients without mutations % agreement was poor: 50.25% and  $\kappa$ =0.11 $\pm$ 0.12. MGIT revealed 16(40%) isolates were phenotypically resistant and 17 (43%) sensitive.

**Conclusion:** The study suggests that the MGIT rifampicin critical concentration should be lowered to increase its predictive values and avoid misclassification of susceptibility. There is a need for the use of minimum inhibitory concentrations (MIC) and patient outcomes data in deriving breakpoints for the susceptibility testing of *Mycobacterium tuberculosis*. Only the rpoB gene was sequenced in these isolates, other resistance mechanisms, including efflux pumps and mutations outside

rpoB, might be clinically important and should be sought after.

rpoB mutations	n (%) strains	MTBDRplus Resistant (n)	GeneXpert/RIF Detected(n)
<b>Resistant on MGIT</b>	<b>16 (40%)</b>		
D516Y	1	1	1
DEL	2	1	2
H526L	1	1	1
H526R	1	1	1
L533P	1	1	1
Q513L	1	1	1
Q513P	1	1	1
S531L	1	0	1
S531Q	2	2	2
S531W	1	1	1
S601T	1	1	1
No mutations**	2	2	1
Mixed strains	1	1	1
<b>Sensitive on MGIT</b>	<b>17 (43%)</b>		
D516Y	1	1	1
H526N	1	1	1
L511P	2	2	2
S531Q	1	1	1
No mutations**	11	6	0
Mixed strains	1	1	1
<b>Lost viability no MGIT result</b>	<b>7 (17%)</b>		
D516Y	2	1	2
H526N	1	1	1
H526R	1	1	1
Q513L	1	1	1
S531L	1	1	1
No mutations	1	0	0

### PD-576-30 Evaluation of a microbead-based method for simultaneous spoligotyping and detection of INH and RIF resistance in *M. tuberculosis* strains

B Molina-moya,<sup>1</sup> M Gomgnimbou,<sup>2,3</sup> C Lafoz,<sup>4</sup> S Samper,<sup>4</sup> C Sola,<sup>2</sup> J Dominguez.<sup>1</sup> <sup>1</sup>Servei de Microbiologia, Institut d'Investigació Germans Trias i Pujol, Badalona, Spain; <sup>2</sup>Institut de Génétique et Microbiologie, CNRS-Université Paris-Sud, Paris, France; <sup>3</sup>Centre Muraz, Centre Muraz, Bobo-Dioulasso, Burkina Faso; <sup>4</sup>Hospital Universitario Miguel Servet, Instituto Aragonés de Ciencias de la Salud, Zaragoza, Spain. e-mail: jadomb@gmail.com

**Background.** A new microbead-based method for simultaneous spoligotyping and detection of resistance to rifampicin (RIF) and isoniazid (INH) named TB-SPRINT has been recently developed. The objective of this study was to evaluate the TB-SPRINT test comparing the results with a) conventional membrane-based spoligotyping, and b) phenotypic drug susceptibility testing (DST) to RIF and INH with Bactec MGIT and sequencing of rpoB.

**Design/Methods.** A total of 69 well characterized *M. tuberculosis* complex strains isolated in Spain were retrospectively selected by inclusion of diverse spoligotypes. Strains were blindly analyzed with the TB-SPRINT method (Gomgninmou et al). Briefly, clustered regularly interspaced short palindromic repeat (CRISPR) region, rpoB, katG and the promoter region of inhA were simultaneously amplified by PCR. Subsequently, PCR product was hybridized to oligonucleotide-precoupled microbeads and detection was performed with a Luminex 200 device and xPonent software. Strains were also subjected to 3R SNP typing (Abadia et al).

**Results.** Of the 69 strains tested, microbead spoligotyping results for two strains were excluded: for one strain DNA concentration was low, and for the other one results suggested the presence of two different populations that was confirmed by MIRU24 and MIRU31 analysis. For two additional strains, membrane- and microbead-based spoligotyping identified different clades, but SNP typing confirmed TB-SPRINT results. Considering the remaining 65 strains, the concordance between spoligotyping methods was 99.6% (2783/2795 spoligotype data points). Regarding the comparison with phenotypic DST, sensitivity of TB-SPRINT to detect resistance to RIF and INH was 66.7% (4/6) and 75.0% (3/4), respectively, and specificity was 98.3% (59/60) and 95.2% (59/62), respectively. Concordance between TB-SPRINT and *rpoB* sequencing was 98.1% (51/52).

**Conclusions.** TB-SPRINT is a rapid and easy to perform test for genotyping and detection of resistance to RIF and INH in a single tube, therefore it may be a useful tool to improve epidemiological surveillance, specially in countries with high burden of drug resistant TB.

#### PD-577-30 Multi-center study to assess the non-inferiority of Nipro NTM+MDRTB and Hain GenoType MTBDRplus V.2 LPAs compared to Hain GenoType MTBDRplus V.1

W Sikhondze,<sup>1</sup> E Valli,<sup>1</sup> D Hillemann,<sup>2</sup> N Ismail,<sup>3</sup> M Joloba,<sup>4</sup> P Nabeta,<sup>1</sup> C Boehme.<sup>1</sup> <sup>1</sup>TB Programme, Foundation for Innovative New Diagnostics (FIND), Geneva, Switzerland; <sup>2</sup>Forschungszentrum Borstel, WHO Supranational TB Reference Laboratory, Borstel, Germany; <sup>3</sup>National TB Reference Laboratory, National Institute for Communicable Diseases, Johannesburg, South Africa; <sup>4</sup>National TB Reference Laboratory, WHO Supranational TB Reference Laboratory, Kampala, Uganda. e-mail: welile.sikhondze@gmail.com

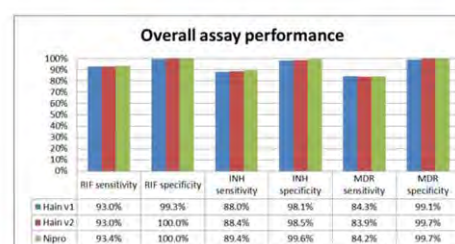
**Background:** In 2008 WHO endorsed the use of line probe assays (LPA) for the rapid detection of MDR TB. An updated version of the Hain GenoType MTBDRplus LPA (Hain V.2) was introduced in 2011. Nipro Corporation updated its NTM+MDRTB LPA (Nipro kit 2) in 2012, which identifies NTMs (*M. avium*, *M. intracellulare* and *M. kansasii*) in addition to the *M. tuberculosis* (*Mtb*) complex. Both assays detect resistance to rifampicin (RIF) and isoniazid (INH). This study aims to determine non-inferiority of the Nipro kit 2 and Hain V.2 kit in comparison to the WHO endorsed Hain GenoType MTBDRplus V.1 on selected strains.

**Methods:** We conducted a multi-center, blinded study to evaluate and compare the performance of the Nipro kit 2 and Hain V.2 for detection of TB, as well as RIF, INH resistance in comparison to Hain V.1, phenotypic drug-susceptibility testing and sequencing. During phase I, 600 selected strains from the ITM/TDR collection were tested. Each participating laboratory (Borstel SNRL, Uganda SNRL and South Africa NICD) received 200 strains (100 RIFr/INHr, 10 RIFs/INHr, 80 RIFs/INHs *Mtb* complex strains, 10 non-*Mtb* complex strains) and were blinded to the phenotypic and sequencing results but not to respective other LPA results.

**Results:** A total of 575 (95.8%) strains were included in the analysis (545 MTB and 30 non-MTB strains) and 25 (4.2%) strains were excluded. Sixteen (64%) of the excluded strains had disputed mutations L533P and H526N, 6 (24%) were excluded due to lack of agreement between sites on the interpretation of WT8 banding pattern and 3 (12%) for possible sample mix-up. For MTB detection, a high specificity of 100% was achieved by all three assays with sensitivity levels of 99.1% (Nipro), 99.5% (Hain v2) and 99.5% (Hain v1). Indeterminate rates were low for the Nipro, Hain v2 and Hain v1 assays for both RIF (1.5% vs 0.6% vs 0.4%) and INH (1.1% vs 0.6% vs 0.6%), respectively. The comparative results for RIF and INH resistance are presented in the attached graph. Both Hain V.2 and Nipro were non-inferior to Hain V.1 for RIF specificity, INH sensitivity and INH specificity. For RIF sensitivity, although the confidence intervals for all three assays cross the lower limit of the non-inferiority margins, the performance of the tests were exactly the same and therefore comparable.

**Conclusion:** Good consistency across testing sites was demonstrated for all assays. The three LPAs showed similar performance in terms of sensitivity and specificity.

Fig 1: Overall assay performance for RIF/INH sensitivity, MDR sensitivity and MTB detection



#### PD-578-30 Evaluation of basic analytical performance of Pure-TB-Lamp

Y Mori,<sup>1</sup> Y Yuki,<sup>1</sup> N Tomita,<sup>1</sup> H Kanda,<sup>1</sup> S Kojiya,<sup>1</sup> T Notomi.<sup>1</sup> <sup>1</sup>Research and Development, Eiken Chemical Co., Ltd., Tochigi, Japan. e-mail: yasuyoshi\_mori@eiken.co.jp

**Background:** Loop-mediated isothermal amplification (LAMP) has been used to detect wide variety of pathogens including bacteria, viruses and protozoa. Because of its easiness and swiftness, LAMP is considered as one of the most promising nucleic acid amplification methods to be applied in the field of point-of-care testing (POCT) system for the resource-limited settings. Recently, the LAMP for *M. tuberculosis* complex detection and its related technology named PURE (Procedure for Ultra Rapid Extraction) for a simple sample processing method (PURE-TB-LAMP) have been developed and evaluated its applicability as simple and fast screening method for TB in rural area of developing countries. Here we report the basic analytical performance of the PURE-TB-LAMP using H37Rv spiked samples.



**Design/Methods:** Sputum samples with a variety of number of TB cells were prepared by spiking cultivated *M. tuberculosis* (H37Rv) to control sputum samples obtained from healthy volunteers and then analyzed by the PURE-TB-LAMP method according to the instructions in the Loopamp MTBC detection kit and Loopamp PURE DNA extraction kit. Bloody sputum samples were prepared by adding blood to control sputum samples and used for evaluating the effect of blood to the sensitivity of the method. Applicability of the method to the samples other than sputum was also evaluated by using of H37Rv spiked urine, simulated gastric fluid and so on.

**Results:** The analytical sensitivity of PURE-TB-LAMP was found to be 100–150 cfu/ml sputum, which is not affected from the presence of an excess amount of *M. avium* cells or human genomic DNA. No cross-reaction was observed from nontuberculosis *Mycobacterium* species tested. It has been found that the PURE method has ability to remove inhibitors in many types of samples including urine and simulated gastric fluid, indicating its possible applicability to the other type of samples than sputum for TB detection.

**Conclusion:** This study on basic analytical performance of PURE-TB-LAMP presents the potential ability of PURE-TB-LAMP as a fast and reliable TB diagnostics.

#### **PD-579-30 Comparison: the performance between Xpert MTB/RIF and line probe tool for diagnosis MDR-TB among MTB and TB-HIV in low prevalence of MDR-TB**

P Kunawarak, <sup>1</sup> S Arunthong, <sup>1</sup> A Jompaeng, <sup>1</sup> S Kongsin, <sup>2</sup> P Pokaew, <sup>1</sup> C Chuchottaworn, <sup>3</sup> C Namwat. <sup>4</sup>

<sup>1</sup> Department of Disease Control, The Office of Disease Prevention and Control, 10, Chiang Mai, <sup>2</sup> Health Administration, Faculty of Public Health, Mahidol University, Bangkok, <sup>3</sup> Department of Medicine, Central Chest Institute of Medical Services, Bangkok, <sup>4</sup> Department of Disease Control, Bureau of Tuberculosis, Bangkok, Thailand. Fax: (+66) 053140773. e-mail: wararakp1@hotmail.com

**Background:** Tuberculosis (TB) continues a major public health problem in Thailand where prevalence of primary drug resistance was over the hot spot level especially among HIV infected individuals. The obstacle of TB control due to lack of effective technology to identify drug resistance tuberculosis and multi-drug resistance tuberculosis (MDR-TB). Xpert MTB/RIF and Line Probe Assay has garnered a significant interest as a high sensitivity and rapid diagnostic tool to improve detection of MDR-TB. The study aimed to compare the effectiveness of MDR-TB diagnosis between Xpert MTB/RIF and Line Probe Assays method (using conventional DST as gold standard).

**Design/Methods:** From May to September 2013, 650 TB patients whose sputum was positive for acid fast bacilli (AFB) were enrolled from the 70 hospitals in upper north of Thailand. All samples had been sent by Express Mail Service to reference laboratory at the Office of Disease and Prevention Control, 10 Chiang Mai for testing by culture, conventional DST, Xpert MTB/RIF and Line Probe Assays.

**Results:** Among 650 cases; only 512 were eligible for the study (24 contaminated, 18 NTM, 3 multiorgan and 93 cases with no growth results from cultures were excluded). Sensitivity, Specificity, Positive predictive value (PPV), Negative predictive value (NPV), Accuracy and Diagnostic Odds of Xpert MTB/RIF to diagnostic MDR-TB was 80%, 98.4%, 33.3%, 99.8%, 98.2%, 50.7%, 0.2% and 249.5, while Line Probe Assays was 40%, 99.2%, 33.3%, 99.4%, 98.6%, 98.6%, 50.7%, 0.6% and 83.83. Among 21 TB-HIV cases, it was found that both Xpert MTB/RIF and Line Probe tool had the same value of Sensitivity, Specificity, PPV, NPV and Diagnostic accuracy at 100% respectively

**Conclusion:** This study show that the performance of Xpert MTB/RIF was better than Line Probe assay for diagnostic MTB with high sensitivity about 2 times. And the performance of both Xpert MTB/RIF and Line Probe assay for diagnostic MDR-TB in TB-HIV group was very good with 100% of all parameter of diagnostic test. Xpert MTB/RIF performance show that it could be placed in decentralized settings to support the reduction of delay in treatment initiation in TB patients and TB with HIV infection.

#### **08. OPENING THE DOOR TO COMMUNITY ENGAGEMENT IN TB**

##### **PD-580-30 Kids role, tuberculosis and health promotion: new communication strategies**

G Israel, <sup>1</sup> C Lima, <sup>1</sup> C Cruz, <sup>2</sup> L Lima. <sup>3</sup> <sup>1</sup>Health Promotion, Rio de Janeiro Health Department, Rio de Janeiro, RJ, <sup>2</sup>General Sub Secretariat, Rio de Janeiro Health Department, Rio de Janeiro, RJ, <sup>3</sup>Praça do Conhecimento, Science and Technology Department, Rio de Janeiro, RJ, Brazil. e-mail: gisrael.br@gmail.com

**Background and challenges to implementation:** Public policies to reach younger audiences using their forms of expression and communication are almost nonexistent, in Brazil and elsewhere. The debate on tuberculosis under the various forms of children and adolescent expression, inside the communities where they live, can greatly contribute to better communicate and to disseminate the relationship of this disease prevention and cure with the promotion of Health, the quality of life, the social mobilization and citizenship. This experience recognizes that children and young people can and should play a leading role in the creation, production and use of products for public policy communication. It also recognizes that the act of playing is relevant to health and stimulates affection, tolerance, solidarity and communication. This has become evident among children of various age groups in the “Favela do Complexo do Alemão” in Rio de Janeiro, since 2010, when this experience began.

**Intervention:** Children have been stimulated to photograph, to film, to design or to show through any other way of expression their understanding on the issue of interest. The debate on tuberculosis emerged related to

quality of life, health promotion, social mobilization and citizenship and got a highlighted place in the children playing agenda.

**Results and lessons learned:** Innovative ways to communicate and disseminate information and campaigns, from childrens' perspective and standpoint, through drafting cards, flyers, video and radio programs, music, and drama performance. This kind of material can be used by Rio de Janeiro Health Department, by NGOs and by the groups that have participated in their production, inside their communities, in the school, and in the various meeting places; there is real evidence of the breaking down of adults resistance in discussing TB issues as they are now joining kids and participating in the activities/games proposed; increased community self esteem and pride; easier dialogue among health care professionals and kids / young people.

**Conclusion and key recommendation:** Children want to take part and to be subjects of their own stories. They show interest and argumentative ability, every time they are asked to express themselves. Children and youth opinions and arguments should often be considered for the decision making of public campaigns, especially those aimed at the victims of inequalities



**PD-581-30 Mobilising community care-givers in providing TB care in hard-to-reach areas of India: experiences of World Vision India and partners**

S Mukhopadhyay,<sup>1</sup> S Cornelius,<sup>1</sup> V K Edward,<sup>1</sup> B Samuel,<sup>1</sup> M Jose.<sup>1</sup> <sup>1</sup>Health, World Vision India, New Delhi, India. e-mail: sugata64@gmail.com

**Background and challenges to implementation:** To overcome challenges like insufficient access to TB services and low TB case detection World Vision India (WVI) and 6 Civil Society partners have been imple-

menting Project Axshya in selected problematic and poorly-performing areas of 74 districts in 7 states (Andhra Pradesh, Orissa, West Bengal, Chhattisgarh, Bihar, Jharkhand, Madhya Pradesh) of India with the help of The Global Fund since Apr'10. The project will continue till Sept'15.

**Intervention or response:** Between Apr'10 to Dec'13, more than 12,000 rural healthcare practitioners, 150 women's self-help groups (SHGs), 1000 community volunteers & workers, 50 workplaces, 80 grass-root level NGOs, 153 HIV Project Managers, 532 PLHIV, and 16,000 school-children gained knowledge on TB as potential community TB care-givers with the help of the project across 74 districts and engaged in 1) TB awareness generation and advocacy in community, b) detection of TB presumptive cases in community & their referral to RNTCP with follow-up (RNTCP: Revised National TB Control Program of India) including sputum collection & transportation, c) provision of DOT to the TB patients.

**Results and lessons learnt:** Those community care-givers generated TB awareness in 31378 villages (out of 48978 villages), added around 12,500 additional TB cases into RNTCP and helped 90% of them to start DOT within 7 days of diagnosis. Around 500 care-givers became DOT-providers. They also retrieved around 3300 defaulted TB cases and brought them back to RNTCP. Active case search by community volunteers in tribal villages & TB advocacy activities by school-children in Chhattisgarh, TB screening camps in difficult-to-reach villages by community volunteers & ASHA in Odissa, TB care by cured TB patients and rural health practitioners in difficult regions of West Bengal, TB/HIV collaboration through PLHIV networks and HIV high risk groups in Andhra Pradesh, TB care by women's SHGs in Bihar, referral of TB presumptive cases and sputum collection & transportation by community volunteers & ASHA in Jharkhand & Madhya Pradesh are good practices created in the project.

**Conclusions and key recommendations:** Engaging community care-givers in TB case detection and care has been gaining appreciation and recognition at various levels of RNTCP and if replicated through program it would be one of the fruitful strategies to help achieving targets of Universal Access of TB Care as recently adopted by the country.

**PD-582-30 Role of NGO to detect hidden tuberculosis cases in Kathmandu urban slum**

RS Gopali,<sup>1</sup> N Ishikawa,<sup>2</sup> L Lochting,<sup>3</sup> R Pant.<sup>4</sup> <sup>1</sup>Public Health, Japan-Nepal Health & Tuberculosis Research Association, Kathmandu, Nepal; <sup>2</sup>International Co-operation, Japan Anti-Tuberculosis Association, Tokyo, Japan; <sup>3</sup>International Cooperation, LHL-International Tuberculosis Foundation, Oslo, Norway; <sup>4</sup>Health, National Tuberculosis Centre, Thimi, Nepal. e-mail: gwala73@hotmail.com

**Background** Urbanization is rapidly increasing in Nepal with many people from village coming to the city. With the increasing urban population, there are growing numbers of urban slum areas. The health and wellbeing

of people in those areas is significantly worse due to poor living conditions, poor access to health services and inappropriate health seeking behavior.

**Aims:** To detect hidden TB cases by designing effective intervention model to mobilize health work forces.

**Intervention** Regular social mobilization and awareness activity in the project sites is conducted by the 50 trained health volunteers and 7 health care providers. Covering approximately 150,000 populations in 2012/13. Persons who had symptoms suggestive of tuberculosis and TB patient's family members were referred to the nearby microscopy centre which was run by NGO clinic. Three sputum samples including one early morning and 2 spots specimens were collected in two consecutive days. For chest x-ray and other additional investigation suspects were advised to visit National Tuberculosis Centre and Medical Colleges where it was appropriate for them.

**Results and lessons learnt:** 343 suspects were referred to the microscopy centre from the community in one year. The mean age was 37 and two third of diagnosed cases were male. Out of 222 all forms of Tuberculosis (TB), 79 (35.59 %) were new smear positive pulmonary TB (PTB), 32 (14.42 %) were smear negative PTB, 14 (6.31 %) were retreatment PTB cases, 79 (35.59 %) were extra-pulmonary cases, and 18 (8.11 %) were others. Treatment outcome of smear positive PTB was as follows; cured 86 %, death 2%, defaulted 4% and transfer out 8%.

**Conclusions and key recommendations:** Regular activity in the community and interaction with health volunteers helps to motivate health volunteers to take part in TB related intervention. Regular mobilization of health volunteers and community leaders can contribute to detect hidden TB cases in hard-to-reach areas where NTP's regular programme could not cover. Introducing similar activity in other parts of the country could be evidence base result for the future expansion and engagement of NGO's working in health and development field.

#### **PD-583-30 Increasing access to TB drug susceptibility testing: a community-based organisation to the rescue of National TB Programme, Mumbai, India**

I Syed,<sup>1</sup> M Khetarpal,<sup>2</sup> A Sreenivas,<sup>1</sup> KS Sachdeva,<sup>3</sup> J Salve,<sup>1</sup> P Malik.<sup>1</sup> <sup>1</sup>Country Office, World Health Organization, New Delhi, <sup>2</sup>Public Health Department, Municipal Corporation of Greater Mumbai, Mumbai, <sup>3</sup>MoHFW, Central TB Division, New Delhi, India.  
e-mail: simfarooq@gmail.com

**Background:** Mumbai, a densely and the most populated city of India (12.8 MN) is economical capital of country. The city is divided into 6 zones and 24 RNTCP districts since 2012. Suburban railways is the lifeline of the city and >7 million commute on daily basis. Post Totally Drug Resistant (TDR) TB episode in Mumbai, the services for DR TB were scaled up. Availability of Revised National TB Control Programme (RNTCP) certified labs was the limiting factor to offer DST. Only 2 certified labs at JJ Hospital & P D Hinduja and that to

were located away from the high risk wards (Govandi, Chembur, and Vikhroli) in Mumbai. One of the schemes under the "RNTCP-Revised Guidelines for NGO/PPs"- "Sputum Pick up and transport" was further modified to suit the needs of Mumbai.

**Intervention:** Review of official communications, interviews with District TB Officers and volunteers of Maharashtra Janavikas Kendra (MJK) were performed for situational analysis and understanding of processes. MJK a community based organization and Mumbai District TB Control Society signed a Memorandum of Understanding. Fresh sputum samples in biosafety were collected on fixed days and transported through trains and other public/private modes, to labs. The reports were conveyed to concerned district TB centres via email minimizing the reporting delay

**Results:** 30 sputum collection centres were established across 24 districts. Due to an efficient mechanism for specimen transport Mumbai was able to expand the criteria for DST offer. 4672 diagnostic and 7381 follow up samples were transported to 6 (4 CBNAATS) labs using trains mainly during 2013 which yielded in diagnosis of 2903 MDR TB cases. If not for the human carrier mechanism the other modes require cold chain and couriers with greater delay in diagnosis

**Conclusion:** A well-defined policy for engagement with community based organizations, NGOs, other sectors should be an integral part of any health policy. Utilization of core competencies of various partners enhances the services. In urban settings where issue of poor human resource is a hitch, community volunteers and organizations come handy. The community based organizations can also be utilized for decentralized treatment and adherence services

Particular	2011	2012	2013	Additional yield over previous year (%)
Certified Labs	1	3	6	3 (100)
CBNAAT	0	1	6	5 (500)
Presumptive TB	97710	117234	128445	11211 (9.6)
Presumptive MDR TB	345	10323	10973	650 (6.3)
Diagnosed MDR TB	181	2195	2903	708 (32.3)

#### **PD-584-30 Collaboration with the Republican Women's Committee to fight tuberculosis in Uzbekistan**

S Gamtsemlidze,<sup>1</sup> J Ismoilova,<sup>1</sup> T Mohr,<sup>1</sup> B Babamuradov,<sup>1</sup> S Sayfiddinova,<sup>1</sup> U Yuldasheva,<sup>1</sup> M Rahimova.<sup>1</sup> <sup>1</sup>Global Health, Project HOPE, Millwood, VA, USA. Fax: (+998) 712371635.  
e-mail: sgamtsemlidze@projecthope.org

**Background:** The USAID Quality Health Care Project aims to improve prevention and treatment of tuberculosis (TB) through increasing public awareness on TB in Uzbekistan. The Uzbekistan Project is implemented by Project HOPE. The Project focuses on community-level interventions in order to institutionalize and scale-up its TB work.



**Methods:** To ensure broad impact of key activities the project collaborates with the Republican Women's Committee - a parastatal organization. A joint work plan to engage communities in TB prevention and care was signed with the Republican Women's Committee and the Republican DOTS Center. This plan supported conducting seminars for representatives from Women's Committees from 11 of 13 regions of Uzbekistan and the Republic of Karakalpakstan. Training participants developed work plans for conducting TB seminars at the district level of their respective regions and subsequently started utilizing their community connections to spread important TB information. Currently Branches of Republican Women's Committees and Khokimiats (mayor's offices) are conducting joint activities on increasing TB awareness based on the action plans developed during training on TB. The Project supported Republican Women's Committee and oblast Khokimiats in 12 regions of Uzbekistan to conduct training and follow up monitoring visits.

**Results:** The collaboration is helping involve more people in the fight against TB and decrease stigma in these places. Khokimiats started to pay increased attention to tuberculosis in their communities. Now the oblast Khokimiats have official activity plans signed jointly with Heads of TB dispensaries on each joint activity. Partnering with the parastatal Women's Committees enabled the project to rapidly expand the geographic reach of project initiated activities.

**Conclusion:** Collaborating with parastatal agencies is an essential activity to multiply the impact of project interventions and to ensure the sustainability of such activities. Involving community members in solving TB issues can help to increase TB awareness of community members and decrease TB stigma among the population.

#### **PD-585-30 Local self-government involvement in tuberculosis control programme in Kasaragod district, Kerala, India: standard for TB care in India**

K Dsa,<sup>1</sup> R Kadambalithaya,<sup>2</sup> PP Sunilkumar,<sup>2</sup> S Balakrishnan,<sup>1</sup> A Sreenivas,<sup>1</sup> S Mrithunjayan,<sup>3</sup> J Subramoniyapillai,<sup>3</sup> A Kumar.<sup>4</sup> <sup>1</sup>Tuberculosis, WHO Country Office for India, New Delhi, <sup>2</sup>District TB Centre, Directorate of Health Services, Kerala, Kasaragod, <sup>3</sup>State TB Cell, Directorate of Health Services, Kerala, Thiruvananthapuram, <sup>4</sup>Research, International Union Against Tuberculosis and Lung Disease (The Union), South-East Asia Regional Office, New Delhi, India.  
e-mail: drdkarthik@yahoo.com

**Background and challenges to implementation:** Kasaragod is the northernmost district of Kerala state in India with 1.3 million populations and register around 25 Drug resistant Tuberculosis (DR-TB) patients annually under Revised National Tuberculosis Control Program (RNTCP). Majority of the DR-TB patients live in households with a monthly income of less than US\$ 40. Local Self Government (LSG) is a three-tier decentralized administrative system in India with elected bodies at the Village, Taluk and District levels which are empowered

with financial resources and administrative powers for the implementation of developmental programmes at the gross root level..

**Intervention or response:** President and executive board members of Kasaragod District Panchayath (KDP) were sensitized from July 2012 to November 2012 individually and through group meetings for the need of Food, Nutrition and social support for DR-TB patients throughout their treatment. Kasaragod District Panchayath understood the importance of their role in community affected with TB and District Tuberculosis Centre (DTC) has submitted the proposal in December 2012.

**Results and lessons learnt:** KDP accepted the DTC proposal, allotted Indian Rupees 2, 00,000 (US\$ 4000) and implemented the Food and Nutrition Support Program for DR- TB Patients in Kasaragod District the financial year 2013–2014 The monthly grocery worth of 20US\$ consisting of Rice - 10 kilogram (Kg), Green gram- 3kg, Toor dal –1Kg, Coconut oil- 1 Litre, Garlic- 500 milligram procured and distributed to the each DR-TB patient's family by DTC in coordination with KDP.

**Conclusions and key recommendations:** Standard 19 of the Standards for TB care in India mentioned that Local self-government /Panchayath Raj Institutions (LSG) have an important role to share the public health responsibility for TB control with the healthcare providers, patients and the community. Food and Nutrition Support Program for DR- TB Patients in Kasaragod District demonstrate a model where empowered decentralised local self-government take the lead in providing nutritional support to DR-TB patients using local resources. This model also show feasibility of TB control programmes to go out of conventional ways and make use of all available local support.

#### **PD-586-30 Community involvement in raising awareness about TB among Somalian population**

M Karels,<sup>1</sup> N Jansen-Aaldring,<sup>2</sup> <sup>1</sup>TB Department, GGD Hollands Noorden, Alkmaar, <sup>2</sup>Regional office the Netherlands & Europe, KNCV Tuberculosisfoundation, The Hague, Netherlands. e-mail: mkarels@ggdhollandsnoorden.nl

**Background and challenges to implementation:** The Netherlands is a low incidence country for TB, with an incidence of 5,7: 100.000. 73% of all TB patients in the Netherlands are foreign born, 18% of them are born in Somalia. The incidence of TB under the Somalian people in the Netherlands is 691: 100.000. Another point is the large proportion of extrapulmonary TB among the Somalian, in 2012 64% of TB cases in this group were extra pulmonary TB. In the region of the Public Health Centre (PHC) Hollands Noorden (a region in the north west of the Netherlands) live around 1500 Somalian. In 2012 there were 5 cases of active TB and in 2013 8 cases of active TB among the Somalian group in this region, 19 and 32% of their total amount of TB patients. The PHC signalized some problems in this group: patient delay is quite long, misunderstanding about TB, a lack of

knowledge about TB although there are education materials available (in Somalian language) and they presumed stigmatizing about TB.

**Intervention or response:** In 2012 the TB- nurse of the PHC discussed with organizations specialized in health problems among the Somali population in the Netherlands (FSAN, PHAROS, KNCV Tuberculosisfoundation) the problems they are facing. They concluded that an important subject for success was that the Somalis their self had to fulfill an active role in a project to raise awareness in their community. The TB nurse contacted a local organization (partner of FSAN) to involve them in the preparation. It was decided to organize meetings. The meetings were organized together with peers. They choose time, location and invite people. After the official meeting people stayed around to eat, drink and speak with each other. The TB nurse gave the information in a short presentation and showed a DVD in Somali about TB. A Somali TB doctor told his experiences about treating TB in Somali and in the Netherlands. People were asked to fill in a questionnaire before and after the meeting.

**Results and lessons learnt:** The meetings were attended by 80 persons (both men and women). The questionnaires showed increase of knowledge, invalidation of misunderstandings, confirmation of the stigma and a preference for information by DVD.

**Conclusions and key recommendations:** Involving peers is very important. Advantage is noticed by the nurses in the involvement and follow up of contact tracing. TB is a topic people are more talking about. The PHC will extend this way of working to other cities in their region.

#### PD-587-30 Civil society initiative in identifying TB patients from key-affected population through community led sputum collection and transportation

R David,<sup>1</sup> Mr Rajesh Singh,<sup>1</sup> A Rahman.<sup>1</sup> <sup>1</sup>Development sector, MAMTA Health Institute for Mother and Child, New Delhi, India. Fax: (+91) 29220575. e-mail: dbabu@mamtahimc.org

**Background** India, has proposed Universal Health Coverage to reduce out-of-pocket expenditure and to minimize catastrophic burden of illness. The key affected population from the vulnerable, marginalized and hard to reach areas access to National TB program is a biggest challenge both in urban and rural set up in India. Project AXSHYA Civil Society initiative to strengthen the TB care and control in India designed activities like referrals and household sputum collection transportation from the vulnerable, marginalized and hard to reach areas in 62 districts across seven states like Bihar, Chhattisgarh, Delhi, Haryana, Maharashtra, Rajasthan & Uttar Pradesh in India.

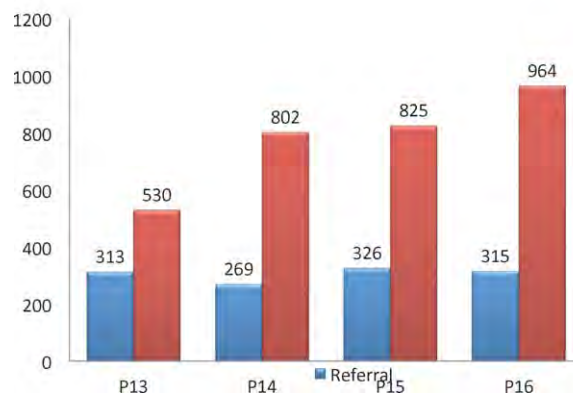
**Intervention:** In order to reach the key population, community volunteers were identified and trained by concerned DTOs with special focus on Sputum collection and transportation, under AXSHYA project from Apr 2013-Mar 2014 from 62 districts, after the training they

were positioned in districts in order to help the key affected population for early diagnosis to the nearest DMCs which resulted in identifying 3121 TB patients from Sputum collection and transport and through referral 1223 TB patients the key affected population in accessing the service public health system without any socio-economic and psychological barriers.

**Results:** The household Sputum collection and diagnosis is an effective model for early diagnosis, which give further scope for initiating treatment and sense of understanding about the public health system facility for the key affected population, the evidence shows that a total of 3121 TB patients were identified and put on treatment through sputum collection and transportation and 1223 TB patients identified through referrals, the positivity rate through sputum collection and transport is comparatively higher than referrals services in all the quarters and annual positivity rate is 8,7% in sputum collection and transportation in comparison to 2.4% of referrals. Thus good Samaritan efforts of civil societies and community volunteers and reduced out pocket expense on travel and treatment of key population.

**Conclusions:** The supportive effort to house hold sputum collection transportation to the nearest DMCs has the potential to improve access to quality of TB services when compared to referrals and overcome barriers like stigma and discrimination, economic burden, distance, time and geographical constraint in accessing early diagnosis without spending from their pockets.

TB Patients Identified through Referrals V/s Sputum collection transportation



#### PD-588-30 Health system gaps in community TB/MCH integration

M Wanjuki,<sup>1</sup> D Seyoum,<sup>1</sup> A Tasew,<sup>1</sup> B Mboya,<sup>1</sup> A Gitimu,<sup>1</sup> S Muhula,<sup>1</sup> M Mungai,<sup>1</sup> S Kuria.<sup>1</sup> <sup>1</sup>Programmes, Amref Health Africa, Nairobi, Kenya. e-mail: meshackn@gmail.com

**Background:** TB is one of the top killers of women in Africa, and a significant cause of childhood illness and death. In 2011, 500,000 women and 64,000 children died of TB. Despite these realities, only 61% new cases of TB in Africa are being notified. There is therefore need to integrate TB interventions into community MCH pro-

grammes in order to reduce the burden of TB among women and children. We identified health system gaps for community TB/MCH integration.

**Design/Methods:** Using a standard questionnaire we collected community TB and MCH integration information from eight (8) Amref Health Africa projects in three countries in Africa, for the data reference period October 2012 to March 2013. We selected eight projects with community TB and MCH components in Ethiopia (2); Uganda (2); and Kenya (4). We collected qualitative information from three key informants using a standardized interview guide. Data was analysed using descriptive and qualitative techniques.

**Results:** All the eight projects worked with a combined total of more than 1100 CHWs to deliver community TB and MCH interventions. Three of the projects worked with CBOs and a similar number had trained CWHs on community TB care. In all the projects, CHWs undertook TB activities including case finding (e.g screening), case holding, stigma reduction and infection control.

The key gaps identified were: program design - no systematic TB/MCH integration; workforce - often no TB or TB/MCH integration training since curriculum at community level lacked explicit TB/MCH integration content e.g FANC training curriculum, had scanty TB content in two projects; service delivery - screening & referral tools not standardized; health information tools rarely captured TB in pregnancy nor referral success; policy & operational guidance on TB/MCH integration lacks.

**Conclusion:** Organizations active in community MCH can integrate TB through CHWs and CBOs, as recently described in the WHO - ENGAGE TB guidelines. For this to happen, they need to address health system gaps especially multi-skilling CHWs, standardizing screening and referral tools as well as job aids to capture pregnancy information and data tools adapted to capture TB/MCH information. This calls for close collaboration between in-country departments of TB, MCH, community health and health information systems. There is need for community trials to determine effectiveness of TB/MCH integration.

#### **PD-589-30 Bridging the gap- Improving the access for TB diagnosis by sputum collection and transport: a field report from Tamilnadu, Southern state in India**

K K,<sup>1</sup> Gane M,<sup>1</sup> A Ramya,<sup>1</sup> A Das,<sup>1</sup> N Krishnan.<sup>1</sup> <sup>1</sup>Health, Resource Group for Education and Advocacy for Community Health (REACH), Chennai, India.  
e-mail: pm.reachaxshya@gmail.com

**Background and challenges to implementation:** TB control program in India, is being implemented through general health system. TB symptomatics attending primary health centers where there were no trained laboratory technicians are referred to the nearest designated microscopy center (DMC). This usually resulted in dropouts in those getting themselves tested at DMC either due to lack of access or for economic

reasons resulting in delayed diagnosis and continued transmission of disease in the community. To address this gap, sputum collection and transport activity was undertaken in Tamilnadu, India and we are reporting the findings

**Intervention or response:** A retrospective analysis of the records on sputum collection and transport maintained by the community volunteers at the district level was undertaken in the 14 districts of Tamilnadu for the period April 2013 to March 2014. As part of ACSM (Advocacy, Communication & Social Mobilization) activities implemented by Project Axshya, a gap analysis was undertaken to identify the non-functioning DMCs in consultation with the DTO. Based on the OPD strength, 114 of these DMCs were selected for implementing the sputum collection and transport activities and based on OPD strength. Medical Officers in the Outpatient department referred TB symptomatics for sputum test. Two sputum samples from these symptomatics were transported by the community volunteer on the same day to the nearest functioning DMC.

**Results and lessons learnt:** Over a 12 months period, 6986 patients in all underwent sputum testing by having their sputum samples collected and transported from primary health centers to the DMCs. Of them, 356 were found to be sputum positive pulmonary TB and started on treatment. Sputum positivity was found to be 5.09%.

**Conclusions and key recommendations:** The above operational findings has highlighted the feasibility of sputum collection and transport in identifying 356 sputum positive pulmonary TB patients, many of whom might not have subsequent diagnosis and would have continued to transmit the disease in the community. This activity has also helped in mitigating the economic impact for the TB symptomatics. However the low sputum positivity of 5.09% needs to be addressed.

#### **PD-590-30 Community empowerment in TB control activities in Myanmar: national TB control programme and INGOs**

L L Win,<sup>1</sup> S Saw,<sup>2</sup> Y T N Oo,<sup>3</sup> T Lwin,<sup>4</sup> T M M Khaing.<sup>5</sup>  
<sup>1</sup>DMR(LM), Ministry of Health, Yangon, <sup>2</sup>Department of Medical Research (Lower Myanmar), Ministry of Health, Yangon, <sup>3</sup>Department of Medical Research, Lower Myanmar, Ministry of Health, Yangon, <sup>4</sup>Department of Health, Ministry of Health, Nay Pyi Taw, <sup>5</sup>Department of Health, Ministry of Health, Yangon, Myanmar. e-mail: yinthe@gmail.com

**Background and challenges to implementation:** TB is one of the national health problems in Myanmar and it ranks 19 of the 22 high TB burden countries. National TB Control Programme (NTP) has been working together with INGOs in TB control activities through various approaches and community empowerment is one approach. Yet, the situation was not assessed, and this study attempted to assess the situation of involvement of community volunteers in TB control activities initiated by INGOs.

**Intervention or response:** A cross-sectional study was carried out during 2012 in 2 selected townships, where different INGO was working for TB control in each



township. This study did not aim to evaluate and compare activities of organizations, and to promote anonymity, only coded alphabets were used such as organization "A" and organization "B" respectively.

**Results and lessons learnt:** The study involved 54 community volunteers for face-to-face interviewing by pretested semi-structured questionnaire and 58 respondents (i.e., TB patients, public health staff and responsible person from the organizations) for in-depth interview and key informant interview by pretested guidelines. Written consent was obtained prior to interview from every interviewee. Findings revealed that the volunteers were contributing to NTP in raising the community awareness, case detection, and treatment completion and treatment success to some extent. Even there were good examples of voluntary free services rendered to the TB patients; sustainability of these voluntary activities should be considered if the external support is phased out.

**Conclusions and key recommendations:** The information from this study will help health system in developing policy on community volunteers' involvement in TB control and strengthening partnership of NTP.

#### **PD-591-30 Novel principles to facilitate cross-cultural community engagement in tuberculosis research**

J Boffa,<sup>1,2</sup> S Ndlovu,<sup>3</sup> M Mayan,<sup>4</sup> D Fisher,<sup>1,5,6</sup> R Cowie,<sup>1,6</sup> D Wilson.<sup>7</sup> <sup>1</sup>Community Health Sciences, University of Calgary, Calgary, AB, Canada; <sup>2</sup>School of Nursing and Health Sciences, University of KwaZulu-Natal, Durban, <sup>3</sup>NGO, Izimbali Zesizwe, Edendale, South Africa; <sup>4</sup>Community and University Partnerships, University of Alberta, Edmonton, AB, <sup>5</sup>Tuberculosis Services, Alberta Health Services, Calgary, AB, <sup>6</sup>Medicine, University of Calgary, Calgary, AB, Canada; <sup>7</sup>Medicine, Edendale Hospital, Pietermaritzburg, South Africa. e-mail: jody.boffa@ucalgary.ca

**Background:** Evaluating population-wide prophylactic interventions for TB in high-HIV settings involves more than assessing clinical outcomes, but also the acceptance and integration of knowledge regarding the risks and benefits of introducing new regimens into a community. In order to assess community perspectives, relationship-building is an important first step to attaining accurate information and interpretation of findings. The principles of community based research were intended to define best practices for relationship-building between scholars and vulnerable communities; however, these principles were originally developed for partnerships in the USA. Conversely, ethnography, which focuses on cross-cultural observation, historically lacks the involvement from the community.

**Methods:** To assess perspectives on the introduction of Isoniazid Preventive Therapy in Zulu communities of KwaZulu-Natal province, South Africa, we set out to develop advisory teams in three community settings (peri-urban, rural, and remote) to help with the development of research tools and interpretation of perspective-based findings. To do so we integrated principles from ethnography and community based

research for use in a cross-cultural environment. The lessons we present are interspersed with stories from our experience in the field.

**Results:** Advisory teams selection and initial meetings were successful with use of the following principles for researchers building partnerships: -strive to be conscious of one's privileged position in society and reflect upon the power imbalance that exists between the research team and community members. Consider how best to minimize imbalance. -internalize the concept of knowledge exchange that critically depends on the expertise derived from the lived experience of community members -make a reasonable effort to learn about social norms, cues, and terms -consider the differences between groups within the community, and try to ensure appropriate representation from those who are most affected by poverty and powerlessness -spend most of your time listening; you are a student of the stories and lessons of community members

**Conclusions:** Assessing perspectives on new community interventions across cultures requires significant community engagement. Using a mix of ethnography and community based research methods helped to ensure participation and positive working relationships between the research team and community advisors.

#### **09. HIV/TB PROGRAMME LINKS: HAND IN HAND SCREENING FOR TB AND HIV**

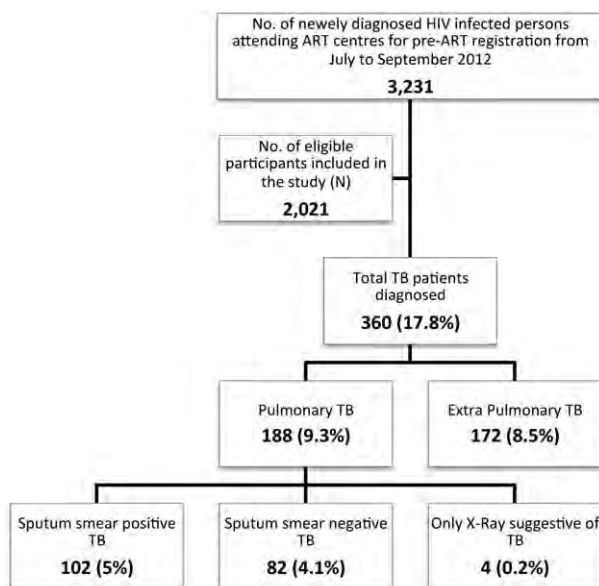
##### **PD-592-30 Assessment of TB prevalence in newly diagnosed HIV infected adults attending ART center in Gujarat, India**

D Kapadiya,<sup>1</sup> P Dave,<sup>1</sup> b Vadera,<sup>1</sup> P Patel,<sup>2</sup> S Chawla,<sup>3</sup> A Shah.<sup>4</sup> <sup>1</sup>Department of Health and Family Welfare, State Tuberculosis Cell, Gandhinagar, Gujarat, <sup>2</sup>Department of Health and Family Welfare, Intermediate Reference Laboratory, Ahmedabad, <sup>3</sup>Department of Health and Family Welfare, Gujarat State AIDS Control Society, Ahmedabad, <sup>4</sup>Department of Medicine, B.J. Medical College, Ahmedabad, India. e-mail: gutbhiv@rntcp.org

**Background:** TB is frequently the first opportunistic infection and leading cause of death among HIV/AIDS patients. Certainly, prevalence of TB is expected to differ between general population and HIV infected persons attending ART centres for pre-ART registration. This study was conducted to determine prevalence of tuberculosis among newly diagnosed HIV infected adults attending ART center for pre ART care and support in Gujarat. Method: Cross sectional study was carried out among pre-ART HIV infected persons attending ART center from July to September 2012. Screening of TB symptoms was done through interview of participants and chest X-ray was done for those who consented. Sputum samples were collected for microscopy with Ziehl Neelsen (ZN) method for all presumptive TB cases and among those diagnosed as pulmonary TB, culture and drug susceptibility test was done. Blood samples were collected for CD4+ T cells count and hemoglobin.

**Results:** Out of 2,021 eligible newly diagnosed HIV infected persons, 63.5% were males and 68.2% were in the age group of 26–45 years. The prevalence of all forms of Tuberculosis was 17.8%. Among 360 patients with TB, 102(28%) had sputum smear positive TB, 82(23%) had smear negative but X-ray chest suggestive of TB, 4(1%) had only X-ray suggestive of TB and 172(48%) were diagnosed as Extrapulmonary TB. Out of 188 pulmonary TB patients, 3(1.6%) were resistant to Rifampicin. Among HIV-TB co-infected patients, 238(66%) had CD4+ T-Cell count below 200 and another 77(21.4%) had CD4+ T-Cell count between 200–349.

**Conclusions:** A high prevalence of TB disease was found among newly diagnosed HIV infected persons attending ART center for pre-ART care. The prevalence of pulmonary and extra pulmonary TB was almost equal. Chances of TB disease were more with depletion of CD4 count. The study highlight urgent need of intensive case finding as well as periodic screening among pre-ART HIV infected individuals.



#### PD-593-30 Assessment of HIV screening and management in children treated for tuberculosis in the Democratic Republic of Congo: results of the 2012 survey

F Kitetele,<sup>1</sup> Eliz Talbot,<sup>2</sup> F Alombah,<sup>3</sup> E Kiangala,<sup>4</sup> D Muteteke,<sup>5</sup> G Bakaswa.<sup>6</sup> <sup>1</sup>Infectious Diseases, Kalembelembe Paediatric Hospital, Kinshasa, Democratic Republic of Congo; <sup>2</sup>Infectious Diseases, Geisel Medical School, Dartmouth, Hanover, NH, <sup>3</sup>TB/HIV, Program for Appropriate Technology for Health (PATH), Washington, DC, USA; <sup>4</sup>PATH/DRC, Program for Appropriate Technology for Health (PATH), Kinshasa, <sup>5</sup>Infectious Diseases, USAID, Kinshasa, <sup>6</sup>National Direction, National TB Programme (PNLT), Kinshasa, Democratic Republic of Congo. e-mail: fkitetele@hotmail.com

**Objective:** Assess nationwide practice of HIV screening and management in children treated for tuberculosis (TB) in the Democratic Republic of Congo (DRC).

**Methodology:** Descriptive cross-sectional assessment of HIV screening and management in children treated for TB in 73 health facilities of 8 out of 11 provinces of the DRC in 2012. A standardized questionnaire was developed, pilot tested, and administered to public sector healthcare workers (e.g., physicians and nurses) in the local language by trained researchers.. Data were analyzed using EpiInfo V7.0.

**Results:** Only 65 (4.2%) of 1554 doctors and 43 (1%) of 4165 nurses in 73 facilities reported having been trained and were active in the management of pediatric TB. Of 2040 children under 15 years of age treated for tuberculosis, 1041 (53%) were female. Only 35 (48%) health facilities reported routinely offering HIV testing to TB patients. Of 496 (24.3%) children screened, 175 (35.3%) were positive for HIV. When coinfection was identified, only 49 (67.1%) and 19 (26%) of health facilities prescribed immediate co-trimoxazole or appropriately timed ARVs, respectively, in spite of national guidelines. A total of 32 (50%) health facilities reported capacity to provide support for TB / HIV co-infection in children and 17 (53.1%) practiced joint management with the HIV centers for coinfecting patients.

**Conclusion:** The present study shows that the TB / HIV coinfection is tragically frequent among children in the DRC, but remains under-diagnosed due to insufficient training and lack of availability of updated national pediatric TB guidelines. Building capacity of the health-care workers and development of clear guidelines appropriate to the local context may dramatically improve the management of TB / HIV coinfection in this pediatric setting.

#### PD-594-30 Presumptive tuberculosis in Zomba district, Malawi: an operational prospective study of outcomes and diagnostic process

M Van Lettow,<sup>1</sup> T Beyeni,<sup>1</sup> H Akello,<sup>1</sup> AK Chan,<sup>1</sup> M Joshua,<sup>2</sup> S Chinomba,<sup>3</sup> J Van Oosterhout,<sup>1</sup> A D Harries.<sup>4</sup> <sup>1</sup>Medical Programs and Operational Research, Dignitas International, Zomba, <sup>2</sup>Ministry of Health, Zomba Central Hospital, Zomba, <sup>3</sup>Ministry of Health, District Health Office, Zomba, Malawi; <sup>4</sup>Operational Research, Union against Tuberculosis and Lung Disease, Paris, France. e-mail: m.vanlettow@dignitasinternational.org

**Background** In Malawi, outpatients who have presumptive tuberculosis (TB), i.e. any-duration cough, fever, night sweats, weight loss in HIV infected and cough of at least 3 weeks duration in HIV uninfected, are registered in 'chronic cough registers'. They should receive a diagnostic work-up with first-step provider initiated HIV testing (PITC) and sputum testing which includes GeneXpert, following a new national algorithm introduced in 2012. Response to antibiotics and radiology determine tuberculosis diagnosis in those with negative sputum testing. Studies before the introduction of GeneXpert and early PITC demonstrated poor outcomes in presumptive tuberculosis patients, mainly related to undiagnosed HIV and TB.

**Methods** We prospectively studied 6-month outcomes of adult outpatients who were registered in chronic cough

registers in Zomba Central Hospital (ZCH) and Matawale peri-urban health center (MHC) between February and September 2013, in the routine setting. ZCH has GeneXpert on-site, MHC sends samples to ZCH. We recorded implementation of the diagnostic protocol and outcomes at 6 months from registration.

**Results** 348 patients were enrolled (257 ZCH, 91 MHC), 47% were male, median age was 40 (IQR 31–50), 21% had previous tuberculosis treatment. At registration 154 (44%) were confirmed HIV positive (90% on ART), 34 (10%) were HIV negative (8 confirmed) and 160 (46%) HIV unknown. Ninety (56% of unknown and unconfirmed) underwent HIV testing. At 6 months 191 (55%) were confirmed HIV positive, 61 (18%) confirmed negative, 26 (7%) unconfirmed negative and 70 (20%) remained HIV unknown. 208 (60%) had sputum AFB followed by GeneXpert according to the protocol (72% in ZCH; 24% in MHC). Tuberculosis diagnosis was made in 53/348 (15%) ; in 8/53 (15%) cases this was based on the GeneXpert result only, and in 26/53 (49%) TB was clinically diagnosed. Coverage of ART in confirmed HIV positives was 89%. After 6 month follow up, 68% were asymptomatic, 14% symptomatic, 6% had defaulted and 11% died (12% in ZCH; 8% in MHC). Mortality among those HIV positive, negative and unknown was 15%, 1% and 11% respectively.

**Conclusion** One quarter of patients with presumptive TB were not HIV tested and among those mortality was high. The impact of GeneXpert on TB diagnosis was limited, independent of whether equipment was available on site. The new national TB diagnostic algorithm needs reinforcement in these clinics and its effectiveness requires evaluation on a wider scale.

### PD-595-30 High indeterminate rates of QFT among HIV-infected individuals in Brazil

S Leone,<sup>1</sup> A Trajman,<sup>2,3</sup> A Paniago,<sup>1</sup> A Ruffino-netto,<sup>4</sup> G Bonecini-almeida,<sup>5</sup> J Croda.<sup>6</sup> <sup>1</sup>Faculty of Medicine, Federal University of Mato Grosso do Sul, Campo Grande, MS, <sup>2</sup>Internal Medicine Graduate Program, Federal University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil; <sup>3</sup>Montreal Chest Institute, McGill University, Montreal, Montreal, QC, Canada; <sup>4</sup>Medical School, USP Ribeirão Preto of University, Ribeirão Preto, SP, <sup>5</sup>Immunology and Immunogenetic in Infectious Diseases Laboratory, Instituto de Pesquisa Clínica Evandro Chagas, Fundação Oswaldo Cruz, Rio de Janeiro, RJ, <sup>6</sup>Faculty of Health Sciences, Federal University of Grande Dourados, Dourados, Dourados, MS, Brazil. Fax: (+067) 91473333. e-mail: sandrinaleone@gmail.com

**Background:** QuantiFERON-TB Gold-in-Tube (QFT-GIT) has replaced tuberculin skin testing (TST) in many high-income countries. However, QFT-GIT can produce indeterminate results in up to 7% in persons living with HIV/aids (PLHA), decreasing its performance and increasing costs from repeated tests. We estimated the prevalence of QFT-GIT indeterminate results and its associated factors among PLHA in Campo Grande, Western Brazil.

**Design/Methods:** 81 consecutive PLHA were submitted to TST and QFT-GIT simultaneously. Stimulated and

unstimulated serum supernatants were frozen and stored for up to 2 months before the ELISA assay. Clinical and epidemiological data were extracted from medical records and BCG scar was searched for.

**Table 1** QuantiFERON®Gold-in-Tube indeterminate results among 81 people living with HIV/aids according to their demographic and clinical characteristics

Characteristics	QFT-GIT results			OR (95% CI) for determinate vs. indeterminate
	Positive n (%)	Negative n (%)	Indeterminate n (%)	
<b>Gender</b>				
Male (n=40)	5 (12)	26 (65)	9 (22)	1.5 (0.5- 4.0)
Female (n=41)	5 (12)	23 (56)	13 (31)	
<b>Age group</b>				
42–84 (n=40)	7 (17)	23 (57)	10 (25)	1.2 (0.4-3.0)
18–41 (n=41)	3 (7)	26 (63)	12 (29)	
<b>Using HAART</b>				
Yes (n=64)	8 (12)	39 (60)	17 (26)	1.1 (0.2–5.0)
No (n=10)	1 (10)	6 (60)	3 (30)	
Missing (n=7)	1 (14)	4 (57)	2 (28)	
<b>Smoker</b>				
No (n= 30)	2 (16)	25 (83)	3 (10)	5.3 (1.4–20.0)
Yes (n= 51)	8 (15)	24 (47)	19 (37)	
<b>Alcohol abuse</b>				
No (73)	8 (10)	46 (63)	19 (26)	1.4 (0.1–16.0)
Yes (03)	1 (33)	1 (33)	1 (33)	
Missing (5)	1 (20)	2 (40)	2 (40)	
<b>BCG scar</b>				
No ( n=22)	3 (13)	14 (63)	5 (22)	1.2 (0.3-3.0)
Yes (n=53)	6 (11)	33 (62)	14 (26)	
Missing (n=6)	1 (16)	2 (33)	3 (50)	
<b>TST</b>				
≥ 5mm (n=18)	8 (44)	5 (27)	5 (27)	1.04 (0.3-3.0)
<5mm (n=63)	2 (3)	44 (69)	17 (26)	
<b>CD4+ T-cells</b>				
≥ 501/mm <sup>3</sup> (n=37)	7 (19)	22 (59)	8 (21)	1.8 (0.6-5.0)
< 500/mm <sup>3</sup> (n= 38)	3 (8)	22 (58)	13 (34)	
Missing (n=6)	-	5 (83)	1 (16)	
<b>HIV viral load</b>				
< 50/mm <sup>3</sup> (n=44)	5 (11)	29 (66)	10 (23)	1.7 (0.6-4.0)
≥ 51/mm <sup>3</sup> (n=32)	5 (16)	16 (50)	11 (34)	
Missing (n=5)	-	4 (80)	1 (20)	
<b>Frozen and store sample</b>				
0–35 days	19 (47)	19 (47)	2 (5)	10 (2.6 a 38)
36–62 days	03 (7)	30 (73)	38 (19)	
<b>Years since HIV/aids diagnosis</b>				
≥ 7 (n=31)	4 (13)	20 (65)	7 (23)	1.4 (0.5-4.0)
< 7 (n=47)	6 (13)	27 (57)	14 (30)	
Missing (n=3)	-	2 (67)	1 (33)	

**Results:** Patients median CD4 count was 422/mm<sup>3</sup> (range 13–1390). TST and QFT-GIT were positive in 18.5% and 12.5% subjects respectively ( $\kappa=0.62$ ). Good concordance was due to the high percentage of negative results. QFT-GIT results were indeterminate in 27.2% (17.8%-38.1%), irrespective of CD4 count, HIV viral load or duration of storage (table). Smokers had a 5.3-fold chance to have indeterminate results



**Conclusion:** We found the high rate of indeterminate QFT-GIT results to be a major limitation for its routine use in PLHA, especially among smokers, regardless of the degree of immunosuppression. Storage may have resulted in the high indeterminate rates, although its duration was not related to results. Although we did not repeat the assays, in programmatic conditions, repeated tests would considerably increase its costs. This should be taken into account in cost-effectiveness analyses.

#### **PD-596-30 Enhancing notification of co-infected cases by engaging networks of PLHIV in TB control activities in Andhra Pradesh, India**

S Mukhopadhyay,<sup>1</sup> AK Kandukuri,<sup>2</sup> S Cornelius,<sup>1</sup> B Samuel,<sup>1</sup> V K Edward,<sup>1</sup> J Banavaliker,<sup>2</sup> U Ramakrishna,<sup>3</sup> A Rameshbabu.<sup>4</sup> <sup>1</sup>Health, World Vision India, New Delhi, <sup>2</sup>Health, Tb Alert, Hyderabad, <sup>3</sup>TB/HIV, State AIDS Control Society, Andhra Pradesh, Hyderabad, <sup>4</sup>Care & Support, Telugu Network of People living with HIV/AIDS (TNP+), Hyderabad, India. e-mail: sugata64@gmail.com

**Background and challenges to implementation:** India has yearly estimate of 130,000 TB/HIV co-infected cases, second highest in the world after South Africa. The present efforts to identify co-infected cases are in the form intensified case findings (ICF) in HIV and TB service delivery sites and cross-referrals between the two sites. The current notification rate of the co-infected case is below 40% in the country which necessitates additional efforts to improve notification. World Vision India (WV India) and TB Alert have been jointly implementing GF-supported Project Axshya in Andhra Pradesh, India to support the State TB Control Program in improving TB case detection in high-risk communities. WV India & TB alert have established partnership with district level networks of PLHIV in 7 districts of Andhra Pradesh to engage them in TB control activities and subsequently improve detection of TB in network members as an additional effort to enhance notification of co-infected cases.

**Intervention or response:** Andhra Pradesh being the highest HIV prevalence of the country has PLHIV networks in all 24 districts with more than 1000 members per district network. World Vision India and TB Alert sensitized around 752 members of 7 district level PLHIV networks on TB with specially designed module between Apr'13 – Mar'14, and engaged the networks in developing their TB action plans, identification TB presumptive cases among PLHIV members and their referral to TB diagnostic services & follow-up, dissemination of TB messages in the networks' outreach activities and networks' participation in WTD.

**Results and lessons learnt:** Between Apr'13 – Mar'14, the networks of 7 districts identified 704 TB presumptive cases in their members by following WHO's updated identification criteria, 696 cases screened for TB and 43 cases were detected (positivity rate 6.2%) with active TB (Sputum positive pulmonary TB) and were put on treatment within 7 days of diagnosis. All these co-infected cases were already on ART. All 7 district networks developed their TB action plan as part of their

network plan. The intervention was found to be highly cost-effective (58 USD spent per co-infection case detection).

**Conclusions:** The intervention showed effectiveness in terms of enhancing co-infected case detection by engaging PLHIV networks in TB control activities. If replicated with other 17 district level PLHIV networks it can help to detect large number of co-infected cases in cost-effective way.

#### **PD-597-30 Scale-up of facility integrated counselling and testing centres and Public-Private Partnership ICTC in India: contribution in HIV testing of TB patients**

R Deshmukh,<sup>1</sup> Rao Raghuram,<sup>2</sup> A Kumar,<sup>2</sup> KS Sachdeva,<sup>3</sup> A Sreenivas.<sup>1</sup> <sup>1</sup>HIV/TB, WHO Country Office of India, New Delhi, <sup>2</sup>Basic Services Division, Department of AIDS Control, New Delhi, <sup>3</sup>TB, Central TB Division, New Delhi, India. e-mail: deshmukhr@rntcp.org

**Background and challenges to implementation:** India's National AIDS Control Programme (NACP) aims to provide universal access to HIV detection and treatment services. Under the NACP the stand alone ICTC were established at health facilities with a counsellor and Lab technician. With the human resource constraint and need for decentralised facilities in the country different approach was necessary.

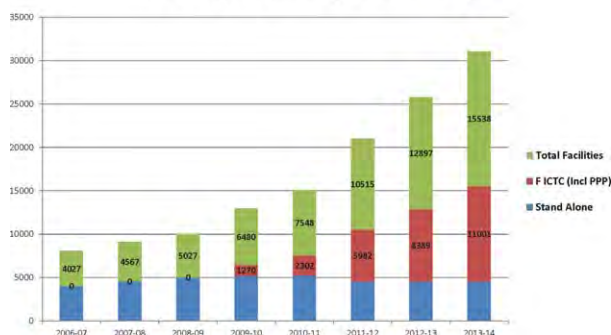
**Intervention:** NACP adopted an innovative approach of Facility-Integrated model of ICTCs (F-ICTC) in collaboration with the general health system, where the existing staff auxiliary nurse midwife (ANM) / staff nurse & laboratory technician were trained to provide HIV counselling and testing services. To involve private sector 'Public Private Partnership (PPP) model ICTCs' were developed, where private sector staff were trained to offer HIV counselling and testing. Strategy to rapidly scale up F-ICTCs & PPP model ICTCs and linkage with Revised National TB Control program (RNTCP) has delivered significant results.

**Results and lessons learnt:** In 2007-08 India had 4567 Standalone ICTCs and the known status of HIV among TB cases was only 11 % (n=38419) ; In 2009-10 the F-ICTC model was introduced. As a result testing HIV among TB cases increased to 25 % (89992) during the year. There was rapid scale up of F-ICTC and PPP model ICTCs, about 9 fold increase in 3 years (1270 in 2009-10 to 11001 in 2013-14). With this intervention the testing of TB patients for HIV increased to 64% (1, 29,964) in 2013 which was three times more than the number which were tested with standalone ICTC. The proportion of presumptive TB cases referred as a part of intensified TB case finding (ICF) activity at ICTC has increased from 6% (n=484617) in 2010 to 9% (620539) in 2013. 10% (n=64506) of the referred cases have been diagnosed as having TB in 2013. The ICF activity has contributed to 4.8% of the total TB cases notified under RNTCP. Although the scale up of F-ICTC has increased there is geographical variation within India. The scale

up of FICTCs and uptake of PPP model ICTCs is less in states with low HIV burden.

**Conclusion and Key Recommendations:** The rapid scale up strategy substantially improved access to HIV screening, and demonstrated the feasibility, as evidenced by increased proportion of HIV testing among TB patients. More F-ICTCs need to be established by strengthening coordination with National Health Mission and through public private partnerships by promoting uptake of revised PPP schemes.

### Scale up of F-ICTCs Including PPP ICTCs, India (2008-14)



### PD-598-30 Streamlining TB-HIV case detection in Ukraine

N Roman,<sup>1</sup> O Pavlova,<sup>2</sup> O Kheylo,<sup>1</sup> M Dolynska.<sup>1</sup> <sup>1</sup>USAID| Strengthening Tuberculosis Control in Ukraine Project, USAID Strengthening Tuberculosis Control in Ukraine Project, Kyiv, <sup>2</sup>Ukrainian Center for Disease Control, Ukrainian Center for Disease Control, Kyiv, Ukraine.  
e-mail: mdolynska@stbcu.com.ua

**Background and Challenges to Implementation:** Ukraine demonstrates high TB incidence and TB mortality in people living with HIV (PLHIV). In addition, detection of dual infection is frequently complicated because of atypical clinical presentation, laboratory confirmations that are much lower for PLHIV than HIV negative individuals, and the lack of standardized diagnostic procedures.

**Intervention:** The USAID Strengthening Tuberculosis Control in Ukraine Project has been promoting screening interviews on symptoms of presumptive TB among PLHIV, who sought any type of medical care since May 2013. The screening interviews introduced a new standardized questionnaire that focused on five main TB symptoms.

**Results and Lessons Learnt:** From May 2013 through March 2014, 32,739 PLHIV were interviewed, 9,841 were found to have a cough, and directed to smear microscopy. Positive smear test results were received in 719 of these cases (7.3%) ; 1,825 patients with negative results of smear tests underwent Xpert/RIF tests, and positive results were received in 57 of these patients (3.1%). During the first months of the intervention, the rate of TB case detection by smear microscopy increased

dramatically from 3.1% in June to 8.4% in December, 2013. In this period, smear-negative patients who underwent Xpert/RIF tests yielded 4.9% TB case detection and a total of 9.1% PLHIV with cough symptoms received TB laboratory confirmation. By March 2014 the smear TB detection rate decreased to 4.8%, and among smear-negative patients TB was detected by Xpert/RIF tests in 0.9%. At the same time coverage by X-ray screening increased from 61.0% in June 2013, to 73.0% in March, 2014, as those patients who had presumptive TB symptoms, other than cough, such as fatigue, weight loss, subfebrile temperature, were directed to X-ray examination. This is a logical result of improved screening quality, as initially more patients with advanced disease signs, as cough, were detected, and then, the patients who were found to have other symptoms, were directed to X-rays or CT, which is the most sensitive method for screening among those patients. Ultimately TB was confirmed among 1,268 patients (3.9% of those, who underwent interview).

**Conclusion:** Consistent use of PLHIV screening based on a simple-to-administer questionnaire is a feasible and effective method which can facilitate patients triage and rapid detection of both contagious and non-contagious TB.

### PD-599-30 Improving TB screening in HIV patients

Y Jean-Noel,<sup>1</sup> J Beauchamp,<sup>1</sup> A Val,<sup>1</sup> J Dieudonne,<sup>1</sup> A Tabois,<sup>1</sup> J Saint-Fleur.<sup>1</sup> <sup>1</sup>Tom White Wing, Hopital Bon Sauveur, Cange, Haiti. e-mail: juddbeauchamp@gmail.com

**Background and challenges to implementation:** The HIV+ population as we know is one of the very vulnerable groups to TB. Despite the systematicity of TB screening among our PLHIV, it was found that the documentation for this screening is not always done. In our reports for 2012 only 51.9% of our patients had evidence of having been screened for tuberculosis. Good number of questions were raised, hence the choice of this project for the identification and resolution of this problem.

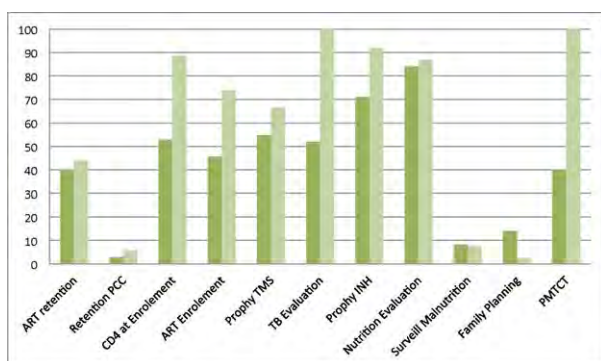
**Intervention or response:** For the six months April to September 2012 only 51% of HIV patients seen were screened and documented in the files. Moving from 51.9 % to 100% over a period of six months from October 2012 to March 2013 is our objective.

**Interventions** were launched progressively 1<sup>st</sup> intervention: Strengthening management of stock. Appointed employees do a bi-weekly inventory to predict a possible pick up in work materials. One month after, we launched the 2<sup>nd</sup>: checking the documentation in the files. The approach was a double check: After consultation, the nurse checks that the MD did and well documented the screening. The data officer in turn verifies this did and any record without TB screening s returned to the MD for action. Updating the electronic system: some electronic records were not entered correctly on EMR causing the discrepancy. The data officer lists all electronic patient records without TB screening. These

patients are put on schedule, are seen in consultation by the doctor, TB assessment and documented information correctly re-entered in the system.

**Results and lessons learnt:** At one month of the initial intervention, we got 0 out of stock, this approach alone after two months increased our target to 66%. At one month of the launch of the second intervention, all TB evaluations are properly documented in the patient record, however, after two months of the launch of the intervention our goals increased from 66% to 77% but we also discovered a discrepancy in the data capture within EMR. 2 months after the start of the third and final intervention of our project is going to score 100%. Lessons learned: 1) verification procedure necessary, 2) staff awareness on TB assessment documentation must be continuous.

**Conclusions and key recommendations:** The low score for TB screening was bound to the lack of documentation of TB evaluation in the appointment sheet by the MD and a delay in updating the electronic system (EMR)



### PD-600-30 Universal TB screening opens the door to integrated health service delivery in a rural border village in Northwest Province, South Africa

M A Uys,<sup>1</sup> E Barnard.<sup>1</sup> <sup>1</sup>Technical Assistance, Foundation for Professional Development, Tshwane, South Africa. Fax: (+27) 11 326 3232. e-mail: margotu@foundation.co.za

**Background** The integration of health services to include TB/HIV services as well as other chronic conditions remains one of the challenges of a comprehensive primary health package. Challenges range from lack of integrated funding to shortage of staff, lack of required clinical skills and infrastructure limitations. Until 2009 primary health care services in South Africa were characterized largely by a lack of integration and a silo approach to disease management. Since 2010 a concerted effort has been made to integrate TB and HIV services. Bray is a rural, border town with Botswana situated in the Kalahari desert (population approx. 12 000) with a high incidence of TB and HIV, mirroring the South African burden of TB and HIV incidence and co-infection (TB incidence 1003/100,000 WHO Global Report 2013 and co-infection >60%). Design/methods: THAT'SIT (Tuberculosis, HIV/AIDS Treatment Support

and Integrated Therapy), a PEPFAR funded TB technical support partner to the Department of Health, initiated the integration of TB and HIV services in this area in 2006 with dramatic improvement of TB outcomes (TB cure rate increased to >90% from <40% in 2006). Similar increases were documented in ART initiation rate. The program introduced the incorporation of all patient clinical information into one standardized file. Universal TB screening was done at the observation station after collection of files and before patient migration to the various other stations. Health counseling and testing (HCT) was monitored on all files and done as required on acute and at least 6-monthly on all chronic patients accessing the clinic. This has resulted in the early detection of TB suspects, early diagnosis of and enrollment into a pre-ART programme for HIV positive patients.

**Results:** The head count for this clinic is approximately 1000/month. In the last three months 268 clients received HCT, 20 tested positive (7.4%) ; 303 were investigated for TB (GeneXpert), 11 tested positive (3.6%). Absolute numbers for TB have declined over the last 6 years – reaching a peak of 176 cases in 2008 to less 60 cases over the last three years. Simultaneously all professional nurses were trained in the required clinical skills.

**Conclusion:** The integrated approach resulted in the provision of a comprehensive health care package, the cornerstone of quality driven primary health care delivery to communities in remote and isolated areas in South Africa.

### PD-601-30 Simplified TB screening algorithms maintaining high sensitivity but with reduced laboratory case load

S Thai,<sup>1</sup> S Sok,<sup>1</sup> R Pe,<sup>1</sup> S Huy,<sup>1</sup> N Lorent,<sup>1,2</sup> J Vangriensvan.<sup>1,2</sup> <sup>1</sup>Infectious Disease Department, Sihanouk Hospital Center of HOPE, Phnom Penh, Cambodia; <sup>2</sup>Research Sciences, Institute of Tropical Medicines, Antwerp, Belgium. Fax: (+855) 023 882 485. e-mail: sopheakthai@sihosp.org

**Background:** A sensitive screening algorithm (cough, fever, weight loss or night sweats for any duration) is currently recommended within tuberculosis (TB) programs. While achieving high sensitivity, the limited specificity yields large amounts of patients that need to undergo laboratory testing, overwhelming the laboratory services. In this study, we evaluated how alternative algorithms performed in terms of TB yield versus the reduced case load of patients requiring laboratory testing, stratified by HIV status.

**Design/Methods:** We conducted a retrospective analysis of routine TB program data in an urban hospital in Phnom Penh, Cambodia. TB screening patients were referred from HIV clinic and Home based care, OPD, Emergency, and IPD of Medical and Surgical department, and Community mobile clinic. The standard algorithm has been used both for HIV infected and unknown or non-HIV infected patients. All adults screened between January 2009 and December 2013 for TB, were included in the study. TB diagnosis followed



WHO recommendations. Relative to standard screening algorithm, we calculated the percentage of TB case diagnosed with simpler algorithms, and the percentage reduction in case load.

**Results:** A total of 2350 HIV positive individuals were evaluated at the TB clinic, of which 200 (8.5%) were diagnosed with TB. Compared to the standard screening algorithm, using "cough more than two weeks and night sweats" still identified 93% of the cases with a 21% reduced case load. A total of 4390 HIV negative or unknown individuals were evaluated at the TB clinic, of which 633 (14.4%) were diagnosed with TB. Compared to the standard screening algorithm, using "cough more than two weeks and weight loss" still identified 95% of the cases with a 10% reduced case load (Table).

**Conclusion:** Several simplified screening algorithms maintained a high TB diagnostic yield and significantly reduced the case load. In the event of logistical and budget constraints, such an approach would make efficient use of limited resources.

**Table: TB screening algorithms among HIV infected and unknown or non-HIV patients**

	Sensitivity (%)	% further investigated	% missed TB cases	% lesser case load
<b>HIV positive patients</b>				
Any cough, weight loss, night sweat, fever	99	94.382979		
Any cough $\geq$ 2 weeks, weight loss, night sweat, fever	99	88.510638	0	5.9
Any cough $\geq$ 2 weeks, weight loss, night sweat	96.5	79.957447	2.5	14.4
Any cough $\geq$ 2 weeks, fever	95.5	78.255319	3.5	16.1
Any cough $\geq$ 2 weeks, night sweat	93	72.893617	6	21.5
Any cough $\geq$ 2 weeks, weight loss	79	60.765957	20	33.6
Cough $\geq$ 2 weeks	56	35.574468	43	58.8
<b>Unknown or non-HIV infected patients</b>				
Any cough, weight loss, night sweat, fever	99.1	98.1		
Any cough $\geq$ 2 weeks, weight loss, night sweat, fever	98.1	95.1	0.9	3.0
Any cough $\geq$ 2 weeks, weight loss, night sweat	96.4	91.7	2.7	6.4
Any cough $\geq$ 2 weeks, weight loss	95.3	87.7	3.8	10.3
Any cough $\geq$ 2 weeks, fever	94.5	90.6	4.6	7.4
Any cough $\geq$ 2 weeks, night sweat	88.2	81.0	10.9	17.1
Cough $\geq$ 2 weeks	75.0	65.6	24.0	32.5

## PD-602-30 Utility of the Xpert MTB/RIF assay on stool specimens for TB diagnosis among people living with HIV in western Kenya

S Mutuku,<sup>1</sup> S Modi,<sup>2</sup> K McCarthy,<sup>3</sup> A Okumu,<sup>1</sup>

J Cavanaugh,<sup>3</sup> K Cain.<sup>1,4</sup>

<sup>1</sup>Research and Public Health Collaboration, Kenya Medical Research Institute/Centers for Disease Control and Prevention, Kisumu, Kenya; <sup>2</sup>Division of Global HIV/AIDS, Centers for Disease Control and Prevention, Atlanta, GA; <sup>3</sup>Division of Tuberculosis Elimination, Centers for Disease Control and Prevention, Atlanta, GA, USA; <sup>4</sup>Division of Tuberculosis Elimination, Centers for Disease Control and Prevention, Kisumu, Kenya. e-mail: smodi@cdc.gov

**Background:** Stool testing for *Mycobacterium tuberculosis* complex (MTBC) may be useful for the diagnosis of extrapulmonary tuberculosis (TB), or pulmonary TB in those who have difficulty producing sputum. Molecular testing with the Xpert MTB/RIF assay (Xpert) is an attractive alternative to culture because it is technically easier and faster, and may detect the presence of MTBC DNA even when the bacteria have been killed during gastrointestinal transit. Studies describing the performance characteristics of Xpert testing using stool are limited.

**Design/Methods:** Stool specimens were collected from HIV-infected participants aged 7 years and older who were enrolled in an Intensified Tuberculosis (TB) Case Finding study at 15 randomly-selected HIV clinics in Nyanza Province, Kenya. Specimens were processed and inoculated to liquid culture according to established protocols. Xpert testing was performed according to manufacturer recommendations for processed specimen pellets.

**Results:** Stool specimens were collected from a total of 308 patients. Xpert testing identified 12 (3.9%) invalid, 16 (5.2%) MTBC and 280 (90.9%) negative specimens. Of those identified with MTBC by Xpert, 2 (12.5%) had indeterminate results for rifampicin resistance and 14 (87.5%) were rifampicin susceptible. By comparison, results of liquid culture were 100 (32.5%) contaminated, 13 (4.2%) MTBC and 195 (63.3%) negative specimens. Nine (69%) of the 13 culture-positive samples were Xpert positive.

**Conclusion:** MTBC can be detected in stool using Xpert, and has no contamination issues and few invalid tests. Xpert may assist with the diagnosis of gastrointestinal TB, or pulmonary TB in patients who have difficulty producing sputum.

### PD-603-30 Incremental yield of Xpert MTB/RIF and liquid culture over Ziehl-Neelsen smear microscopy among patients with HIV and tuberculosis

J Cavanaugh,<sup>1</sup> S Modi,<sup>2</sup> A Okumu,<sup>3</sup> H Alexander,<sup>2</sup> K McCarthy,<sup>1</sup> B Burmen,<sup>3</sup> S Musau,<sup>3</sup> K Cain.<sup>3,4</sup> <sup>1</sup>Division of Tuberculosis Elimination, and <sup>2</sup>Division of Global HIV/AIDS, Centers for Disease Control and Prevention, Atlanta, GA, USA; <sup>3</sup>Research and Public Health Collaboration, Kenya Medical Research Institution/Centers for Disease Control and Prevention, Kisumu, <sup>4</sup>Division of Tuberculosis Elimination, Centers for Disease Control and Prevention, Kisumu, Kenya. e-mail: smodi@cdc.gov

**Background:** Sputum smear microscopy with Ziehl-Neelsen (ZN) staining is the principal diagnostic test for tuberculosis (TB) in Kenya, but it lacks sensitivity in HIV-infected persons. We sought to establish the benefit of Xpert MTB/RIF (Xpert) assay or liquid culture over smear microscopy in Kenya.

**Design/Methods:** We requested sputum specimens from patients 7 years or older and newly enrolled in HIV care in Nyanza Province, Kenya, regardless of symptoms. We performed ZN microscopy, Xpert assay, and liquid culture, each on two specimens. A TB case was confirmed if at least one Xpert or culture identified *Mycobacterium tuberculosis* complex.

**Results:** Among 779 patients, the laboratory confirmed TB in 88. Among 74 cases whose sputum received two ZN microscopy examinations and two Xpert tests, 25 (33.8%) were diagnosed by ZN microscopy; one Xpert test yielded an additional 18 (24.3%) cases, a second Xpert yielded an additional 13 (17.6%) cases. Among 82 cases whose sputum received two ZN microscopy and two cultures, 27 (32.9%) were diagnosed by ZN microscopy; one culture yielded an additional 35 (42.7%) cases, a second culture yielded an additional 11 (13.4%) cases.

**Conclusion:** Among people living with HIV (PLHIV), smear microscopy of 2 specimens missed two-thirds of TB cases. A single Xpert almost doubled the yield of microscopy, while a single culture more than doubled the yield. A second Xpert or culture test yielded an additional 15% above and beyond the first specimen. International recommendations to implement Xpert as the initial diagnostic test for symptomatic PLHIV should be implemented.

## 10. COMMUNITY COMMITMENTS TO IMPROVING TB TREATMENT ADHERENCE

### PD-604-30 Tuberculosis in homeless population of Delhi

D Kundu,<sup>1</sup> A Narnoliya,<sup>2</sup> M Kumar,<sup>3</sup> B S Banerjee,<sup>3</sup> A Sreenivas.<sup>1</sup> <sup>1</sup>RNTCP, WHO Country Office for India, Delhi, <sup>2</sup>RNTCP, Desraj Choudhary Chest Clinic, Delhi, <sup>3</sup>Home for special need children, Ashakiran, Delhi, India. e-mail: debashishkundu@yahoo.com

**Background and challenges to implementation:** Tuberculosis (TB) is a social disease and homeless population,

such as homeless labours, rickshaw pullers, beggars, vagabonds, mentally retarded orphans, etc. increases TB related morbidity and mortality among such vulnerable population and surrounding communities. An effective collaboration between Homeless and Governments and Non-Government Organizations are required to ensure early TB diagnosis and treatment. In order to ensure universal access to TB care, it is important to reach out to these homeless population, not accessing TB diagnostic and treatment services, though reasonably better accessed by other population of the society.

**Intervention or response:** Desraj Choudhary Chest Clinic in the Delhi's north west revenue district, under the Revised National TB Control Programme (RNTCP), collaborated with 'Ashakiran', a Delhi Government Organisation for special need children, home for mentally retarded orphans, to provide TB treatment and care services since 2004. 'Ashakiran' provides accommodation, medical care (through a medical unit team headed by a Chief Medical Officer), nutritional support, basic education and training to the 1050 mentally retarded children and adults, both male and female. All inmates in the home are subjected to routine medical examination by the medical care unit.

**Results and lessons learnt:** Data of last 8 years shows that among the paediatric (below 14 years), adolescent (15–18 years) and adult (above 18 years) age group, 121, 36 and 283 were put on TB treatment respectively. Of which 109 (90%) children, 35 (97%) adolescent and 269 (95%) were successfully treated. All TB patients were screened for HIV since 2010 at the nearest ICTC centre and one adult was found to be TB-HIV co-infected.

**Conclusions and key recommendations:** High success rate of TB treatment among the homeless population in 'Ashakiran' is pre-dominantly due to domiciliary DOT provided in this home by trained staff nurses, minimising the chances of 'loss to follow-up' in such vulnerable population. 'Ashakiran' Home provides residence to 1050 inmates as against 350 inmate capacities, which calls for an urgent need to create a homeless shelter plan by the state. Active collaboration with specialised shelters to homeless, run by Government and Non-Governmental Organizations, should be included in the national strategy for partnership for effective TB Control in India.

### PD-605-30 Strengthening TB treatment adherence in Kazakhstan: a multidisciplinary approach

S Amatya,<sup>1</sup> Z Beisembinova,<sup>2</sup> F Ginnett.<sup>1</sup> <sup>1</sup>Partnership Development, British Red Cross, London, UK; <sup>2</sup>Health, Kazakhstan Red Crescent Society, Almaty, Kazakhstan. e-mail: amatyasumi@yahoo.com

**Introduction:** In 2012 the National Centre for Tuberculosis (TB), Kazakhstan reported a TB incidence of 81.7 per 100,000 populations, while MDR TB rate was 14% among newly diagnosed and 45% among previously treated case. TB incidence is 522.5 per 100,000

prisoners. HIV prevalence among TB cases increased from 1.4 % in 2011, to 2.1% in 2012. Prisoners, injecting drug users, sex workers, migrants (MARPs) face risk and double burden of TB/MDR TB and HIV. Challenges of unemployment, homelessness, poverty, malnutrition, health inaccessibility, stigmatization and discrimination are barriers for TB treatment completion.

**Response:** Since 2012, the EU and British Red Cross supported Kazakhstan Red Crescent Society to provide rehabilitation support to TB patients and PLWHA including former prisoners through multidisciplinary teams (MDT) of a social worker, psychologist and lawyer. Friendly Centres were established in 5 regions to deliver services, host peer support groups (PSG), and disseminate TB/HIV information to the communities. A strong partnership with the National TB, HIV, Narcotic centres and Regional Penitentiary Department (KUIS), ensured cross referral of TB/HIV patients. Referred patients were assessed on their status and needs, if then registered on the program clients received varied forms of support to encourage treatment adherence:

- Psychosocial
- Nutritional
- Civil and social legal aids (housing, pensions and medical access)
- Further referrals for specialised treatment.
- PSGs with clients and family members were facilitated by the social worker and former clients taking on role of volunteer instructors.

**Results:** 1564 patients received program services. 50.6% of all patients were former prisoners. 889 patients received counselling and social support, 960 patients received legal aid, and 3000 food parcels distributed. 1,732 specialised treatment referrals were made. By December 2013, 93% of supported TB clients continued treatment without any interruption, with 63% achieving treatment completion. The overall TB treatment default rate was 1.5%, significantly lower than the WHO rate of <5%.

**Conclusion:** Through collaborative effort with TB and HIV centre, multidisciplinary approach for psychosocial, nutrition and legal care can achieve success in TB treatment. The additional aspect of peer involvement for self-recovery and family engagement has proved critically important in providing a holistic system of support for MARPs living with TB/HIV.



**Figure 1** Multidisciplinary team of social worker, psychologist and lawyer support to TB and HIV clients

### PD-606-30 High loss-to-follow-up among HIV-infected children registered for Pre-antiretroviral therapy care at Madurai, south India

V Pooranagangadevi,<sup>1</sup> A Kumar,<sup>2</sup> P Chinnakali,<sup>3</sup> S Sahu,<sup>3</sup> M Selvaraj,<sup>4</sup> A S Valan,<sup>5</sup> S Swaminathan.<sup>1</sup> <sup>1</sup>Department of clinical research, National Institute for Research in Tuberculosis, Madurai, <sup>2</sup>Research, International Union Against TB and Lung Disease, Bangalore, <sup>3</sup>Preventive and Social Medicine, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, <sup>4</sup>ART centre, Government Rajaji Hospital, Madurai, <sup>5</sup>Care, support and Treatment, Tamil Nadu State AIDS Control society, Chennai, India. e-mail: drpooranadevi@yahoo.co.in

**Background** Information on the follow-up of HIV-infected children enrolled into pre-antiretroviral therapy (Pre-ART) care (and not eligible for ART) under routine program settings is limited in India. Knowledge on the magnitude of loss to follow up (LFU) and its reasons will help program to retain children in HIV care. We aimed to assess the proportion of children lost to follow up (LFU) in Pre-ART care and its associated factors. **Methodology** In this retrospective cohort study, we reviewed the records of all HIV infected children (aged <15 years) registered from April 2004 to December 2012 at an ART centre, Madurai, South India. Lost to follow up (LFU) during pre-ART care was defined as having not visited the ART centre within a year of registration. Children who were transferred-in on ART were excluded.

**Results** Of 427 children enrolled in Pre-ART care, 211 (49%) were females and 302 (71%) were in the 5–14 years age group. At one year of registration, 349 (82%) were lost to follow-up. Of 349, 61 returned to care after one year of enrolment while 288 (67%) were permanently lost-to-follow-up. The proportion of LFU has remained high from 2004 to 2012. Only 23 (5%) of this cohort were documented to have had any opportunistic infection (OI) of whom 10 (40%) had Tuberculosis. Children in WHO clinical stage 2 (RR=1.14; 95% CI: 1.05-1.25), history of opportunistic infections (RR = 0.68; 95% CI: 0.47-0.98) were associated with LFU. Age, sex, baseline CD4 count were not significantly associated with LFU.

**Conclusion** LFU was high indicating suboptimal clinical and programmatic monitoring among HIV-infected children enrolled in pre-ART care. Qualitative research is needed to understand the exact reasons for LFU based on which effective interventions may be planned for reducing such losses.

### PD-607-30 Experience organising TB patient support groups in the Republic of Kazakhstan

B Babamuradov,<sup>1</sup> Y. Belova,<sup>1</sup> T Mohr,<sup>1</sup> Y. Radionova.<sup>2</sup> <sup>1</sup>Tuberculosis, Project HOPE, Almaty, <sup>2</sup>Social Support, CBO "Kos Kanat Zhetisu", Taldikurgan, Kazakhstan. e-mail: bbabamuradov@projecthope.org

**Background:** Tuberculosis is a serious public health threat in Kazakhstan. Studies show that lack of knowledge among TB patients about their disease may



lead to treatment interruption. Project HOPE under the auspices of the USAID Quality Health Care Project implemented Patient Support Groups (PSGs) to enable patients to take more responsibility for their health, to reduce stigma and discrimination, and to improve treatment adherence. PSGs also aimed to improve the effectiveness of work with TB patients and to reduce the workload of health care workers. In 2012, Project HOPE, with the support of Kazakhstan's NTP and local Community Based Organization (CBO) "Kos kanat Zhetisu", established PSGs in Taldikurgan city (Almaty Oblast).

**Setting:** Taldikurgan city of Almaty Oblast, Kazakhstan.

**Methods:** Preparatory activities were conducted prior to organizing PSGs. These included: agreeing with health care institutions to organize PSGs, involving CBOs in patient support, and training CBOs on how to work with patients. Once preparatory work was completed a CBO began functioning as "a bridge" between patients and health care professionals. In some location PSGs were formed without CBO involvement. PSGs include doctors and current, and former patients who share their experiences to improve adherence to treatment and support each other on the path to cure.

**Results:** From October 2012 to December 2013 monthly PSG meetings were held in City polyclinics. CBO staff and health institutions actively helped address problems patients identified that create barriers to receiving and finishing treatment. In total, 165 TB patients participated in the PSG meetings, including 62 men (37.6%) and 103 women (62.4%). On average, 11 patients participated; the percentage of patients participating in PSGs averaged 56.1% and ranged from 36.4% to 77.8%. Among patients who participated in PSG meetings, 117 completed treatment with the outcome "cured" or "treatment completed" and 48 continue treatment as of March 2014.

**Conclusion:** The high percentage of patients attending PSGs reflects the interest of patients in this activity. Reduction in treatment interruptions and defaults confirm the value of PSGs for TB patients, including the involvement of CBOs which helps improve patient adherence to treatment, and reduces stigma and discrimination.

#### **PD-608-30 Social movements and the Directly Observed Treatment of tuberculosis in Rocinha, Rio de Janeiro, Brazil: perceptions of nurses**

F Assumpção De Souza,<sup>1</sup> G Schuabb,<sup>1</sup> J Siqueira Lima,<sup>1</sup> TC Scatena Villa,<sup>2</sup> A Ruffino-netto.<sup>2</sup> <sup>1</sup>DEMC, Federal University of the Estate of Rio Janeiro - UNIRIO, Rio de Janeiro, RJ, <sup>2</sup>Enfermagem Materno Infantil e Saúde Pública, University of São Paulo - USP, Ribeirão Preto, SP, Brazil. e-mail: glaucialschuabb@gmail.com

**Introduction:** The incidence rate of tuberculosis (TB) in Rocinha/ RJ community is 300/100.000 inhabitants, the largest in the country, which has the average 46/100.000 inhabitants. Popular participation in TB control activities becomes important due to the fact that the actors

become able to point out the problems and solutions concerning their actual demands.

**Objectives:** To identify and analyze the performance of social movements in Directly Observed Treatment (DOT) of TB in the community of Rocinha, in the perception of nurses.

**Methods:** A qualitative study using content analysis. Semi-structured interviews with 26 nurses from Rocinha Family Health Strategy (FHS) were performed. For the analysis of the responses, we used the Atlas -ti 6.2 software that enables the encoding of speech according to the categories of analysis. The study was approved by the Ethics Committee in Research of the Municipal Health Secretariat of Rio de Janeiro.

**Results:** While some nurses FHS Rocinha reported knowing the social movements that carry TB control activities in the community, others reported unknown them. The majority of respondents have heard about a social movement that works with the reintegration of patients and former patients of TB in society, however, nurses do not maintain contact with it, mainly due to high demand and intense day of work which are submitted. In relation to DOT, nurses reported non-participation of social movements exist in this process, which is established only between community health worker and the patient.

**Conclusion:** More than half of respondents know the social movements that carry TB control activities in Rocinha; and in relation to the specificities of supervision of TB treatment, respondents are unaware of the existence of social movements active in this process. Nurses recognize the contribution of representative groups of society in the fight against TB in the community but there are no communication and integration activities of such groups and nurses.

#### **PD-609-30 Home-based tuberculosis care in Armenia**

H Armen,<sup>1</sup> V Khachadourian,<sup>1</sup> M Hovhannisyan,<sup>1</sup> Z Koloyan.<sup>2</sup> <sup>1</sup>National Tuberculosis Control Office, Ministry of Health, Yerevan, <sup>2</sup>Yerevan Home Care, Yerevan Home Care, Yerevan, Armenia. e-mail: vahe.khachadourian@gmail.com

**Background:** One of the major factors contributing to tuberculosis control is successful treatment of the disease. There are various factors associated with tuberculosis treatment outcomes. Non adherence to the treatment regimen has been identified as one of the main reasons for treatment failures. Very often, because of physical illnesses, patients are unable to visit TB outpatient centers to take their daily medications. To tackle the problem and make the TB care accessible to such patients a pilot program was suggested to provide home based TB treatment for patients living in Yerevan.

**Intervention or response:** The program was initiated during the year 2013 through involving TB patients according to specific criteria. According to the criteria, those patients with severe mobility disorders, those with critical illnesses and unstable condition, and those with vertebral TB were eligible to be included in the program.

The inclusion of the patients was made and verified by the responsible physician and the corresponding TB specialist working at the national TB control office.

**Results and lessons learnt:** Out of 57 TB patients included in the program, 21% (12) were included for a short period of time (temporary treatment) and 79% (45) for their entire treatment (full treatment). Out of 45 patients in full home based treatment, 51% (23) have completed and 49% (22) are still on treatment. 23 of the patients in the full home based treatment who completed the treatment have had 91% (21/23) successful treatment outcome, and 2 of the patients 9% (2) died due to non TB reasons. The treatment of all patients, involved in temporary home based program, were transferred to TB outpatient centers, because of improved health status.

**Conclusions and key recommendations:** The high rates of successful treatment outcomes among patients with high rates of morbidity and mobility problems highlighted the potential effectiveness of home based TB care program. The project increased the accessibility of the treatment, improved adherence of patients to treatment regimen and consequently resulted to better treatment outcomes. Based on the pilot study results we recommend scale-up the project and after confirmation of the results in a larger project incorporating the approach in the National tuberculosis control strategy. The program can also be implemented in other countries with similar health care structure and available resources.

#### **PD-610-30 Christmas break not treatment break- promoting TB treatment adherence among mine workers in Swaziland**

N Shongwe,<sup>1</sup> Y G Ghebreyesus,<sup>1</sup> S Haumba,<sup>1</sup> C Dlada,<sup>2</sup> V Jele,<sup>3</sup> E Phiri,<sup>4</sup> J Ongole.<sup>1</sup> <sup>1</sup>TB/HIV USAID ASSIST PROJECT, University Research Swaziland, Mbabane, Swaziland; <sup>2</sup>World Bank Project, University Research South Africa, Pretoria, South Africa; <sup>3</sup>Migrant Workers, Swaziland Mine Workers Association, Nhlalanga, <sup>4</sup>TB/HIV, National TB Control Program, Manzini, Swaziland. Fax: (+268) 24047199. e-mail: ntombifuthis@urc-sa.com

**Background and challenges to implementation:** Stop TB Partnership figures reveal that TB incidence among South Africa's mineworkers is 3000 to 7000/100 000 miners compared with the global incidence rate of 128/100 000. The mines have traditionally attracted workers from Swaziland, albeit limited TB control policies. A campaign themed "Christmas Break not Treatment Break" was launched focusing on providing continued support to South African based miners who were on festive holidays.

**Aim:** Sensitizing and raising awareness of the mine workers on the importance of TB treatment adherence; supporting mine workers on TB treatment returning to Swaziland during the holidays, through ensuring continued access to TB medicines.

**Intervention or response:** URC Swaziland, NTCP and SWAMMIWA agreed to develop an emergency plan to ensure continued treatment for miners during the Christmas break. Media messages (both in Siswati and English) were developed. Sensitization and awareness

training activities were conducted at 2 of the country's main border posts provided by 5 community based volunteers trained to teach returning miners, ex-miners and their families about the TB treatment adherence. Information pamphlets on treatment adherence and support during the Christmas break were available. A call line was provided and advertised on the radio, dedicated to mine workers concerns on TB and treatment. The campaign hosted an interactive event between Ministry of Health directorate and the miners.

**Results and lessons learnt:** Radio messages on treatment adherence were broadcasted to reach mine workers from 24 December 2013 until 5 January 2014. A total of 402 mine workers were reached at the Mahamba and Oshoek border posts through 5 community volunteers. Education sessions covered: TB treatment adherence, alcohol abstinence while on treatment, importance of disclosure and openness to family support, side effect management, and infection prevention and control in the home and community. Miners appreciated efforts by Government and the Mining Association; and requested that such campaigns be communicated in advance (at the mines) and for more educational interventions on TB treatment and management.

**Conclusions and key recommendations:** The 'Christmas break not Treatment Break' campaign was a success. Such informative initiatives will improve TB treatment adherence, reduce disease transmission and limit development of drug resistance.

#### **PD-611-30 Social determinants of health and adherence to tuberculosis therapy for patients living in Karachi: a qualitative study**

AA Khan,<sup>1</sup> U Rabbani,<sup>1</sup> S Bawani,<sup>1</sup> M Zafar,<sup>2</sup> A Ahsan,<sup>1</sup> Z Fatmi.<sup>1</sup> <sup>1</sup>Department of Community Health Sciences, Aga Khan University, Karachi, <sup>2</sup>Department of Community Medicine, Dow university of Health Sciences, Karachi, Pakistan. e-mail: unaib\_dr@yahoo.com

**Background:** The treatment of TB is a long term therapy and therefore adherence to the treatment is crucial for good outcomes, however, in low and middle income countries there obstacles to compliance. Pakistan has a high burden of tuberculosis (TB) and treatment compliance is known to be low with high default rates. The latter has resulted in the emergence of multi-drug resistant TB. This study aimed to identify the social determinants of adherence to Anti Tuberculosis Therapy (ATT) among TB patients in selected towns of Karachi.

**Methods:** The research objective of this research was to identify the determinants of compliance to Anti Tuberculosis Therapy (ATT) among TB patients in towns of Karachi, Pakistan. A qualitative study was carried out in Karachi from January 2012 to March 2012 to identify the key social determinants of adherence (or compliance) ATT. In this respect, 10 TB patients and 5 physicians were interviewed using a semi-structured instrument based on a theoretical framework for health related behavior. The notion of judgment in qualitative sampling was used to select potential study participants.

**Results:** Both facilitating and impeding determinants that influence participants' adherence towards TB treatment were identified. Determinants that positively affect an individual's adherence include good behavior of the doctor, family support and correct knowledge about the disease. Barriers to treatment adherence include poor knowledge about the disease, lack of adequate counseling by health personnel, low financial status and distant health facilities. Were there any differences between men and women? Was there any difference between ages?

**Conclusion:** Various factors related to the social determinants of health from an individual level (e.g. education, access, economic status), to the health care system level where the behavior of health professionals played a role in treatment adherence. Human Resource Managers and Policy makers need to focus on improved communication skills of health care providers, fostering awareness among the patients about adverse outcomes of non-adherence and establishment of diagnostic and treatment facilities in the distant areas could improve adherence to ATT.



Fig. 1 Cumming's Theoretical framework

Source: Bringing the models together: an empirical approach to combining variables used to explain health actions by Cummings KM, Becker MH, Maile MC. *Journal of Behavioral Med.*

### PD-612-30 Interest of the community involvement in the control of tuberculosis in Burkina Faso

F M G Coulibaly Donessoune,<sup>1</sup> K Lougué.<sup>1</sup> <sup>1</sup> Civil Society, PAMAC, Ouagadougou, Burkina Faso.  
e-mail: couldaley@yahoo.fr

**Background:** According to WHO estimates, it was expected in 2013 in Burkina Faso, 9342 new cases of tuberculosis and relapse. However, the 2013 report of the national program against tuberculosis highlights 6290 on expected 9342. Indicators are below target. the NTP sought PAMAC (the national civil society support programme) to improve detection of TB cases through the implementation of community activities. Description of the procedure. Specialized associations in community support hotlines hold in the DTC, do research absent treatment, conduct home visits and make the search for suspects around sick. Those specialized in Information, Education and communication educate people who have "less access to information."

**Results:** During the year 2013, through sensitization, 841 TB suspects were referred to health centers by Community Health worker and 113 tuberculosis all forms were detected (including 14PTB -). There are 4479/5520 registered patients (over 80 %) who received Community support, allowing to recover the 162 missing treatment. Finally, 457 cured patients have benefited from community DOTS (25% of patients).

**Lessons learnt:** The community health worker partnership with health Care services actors provides comprehensive care of the patient and the implementation of a patient-centered approach. Community health worker well-trained plays an important role in the control of TB, and solved the lack of human resources in the DTC.

### PD-613-30 Social approach to reach vulnerable and marginalised communities for tuberculosis, care and control

A K Singh,<sup>1</sup> R David.<sup>1</sup> <sup>1</sup>TB, MAMTA-HIMC, New Dehi, India.  
e-mail: alok@mamtahimc.org

**Background and challenges to implementation:** Axshya Project initiative of MAMTA is a Sub-Recipient of The Union under Global Fund Round-9. MAMTA is implementing this project in 62 districts across 7 States. The current study is based on the result of the project implementation in 11 districts of Uttar Pradesh over a period of one year i.e. April 2013 to March 2014. The project aims to address problems of tuberculosis among the communities through the advocacy, communication and social mobilisation by engaging civil society. It also intends to bring about a change in social perception and enhance the information needs of community people about tuberculosis, its diagnosis and treatment over a period of time. The specific challenges to program implementation included the needs assessment of the project, mapping of the selected districts highlighting the vulnerable and marginalised population, developing model Axshya villages, and overall initiation of policy to action at the outreach.

**Intervention or response:** The analysis of the collected data was done through the MS-Excel in a pre-designed format which presented the data measurable in terms of achievement, social progression, increased awareness, and indicators showing increased performance of overall activity of Axshya project in the district. It was evident from this project that more a person aware about tuberculosis more likely he is to seek timely diagnosis and treatment and also he is less likely to default.

**Results and lessons learnt:** The project activities such as referrals through 84933 numbers of Axshya Samvad (household visits) yielded 244 patients being put on DOTS; referrals through 332 numbers of trained RHCPs engaged in Axshya has resulted 137 patients being put on DOTS; and referrals through 2623 numbers of Community meetings in Axshya resulted in 221 patients being put on DOTS over a period of one year. Similarly another output indicator such as Sputum Collection and Transportation (SCT) has shown encouraging results i.e. SCT through 84933 numbers of Axshya Samvad returned 405



patients being put on DOTs; SCT through 332 numbers of trained RHCPs engaged in Axshya returned 355 patients being put on DOTs.

**Conclusions and key recommendations:** The learning from the implementation of this project is of immense help in shaping the future strategy to design a project that is socially more viable, measurable in terms of project performance and socially intact.

Indicators (Referral performance indicators)										
Sr. No.	Quarter	Activity		Referrals through IORA						
		No. of IORA conducted		TB Symptomatic Referred	Underwent sputum examination	Diagnosed as TB patients	No. put on DOTs		Positivity Rate (%)	
1		No.	%	No.	No.	No.	No.	%	Quarterly	Annual (Average)
	Q1	7837	9%	622	185	32	31	13%	17%	
	Q2	18896	22%	1417	713	65	62	26%	9%	
	Q3	23752	28%	1965	612	61	61	25%	10%	
	Q4	34448	41%	2787	1166	90	90	36%	8%	
Yearly	Total	84933		6791	2676	248	244			11%
Sr. No.	Quarter	Trained RHCPs Engaged		Referrals through RHCPs						
		No.	%	No.	No.	No.	No.	%	Quarterly	Annual (Average)
2	Q1	16	5%	378	151	18	18	13%	12%	
	Q2	72	22%	712	336	32	30	22%	10%	
	Q3	108	33%	980	376	44	44	32%	12%	
	Q4	136	41%	1200	468	45	45	33%	10%	
Yearly	Total	332		3270	1331	139	137			11%
Sr. No.	Quarter	Community meetings/MM Conducted		Referrals through Other Groups (Community meetings/ special groups/facility based)						
		No.	%	No.	No.	No.	No.	%	Quarterly	Annual (Average)
3	Q1	650	25%	1794	625	102	94	43%	16%	
	Q2	586	22%	1263	741	59	46	21%	8%	
	Q3	668	25%	1649	561	44	44	20%	8%	
	Q4	719	27%	2271	716	37	37	17%	5%	
Yearly	Total	2623		6977	2643	242	221			9%
Indicators (SCT performance through IORA)										
Sr. No.	Quarter	Activity		SCT indicators				Positivity Rate (%)		
		No. of IORA conducted	No. of patients (SCT done)	No. diagnosed as TB patients	No. put on DOTs	No.	No.	%	Quarterly	Annual (Average)
4	Q1	7837	9%	295	26	26	6%	9%		
	Q2	18896	22%	1417	154	114	28%	10%		
	Q3	23752	28%	1965	139	119	29%	10%		
	Q4	34448	41%	2787	177	146	36%	9%		
Yearly	Total	84933		4209	406	405		10%		
Indicators (SCT performance through RHCP Engagement)										
Sr. No.	Quarter	No. of trained RHCPs Engaged		SCT indicators				Positivity Rate (%)		
		No.	%	No.	No.	No.	No.	%	Quarterly	Annual (Average)
5	Q1	16	5%	829	71	68	19%	9%		
	Q2	72	22%	1024	85	85	24%	8%		
	Q3	108	33%	946	90	90	25%	10%		
	Q4	136	41%	1138	112	112	32%	10%		
Yearly	Total	332		3937	358	355		9%		
Indicators (SCT performance through Other Groups (Community meetings/ special groups/facility based))										
Sr. No.	Quarter	Community meetings/MM Conducted		SCT indicators				Positivity Rate (%)		
		No.	%	No.	No.	No.	No.	%	Quarterly	Annual (Average)
	Q1	650	25%	433	46	45	17%	7%		
	Q2	586	22%	825	76	88	34%	13%		
	Q3	668	25%	791	74	74	28%	11%		
	Q4	719	27%	679	57	55	21%	8%		
Yearly	Total	2623		2728	253	262		10%		

## 11. RETROSPECTIVE TB DATA ANALYSIS: CASE IDENTIFICATION, TREATMENT AND CONTROL

### PD-614-30 Co-infection of TB and HIV in Russia in the beginning of the XXI century (2004–2013)

E Tsybikova.<sup>1</sup> <sup>1</sup>Health Statistics, Federal Research Institute for Health Organization and Informatics, Moscow, Russian Federation. Fax: (+7) 4956193840. e-mail: erzheny2014@yandex.ru

**Background:** The first decade of the XXI century in Russia was characterized by the essential growth of cases of co-infection of TB and HIV. As a result, the number of

regions with high prevalence came up to 43 i.e. doubled in comparison with 2000.

**Aim:** To study epidemiology of co-infection of TB and HIV in Russia in the beginning of the XXI century (2004–2013).

**Design/Methods:** Co-infection prevalence indicators were calculated using official reporting forms of Federal State Statistics Service and Ministry of Health of Russia. Data from 81 TB dispensaries of Russia were used to determine causes of death and age distribution of deaths from lung TB. Correlation analysis was conducted.

**Results:** Prevalence of co-infection of TB and HIV in Russia during 2004–2013 is increasing. Cumulative rate of prevalence of co-infection of TB and HIV estimated 777% in 2013 in comparison with 2004 including growth during 2004–2008 – 425% and during 2009–2013 – 33.3%. Growth of number of patients is mainly registered in 25–34 and 35–44 age groups estimating 52.9% of their total number in 2013. Mortality from HIV in these age groups reached 86% of the total number of deaths in HIV patients. Correlation analysis showed that share of deaths from TB was inversely proportional to share of all other deaths: Pearson correlation coefficient – 0.61 (p=0.002). Currently, variance of mortality level in newly diagnosed TB patients in Russian regions is determined not by mortality from TB but by mortality from HIV. Growth of number of deaths from co-infection of TB and HIV is followed by increase of HIV mortality and also by reduction of TB mortality. Summary rate of reduction of mortality from TB in Russia during 2004–2012 estimated –41.3% and rate of growth of mortality from HIV +950.0%. Number of patients with tuberculosis meningitis is increasing, especially in 25–34 and 35–44 age groups, and their share doubled since 1999 and estimated in 2013 69.8% of the total number. Up to now dynamics of indicators of co-infection of TB and HIV evidences that the number of new cases of TB is increasing mainly due to HIV patients. **Conclusion:** Dynamics of prevalence of co-infection of TB and HIV in Russia in 2004–2013 demonstrates the ascending trend. The main share of deaths among patients with co-infection of TB and HIV falls to 25–34 and 35–44 age groups. Their summary share in 2011 estimated 86% of the total number.

### PD-615-30 Outpatients: treatment outcomes after cross-checking registers and records in Lusaka, Zambia

V Mfungwe,<sup>1,2</sup> M Ota,<sup>1,3</sup> H Ogata,<sup>1,3</sup> N Kapata,<sup>2,4</sup> K Koyama,<sup>1,3</sup> G Samungole.<sup>2,4</sup> <sup>1</sup>Tuberculosis/HIV, The Research Institute of Tuberculosis/Japan Anti TB Association (RIT/JATA) Zambia, Lusaka, <sup>2</sup>Health, Health Professionals Association of Zambia, Lusaka, Zambia; <sup>3</sup>Tuberculosis, The Research Institute of Tuberculosis/Japan Anti TB Association (RIT/JATA) Japan, Tokyo, Japan; <sup>4</sup>Tuberculosis, Ministry of Community Development, Mother and Child Health, Lusaka, Zambia. e-mail: mfungwev@gmail.com

**Background:** Low tuberculosis (TB) treatment success rates in large urban settings in low-income countries like Zambia are a challenge in TB control. Follow up of

transferred out cases is often neglected and the actual treatment outcomes of these cases may not be fully known, contributing to a lower treatment success rate. Lusaka urban district, the capital city of Zambia has a current population of 2 340 000. It accounts for over 32% of the total urban population in the country. A diagnostic center serving three major satellite treatment facilities representing 5% of the population in Lusaka was selected. This diagnostic center registers about 700 cases of all types of TB every year, of which on average 60% resides outside its catchment area and are transferred to the three satellite health facilities to provide them with easier access to treatment. **Objective:** to assess the treatment outcomes of "transfer out" cases at a diagnostic centers serving three major satellite treatment facilities in Lusaka

**Design/Methods:** A retrospective cohort study was conducted on treatment outcomes for new smear-positive TB cases registered from 1 July to 31 December 2012 at the diagnostic center. The recorded treatment outcomes of TB cases that had been transferred out to three satellite treatment facilities were reviewed and compared with those in the diagnostic center TB register. In-depth group discussions with TB corner nurses at all the four facilities were held to make sure the treatment outcomes were accurate

**Results:** Forty-nine new smear positive cases were transferred out to the three satellite health facilities, of which, 30 (61%) had the same and 19 (39%) had different treatment outcomes recorded in the registers and treatment cards. Of the 19 pairs of different records, ten (53%) records had to be updated in the TB register of the diagnostic center and thirteen (47%) in the three satellite facilities, reducing the proportion of "transfer out" cases from 18% to 7% at the diagnostic center

**Conclusion:** Review and crosscheck of the TB registers at the diagnostic center and satellite facilities led to a significant reduction of non-assessed cases. TB registers between the diagnostic center and treatment facilities should frequently be crosschecked to be able to monitor the actual treatment outcomes of the TB cases registered at the diagnostic center

**Table 1.** The difference in treatment outcomes for all new smear-positive patients enrolled from 1 July to 31 December 2012 before and after register update.

	New SM+	TSR	Cure	TC	LF	TO	DIED	TF
Before update	85	65%	40 (47%)	15 (18%)	9 (11%)	15 (18%)	4 (5%)	2 (2%)
After update	85	74%	44 (52%)	19 (22%)	9 (11%)	6 (7%)	5 (6%)	2 (2%)
Difference	0	+7%	+5%	+4%	0%	-11%	+1%	0

SM: smear, TSR: treatment success rate, C: cured, TC: treatment completed, LF: lost to follow up, TO: transfer out/not evaluated, TF: treatment failure

### PD-616-30 Tuberculosis control in security challenged States of north-east Nigeria. Is there significant impact?

M Gidado,<sup>1</sup> Josh Obasanya,<sup>2</sup> J Onazi,<sup>1</sup> R Eneogu,<sup>2</sup> N Chukwueme,<sup>2</sup> T Odusote,<sup>3</sup> J Kuye,<sup>2</sup> S Useni.<sup>1</sup> <sup>1</sup>Program, KNCV/TB CARE I Project, Abuja, <sup>2</sup>Public Health, National TB & Leprosy Control Program, Abuja, <sup>3</sup>TB/HIV Unit, USAID, Abuja, Nigeria. e-mail: gidadom@kncvnigeria.org

**Background:** Nigeria in the past few years is faced with various security challenges in different parts of the country. The most severe in the last three years has been the crisis in northern Nigeria and specifically the north-eastern States, where three of the States have been under emergency rule for a year. Health care delivery system is usually one of the major casualties in a security challenged environment leading to unavailability or low utilization of services. The aim of this paper is to share the experience of TB services in states under emergency rule.

**Methodology:** A retrospective review of program data (reportable indicators for TB case finding, TB/HIV and treatment outcome) were reviewed for a period of six years comparing national data with north-east and the three states most affected by security challenges (Borno, Adamawa & Yobe).

**Results:** National TB case notification and treatment success rate increased marginally by 6.7% and 4.5% between 2008 to 2013 respectively (total cases of 90,311 in 2008 to 100,401 in 2013; TSR of 82.5% in 2008 to 87% in 2013). While for same indicators in north-east; the increase was less than 1% for case notification; and 4% for TSR. There were variation among the three most affected states (Borno, Yobe & Adamawa) for periods between 2008 - 2013, with a decrease in cases notification of 18.7% and increase in TSR of 7% for Borno; 34.4% reduction in total cases notified and decrease of 3% for TSR for Adamawa; and 3% increase in case notification and 3% reduction on TSR for Yobe. TB/HIV indicators are on a positive trend nationally; the north-east zone; and two states under the emergency rule (Adamawa & Yobe).

**Conclusions;** Insecurity can pose a challenge for TB control activities especially case finding, therefore the need for innovative approaches for case finding in areas of insecurity. Other areas affected are expansion of services, quality supervision, and logistics management system especially ensuring availability of supplies.

### PD-617-30 Clinical audit to evaluate quality of care for cases with TB-HIV co-infection in the Republic of Moldova

S Bivol,<sup>1</sup> V Vilc,<sup>2</sup> V Soltan,<sup>1</sup> S Popovici,<sup>3</sup> O Scutelnicu.<sup>4</sup> <sup>1</sup>PAS Center, Center for Health Policies and Studies, Chisinau, <sup>2</sup>Department of Phtysiopneumology, N Testemiteanu State Medical and Pharmaceutical University, Chisinau, <sup>3</sup>HIV Department, Dermatology and Communicable Diseases Hospital, Chisinau, Moldova; <sup>4</sup>Regional Office for Europe and Central Asia, UNAIDS, Almaty, Kazakhstan. Fax: (+373) 22226843. e-mail: stelatic@yahoo.com

**Background:** Tuberculosis (TB) is the top cause of mortality among people living with HIV (PLHIV) in

the Republic of Moldova. To evaluate the quality of clinical care and case management of the TB/HIV co-infection cases and the coordination between TB and HIV service, a clinical audit of all registered TB/HIV cases between 2007 and 2011 was performed.

**Methods:** retrospective cohort analysis based on a structured questionnaire applied to clinical records of TB/HIV cases registered in the national TB database. Cross check of all cases with death outcome with national mortality database.

**Results:** 921 cases met the clinical chart audit criteria for the period 2007–2011. TB/HIV cases had a high prevalence of social vulnerabilities (81% unemployment, 92% history of drug use, 39% history of incarceration). HIV cases presented late for HIV clinical follow-up: 27% of cases have not seen a doctor for HIV before TB diagnosis; at the time of TB diagnosis 46% had CD4 counts  $< 200$  cells/mm<sup>3</sup>; of those in HIV clinical follow-up, 57% were on ARV treatment. TB screening was inadequate: 11% of cases had record of TB screening in the past 12 months, of which 95% with X-ray. None of PLHIV received preventive treatment with Isoniazid. On average, 28 days (SD 94 days) elapsed between first TB suspicion and start of TB treatment. Among TB/HIV cases, 26% had confirmed MDR TB, and 8% had mono or poly-resistance, yet only 2% received DOTS+ treatment regimen. Only 25% were administered cotrimoxazol for prevention of *Pneumocystis Carinii* Pneumonia prevention. Clinical outcomes: 15% cured, 21% completed treatment, 32% deceased, 16% treatment default, and 11% treatment failure (5% not evaluated at the time of audit).

**Conclusions:** Clinical audit quantified deficiencies in both HIV and TB clinical management and care coordination, with main bottlenecks being late HIV diagnosis, reduced ART coverage, poor TB screening and preventive treatment, excessive time to diagnose TB, inadequate TB treatment regimen and poor case-management.

#### **PD-618-30 Inner-urban environmental predictors of tuberculosis infection sites according to the activity space in Shinjuku, Tokyo from 2003 to 2011**

K Izumi,<sup>1,2</sup> A Ohkado,<sup>1</sup> K. Uchimura,<sup>1</sup> Y Murase,<sup>3</sup> Y Tatsumi,<sup>4</sup> K Fukuuchi,<sup>5</sup> H Watanabe,<sup>6</sup> N Ishikawa.<sup>4</sup>

<sup>1</sup>Epidemiology and Clinical Research, Japan Anti-Tuberculosis Association, Research Institute of Tuberculosis, Kiyose,

<sup>2</sup>Graduate School of Biomedical Sciences, Nagasaki University, Nagasaki, <sup>3</sup>Mycobacterium Reference and Research, Japan Anti-Tuberculosis Association, Research Institute of Tuberculosis, Kiyose, <sup>4</sup>Director's Office, Japan Anti-Tuberculosis Association, Research Institute of Tuberculosis, Kiyose, <sup>5</sup>Director's Office, Koto Public Health Center, Koto, <sup>6</sup>Health, Shinjuku Public Health Center, Shinjuku, Japan. e-mail: kizumi95@gmail.com

**Aim:** To assess the possible predictors of tuberculosis (TB) transmission sites using selected demographic and urban environmental variables from an inner-urban setting in Japan.

**Methods:** This retrospective ecological study included notified bacillus-positive TB patients in Shinjuku, Tokyo during 2003–2011. The primary outcome was the annual number of TB patients per km<sup>2</sup> (TB patient density) according to the census tracts where they had mostly resided during waking hours. All TB bacilli isolated from each enrolled TB patient were subjected to restriction fragment length polymorphism (RFLP) analysis. A genotype cluster was defined as a group of patients with identical RFLP-band patterns. We set 2 dependent variable groups for the multivariate Poisson regression models: Group I, 22 demographic and urban environmental variables; and Group II, 4 classes of Land Use Zones that determine specifications concerning the construction and use of buildings within the zone. Each model was stratified and analyzed according to residential status, including general inhabitants (non-homeless), foreigners, and the homeless.

**Results:** Multivariate analysis identified various predictive trends across different residential and genotype cluster statuses. Except for the “commercial zone,” none of the significant predictors of general inhabitants overlapped with those of the homeless. Additionally, the “day and night population ratio” associated negatively with general inhabitants but positively with the homeless, although the regression coefficient was very low. For general inhabitants, the “daytime population density” ( $p < 0.05$ ), “social insurance, social welfare, and care services” ( $p < 0.01$ ), and “commercial zone” ( $p < 0.001$ ) were positive predictors of genotype clustering and suggested a recent infection occurrence; these variables were not significant for the non-clustered. Unlike general inhabitants, both the genotype- non-clustered and clustered homeless displayed similar trends for nearly all variables; in particular, all significant predictors for the former were significant predictors for the latter. In Group II, “commercial zone” had the highest partial regression coefficient value in all models, especially for the homeless (13.75,  $p < 0.001$ ).

**Conclusion:** The predictors appeared to vary among the residential status and genotype-clustering subgroups and were relevant for the assessment of spatial risk factors.

#### **PD-619-30 Evolución y características epidemiológicas de los casos de tuberculosis diagnosticados en Galicia, 1996–2012**

E Cruz-Ferro,<sup>1</sup> MI Ursúa-Díaz,<sup>1</sup> JA Taboada-Rodríguez,<sup>1</sup> X Hervada-Vidal,<sup>1</sup> Grupo de Trabajo DEL Programa Galle.<sup>1</sup> <sup>1</sup>Programa Galego de Prevención e Control da Tuberculose, Consellería de Sanidade. Dirección Xeral de Innovación e Xestión da Saúde Pública, Santiago de Compostela, Spain. Fax: (+34) 881542971. e-mail: elena.cruz.ferro@sergas.es

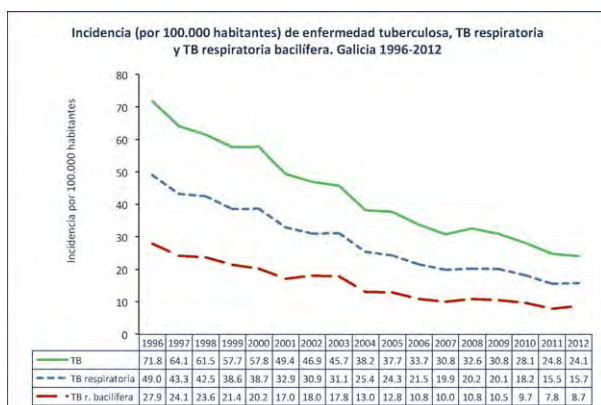
**Antecedentes:** El Programa Gallego de Prevención y Control de Tuberculosis se basa en siete Unidades de Tuberculosis, que realizan una captación y seguimiento activo de todos los casos de enfermedad e infección tuberculosa. Objetivo: describir la evolución y las



principales características de los casos de tuberculosis (TB) de Galicia en el período 1996–2012.

**Métodos:** Estudio observacional descriptivo retrospectivo. Fuente: Sistema de Información de Tuberculosis. Período: 1996–2012. Ámbito: Galicia. Variables: sexo, edad, localización, radiografía de tórax, bacteriología, coinfección VIH, inmigración, retraso diagnóstico, tratamientos supervisados y situación final del tratamiento. Resultados: Número de casos (incidencia por 100.000 habitantes): 1.963 (71,8) en el año 1996; 669 (24,1) en 2012. Disminución por término medio anual: –6,6%. Incidencia de TB respiratoria y TB respiratoria bacilífera: 49,0 y 27,9 en 1996; 15,7 y 8,7 en 2012, respectivamente. Sexo: 60,5% hombres (1996–2012). Grupo de edad más afectado: entre 15–24 años ( $97,7/10^5$ ) en 1996; entre 25–34 años ( $28,7/10^5$ ) y  $>74$  ( $30,0/10^5$ ) en 2012. Incidencia en  $<15$  años:  $33,0/10^5$  en 1996;  $9,5/10^5$  en 2012. Localización: 59,2% exclusivamente respiratoria; 32,6% sólo extrarrespiratoria y 8,2% ambas localizaciones (1996–2012). Radiografía de tórax de la TB respiratoria con imagen cavitada: 33,0% en 1996; 26,9% en 2012. Baciloscopia de esputo positiva: 54,2% (1996–2012). Confirmación de TB respiratoria: 70,5% en 1996; 82,4% en 2012. Confirmación de TB extrarrespiratoria: 39,2% y 40,9% respectivamente. Antibiógramas (desde el año 2004 se hace antibiógrama a todos los casos de TB): resultados del año 2012: 89,8% sensibles a los 5 fármacos de 1ª línea; 3,4% resistencia primaria a isoniazida; 0,7% (3 casos) TB multirresistente. Coinfección TB/VIH: 178 (9,1%) en 1996; 24 (3,6%) en 2012. TB/inmigración: 0 en 1996; 45 (6,7%) en 2012. Retraso diagnóstico de TB respiratoria: 52,5 días de mediana (año 2012). Tratamientos supervisados: 99 (5,0%) en 1996; 287 (43,0%) en 2012. Resultados satisfactorios: 82,1% en 1996; 88,5% en 2012.

**Conclusiones:** La evolución de la TB en Galicia es satisfactoria, pero el retraso diagnóstico continúa siendo importante (lo que favorecería una mayor incidencia en niños). La asociación TB/VIH o TB/inmigración no es relevante. Hay un bajo porcentaje de TB resistente y multirresistente. Los resultados satisfactorios de todos los casos de TB son próximos al 90%.



## PD-620-30 Sistema de información de tuberculosis de Galicia: búsqueda activa de casos no declarados, Galicia, 2008–2012

E Cruz-Ferro,<sup>1</sup> MI Ursúa-Díaz,<sup>1</sup> JA Taboada-Rodríguez,<sup>1</sup> X Hervada-Vidal,<sup>1</sup> Grupo de Trabajo del Programa Galle.<sup>1</sup> <sup>1</sup>Programa Galego de Prevención e Control da Tuberculose, Consellería de Sanidade. Dirección Xeral de Innovación e Xestión da Saúde Pública, Santiago de Compostela, Spain. Fax: (+34) 881542971. e-mail: elena.cruz.ferro@sergas.es

**Antecedentes:** La tuberculosis (TB) es una enfermedad de declaración obligatoria nominal, pero aun así se sospecha que existe un alto porcentaje de casos no declarados. El Sistema de Información de Tuberculosis de Galicia (SITUB) registra todos los casos de TB y sus principales características, bien fueran declarados pasivamente al Programa Gallego de Prevención y Control de la Tuberculosis o detectados por búsqueda activa. Objetivo: describir la evolución de la declaración de casos de TB en Galicia según la fuente de información en el período 2008–2012.

**Métodos:** Estudio observacional descriptivo retrospectivo. Fuente: SITUB. Período: 2008–2012. Ámbito: Galicia.

**Resultados:** El número de casos nuevos de TB registrados en el período 2008–2012 fue: 909; 862; 786; 691 y 669, respectivamente. En cada uno de estos años se detectaron los siguientes casos por búsqueda activa: 312 (34,3%) ; 380 (44,1%) ; 354 (45,0%) ; 283 (41,0) y 291 (43,5%), respectivamente. La fuente en la que más casos se detectaron fue el servicio de microbiología, con 976 (24,2%) casos en el período 2008–2012 y el que menos el registro de sida (1 caso) y el de mortalidad (0 casos). En la tabla se presenta, con más detalle, el origen de la información de todos los casos nuevos de TB registrados en el período 2008–2012.

	2008		2009		2010		2011		2012	
	Nº	%	Nº	%	Nº	%	Nº	%	Nº	%
Declaración pasiva	897	65,7	482	55,9	432	55,0	406	59,0	378	56,5
Servicio de Microbiología	165	18,2	214	24,8	197	25,1	174	25,0	197	29,4
Servicio de Farmacia	5	0,6	5	0,6	5	0,6	6	0,9	2	0,3
Servicio de Anatomía Patológica	13	1,4	15	1,7	19	2,4	0	0,0	7	1,0
Registros de altas hospitalarias	10	1,1	9	1,0	18	2,3	13	1,9	10	1,5
Contactos con enfermos de TB	45	5,0	40	4,6	41	5,2	25	3,6	22	3,3
Otros servicios sanitarios	63	6,9	90	10,4	67	8,5	51	7,3	53	7,9
Registro gallego de sida	0	0,0	0	0,0	0	0,0	1	0,1	0	0,0
Registro de mortalidad	0	0,0	0	0,0	0	0,0	0	0,0	0	0,0
No conocidos/comunicado	11	1,2	7	0,8	7	0,9	1	0,1	0	0,0
<b>Total casos nuevos de TB</b>	<b>909</b>		<b>862</b>		<b>786</b>		<b>691</b>		<b>669</b>	

**Conclusiones:** El 40% de los casos de TB de Galicia de los 5 últimos años analizados se detectaron por búsqueda activa, siendo la fuente que más casos aportó el servicio de microbiología. Es fundamental insistir en la importancia de la declaración de todos los casos de TB y continuar con el sistema de búsqueda activa de posibles casos no declarados, para conocer la realidad de la enfermedad en la región y para organizar los estudios de contactos en aquellos casos que así lo precisasen, cortando así la cadena epidemiológica de transmisión de la enfermedad.

Grupo de Trabajo del Programa Gallego de Prevención y Control de la Tuberculosis: Abdelkader Hasan A, Anibarro García L, Castro-Paz Álvarez-Buylla MA, Cruz Ferro E, Ferreiro Fernández L, Hervada Vidal X, Otero Santiago M, Penas Truque A, Rodríguez Canal A,

Taboada Rodríguez JA, Ursúa Díaz I, Valiño López P, Vázquez Gallardo R, Vázquez García-Serrano E

### PD-621-30 Data quality assessment of routine tuberculosis data in Kenya: where are we?

H K Kipruto,<sup>1</sup> E Klinkenberg,<sup>2</sup> J Kioko,<sup>3</sup> A Ronoh,<sup>3</sup> F Ngari,<sup>3</sup> B Langat,<sup>3</sup> J Nabongo,<sup>4</sup> M Mwakala.<sup>3</sup> <sup>1</sup>KCO, WHO, Nairobi, Kenya, <sup>2</sup>TUB, KNCV, Nairobi, <sup>3</sup>NLTLD-Unit, Ministry of Health, Nairobi, <sup>4</sup>CRDR, KEMRI, Nairobi, Kenya. e-mail: kiprutoh@gmail.com

**Objectives:** To assess the quality of routine TB surveillance data at health facility level

**Background and Methods:** Data quality assessment in routine settings assures government and all stakeholders that the data provided is of good quality. Routine DQA provides trends over time on performance of the TB surveillance system. It identifies weaknesses and strengths in the surveillance system and provides an opportunity to mitigate the observed challenges. Kenya conducted its last country-wide data quality audit (DQA) in 2010, therefore another DQA was timely. A retrospective cross sectional survey was conducted in June – July 2013 to assess the quality of TB surveillance data reported through the Kenya national TB surveillance system. The survey was conducted in a country representative sample covering all 12 TB control regions consisting of 215 health facilities. Levels of agreement were measured using the kappa scores for completeness and consistency, while accuracy was measured by acceptable proportions of concordance with (100 ±5) % considered as acceptable.

**Results:** Concordance between the facility and the district register was acceptable ranging from 97% to 102%. However there was poor concordance, as low as 14% between the patient record card and the district register. The use of the patient record cards was observed to be sub-optimal. Body Mass Index (BMI) was the most incomplete variable reported. The level of agreement for age and sex between facility register and district register was almost perfect at 0.821 and 0.816 respectively. Patient type and disease type scored moderate level of agreement at 0.746 and 0.699 respectively. The level of agreement of patient records on treatment outcome was moderate

**Conclusion:** There was general consistency of reporting between the facility register and the district register. However there was poor consistency between the patient record card and the district register. Supportive supervision at both regional and national levels should be strengthened by incorporating on site data verification (OSDV) as part of the tasks to be undertaken routinely, provide documented feedback to facilities on data issues, provide on job training on BMI calculation.

### PD-622-30 Focused interventions to optimise performance under Revised National TB Control Programme, Karnataka, India

NS Vishwanath,<sup>1</sup> S Shastri,<sup>1</sup> P Bhat,<sup>2</sup> S Managuli.<sup>1</sup>

<sup>1</sup>Department of Health and Family Welfare Services, Lady Willingdon State TB Centre, Bangalore, <sup>2</sup>Department of TB Control, WHO country office for India, New Delhi, Bangalore, India. e-mail: susha007@gmail.com

**Background** Karnataka, a south Indian State with 63 million population is implementing Revised National TB Control Programme (RNTCP) since 2000. While the State is having fairly good health infrastructure and processes under the programme, it has consistently underperformed to achieve the national average in various case finding and treatment outcome indicators. Karnataka has 31 districts and 125 sub-district level TB units for the purpose of programme administration and monitoring. There were field observations that only few TUs were performing consistently low in few parameters. We sought to identify specifically the consistently underperforming tuberculosis units in case finding and treatment outcome indicators.

**Methods** In this retrospective cohort analysis, the programme records were reviewed for all 125 TUs from January 2009 to September 2013. All the available data were reviewed to identify the consistently underperforming TUs.

**Results** Of the 125 TUs reviewed, 16 (13%) were examining less than 800 TB suspects per 100,000 population per annum, 33 (26%) could not reach the benchmark of 53 new smear positive TB cases per annum, 5 (4%) could not reach national average of 85% treatment success rate during the study period of 19 quarters.

**Conclusion** Only few TUs in the State of Karnataka were identified responsible for undermining the larger good performance of the State in TB control. A focussed action plan was prepared and in force to find out the reasons for underperformance in these identified TUs. A detailed support intervention was also planned to improve the programme parameters in these TUs.

### PD-623-30 The incidence rate and risk factors of tuberculosis among people living with HIV in Osaka, Japan

A Ohkado,<sup>1</sup> T Shirasaka,<sup>2</sup> T Goto,<sup>3</sup> M Shirano,<sup>3</sup>

A Shimouchi.<sup>1</sup> <sup>1</sup>Epidemiology and Clinical Research, Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association, Kiyose, <sup>2</sup>AIDS, Osaka Medical Center, Osaka, <sup>3</sup>Infectious Diseases, Osaka City General Hospital, Osaka, Japan. Fax: (+81) 424 92 8258. e-mail: ohkadoa@jata.or.jp

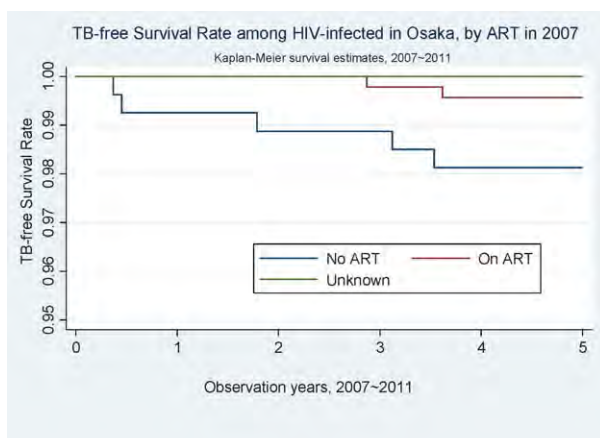
**Background:** Few studies have described the incidence rate and risk factors of tuberculosis (TB) among people living with HIV (PLWH) in Japan. This study aimed to explore the incidence rate and risk factors of TB among PLWH who were followed by 2 major hospitals in Osaka, Japan.

**Design/Methods:** The design was retrospective cohort study. We retrospectively observed PLWH registered at 2

hospitals in Osaka City from January 1, 2007 to December 31, 2011. Observation end points were defined as the date of TB diagnosis, when patients were lost to follow up, or when a patient died of any cause. Data was collected through medical chart review at the 2 hospitals. The annual incidence of TB per person-year was calculated. Hazard ratios were analyzed by possible attributable factors through Cox regression analysis. TB was diagnosed at both hospitals by physicians in accordance with standard TB diagnosis procedures. Definitive diagnosis of TB required any specimens from presumptive TB patients to be bacteriologically positive. TB was also diagnosed clinically with the treating doctor's recommendation to commence TB treatment without bacteriological evidence.

**Results:** The study cohort was comprised of 739 PLWH. 7 patients were diagnosed with TB during the observation period, but none were lost to follow up or died. The observation person-years totaled 3673.251. The total TB incidence rate among PLWH was 0.0019057 per person-year (95% confidence intervals [CI], 0.0009–0.0040). The TB incidence rate among PLWH in Osaka was 4.6 times higher than the annual TB notification rate in the entire population of Osaka City. The TB incidence rate among PLWH receiving anti-retroviral treatment indicated a relatively low hazard ratio of 0.23 (95% CI, 0.04–1.17), compared with the ratio among those who did not receive anti-retroviral treatment, although this difference was not statistically significant ( $p = 0.08$ , Figure). The TB incidence rate among PLWH with whole blood CD4 counts  $\geq 500/\mu\text{L}$  also indicated relatively low risk levels among those patients with no statistical significance (hazard ratio, 0.13; 95% CI, 0.01–1.22;  $p = 0.07$ ).

**Conclusion:** This study found high total TB incidence rate per person-year among PLWH in Osaka. This observation implies that intensified TB screening of this high-risk group is necessary to detect and treat early stages and to limit TB transmission in Osaka, Japan. Further study to describe the risk factors of TB among PLWH in the setting of Japan is needed.



## PD-624-30 Burden of tuberculosis in nine sub-Saharan African countries

O Adetokunboh,<sup>1</sup> M Oluwasanu,<sup>2</sup> T Balogun.<sup>1</sup>

<sup>1</sup>Interdisciplinary Health Sciences, Stellenbosch University, Cape Town, South Africa; <sup>2</sup>Health Promotion, University of Ibadan, Ibadan, Nigeria. e-mail: adetok\_sic@yahoo.com

**Background:** Tuberculosis (TB) is a major global public health concern. It was estimated that about 8.6 million people had active TB and 1.3 million died from TB in 2012. TB remains the leading cause of death among the people living with HIV, causing about one fifth of all deaths. There has been decline in the rate of new TB infections globally but the African region is not on track to achieve the mortality and prevalence targets. Sub-Saharan Africa has the highest new cases per population with more than 255 cases per 100 000 population in 2012. Nine countries from sub-Saharan Africa are part of the 22 countries with the highest burden of TB globally. The objective of this study is assess the trend in the burden of TB among the nine high burden African countries after launching of the directly observed treatment- short course.

**Design/Methods:** Study data was obtained from the 2013 World Health Organisation (WHO) global TB database. We estimated trends in TB mortality rates, prevalence and incidence (1995–2012). The estimated TB mortality excludes TB deaths among HIV-positive people. The values used are the best estimates for the 9 countries. Paired data mean- comparison test was conducted to determine the mean difference (MD) of TB mortality rates, prevalence rates and incidence (in number and rates). The rates are per 100,000 population and numbers are in thousands.

**Results:** Mortality rates reduced from 42.3 to 31.2, MD 11.1, 95%CI –29.1–6.9,  $p=0.1929$  while the prevalence rates also reduced from 438.1 to 382.8, MD 54.3, 95%CI –240.9–132.2,  $p=0.5207$ . Incidence in number increased from 112.9 to 181.2, MD 68.3, 95%CI –31.9–168.6,  $p=0.1546$  and incidence rates also increased from 344.4 to 379.1, MD 94.6, 95%CI –183.4–252.8,  $p=0.7235$ . Only four of the African countries had reduction in incidence rates with Uganda leading the pack with 67% while South Africa had an increase of 215% in the period under review.

**Conclusion:** African countries with high burden of TB infections has made some progress in tackling the TB burden. TB mortality and prevalence rates has reduced from the mid-1990s level but this reduction is not significant. A big challenge to the control of TB is the increasing new infections in many of the African countries. There is need to check the increasing trend of new infections by changing in approaches to public health implementations in these countries. More research and prompt implementation are needed to achieve significant reduction.



**PD-625-30 Risk of tuberculosis: a ten-year follow-up study of contacts in Amsterdam**

R Sloot,<sup>1</sup> M Schim Van Der Loeff,<sup>2,3</sup> P Kouw,<sup>2</sup> M W Borgdorff.<sup>2,3</sup> <sup>1</sup>Department of Clinical Epidemiology, Biostatistics and Bioinformatics, Academic Medical Center, University of Amsterdam, Amsterdam, <sup>2</sup>Department of Infectious Diseases, Public Health Service, Amsterdam, <sup>3</sup>Center for Infections and Immunity Amsterdam (CINIMA), Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands. e-mail: r.sloot@amc.uva.nl

**Objective:** To determine the risk of tuberculosis (TB) after recent exposure in a low incidence setting.

**Methods:** A retrospective cohort study was performed using records of contacts of pulmonary TB (PTB) patients at the Public Health Service Amsterdam (PHS), 2002–2011. Demographic data, tuberculin skin test (TST) results, BCG status and information on preventive therapy were recorded. The PHS TB electronic registration system was used to identify TB cases during follow-up until October 2012: defined as co-prevalent if <180 days and incident if ≥180 days after TB diagnosis of index patient. Correlates of co-prevalent TB were identified by logistic regression using generalized estimating equations (GEE). Kaplan-Meier curves were used to estimate cumulative TB risk. Multivariable Cox proportional hazard models were used to assess risk factors for incident TB.

**Result:** The Kaplan-Meier cumulative risk of TB after 2-years was 1.0% (95%CI=0.8–1.3) among all 9,332 contacts under study and 9.7% (95%CI=7.6–12.4) among 739 contacts with latent tuberculosis infection (LTBI). Among 739 contacts with evidence of infection 57 (7.7%, 95%CI=6.0–9.9) had co-prevalent TB and 14 (1.9%, 95%CI=1.1–3.2) developed incident TB. Of patients with LTBI and without co-prevalent TB, 45% received preventive therapy.

**Conclusions:** While the risk of TB was consistent with previous estimates, the incidence of TB among contacts with LTBI and without co-prevalent TB was low, suggesting limited impact may be expected of expanding preventive therapy.

**12. TB AND DIABETES: THE RISING BURDEN****PD-626-30 Burden of diabetes among patients with tuberculosis: ten-year experience from an Indian tertiary care teaching hospital**

D Christopher,<sup>1</sup> S Mitra,<sup>1</sup> J Sarojini,<sup>1</sup> V Balaji,<sup>1</sup> M Gupta,<sup>1</sup> M Therese,<sup>1</sup> B Yadav,<sup>1</sup> L Jeyaseelan.<sup>1</sup> <sup>1</sup>Pulmonary Medicine, Christian Medical College, Vellore, India. Fax: (+91) 416 2211570. e-mail: djchris@cmcvellore.ac.in

**Background:** Diabetes mellitus (DM) has become a global epidemic, especially in low- and middle-income countries, where 80% of DM-related mortality is estimated to occur. Currently, there are more than 61 million people living with DM in India. A similar scenario is true for Tuberculosis with nearly a third of

the world's population being infected with *Mycobacterium tuberculosis*. India also has a huge TB burden, with an estimated 2.3 million new cases every year. There is good evidence that the risk of TB among people with DM is three times higher than in those without DM. This study was designed to study the burden of Diabetes among TB patients in India.

**Design/Methods:** This is a retrospective descriptive study. All patients (inpatients and outpatients) above the age of 16 years; who were diagnosed to have tuberculosis, under the departments of Internal Medicine-Unit II and Pulmonary Medicine of Christian Medical College, Vellore, India from 1<sup>st</sup> January 2001 to 31<sup>st</sup> December 2011, were selected for the study, from the hospital computerised database of outpatients, inpatients, the microbiology and histopathology laboratories. Data related to tuberculosis and diabetes were collected.

**Results:** During the study period, a total of 2224 patients had been diagnosed to have Tuberculosis. Analysis was carried out in 1980 TB patients in whom plasma glucose values were available- mean age(SD) = 39(15.6) ; Male-1405(71%) and Female-574(29%). The prevalence of Diabetes [Diabetes Mellitus(DM) or Pre-diabetes mellitus(PDM) ] was 472(23.8%) - type 2 DM-432(91.5%), type1 DM- 7(1.5%) and PDM- 33(7%). In all; 319(16.1%) had extra-pulmonary TB (EPTB) and 1660(83.9%) had pulmonary TB (PTB) - 964(58.1%) were sputum smear +ve and 696(41.9%) smear – ve. Of these, 281(28.4%) of the smear positive and 145(20.8%) of the smear negative PTB patients and 46(14.4%) of the EPTB patients were Diabetic(DM or PDM). Among the PTB patients, there were significantly higher smear positive disease among Diabetics 65.96% VS 55.35% (P <0.0001 ). More men with PTB compared to women 28% VS 19.6% had Diabetes (P<0.001) and more smear positive men compared to women 18.8% VS 11.6% were Diabetic (P<0.001). There was no difference in Diabetes prevalence between men and women with extra-pulmonary TB - 13.8% VS 15.3% (P>0.05). A total of 1980 TB patients were screened to diagnose 472 Diabetic patients; thus the number needed to screen (NNS) was 4.2.

**Conclusion:** The prevalence of diabetes or pre-diabetes is high (23.8%) in an Indian tertiary care hospital cohort of TB patients. Diabetic patients had more smear positive PTB. Men with PTB and with smear positive PTB had a higher prevalence of DM, compared to women. Screening for Diabetes is extremely cost effective.

**PD-627-30 Mitochondrial mutational load in diabetes: toward a better understanding of diabetes in tuberculosis**

W Wangh,<sup>1</sup> A Osborne,<sup>1</sup> K.C. Hayes.<sup>1</sup> <sup>1</sup>Dept. of Biology, Brandeis University, Waltham, MA, USA. e-mail: wangh@brandeis.edu

**Background:** Worldwide there are now more patients afflicted by tuberculosis (TB) and diabetes, than patients co-infected with TB and HIV. Diabetics are three times

more likely to develop active TB than non-diabetics. Having diabetes and TB adversely affects drug treatment and prognosis. Thus, it is critical to test TB patients for diabetes and to develop rapid diagnostic DNA biomarkers to identify pre-diabetics at risk of developing the disease. Because insulin-resistance and diabetes are linked to mitochondria dysfunction, we investigated whether diabetes is associated with mitochondria DNA (mtDNA) mutations in the liver and whether the number of mutations correlates with the severity of the disease.

**Methods:** Diabetes is studied in the Nile Rat (*Arvicanthus niloticus*), a model system of diet-induced diabetes that recapitulates the human disease. Diabetic and non-diabetic wild-type animals were scored for disease severity by following random blood glucose over several weeks. Age-matched diabetic and healthy Nile rats were screened for mutations in the D-loop and ND3 regions of liver mtDNA using digital LATE-PCR with Lights-On/Lights-Off probes.

**Results:** Every diabetic animal ( $n = 5$ ) tested exhibited higher numbers of random mtDNA mutations in comparison to healthy controls ( $n = 7$ ). In all cases, the increase in mutations was significant ( $p < 0.05$ ). Mutation numbers did not correlate with the severity of the diabetes, and some healthy rats had a high number of mtDNA mutations, suggesting that mutations might precede the onset of diabetes.

**Conclusions:** This is the first study to document mtDNA mutations with diabetes. Our findings suggest that mtDNA mutations may serve as a diagnostic biomarker for diabetes and may play a role in disease development. Currently we are investigating whether mtDNA mutations come before or after onset of diabetes. The next step will be to establish whether anti-TB and anti-HIV drugs known to mutate mtDNA, increase the rate or severity of diabetes progression in Nile Rats.

### PD-628-30 Does HIV modify the association between diabetes mellitus and active tuberculosis?

SL Bailey,<sup>1,2</sup> S Floyd,<sup>1</sup> JS Yudkin,<sup>3</sup> P Godfrey-Faussett,<sup>1</sup> H Ayles.<sup>1,2</sup> <sup>1</sup>Clinical Research and LSHTM TB Centre, London School of Hygiene and Tropical Medicine, London, UK; <sup>2</sup>Clinical Research, Zambart, Lusaka, Zambia; <sup>3</sup>Medicine, University College London, London, UK.  
e-mail: slbailey@doctors.org.uk

**Background:** HIV and diabetes mellitus (DM) are independently associated with an increased incidence of active tuberculosis (TB). However, the dual effect of HIV and DM on the risk of developing TB disease is unclear. This study aims to determine if HIV modifies the association between DM and active TB.

**Methods:** This is an ongoing unmatched case-control study among adults in Lusaka, Zambia, with diagnosed active TB disease as the outcome and DM as the exposure of interest. Cases with TB were recruited from TB clinics in Lusaka, data for the community controls were taken from a recently conducted population-based cross-sectional study (the ZAMSTAR prevalence survey). DM is defined as a capillary random blood glucose

concentration of  $\geq 11.1$  mmol/L. HIV status is determined by serological result. Logistic regression was used to explore HIV as a potential effect modifier, adjusting for age, sex, education, body mass index, smoking history and community.

**Results:** The table gives the results to date, showing the estimates of the odds ratios for active tuberculosis overall and by HIV and diabetes interaction.

Category		Number of Cases (Column %)	Number of Controls (Column %)	Adjusted OR (95% CI)
DM	-	1,253 (98.7)	5,778 (98.5)	1
	+	16 (1.3)	89 (1.5)	1.45 (0.68-3.06)
HIV	-	416 (33.3)	4,320 (82.4)	1
	+	832 (66.7)	926 (17.7)	9.28 (7.67-11.22)
HIV- DM-		411 (98.8)	4,146 (98.3)	1
	DM+	5 (1.2)	71 (1.7)	0.73 (0.25-2.11) *
HIV+ DM-		822 (98.8)	904 (99.5)	1
	DM+	10 (1.2)	5 (0.5)	6.36 (1.34-30.20) *
DM- HIV-		411 (33.3)	4,146 (82.1)	1
	HIV+	822 (66.7)	904 (17.9)	9.07 (7.50-10.99) **
DM+ HIV-		5 (33.3)	71 (93.4)	1
	HIV+	10 (66.7)	5 (6.6)	79.12 (12.10-517.17) **

OR=odds ratio; CI=confidence interval; 26 cases & 2,179 controls excluded from analysis due to missing data; main confounding factors=sex, age, body mass index and community; \*OR for TB comparing individuals with DM to those without; \*\*OR for TB comparing individuals with HIV to those without; p-value for interaction=0.017

**Conclusions:** As expected, HIV is a strong risk factor for TB in this population. These preliminary results suggest that the effect of HIV on TB may be greater for individuals with DM than for those without. The current analysis suggests that the effect of DM on TB may be greater for individuals with HIV than for those without, but overall there is as yet no evidence that DM is associated with active TB in this population. Confidence intervals are wide and the study is ongoing so findings will become more definitive later.

### PD-629-30 Cost analysis of integrating diabetes screening with a tuberculosis active case finding programme in the private sector

M Basir,<sup>1</sup> A Zaidi,<sup>1</sup> H Hussain,<sup>1</sup> S Khowaja.<sup>1</sup> <sup>1</sup>Community Health Solutions, Interactive Research & Development (IRD), Karachi, Pakistan. e-mail: mashal.basir@irdresearch.org

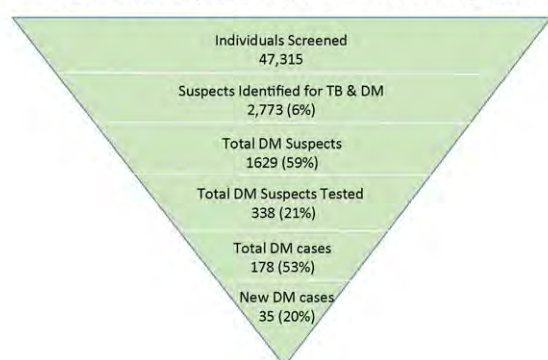
**Background:** The Collaborative Framework for Care and Control for Tuberculosis (TB) and Diabetes Mellitus (DM) has called for the development of "synergies of collaborative activities" for controlling dual epidemics. In countries such as Pakistan with a high prevalence of TB and DM, screening programs could benefit from integrating case-finding activities for both diseases. Active case-finding for TB has been shown to be effective in high burden countries. Additional costs of DM screening, however, need to be justified by high yield of case-detection. The aim of this study was to conduct a cost-analysis of integrating screening for DM in a TB screening program in a high TB and DM burden setting. **Methods:** Costing and case-detection was investigated for a subsample of 15 screeners that were part of a TB

Reach Initiative in Karachi, Pakistan, over a 2-month period. Screening was carried out at private sector clinics. Community laypeople were provided a base-stipend and incentives for total individuals screened, referred for testing and cases identified. TB suspects were identified based on any TB symptoms and were referred for diagnosis using chest X-ray and GeneXpert MTB/Rif. DM suspects were identified based on age, BMI and family history of DM and tested using point-of-care capillary blood-glucose testing.

**Results:** A total of 47,315 individuals were screened and 2,090 TB and 1,629 DM suspects were identified. A total of 15 TB cases and 178 DM cases were identified of which 35 cases were newly-diagnosed diabetics. Costs relevant for screening of both diseases were USD 3,078 and included costs of equipment, training and materials. Screener base-stipend was apportioned between TB and DM on a ratio of 4 to 1 using activity-based costing. Costs specific to TB were USD 2,005 and included costs for X-rays, GeneXpert testing, sputum processing materials and incentives for TB suspects and cases detected. Costs specific to DM were USD 655 and included costs of glucometers, testing materials and screener incentives for glucose testing. The total cost per TB and DM case detected was USD 383 and USD 164, respectively. The added cost for a newly diagnosed DM case was USD 18.

**Conclusion:** Integration of DM screening in existing TB screening programs provided a low-yield for DM case detection in the individuals presenting at private clinics. However, the low-cost per case detected warrants consideration of the joint-approach in other settings with a high burden of TB and DM.

**Integrated Mass-Screening of TB and Diabetes Testing in the Private Sector in Karachi, Pakistan (Feb 1<sup>st</sup> – March 31<sup>st</sup>, 2014)**



## **PD-630-30 High prevalence of latent tuberculosis infection among adults with type 2 diabetes mellitus in Karnataka, India**

M Foote,<sup>1</sup> PA Mahesh,<sup>2</sup> R Kempker,<sup>1</sup> KM Narayan,<sup>3</sup> V Mohan,<sup>4</sup> BS Jayaraj,<sup>2</sup> SM Ray.<sup>1</sup> <sup>1</sup>Division of Infectious Diseases, Department of Medicine, Emory University School of Medicine, Atlanta, GA, USA; <sup>2</sup>Department of Pulmonary Medicine, J.S.S. Medical College and Hospital, Mysore, India; <sup>3</sup>Hubert Department of Global Health, Rollins School of Public Health, Emory University, Atlanta, GA, USA; <sup>4</sup>Diabetology Department, Madras Diabetes Research Foundation, Chennai, India. e-mail: mary.foote@emory.edu

**Background:** India has the highest TB case burden in the world and is experiencing a rapidly expanding diabetes mellitus (DM) epidemic. DM has been shown to increase the risk of active tuberculosis (TB), potentially due to hyperglycemia induced immune suppression. However, little is known about the risk of latent TB infection (LTBI) in persons with diabetes. We aim to describe the prevalence of LTBI in persons with and without diabetes in a high TB prevalence setting in Karnataka, India.

**Methods:** We recruited adults with known diagnosis of DM (n=204) from an outpatient medical clinic at a large tertiary hospital in Mysore, India. In addition, anyone found to have A1C levels  $\geq 6.5\%$  during community-based screenings to recruit non-DM controls (which is ongoing) were included as newly diagnosed DM cases (N=22). All were evaluated for LTBI with QuantiFERON-TB Gold In-Tube (QFT-GIT). Glycosylated hemoglobin A1C levels and capillary blood glucose levels were used to determine glycemic control. Subjects with a positive TB symptom questionnaire were referred for chest X-ray.

**Results:** Among 226 patients with DM, 22 (10%) were newly diagnosed through community screening, 58% were male, median age was 58, mean BMI of 27.4, and mean HbA1C was 8.1%. The median duration of diabetes was 5.8 years and 55 (27%) reported regular insulin use. In total, 113 (54%) had a positive QFT-GIT, 86 (41%) were negative and 12 (6%) had indeterminate results. The only significant risk factor for a positive QFT-GIT was increasing age, per year (OR 1.04, 95% CI 1.02-1.07). Other risk factors included tobacco use (OR 1.6, 95% CI 0.6-4.1), alcohol use (OR 3.29, 95% CI 0.9-12.0), and A1C  $>9\%$  (OR 1.57, 95% CI 0.8-3.2), although none reached statistical significance. Of 87 cases with a positive QFT-GIT or TB symptom screen referred for CXR, 24 (28%) were reported as abnormal, including 1 with cavitory lesions and 8 (9%) with pulmonary infiltrates identified.

**Conclusions:** The prevalence of 54% LTBI among adults with diabetes in this Indian cohort is significantly higher than the reported national prevalence of 40%. This could have significant implications for TB control efforts in the future and supports the need for active case finding among patients with DM. Although unconfirmed, our data suggest that higher A1C levels may be associated with risk of QFT-GIT positivity, and further investigation on possible mechanisms is warranted.



Table 1: Risk Factors for a positive QFT

Characteristic	QFT + N=113	QFT - N=86	OR	95% CI
Mean Age (SD)	59 (11)	54 (12)	1.04	1.02-1.07
Male Sex (%)	72 (64)	49 (57)	1.33	0.75-2.35
Illiterate	37 (33)	30 (35)	0.91	0.50-1.64
Mean BMI (SD)	25.0 (4.7)	26.2 (4.6)	0.95	0.89-1.01
Rural Home Location	76 (67)	62 (72)	0.80	0.43-1.47
<b>DRUGS</b>				
Daily TOB exposure	19 (17)	18 (21)	0.76	0.37-1.56
Smoker	14 (12)	7 (8)	1.60	0.62-4.14
Current Alcohol Use	12 (11)	3 (4)	3.29	0.90-12.0
<b>DIABETES</b>				
A1C < 7	35 (31)	32 (37)	1.00	-
A1C 7-9	42 (37)	33 (38)	1.16	0.60-2.26
A1C > 9	36 (37)	21 (24)	1.57	0.76-3.22
Years with DM	6.6 (7.4)	5.9 (6.4)	1.01	0.97-1.06
Insulin Use	26 (24)	29 (35)	0.59	0.32-1.12
<b>TUBERCULOSIS</b>				
History of TB Exposure	12 (11)	5 (6)	1.92	0.65-5.69
History of TB Treatment	3 (3)	2 (2)	1.15	0.19-7.01

### PD-631-30 Has diabetes mellitus had an impact on tuberculosis rates in Mexico? Analysis of the Mexican registry of tuberculosis, 2000–2012

L Garcia,<sup>1</sup> Mart Castellanos,<sup>2</sup> G Delgado-Sánchez,<sup>1</sup> L Cruz-Hervert,<sup>1</sup> V Ortega Baeza,<sup>1</sup> LD Ferreyra-Reyes,<sup>1</sup> EE Ferreira-Guerrero,<sup>1</sup> A Hernández.<sup>3</sup> <sup>1</sup> Centro Investigación Enfermedades Infecciosas, Instituto Nacional de Salud Pública, Cuernavaca, <sup>2</sup>Control de Tuberculosis, Programa Nacional de Prevención y Control de Tuberculosis, Secretaría de Salud, México, DF, <sup>3</sup> Vigilancia Epidemiológica, Instituto Nacional de Enfermedades Respiratorias "Ismael Cosío Villegas", Mexico City, Mexico.  
e-mail: garcigarm@gmail.com

**Background:** Tuberculosis (TB) continues to be a health problem in Mexico while the incidence of diabetes mellitus type 2 (DM) has experienced rapid growth in recent years. The purpose of this study was to analyze the trends of incidence rates (IR) of TB with and without DM and to determine if a prior diagnoses of DM was associated with a greater likelihood of treatment failure  
**Design/Methods:** We analyzed the official Mexican Registry of Tuberculosis from 2000 to 2012. We included patients >20 y. Three indicators of TB IR were estimated for each successive 12-month period: IR of all forms of TB (with, without DM and total); of pulmonary TB (PTB) (with, without DM and total) ; and of extrapulmonary TB (ETB) (with, without DM and total). We used the estimated annual general population for persons > 20 y as the denominator. We used the  $\chi^2$  test for trends to detect significant trends. To determine the association between DM comorbidity and treatment failure, we used multiple logistic regression analyses and estimated odds ratio (OR) and 95% confidence intervals (CI).

**Results:** 205,431 cases were registered during the study period. On 194,717 (94.78%) information on prior DM diagnosis was available; 17.49% (34,059) suffered DM comorbidity. The IR of all forms of TB with DM increased by 90.14% from 2.94 to 5.59, ( $p<0.001$ ) while the rate of TB without DM decreased by 0.47% from

21.3 to 21.2, ( $p<0.001$ ). Total rates increased 10.48% from 24.24 to 26.78, ( $p<0.001$ ). The IR of PTB with DM increased by 82.98% from 2.82 to 5.16, ( $p<0.001$ ) while the rate of TB without DM decreased by 9.95% from 18.89 to 17.01, ( $p<0.001$ ). Total rates increased 2.12% from 21.71 to 22.17, ( $p<0.001$ ). The IR of EPTB with DM increased by 290.91% from 0.11 to 0.43, ( $p<0.001$ ) while the rate of TB without DM increased by 72.73 % from 2.42 to 4.18, ( $p<0.001$ ). Total rates increased 82.21% from 2.53 to 4.61, ( $p<0.001$ ). Treatment outcomes were as follows, 81.56% experienced treatment success, 1.52% failed, 7.58% defaulted, and 1.52% died. Patients with a prior diagnosis of DM had a greater likelihood of failing treatment (adjusted OR, 1.24; 95% CI 1.12, 1.37;  $p<0.001$ ).

**Conclusion:** Our data indicate that the growing DM epidemic has probably had an impact on TB incident rates in Mexico. In addition, patients suffering from both conditions have a greater likelihood of treatment failure. The content of this poster reflects the personal position of the researchers and does not represent the position of INSP.

### PD-632-30 Joint management of patients with pulmonary tuberculosis and diabetes mellitus is feasible and appears to improve treatment outcomes in Mexico

L Garcia,<sup>1</sup> Mart Castellanos,<sup>2</sup> G Delgado-Sánchez,<sup>1</sup> L D Ferreyra-Reyes,<sup>1</sup> L Cruz-Hervert,<sup>1</sup> E E Ferreira-Guerrero,<sup>1</sup> M Jiménez-Mendoza,<sup>2</sup> A Ponce-de-León.<sup>3</sup> <sup>1</sup>Centro de Investigación sobre Enfermedades Infecciosas, Instituto Nacional de Salud Pública, Cuernavaca, Morelos, <sup>2</sup>Programa Nacional de Prevención y Control de Tuberculosis, Secretaría de Salud, Mexico DF, <sup>3</sup>Instituto Nacional de Nutrición y Ciencias Médicas Salvador Zubirán, Secretaría de Salud, Mexico DF, Mexico. e-mail: garcigarm@gmail.com

**Background and challenges to implementation:** Recently, the WHO and the IUATLD published a Collaborative Framework for the Care and Control of Tuberculosis (TB) and Diabetes (DM) (CFTB/DM) proposing bidirectional screening and joint management.

**Intervention or response:** The WHO/ IUATLD CFTB/DM was adapted and implemented according to official Mexican guidelines. TB and DM screening was conducted from 07/2012 to 09/2013 in patients aged  $\geq 20$  y who had been diagnosed with DM or pulmonary TB respectively and sought care at 15 medical units in 5 states. Consenting patients who were diagnosed with DM and TB were jointly managed by the TB and DM local programs. TB treatment outcomes were compared with those obtained in patients treated in the same clinical units in 2010 and 2011.

**Results and lessons learnt:** Of 783 DM patients, 38 (4.9%) were diagnosed with TB, of whom 11 were unaware of this diagnosis. Of 361 TB patients, 70 (19.4%) were diagnosed with DM of whom 16 were unaware of their DM. The probability of a TB diagnosis was higher in men and in patients who had already suffered a previous TB episode or who had contact with a

TB patient. The probability of a DM diagnosis was associated with older age, having parents with DM and with recent weight loss, polydipsia or polyuria. Ninety-five TB/DM patients consented to be jointly managed, 84 (88%) experienced TB treatment success. As TB treatment progressed, the medians of HbA1c, serum glucose and casual glucose decreased significantly ( $p < 0.001$ ). Average decrease of HbA1c and casual glucose was larger among patients with treatment success ( $p < 0.001$ ). Patients treated under joint management were more likely to experience treatment success than patients treated during 2010–2012 in the same clinical units (adjusted odds ratio, 4.07; 95% CI 1.46–11.34).

**Conclusions and key recommendations:** Joint management of TB and DM is feasible and appears to improve treatment outcomes. We found that 71 DM and 23 TB patients would need to undergo screening to detect a new case of TB and of DM respectively. Comparison of the characteristics between patients in whom TB or DM was detected allowed identification of a profile of patients among whom screening could be optimized. We identified problems that need to be addressed in the future in order to improve the efficiency of this approach. The content of this poster reflects the personal position of the researchers and does not represent the position of INSP.

#### PD-633-30 Variation in TB treatment outcome: the need for population specific interventions

I Mgbakor,<sup>1</sup> T Badru,<sup>1</sup> M Odo,<sup>2</sup> I Mogaba,<sup>1</sup> O Adebayo,<sup>1</sup> O Itua,<sup>3</sup> B Olusola-Faleye,<sup>2</sup> T Odusote.<sup>3,4</sup> <sup>1</sup>Monitoring and Evaluation, FHI360, Abuja, <sup>2</sup>Prevention, Care and Treatment, FHI360, Abuja, <sup>3</sup>Prevention, Care and Treatment, Acheiving Health Nigeria Initiative, Benin, <sup>4</sup>TB/HIV, USAID Nigeria, Abuja, Nigeria. e-mail: ifunanyaigbojekwe@gmail.com

**Background:** Tuberculosis (TB) is the second greatest global killer after HIV/AIDS with high mortality (95%) in low- and middle-income countries. Hence the need to actively monitor the treatment course and ensure successful treatment outcome for all cases. Enhanced understanding of the treatment outcome patterns and its predictors is key to empowering the National TB control Program (NTP) design targeted interventions towards achieving its goal of eliminating TB.

**Design/Methods:** Records of TB cases notified from October 2011 to October 2013 across 9 LGAs in 2 states in Nigeria were retrospectively assessed. Treatment outcomes were reported in percentages. Unsuccessful treatment outcome was interpreted based on WHO definition as treatment failure, default or death. Multi-variable Logistic Regression analysis was conducted using Stata (11.0) to identify predictors of unsuccessful treatment outcome.

**Results:** A total of 1,946 TB cases were analyzed. Of these, 331 (17%) had an unsuccessful TB treatment outcome. In total, 174 (8.94%), 119 (6.12%) and 38 (1.95%) died, defaulted and failed respectively. Treatment failure was the same for both males (17%) and females (17%). However, treatment failure was significantly higher among HIV-positive (22%) than HIV-negative (15%) patients ( $p < 0.001$ ). In multivariable analysis, unsuccessful

ful treatment outcome was associated with age  $> 60$  years (AOR 1.75,  $p = 0.03$ ), being HIV-positive (AOR=1.61,  $p = 0.01$ ) and urban resident (AOR 1.32;  $p = 0.05$ ).

#### Conclusion

**Results** indicate that our aging population of TB cases and TB/HIV co-morbid individuals are less likely to achieve successful treatment outcome. These findings merit targeted and innovative approaches for improving treatment outcomes amongst the elderly, TB/HIV co-morbid individuals and urban residents. Improved support system, intensified patient/treatment-supporter education and active monitoring within the failing groups is highly recommended.

#### PD-634-30 Epidemiology of TB, diabetes and non-communicable diseases risk factors in an urban Cape Town township

T Oni,<sup>1,2</sup> R Goliath,<sup>1</sup> N Levitt,<sup>3</sup> R Wilkinson.<sup>1,4,5</sup> <sup>1</sup>Clinical Infectious Disease Research Initiative, Institute of Infectious Disease and Molecular Medicine, University of Cape Town, Cape Town, <sup>2</sup>Center for Infectious Disease Epidemiology Research, School of Public Health, University of Cape Town, Cape Town, <sup>3</sup>Department of Medicine, Groote Schuur Hospital, University of Cape Town, Cape Town, South Africa; <sup>4</sup>Department of Medicine, Imperial College London, London, <sup>5</sup>Medical Research Council, National Institute for Medical Research, Cape Town, UK. e-mail: tolullahoni@doctors.org.uk

**Background:** South Africa has one of the highest burdens of TB and is undergoing rapid urbanisation & epidemiological transition; characterized by lifestyle and dietary changes. This is contributing to a rise in non-communicable diseases (NCD) (particularly diabetes (T2DM) and hypertension (HPT)), and is predicted to increase significantly over the next few decades. Furthermore T2DM is associated with a 2–3 fold higher risk of TB; and could further derail TB control. As part of an ongoing study investigating the contribution of T2DM to the TB epidemic, we describe the prevalence of T2DM, hypertension (HPT), and obesity among patients presenting for TB screening.

**Methods:** We present results from 564 consecutive patients with TB symptoms attending a TB clinic in Khayelitsha, Cape Town for TB screening between July 2013–April 2014. Study participants were screened for T2DM with a fasting glucose (FG), HbA1c, and oral glucose tolerance test at presentation for TB screening. T2DM was defined as FG  $\geq 7.1$  mmol/l, HbA1c  $\geq 6.5\%$ , or OGTT  $\geq 11.0$  mmol/l. Patients were screened for HPT using 2 measurements recorded at different time points and HPT defined as 2 measurements  $> 140/90$  mmHg. The body mass index (BMI) of patients was recorded and the proportion of underweight (BMI  $< 18$ ) and overweight/obese (BMI  $> 25$ ) patients noted.

**Results:** We found a 13.3% (95% C.I. 10.2–17.0%) prevalence of T2DM among patients presenting for TB screening. Of the T2DM patients identified at TB screening, only 14% had a prior diagnosis of T2DM. Similarly, a 25% (95% C.I. 21.9–29.4%) prevalence of elevated systolic and/or diastolic blood pressure was

found among TB suspects; 25% of which had a prior diagnosis of HPT. We also examined BMI and when compared to TB controls, a greater proportion of TB cases were underweight (11.7%; 95% C.I. 6.5–20%) compared to TB controls (6.9%; 95% C.I. 4.9–9.7%). However, among TB cases, a greater proportion were overweight/obese (26.4%; 95% C.I. 17.6–37.6%) versus underweight (11.7%; 95% C.I. 6.5–20%).

**Conclusion:** Our results demonstrate a high prevalence of T2DM and HPT among patients undergoing TB screening at a primary care clinic. We also show a greater prevalence of overweight/obese than underweight TB patients. These results highlight a need for screening for prevalent NCDs and associated risk factors among patients presenting for TB screening and/or TB treatment as part of an integrated approach to the management of chronic infectious and non-communicable diseases.

### PD-635-30 Prevalence of diabetes mellitus among tuberculosis patients in medical colleges of Tamil Nadu, India

HR Shivaramakrishna,<sup>1</sup> D Ranganathan,<sup>2</sup> S Anjum,<sup>1</sup> J Arivoli,<sup>3</sup> K Ganesh Kumar,<sup>4</sup> S A,<sup>1</sup> P Moonan.<sup>5</sup> <sup>1</sup>TB, WHO country Office India, New Delhi, <sup>2</sup>TBCD, Madras Medical College, Chennai, <sup>3</sup>RNTCP, State TB Officer, Chennai, <sup>4</sup>RNTCP, District TB Officer, Salem, India; <sup>5</sup>Epidemiology, US Centers for Disease Control and Prevention, Atlanta, GA, USA. e-mail: shivaramkrishanh@rntcp.org

**Background:** Diabetes mellitus (DM) triples the risk of developing tuberculosis (TB). Persons with TB and DM are at high risk of poor treatment outcomes and may respond to treatment more slowly. Because of the rapidly growing prevalence of diabetes globally, the World Health Organization and the International Union against Tuberculosis and Lung Disease developed a collaborative framework for care and control of diabetes and tuberculosis. It recommends the routine implementation of bi-directional screening for the two diseases. Medical colleges account for about 25% of all new TB cases reported in India each year, yet it is unknown how many patients have both TB and DM in this setting. This study aims to estimate the prevalence of DM and determine risk factors associated with DM among the adult patients with TB in four medical college hospitals of Tamilnadu, India.

**Design/Methods:** This facility-based cross-sectional study was conducted at 4 randomly selected government medical college hospitals during January to March, 2014. All persons with TB >15 years of age were screened for DM using the diagnostic criteria of a fasting plasma glucose level of  $\geq 126$  mg/dl or a self-reported history of taking anti-diabetic drugs after diagnosis by a medical professional. We reviewed medical records to record select demographic, behavioural, and clinical characteristics. Odds ratios and 95% confidence intervals were calculated to determine potential factors associated with DM.

**Results:** A total of 795 TB cases were identified during the study period. Among these 728 (92%) were tested for DM and 226 (31%) had DM (previously diagnosed DM:

22%; newly diagnosed DM: 9%). DM was significantly associated with older age, family history of diabetes, consumption of alcohol

**Conclusion:** Our findings highlight a high prevalence of DM among newly diagnosed TB patients. Screening TB cases for fasting plasma glucose estimation will help in early detection of diabetes. Our study highlights in people with TB, it may be appropriate to actively screen for DM. Prevention, screening, and treatment of both diseases together, a model similar to the TB-HIV program, may be the best approach.

## 13. TB PUBLIC PRIVATE MIX: INDIA

### PD-636-30 A community based approach in designing a model TB sensitization programme for Self Help Groups (SHGs): a study from south India

B Thomas,<sup>1</sup> B Watson,<sup>1,2</sup> B Priscilla,<sup>1</sup> R Vijayalakshmi,<sup>2</sup> S Swaminathan.<sup>3</sup> <sup>1</sup> Department of Social and Behavioral Research, National Institute for Research in Tuberculosis, Chennai, <sup>2</sup>Department of Statistics, National Institute for Research in Tuberculosis, Chennai, I, <sup>3</sup>Director, National Institute for Research in Tuberculosis, Chennai, India. Fax: (+91) 04428362528/2525. e-mail: beenaelli09@gmail.com

**Background:** With tuberculosis (TB) continuing to be a major public health problem, innovative community based TB prevention and intervention strategies aimed at TB control is crucial. A powerful community task force has gained momentum in many districts in South India by way of Self Help Groups (SHG). This group could be involved in TB control activities considering their reach in communities especially at the grass root level. A community driven TB sensitization model based on participatory action approach using self help groups in TB control activities was therefore explored

**Study design:** This was an experimental study done in three phases and involved a quantitative and qualitative design. The first phase was the qualitative phase to test the acceptability of SHGs in the community and the level of awareness on TB. The second phase was to develop a TB sensitization intervention strategy through a community based approach. The third phase was a randomized control trial (RCT) to test the intervention through an experimental (Exp) design. The sample included 1560 SHG representatives (796 in the intervention and 764 in the control group). Participants were assessed at 0, 3 and 6 months.

**Results:** The involvement of SHGs in TB control activities (spreading awareness on TB, identification and referrals of chest symptomatics and registration as DOT providers) was compared in both groups. With regard to TB advocacy, there was no significant difference between the groups (86% in Control vs. 88% in Exp). However, identification and referrals of chest symptomatics was significantly higher in the Exp group (7.8% in Control vs 13.7% in Exp;  $p < 0.001$ ). The number of SHG participants who registered to be



community DOTS providers was also significantly higher in the intervention group (16.4% in Control vs 23.9% in Exp.;  $p=0.01$ ).

**Conclusions:** A community driven TB sensitization model based on participatory action approach using self help groups in TB control has proven to be an effective strategy in TB control. Once sensitized they can be considered a powerful task force in promoting TB awareness, identification and referral of chest symptoms and also as community DOTS providers.

### PD-637-30 Public-Private partnership in drug-resistant TB care: a case study of Nagpur model, India

R Deshmukh,<sup>1</sup> B.O Tayade,<sup>2</sup> A Sreenivas,<sup>1</sup> S P Patil.<sup>3</sup> <sup>1</sup>TB, WHO Country office of India, New Delhi, India, <sup>2</sup>Pulmonary medicine, NKP Salve Medical college and DRTB centre, Nagpur, India, <sup>3</sup>Joint Director TB office, State TB cell, Pune, India. e-mail: deshmukhr@rntcp.org

**Background and challenges to implementation:** Emergence of Drug resistant TB (DRTB) in India is threatening the efforts of TB control. India has one of the largest private sectors and this is often the first point of contact for a significant number of DRTB suspects and patients. There are limited Drug resistant TB centres (DRTBC) in India and there is felt need for decentralised service delivery with involvement of Private, NGO and corporate sector. In Nagpur, the public sector hospital providing DRTB services was not functional and the DRTB patients had to travel long distances to get admitted in another public sector hospital. A unique initiative was taken to involve local private medical college hospital as Public Private Partnership (PPP) to provide decentralised service delivery for DRTB patients.

**Intervention:** To address the challenge of providing DRTB services to 10 million populations in Nagpur zone, Government authorities approved a DRTBC in private medical college with 900 bedded hospital and pulmonary medicine specialities. The public sector supported private hospital with Human resource, Training of specialist and staff involved in DRTB services, Maintenance cost and up gradation of DRTBC as per airborne infection control guidelines, Facility for free investigations and free drugs. Private sector institute provides specialist care to DRTB patients along with infrastructure and nutritional support for the patients.

**Results and lessons learnt:** 'Nagpur PPP model' delivers clinical services to TB, DRTB and Nutritional supplementation for patients. Since Jan 2013, 112 MDRTB patients and 1XDRTB patients have been initiated on treatment from seven districts of Nagpur zone linked to the DRTB centre. Quality services are provided by specialist trained in DRTB at National level. DRTBC has been renovated as per the airborne infection control guidelines in India. Partnership has shown increase case detection rates, reduce diagnostic delays and cost to the patients.

**Conclusions and key recommendations:** Private sector Involvement leads to quality healthcare delivery as seen

in the case of the 'Nagpur model'. PPP approaches are necessary for early diagnosis, decentralised DRTB treatment services, to reduce costs to DRTB patients, prevent the emergence of XDR and spread of drug-resistant TB. Continuous interaction and mutual trust between the public and the private sectors are essential prerequisites for the success of the collaboration.



Image 1: Dean of the private Institution (NKP5 medical college, Nagpur India) along with Public health department Director STDC providing free DRTB drugs to Patient.

### PD-638-30 Perceptions of private practitioners about "Standards for TB care in India" and its probable impact on their involvement in TB programme, India

P Dave,<sup>1</sup> S Bharaswadkar,<sup>2</sup> K Pujara,<sup>1</sup> b Vadera,<sup>2</sup> K Rade,<sup>2</sup> A Sreenivas.<sup>2</sup> <sup>1</sup>Department of Public Health, Government of Gujarat, Office of Commissionerate, Gandhinagar, <sup>2</sup>WHO RNTCP Technical Support Network, World Health Organization, Country office for India, New Delhi, India. e-mail: bharaswadkars@tbcindia.nic.in

**Background:** Private Practitioners (PP) are primary source of health care for patients in India. Revised National TB Control Programme (RNTCP) in consultation with other stakeholders conceived Standards for TB care in India (STCI) to facilitate quality management of TB by all health care providers. Assessment of perception of PP about STCI is crucial to forecast application of STCI into practice by all health care providers moreover it will help programme assess probable impact STCI may have on involvement of PP in RNTCP.

**Design/Methods:** Cross sectional study in 3 urban districts of Gujarat (Ahmedabad, Bhavnagar, and Jamnagar) in India. Structured questionnaire administered to qualified PP (n=152) attending Continuation Medical Education (CME). Data entry and analysis done in Epi data. Diagnosis- 74% PP consented with policy of using X ray chest as screening tool for diagnosis of TB. 62% PP agreed with banning of serological tests for TB. 40% of PP agreed with use of CBNAAT for diagnosis of pediatric TB and HIV associated TB. Treatment- 67% PP agreed with daily regimen for treatment of TB 90% of PP felt that patient support system is necessary to ensure compliance though 20% of them opted for system other than treatment provider. TB-HIV- 43% PP agreed that

Isoniazid Prophylaxis Therapy (IPT) may be offered to HIV infected persons in whom active TB is ruled out. Public Health Responsibility- 84% of PP agreed that TB cases must be notified to public health authorities. 93% of PP felt that written record of TB patients should be maintained though 22% out of them felt that it may be unfeasible. >85% of PP opined that they will refer/notify TB patients and allow health staff to extend soft benefits to their TB patients if STCI is implemented in RNTCP.

**Conclusion:** There is a need of sensitization of PP on newer initiatives including CBNAAT, IPT and ban on sero Diagnostics. Components of newer initiatives may be included into curriculum of CME for PP. Standards of daily regimen, FDC may be implemented into the programme in order to further build trust of private sector into the programme. Programme may consider utilizing other methods like information technology tools to monitor compliance of treatment of patients making treatment of TB more patient friendly. Programme may expedite implementation of STCI into programme which may ensure more involvement of PP and thus universal access of TB care.

#### **PD-639-30 Experience of Public-Private Partnership (PPP): perception of collaboration by public and rural health-care providers in Karnataka, India**

S Gadala,<sup>1</sup> KR Vishwanath,<sup>1</sup> T Thomas,<sup>1</sup> M Krithika,<sup>1</sup> P Banuru Muralidhara,<sup>2</sup> D Bharati.<sup>1</sup> <sup>1</sup>Project Axshya, Catholic Health Association of India, Hyderabad, India, <sup>2</sup>Project Axshya, Union Against Tuberculosis & Lung Diseases, New Delhi, India. Fax: (+91) 40-27811982. e-mail: srinivasa-rao@chai-india.org

**Background:** Over the decade multi stakeholder partnership approach involving stakeholders such as non-government organizations, private practitioners, medical colleges and corporate sectors is key strategy in India. Despite the robust collaboration, TB prevention and control is faced with several programmatic challenges like limited community awareness, less community ownership, alarming rate of MDR and inadequate professionals. In the districts of Hassan and Tumkur rural healthcare providers (RNCPs) are engaged with project Axshya from 2010. The programme often considers engagement of healthcare providers and when implemented there are unexplained barriers. This abstract makes an attempt to enumerate the barriers of engagement of unqualified RHCPs with the programme. **Method:** A structured questionnaire was administered to 15 RNTCP staff at public facilities through a one-to-one interview to understand the perception of engagement of unqualified practitioners. They were assessed on a three point scale. Similarly, interview was conducted with RHCPs.

**Results:** In terms of information, 80% RNTCP staff were of the opinion that RHCPs are providing inadequate information about TB while 55% RHCP reported that they are not receiving any information from RNTCP. Majority of the RNTCP staff (90%) presumed that RHCP do not adhere to the treatment guidelines

provided which results in default cases. Also they stated (85%) that RHCPs refer only low income patients to the DOTS centre. With regard to DOTS provision, RHCPs were found to have a more negative attitude towards RNTCP. More than half of the RHCP (54%) experience that government DOT providers need to change their attitude towards TB patients and around 60% also felt that referring to RNTCP services would lead to lower clientele in their clinics. In addition, 36% were also of the opinion that patients are denied of regular treatment due to the unavailability of drugs at the DOTS centre. On the other hand, 60% RNTCP believed that default rate increases if TB patient continues treatment through the rural practitioner.

**Conclusion:** PPP is an effective approach for scaling up the quality health care services however lack of co-ordination can result in failure. There is a need for regular dialogue, capacity enhancement and greater collaboration to ensure an effective partnership approach.

#### **PD-640-30 Reaching the "missing" tuberculosis cases: are private health care providers in Pune, India notifying TB patients to the national programme?**

R Yeole,<sup>1</sup> K Khillare,<sup>2</sup> V Chadha,<sup>3</sup> A Kumar.<sup>4</sup> <sup>1</sup>Revised National Tuberculosis control programme, World Health Organization (WHO) Country Office in India, New Delhi, <sup>2</sup>Public Health Department, City TB Office, Pimpri Chinchwad Municipal corporation (PCMC), Pune, <sup>3</sup>Epidemiology and Research Division, National Tuberculosis Institute, Bangalore, <sup>4</sup>South-East Asia Regional Office, International Union against Tuberculosis and Lung Disease (The Union), New Delhi, India. e-mail: rdyeole@rediffmail.com

**Background:** In India, it is widely acknowledged that many tuberculosis (TB) patients are diagnosed and managed outside the national programme by private health care providers (PP). To capture these 'missing' TB cases, the Government of India declared TB a nationally notifiable disease in May 2012 that mandates all the health care providers in the country to report information on TB cases managed by them. We aimed to assess the extent of involvement of PPs in Pimpri Chinchwad Municipal Corporation (PCMC), Pune, India and determine the challenges involved in TB notification.

**Design/Methods:** The study had two components. The quantitative component involved a review of programme records to assess the number of PPs who participated in TB notification and the number of TB patients notified during February-April 2013 by them. The qualitative component involved in-depth interviews of PPs to assess their perceived barriers to notifying TB cases. We used inductive analysis for the qualitative data obtained from provider responses to identify themes.

**Results:** Of 831 PPs/health establishments in PCMC, 533(64%) participated in notification and of these, 87 (16%) notified at least one TB case during the study period. A total of 138 TB cases were notified by PPs which represented 20% (n=695) of all TB cases notified to the programme from all sources. The challenges and

barriers perceived by PPs were grouped into four themes: lack of knowledge about TB notification, concern about breach of confidentiality of TB patients, lack of a simplified operational mechanism for notification, and lack of trust and coordination with government health system.

**Conclusion:** It was encouraging to note that nearly two-thirds of PPs agreed to participate and contributed to one-fifth of all TB cases notified to the national programme. However, we noted a number of challenges, which needs to be addressed urgently. We recommend that the national TB programme should plan and implement a targeted, advocacy, communication and social mobilization campaign to allay the concerns of PPs and simplify the operational mechanisms to notify TB cases by establishing alternate channels (toll-free number, using short-message services of mobile phones, web-based mechanisms) of communication.

#### **PD-641-30 Civil society, key shareholder in TB control programme: a solution in increasing TB suspects and cases to 2 times over a period of 24 months**

S Nayak,<sup>1</sup> T Nandy,<sup>2</sup> G Singh,<sup>3</sup> U Bajpai,<sup>4</sup> M S Rana.<sup>4</sup> <sup>1</sup>The Union South-East Asia Office, IUATLD, Jharkhand, <sup>2</sup>Project Axshya, Population Service International (PSI), Punjab, <sup>3</sup>The Union South-East Asia Office, IUATLD, New Delhi, <sup>4</sup>Project Axshya, Voluntary Health Association of India, New Delhi, India. Fax: (+91) 1146054430. e-mail: snayak@theunion.org

**Background:** TB in urban slums a major challenge in India. Ludhiana, a state of Punjab is one of them. Global fund supported Project Axshya is being implemented in 300 districts of India through the Union which include 15 districts of Punjab. Ludhiana having 3 million populations with 3:2 urban to rural ratio is one of them. 25% of the entire slum populations of Punjab live in Ludhiana and the district contributes about 15% of total TB cases of Punjab. Getting adequate number of referrals from urban slums is a major concern for the TB programme. This paper analyses the impact of strategic initiatives in urban slums through civil society in a specific Microscopic Centre area of the city.

**Intervention:** Population Service International (PSI), Sub Recipient to The Union in Axshya Project, conducts TB Info Mela (information campaign in strategic locations) and training of non-allopathic doctors since April 2011 in selected slums of Ludhiana City including 'high vulnerable and low performing' Janata Nagar DMC. During May 2011 to Dec 2012, around 800 community level TB Info Melas (Individual and group sensitisation on TB in strategic locations) have been conducted along with training of 105 non-allopathic doctors on TB. Referrals are being made from both the interventions and also through 1-1 IPC by the field staff.

**Results and Lessons Learnt:** Out of three intervened DMCs, impact analysis was made in Janata Nagar DMC by comparing the status before (2010) and after (2012) intervention. Suspects examination increased by 95% during 2010 (512) to 2012 (996). Quite significantly, numbers of sputum positive cases diagnosed increased by

129% (63 to 144). The positivity rate also increased from 12% to 14%. The intervention has two dimensional effect i.e. (i) 25% contribution of suspects and sputum positive cases diagnosed through direct referrals and (ii) significant improvement in persons accessing the service delivery points as the indirect effect.

**Conclusion:** Civil Society, the key shareholder is a major means of solution in TB control by increasing suspect referrals and turned a low performing microscopic centre to high performing. Secondly, the innovative method of information dissemination penetrated into the slums to access the health services. Partnering with Civil society is highly crucial in vulnerable areas both for community and for the system. TB control policy though envisages the importance of NGO participation, need to foster the pace of involvement.

#### **PD-642-30 Community involvement by community pharmacists in India for TB care and control**

M Gharat,<sup>1</sup> S Prasad.<sup>2</sup> <sup>1</sup>Community Pharmacy, Indian Pharmaceutical Association, Mumbai, <sup>2</sup>Lilly MDR TB Partnership, Eli Lilly and Company, Gurgaon, India. e-mail: symghar@yahoo.com

**Background and challenges:** Revised National Tuberculosis Control Programme (RNTCP) offers free diagnosis and free treatment of Tuberculosis. RNTCP uses the DOTS (Directly Observed Treatment, Short course) strategy. In spite of efforts, large populations still remain unaware about free public sector treatment, posing a challenge. Further efforts are needed to increase community awareness about TB and DOTS. One of the efforts made by Indian Pharmaceutical Association (IPA) is development of Public private partnership engaging community pharmacists in many parts of India. Pharmacists, being first point of contact for most patients, are in suitable position to engage community to increase awareness about TB and DOTS. The paper discusses variety of ways by which pharmacists work closely with the community for TB care and control.

##### **Methods and Results:**

**Training of pharmacists:** During 2010–2012, Indian Pharmaceutical Association, in collaboration with Revised National Tuberculosis Control Programme, (RNTCP) and with support of Lilly MDR TB Partnership trained about 350 community pharmacists from various parts of State of Maharashtra. Training involved details of TB basics, DOTS protocols, role of pharmacists and communication skills. Post training, a variety of ways of community outreach are being successfully tried through these pharmacies.

##### **Community Outreach**

**Methods:** a) Display of prominent boards outside the pharmacies with message about TB symptoms, free medicines and appealing to ask pharmacist for any further information. b) Awareness lectures by pharmacists for schools, prisons, citizens fora, mill workers etc c) ACSM material distribution through Pharmacies d) Counseling of TB patients and TB suspects Above



methods have proved effective in reaching out to the community. Several patients in private sector, who would have been probable defaulters, could be converted to DOTS as well as several new cases could be detected. Pharmacists have become focal points for community help. Pharmacists have gained high respect and status in the eyes of the public as well as the Government. Media has been giving excellent visibility to the pharmacists' work.

**Conclusion:** Pharmacists have huge potential for involving community in TB matters

**Interventions** by pharmacists provide innovative solutions to reach out to the community to improve TB care and control.

**Key Recommendation:** In every high TB burden country, pharmacies should be actively involved in TB control programme.

#### **PD-643-30 Targeted intervention with private practitioners in urban areas for notification under India's national TB programme**

M Kohli,<sup>1</sup> A Moitra,<sup>2</sup> S Bhargava,<sup>3</sup> V Chhajlani,<sup>4</sup> M Jain,<sup>5</sup> R Sinha.<sup>1</sup> <sup>1</sup>Tuberculosis, International Union Against Tuberculosis and Lung Disease, South East Asia Office, New Delhi, <sup>2</sup>World Health Organization Country Office for India, New Delhi, <sup>3</sup>Department of Chest Medicine, MGM Medical College, Indore, <sup>4</sup>District Tuberculosis Centre, Revised National Tuberculosis Control Programme, Indore, India; <sup>5</sup>Rollins School of Public Health, Emory University, Atlanta, GA, USA. e-mail: mohanpskohli@gmail.com

**Background and challenges to implementation:** The private sector plays a critical role in TB treatment, however their involvement in India's Revised National TB Control Program (RNTCP) is sub optimal. RNTCP involves private practitioners through public private partnership (PPM) projects and NGO PP schemes. The efforts of this partnership have been limited and not to scale. Out of an estimated over 1 million private practitioners, only 14000 are aligned with RNTCP for TB control. Currently, RNTCP has limited capacity to engage with private practitioners, private sector on the other hand is apprehensive about losing patients. In 2012, the Government made Notification of TB cases mandatory, to aid TB control measures. So far, the response from private sector has been inadequate.

**Intervention or response:** Under an initiative to make Indore, a city in the Indian State of Madhya Pradesh, TB free by 2020, the Collaborative for Elimination of TB from Indore (CETI) undertook a pilot project to involve private practitioners in TB control. An initial meeting with 75 doctors resulted in identification of 11 doctors as change agents/physician champion, who further interacted with the doctors' community garner their support. The staff of selected doctors were trained on record keeping for TB notification. Utilizing short messaging service (SMS) messages were sent to 100 doctors on TB and motivate them to learn more through online CETI resources. Utilising short messaging services to send information, reminders and updates to 100 doctors on

TB and motivate them to learn more through online CETI resources.

**Results and lessons learnt:** Starting with a base of 25 doctors notifying TB cases in Feb. 2013, the number went up to 200 doctors by Dec. 2013 through DTO, the nodal person for notification under RNTCP. Joint efforts of RNTCP and CETI facilitated notification of over 1000 cases including government cases through 69 hospitals and nursing homes, wherein physician champions played a vital role. Sending repeated SMSes helped build recall; but maintaining records remains a challenge.

**Conclusions and key recommendations:** Focused intervention using motivated doctors as champions within the doctors' community, and training of their staff will give a boost to notification from the private sector. Sustained reminders through SMSes or by any other means to promote notification yields positive results.

#### **PD-644-30 Engaging private pharmacies in the Public-Private Partnership for TB control in Chennai city, India**

R Ananthakrishnan,<sup>1</sup> P Sujatha,<sup>1</sup> S Augusteen,<sup>1</sup> N Krishnan,<sup>1</sup> S Prasad.<sup>2</sup> <sup>1</sup>OR, REACH, Chennai, <sup>2</sup>Eli Lilly and Company (India), Lilly MDR TB Partnership, New Delhi, India. e-mail: ramyardr@gmail.com

**Background and challenges to implementation** Pharmacies are often the first point of contact for more than 50% of TB patients is the private sector. Private pharmacies form a vital component of any PPM (Public Private Mix) because they are closest to the community and are hence also in a position to influence patients' treatment choices. Chennai city with 4.7 million population has a presence of huge and vibrant private health sector and pharmacies.

**Intervention** A sustainable partnership for TB control with the Private pharmacies in Chennai city (i). to facilitate the private pharmacies in actively notifying the number of TB patients receiving anti-TB drugs from them, (ii). To encourage referrals from private pharmacies of symptomatic to TB control program, (iii). To promote awareness and education on TB and DOTS to TB patients by the private pharmacies, (iv). To facilitate pharmacists to act as DOT providers

**Results** Between January 2013 to March 2014, 550 pharmacists attended the TB orientation workshop following which there were 382 (documented and validated) referrals over 15 months period. Of these referrals 252 were chest symptomatics and 130 were TB patients diagnosed in the private sector. Of the symptomatics, 70 % underwent sputum examination and 39 were found to be sputum positive. Overall, 76 TB patients were started on TB treatment with 68% of them receiving treatment under government DOTS program. 23 TB patients receive DOT from the pharmacists.

**Conclusion** The above findings has shown that pharmacists could be successfully engaged in TB control efforts. Through the pharmacists, the TB patients on private treatment could be assessed and they received counseling and motivation for completion of the course. In addition,

the pharmacists had educated patients by displaying posters, directing them to appropriate treatment choices and by motivating patients for completion of the treatment course. The findings has reiterated the need to look at all stakeholders in the private health sector. The contribution of private pharmacists towards DOTS program could be considerable and it is critical to engage with them in a sustained manner.

### PD-645-30 Demonstrating PPIA (Private Provider Interface Agency) as mandated by India's national strategic plan for TB control: mid-course results

O George,<sup>1</sup> R Washington,<sup>2</sup> H Gururaj,<sup>2</sup> R Ganesan,<sup>1</sup> R Swamickan.<sup>3</sup> <sup>1</sup>SHOPS, Abt Associates Inc., New Delhi, <sup>2</sup>Management, KHPT, Bengaluru, <sup>3</sup>Health Division, USAID, New Delhi, India. Fax: (+91) 112653 5172. e-mail: oommen.geo@gmail.com

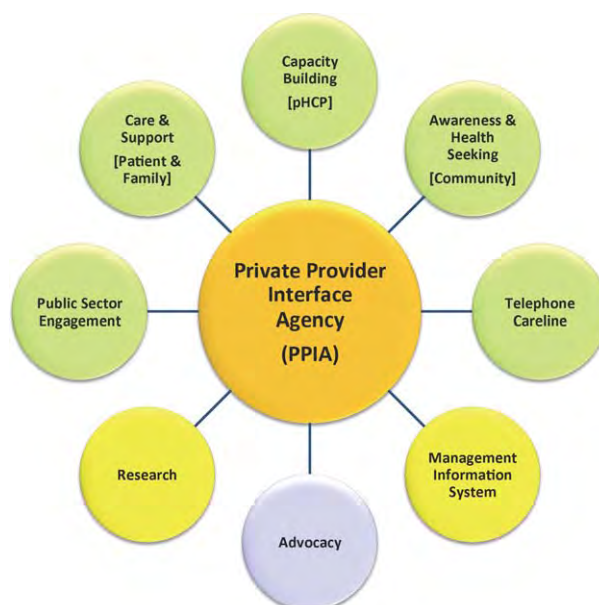
**Background:** India's national strategic plan for RNTCP recommends using private provider interface agencies (PPIA) to engage private health care practitioners (pHCP) in TB control. The USAID-funded Strengthening Health Outcomes through the Private Sector (SHOPS) project led by Abt Associates Inc. in partnership with KHPT designed and initiated a PPIA model to bridge gaps in health-seeking, diagnosis, notification, treatment and follow through in TB. This abstract presents mid-course results at 10 months of intervention.

**Methods:** Presented with gaps in TB prevention and care under 3 categories – community, pHCP, public sector RNTCP – SHOPS developed behavior change strategies to promote health-seeking (community, TB symptoms), bacteriological diagnosis (pHCP), standardized treatments (pHCP), notification (pHCP, public sector) and follow up care and support (patient, pHCP, RNTCP). These principles are promoted through a PPIA, addressing gaps and barriers between the 3 stakeholder groups. Keys to the success of this simple, but innovative, model are its participatory and patient-centric approach with community, pHCP and RNTCP and its focus on continuum of care.

**Interventions** are supported by phone-based learning for pHCP, a telephone Careline for patients, web-based MIS, research and advocacy. The model facilitates and provides services to a million people from urban slums in 42 towns of Karnataka.

**Results:** This first-of-its-kind model improves universal access to quality primary TB care among urban slum populations. The state government and PPIA collaborate and are co-dependent. It enables universal engagement of qualified and informal pHCP. 2984 TB patients were diagnosed and reported to SHOPS from Jun-13 to Mar-14; 39% from target slums, and 61% from non-slum populations. Among in- and out-of-slum patients, 54% are managed privately and 46% under RNTCP. 17% diagnosed are children; 11% less than 5 years. SHOPS-cognizant annualized total case notification rate is 210 (143 under RNTCP; 67 under private management) for people from intervention slums [context: Karnataka, 98;

Bangalore Urban district, 166]. Wider RNTCP data is being collected to appreciate the full impact of the model. **Conclusions:** SHOPS initiated an innovative, comprehensive, model to address gaps in TB continuum of care in India. Mid-course results are exciting. Additional information covering notification, solutions, cost benefits and delays, are expected over the remaining 3 project quarters.



### PD-647-30 Chemists and less-than-fully-qualified providers dominate Mumbai's health provider universe

S Vijayan,<sup>1</sup> M Khetarpal,<sup>2</sup> Mohu Datta,<sup>1</sup> I Syed,<sup>3</sup> R Chopra,<sup>4</sup> P Sugendran,<sup>1</sup> V Jondhale,<sup>1</sup> R Gandhi.<sup>1</sup> <sup>1</sup>PPIA -Mumbai, PATH, Mumbai, <sup>2</sup>Tuberculosis, Municipal Corporation of Greater Mumbai, Mumbai, <sup>3</sup>Tuberculosis, WHO, Mumbai, India, <sup>4</sup>Business Consulting, Intellectap, Mumbai, India. Fax: (+91) 1146054430. e-mail: shibuvij@gmail.com

**Background:** Mumbai is the largest, most densely populated city in India, and 62 % of residents live in slums. Healthcare in Mumbai is highly privatized, yet no comprehensive listing and mapping of private health services was available. Existing legal frameworks require registration of qualified doctors, licensed chemists, and diagnostic centres with health authorities; yet a huge less-than-fully qualified provider population serves a major source of healthcare. Comprehensive listing and profiling of all private providers was required in Mumbai to plan and deploy private sector engagement efforts for TB.

**Methods:** We conducted mapping of private practitioner and chemist in 15 wards of Mumbai, covering 8.9 million population, comprising ~85% of slum population (census 2001). Data were captured from the signboard of the standalone clinics, name, degree and address of the clinics. Locations were geocoded. Details of the doctors practicing in hospitals were collected from the reception.

Given legal guidelines on prescribing authority for anti-TB drugs, we defined qualified providers as having at least MBBS degree, less than fully qualified (LTFQ) as having a diploma or degree in Ayurveda, Unani, Indian systems of medicine, or homeopathy. Unclassified providers were those with other certification not fitting into the above two classification. Chemists were those supplying prescription medicines

**Results:** After removing the dental clinics we identified 8519 providers including chemists (1 per 100,000 population), with a total of 276 different degrees, diplomas, and certifications; amongst these unclassified accounts for 233 variety of degrees. Among the total universe qualified providers were 1852 (22%), LTFQ 3416 (40%), Chemist 2763 (32%) and unclassified 488 (6%). Analysis of slum non slum provider distribution was done for two wards and the proportion of LTFQ is more in non-slum areas compared to slum areas in these two wards and the difference is significant ( $p < .001$ ) (Table)

Type of provider	Slum	Non Slum	Total
Qualified	29.4 (249)	40.5 (128)	32.4 (377)
Less than fully qualified	59.2 (502)	44.0 (139)	55.1 (641)
Unclassified	11.4 (97)	15.5 (49)	12.5 (146)

$p < .001$

**Conclusions:** Mumbai's private provider universe is large but dominated by LTFQ and chemists, particularly in the slum areas. A bewildering multiplicity of qualifications was claimed, and such claims provided no guide or reference to quality of care. Strategies for early detection of TB will require extensive utilization of these LTFQ provider groups.

## 14. DIAGNOSTIC EVALUATION OF TB: WHAT DOES AND DOESN'T WORK

### PD-648-30 Source of sputum smear positive tuberculosis patients in Rajnandgaon district, Chhattisgarh, India

P Nayak,<sup>1</sup> Pawa Jethani,<sup>2</sup> T K Agrawal,<sup>2</sup> S Chandraker,<sup>2</sup> S Anjum,<sup>1</sup> K Sharma,<sup>1</sup> A Sreenivas.<sup>1</sup> <sup>1</sup>Country Office, India, World Health Organization, New Delhi, <sup>2</sup>State Tuberculosis Cell, Directorate Of Health Services, Raipur, Chhattisgarh, India. e-mail: pikoo.2007@gmail.com

**Background and challenges to implementation:** Revised national tuberculosis control programme (RNTCP) aims to achieve universal access to tuberculosis (TB) care services across the country. To achieve this, all TB patients in the community should have access to early diagnosis and treatment. A number of health care providers contribute to referring these presumptive TB patients to the designated microscopic centres (DMC), a proportion of which turns out to be sputum smear positive. Studying this source of referrals and the proportion of positive cases amongst them can give us information about the distribution of TB cases amongst

various health care providers (HCP). This study aims to assess the utilization of RNTCP diagnostic services (DMC) by HCPs in Rajnandgaon district of Chhattisgarh, India

**Intervention or response:** In this cross sectional study among all presumptive TB patients examined during January-December 2013 in Rajnandgaon district of Chhattisgarh, we reviewed the laboratory forms and registers at the DMC and the treatment card of patients to extract the desired information

**Results and lessons learnt:** Of 9074 presumptive TB patients examined (69% male; median age of 36 years), 956 (11%) were found to be sputum positive. About 12 % (691/5628) sputum positivity is observed among the presumptive TB patients reporting at the outpatient department (OPD) whereas 6% (9/149) positivity is through sputum collection center and transportation (SCCT) model. We found 10% (193/2371) positivity among the presumptive TB patients referred by health care workers. Among the contacts of tuberculosis patients examined, 3 % (21/606) positivity was observed. The private sector contributed to 13% (41/320) of sputum smear positive cases.

**Conclusions and key recommendations:** This study describes the source of sputum smear positive TB patients and the pathway followed by them in the health system. Engagement of private sector and implementation of SCCT model can be envisaged to reach out to the TB patients in the community. Enhanced efforts towards training of field staff and greater involvement of general health system can improve the sputum smear positive case detection of tuberculosis

### PD-649-30 Epidemiology and diagnostic techniques of tuberculous lymphadenitis in a TB low-burden country

I Los Arcos,<sup>1</sup> F Salvador,<sup>1</sup> A Sánchez-montalvá,<sup>1</sup> T Tortola,<sup>2</sup> A Curran,<sup>1</sup> A Villar,<sup>3</sup> J Castellví,<sup>4</sup> I Molina.<sup>1</sup> <sup>1</sup>Infectious Diseases, <sup>2</sup>Microbiology, <sup>3</sup>Pneumology, and <sup>4</sup>Pathology, Vall d'Hebron Teaching Hospital, Barcelona, Spain. e-mail: ibai.losarcos@gmail.com

**Background:** Tuberculous lymphadenitis (TL) is the most common form of extra-pulmonary tuberculosis. The diagnosis can be made by culture, polymerase chain reaction (PCR) or histological techniques, performed on samples obtained through an excisional biopsy or by fine-needle aspiration (FNA). We studied the profitability of the different diagnostic techniques and the epidemiology of TL in a TB low-burden country.

**Methods:** A retrospective study was conducted to recruit all cases of TL in adults diagnosed in a tertiary hospital (Vall d'Hebron Teaching Hospital, Barcelona, Spain) from January 2001 to December 2013. We included confirmed TL (by bacilloscopy, mycobacterial culture or PCR through Xpert MTB/RIF test) and probable TL (suspected by clinical presentation, suggestive anatomopathological features and clinical improvement after specific treatment). Clinical, epidemiological and microbiological data were collected from medical records.



**Results:** Overall, 123 patients met the inclusion criteria. Fifty-four (43.9%) patients were men, median age was 38 (18–83) years and median time from the beginning of symptoms to consultation was 2 (1–48) months. Fifty-three out of 123 (43.1%) patients were born in Spain and 70 (56.9%) patients were foreign-born: 21 (17.1%) were from Pakistan, 17 (13.8%) were from Morocco, 9 (7.3%) were from Ecuador, 6 (4.9%) were from Bolivia and 17 (13.8%) were from other countries. HIV test was performed in 104 patients, from whom 16 (15.4%) resulted positive. In 37 out of 123 (30.1%) patients, extranodal involvement was reported, being pulmonary involvement the most frequent one (22 patients, 17.9%). Diagnosis was confirmed microbiologically in 86 (69.9%) patients, and probable TL was diagnosed in 37 (30.1%) patients. Profitability of the different diagnostic techniques is summarized in Table 1.

**Conclusion:** The number of TL diagnosed in our hospital during the last decade has progressively increased; this increase has been at the expense of an increase of TL in foreign-born patients. The profitability of Ziehl-Neelsen stain detection and mycobacterial culture in both techniques (FNA and biopsy) were similar, but granulomatous inflammation was observed much more frequently in biopsy samples. Although PCR was performed in a low number of patients in our study, it yields a sensitivity of 77.3% when performed in FNA-obtained samples, lower than previous studies, but higher than mycobacterial culture.

Table 1. Profitability of different diagnostic techniques.

	Fine-needle aspiration	Biopsy
<b>Results in samples for histopathological study:</b>		
Granulomatous inflammation	40/73 (54.8%)	61/63 (96.8%)
Positive Ziehl-Neelsen stain	10/54 (18.5%)	15/62 (24.2%)
Positive PCR (from paraffin-embedded tissues)	-	1/7 (14.3%)
<b>Results in samples for microbiological study:</b>		
Positive Ziehl-Neelsen stain	16/64 (25%)	10/47 (21.3%)
Positive mycobacterial culture	40/64 (62.5%)	32/49 (65.3%)
Positive PCR	11/15 (73.3%)	6/14 (42.9%)

NOTE. Data are reported as number (%) of patients.

### PD-650-30 Added value of including Xpert MTB/RIF in an algorithm to diagnose smear-negative tuberculosis in a HIV prevalent resource-constraint setting

H Huerga,<sup>1</sup> G Ferlazzo,<sup>2</sup> P Bevilacqua,<sup>1</sup> B Kirubi,<sup>3</sup> E Oduor,<sup>3</sup> E Ardizzoni,<sup>2</sup> J Sitienei,<sup>4</sup> M Bonnet.<sup>1</sup> <sup>1</sup>Clinical Research, Epicentre, Paris, <sup>2</sup>Medical, Médecins Sans Frontières, Paris, France; <sup>3</sup>Medical, Médecins Sans Frontières, Nairobi, <sup>4</sup>National Tuberculosis, Leprosy and Lung Disease Unit, Ministry of Health, Nairobi, Kenya.  
e-mail: helena.huerga@epicentre.msf.org

**Background:** Diagnosis of tuberculosis (TB) remains a challenge in resource-limited countries. Xpert MTB/RIF

has shown good performance but there is few data on diagnostic algorithms including the assay in routine field conditions. We evaluate an algorithm including Xpert to diagnose smear-negative TB at district level in a HIV prevalent setting.

**Design/Methods:** Prospective cohort study. Consecutive smear-negative pulmonary TB (PTB) suspects living in the area were eligible. At first consultation, patients received clinical exam, one Xpert MTB/RIF test (results on the same day), chest X-ray (if Xpert negative) and MTB culture (Thin Layer Agar and Lowenstein Jensen). Patients not started on TB treatment received 5 days amoxicillin course and were re-assessed clinically and with microscopy and Xpert. Patients' outcomes were assessed at 6 months. We used TB treatment initiation as primary end point and MTB culture as reference.

**Results:** Of 613 PTB suspects, 400 (65.3%) smear-negative patients were included. Median age was 37 years, 59.2% were women, 29.0% had past TB history, and 68.5% (267/390) were HIV positive. MTB culture was positive in 13.8% (52/376). TB treatment was started in 161 (40.3%) patients using the diagnostic algorithm. Additional 8 (2.0%) patients received TB treatment after positive culture result and tracing (Figure). Sensitivity and specificity of the diagnostic algorithm for treatment initiation were: 84.6% (CI95%: 71.9–93.1) and 66.0% (CI95%: 60.6%–71.2%) respectively. Positive and negative predictive values were: 28.6% (CI95%: 21.6–36.4) and 96.4% (93.0–98.4) respectively. Sensitivity and specificity of the first Xpert were: 58.8% (30/51) and 97.2% (314/335) respectively. Mortality at 6 months was not significantly different in culture positive patients compared to negative but was higher in those started on TB treatment through the diagnostic algorithm (9.0%) vs those not started on treatment (3.1%),  $p=0.03$ .

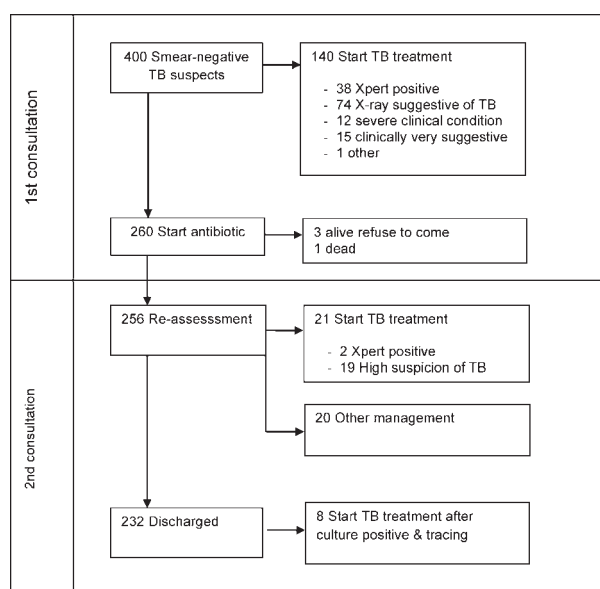


Figure 1 : Diagnostic and treatment pathway of 400 smear-negative TB suspects

**Conclusion:** Including Xpert in the diagnostic algorithm led to a majority of the confirmed smear-negative TB cases initiated on TB treatment but did not prevent the risk of overtreatment despite the rapidity of the results. An important proportion of cases not confirmed by culture were also treated. Although some of them might have been true culture negative TB cases, many were probably non TB cases wrongly started on TB treatment, which may explain the higher mortality in this group of patients.

### PD-651-30 Health-care worker TB investigation practices: did Xpert MTB/RIF change testing practice?

V Chihota,<sup>1,2</sup> K Fielding,<sup>3</sup> S Ginindza,<sup>1</sup> K McCarthy,<sup>1</sup> G Churchyard,<sup>1,2</sup> A Grant.<sup>4</sup> <sup>1</sup>Research, Aurum Institute, Johannesburg, <sup>2</sup>School of Public Health, University of Witwatersrand, Johannesburg, South Africa; <sup>3</sup>Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, <sup>4</sup>Clinical Research, London School of Hygiene and Tropical Medicine, London, UK.  
e-mail: vchihota@auruminstitute.org

**Background:** As part of a pragmatic cluster randomised trial ("XTEND" study), evaluating the effect of Xpert MTB/RIF implementation in South Africa, we describe health care worker (HCW) practices in the investigation of TB. The aim of the study was to determine the proportion of adults attending primary health clinics (PHC), reporting  $\geq 1$  TB symptoms who had sputum requested by HCW and to compare this between clinics using smear microscopy vs Xpert as an initial test.

**Design/Methods:** A systematic sample of adults leaving PHC (20 Xpert arm, 20 microscopy arm) who reported one or more TB symptoms were enrolled. The primary outcome was whether a sputum sample had been requested by a HCW during that clinical encounter.

**Results:** 3604 participants (1676 in Xpert arm, 1928 in microscopy arm) were enrolled; (median age 38 yrs, 71% female, 39% reported being HIV-positive). 71% and 31% reported cough and fever respectively with equal proportions (42%) reporting weight loss and night sweats. For 1267 participants (35%) the main reason for attending the clinic was due to TB symptoms. Overall 2130 (59%) had reported TB symptoms to HCW. 23% (818/3604) of participants had sputum requested by HCW. Though participants in the Xpert vs microscopy arm were more likely to have sputum requested by HCW, this was not significantly different: overall (26% [436/1676] vs 20% [382/1928]; adjusted prevalence ratio [aPR] 1.31, [95% CI 0.78-2.20]). This was not changed when restricted to those presenting at clinics due to symptoms (49% [260/530] vs 30% [220/737]; aPR 1.38 [0.89-2.13]); and when restricted to those reporting being HIV-positive (29% [190/647] vs 21% [156/749]; aPR 1.38 [0.88-2.16]). A weak association was observed among those that had reported symptoms to HCWs (42% [384/905] vs 28% [345/1225]; aPR 1.47 [0.99-2.16]). Among the group who attended the clinic due to TB symptoms, participants were more likely to have sputum requested by a HCW if they had a higher number of TB symptoms, longer duration of cough, unintentional weight loss and night sweats,

were HIV-positive and not on ART vs HIV-negative; and if they reported symptoms to HCW (Table 1).

**Conclusion:** A large proportion of participants with TB symptoms who attended PHCs did not get tested for TB. The implementation of Xpert MTB/RIF did not substantially change the probability of testing for TB. There is need to improve adherence to guidelines for TB screening of persons presenting at PHCs.

Table 1: Factors associated with having sputum requested for TB investigations among clients attending clinic because of symptoms suggestive of TB (n=1267)

	Total	Sputum requested by HCW N (row %)	OR* (95% CI)	P value
All patients	1267	480 (37.9)		
Age, years				
18-29.9	380	139 (36.6)	1	0.14
30-34.9	187	71 (38.0)	1.17 (0.79-1.75)	
35-39.9	136	61 (44.9)	1.41 (0.91-2.19)	
40-49.9	253	108 (42.7)	1.54 (1.07-2.20)	
$\geq 50$	311	101 (32.5)	1.06 (0.75-1.51)	
Gender				
Male	454	207 (45.6)	1	0.0005
Female	813	273 (33.6)	0.63 (0.49- 0.82)	
Cough duration				
No cough	220	41 (18.6)	1	<0.0001
$\leq 2$ weeks	656	236 (36.0)	3.04 (2.02-4.58)	
>2 weeks	391	203 (51.9)	5.08 (3.30-7.81)	
Duration night sweats				
None	697	216 (31.0)	1	<0.0001
$\leq 2$ weeks	299	138 (46.2)	2.05 (1.51-2.78)	
>2 weeks	271	126 (46.5)	1.73 (1.25-2.88)	
Weight loss duration				
None	700	229 (32.7)	1	0.0024
$\leq 2$ weeks	189	86 (45.5)	1.80 (1.26-2.58)	
>2 weeks	378	165 (43.7)	1.39 (1.04-1.86)	
Fever duration				
None	795	316 (39.8)	1	0.76
$\leq 2$ weeks	337	117 (34.7)	0.98 (0.72-1.34)	
>2 weeks	135	47 (34.8)	0.85 (0.55-1.31)	
Number of WHO symptoms				
One	419	111 (26.5)	1	<0.0001
Two	430	166 (38.6)	1.96 (1.42-2.69)	
Three	295	137 (46.4)	2.73 (1.92-3.89)	
Four	123	66 (53.7)	3.83 (2.39-6.12)	
HIV status				
HIV negative	458	144 (31.4)	1	<0.0001
HIV+/on ART	167	56 (33.5)	1.27 (0.84-1.91)	
HIV +/not on ART	181	111 (61.3)	2.83 (1.91-4.19)	
HIV unknown	461	169 (36.7)	1.18 (0.87-1.60)	
Informed health worker of symptoms				
No	188	22 (11.7)	1	<0.0001
Yes	1079	458 (42.5)	5.84 (3.56-9.56)	

\* controlling for clinic using a random effects model

### PD-652-30 Culture positivity rate for *Mycobacterium tuberculosis* in migrants from Pakistan before immigration to other countries

K Jabeen,<sup>1</sup> Y Shafqat,<sup>1</sup> M Irfan,<sup>2</sup> R Hasan.<sup>1</sup> <sup>1</sup>Pathology Microbiology, Aga Khan University, Karachi, <sup>2</sup>Medicine, Aga Khan University, Karachi, Pakistan.  
e-mail: kausarjabeen@aku.edu

**Background:** Pakistan is high tuberculosis (TB) burden country and TB screening is demanded by many countries for every Pakistani individual before immigration. We studied culture positivity rate in the asymptomatic individuals migrating from Pakistan who were screened for TB by chest radiograph and Mantoux test. Sputum for TB culture was sent if there was Mantoux positivity and radiological changes suggestive of TB.

**Design/Methods:** All cases that are referred from immigration health centers in Karachi to Aga Khan University pulmonology clinics were recruited in the study. Sputum culture from these cases were also directly referred to Aga Khan University laboratory from these centres. TB culture data from 2008 to February 2014 was retrieved. TB cultures were performed at the Aga Khan University laboratory using standard methods.

**Results:** A total of 81 cases were included for which both TB smear and culture was requested. TB smear was positive in 2/81 (2.5%) and TB culture was positive in 4/81 (4.9%) cases. One case was TB smear positive and culture negative. Two cases were positive for non tuberculous *Mycobacteria* (NTM)

**Conclusion:** Our data shows a high rate of culture positivity in otherwise asymptomatic cases screened for TB for immigration purposes. Use of rapid diagnostic tests like Xpert in such cases may lead to an early diagnosis and treatment.

### PD-653-30 Infectiousness of untreated, drug susceptible tuberculosis patients in South Africa, using microscopy and geneXpert for diagnosis

A Stoltz,<sup>1</sup> M Mphahlele,<sup>2</sup> E De Kock,<sup>3</sup> M Van Der Walt,<sup>2</sup> A Dharmadhikari,<sup>4</sup> E Nardell.<sup>4</sup> <sup>1</sup>Medicine, University of Pretoria, Pretoria, <sup>2</sup>Tuberculosis Epidemiology and Intervention Unit, South African Medical Research Council, Pretoria, <sup>3</sup>Retrasol, Retrasol, Pretoria, South Africa; <sup>4</sup>Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA. e-mail: adharmadhikari@partners.org

**Background:** The infectiousness of untreated TB patients is generally unknown but most likely varies from person to person. Contact studies reflect variable environmental conditions including exposure duration and susceptibility of exposed contacts. In the context of a Gates Foundation funded study to assess the efficacy of BCG vaccination to protect guinea pigs exposed to human TB patients under controlled conditions, we had the unique opportunity to assess the infectiousness of a series of 48 newly diagnosed, drug susceptible TB patients in South Africa.

**Design/Methods:** Tuberculosis patients newly diagnosed using microscopy and geneXpert with early reporting occupied the Airborne Infections Research (AIR) Facility in Mpumalanga Province for 48 hours before initiating standard treatment. In the AIR Facility, exhaust air from patient rooms is delivered to animal exposure chambers containing guinea pigs. Here we report on the infectiousness of a series of 48 patients for 90 control, unvaccinated guinea pigs after approximately 48 hours exposure.

**Results:** Among 680 TB suspects screened, 53 (7.8%) were geneXpert positive, a rate somewhat lower than the national average. Of the patients admitted to the AIR facility, 5 were promptly discharged and admitted to hospital and started on therapy due to rapid progression of community acquired pneumonia. Although data were incomplete, 15 of 27 patients (55%) were HIV positive by history. Thirty four patient chest x-rays were available for review. Of these, 18 (53%) had lung cavities, 26 (76%) had findings in keeping with tuberculosis and 3 (9%) were normal. Radiographic scoring to quantitate severity of disease is in progress. Although the goal of the study was to infect the guinea pigs, and sputum smear positivity was desirable, sputum microscopy values ranged from negative in 23 patients (48%) to three plus in 3 patients (6%). Among unvaccinated animals, only 5.5% converted to TST positive after approximately 96 person-days exposure.

**Conclusion:** Newly diagnosed, untreated, drug susceptible patients in this study from South Africa were unexpectedly less infectious than anticipated.

### PD-654-30 Challenges and lessons learnt In conducting national TB prevalence survey in a high-burden and limited-resource country

DB Lolong,<sup>1</sup> Iam Pangaribuan,<sup>1</sup> An Musadad,<sup>1</sup> DE Mustikawati,<sup>2</sup> B Dwihardiani,<sup>3</sup> S Meharwal.<sup>4</sup>

<sup>1</sup>Ministry of Health, National Institute of Health Research and Development, Jakarta, <sup>2</sup>Ministry of Health, National TB Program, Jakarta, <sup>3</sup>Infectious Diseases, World Health Organization, Jakarta, <sup>4</sup>Project, USAID DELIVER, Jakarta, Indonesia. Fax: (+62) 2142872392.  
e-mail: dina\_lolong@yahoo.com

**Background:** TB remains a leading cause of death and rank 2nd among all causes of deaths in Indonesia. A National TB Prevalence survey was planned for 2013-14 to better understand the disease and the ways to improve the control. The aim was to assess the prevalence of bacteriological confirmed pulmonary TB.

**Methods:** Total 78,000 participants aged 15 years and older from 3 regions in both urban and rural areas were included. There were total 156 clusters and each cluster had 500 participants. Interviews and digital Chest X-ray used for screening. Individuals with TB symptoms and/or abnormal x-ray were considered as eligible. Two sputum specimens were collected from each participant and transported to labs for smear and culture examinations. All the smear positives were confirmed by GeneXpert and cultures were identified by MPT64 and/or Niacin test.



**Challenges and Lessons Learnt:** 1) Indonesia is a widely diverse, multicultural and multiethnic country having around 17500 Islands. Geography, culture and language barrier posed a challenge in collecting and transporting the specimens. Concrete planning and lab mapping should be done to save the transportation time and cost. A translator was a great help. 2) Digital X-ray was a new experience. Capturing large no. of images were difficult as the machine used to heat up after few images; a high throughput and easy to handle machine should be procured. Radiologists need to be trained to read a digital image. 3) Natural disasters (flood, landslide, volcano) or unforeseen condition (security threat, unrest) decreased the participation. We had to extend or postponed the activity in some places that impacted the budget heavily. Extra budget should be secured for these kinds of situations. 4) Participation was low in urban settings, more socialization such as door-to-door visits and mopping is required. 5) Higher contamination rate was observed in some labs and few labs complained overburdened, so, selection of a well-equipped lab with sufficient manpower is important. Impact on regular lab services was also reported. 6) Data collection from the field and lab was not easy. Regular supervision and data cleaning should be done. 7) Follow-up of diagnosed cases was a challenge, strong collaboration with stakeholders and local authorities is essential. 8) Proper budgeting is important to avoid stock out and discontinuation of activity. Sufficient supplies for field and labs should be arranged in advance. Faster procurement during the survey was challenging.

**PD-655-30 Pre-entry screening of migrants to the UK: using probabilistic matching to identify cases of tuberculosis post-migration**

R Aldridge,<sup>1,2</sup> M Muzyamba,<sup>2</sup> P Dhavan,<sup>3</sup> D Zenner,<sup>1,2</sup> A Hayward,<sup>1</sup> I Abubakar.<sup>1,2</sup> <sup>1</sup>Research Department of Infection and Population Health, University College London, London, <sup>2</sup>Centre for Infectious Disease Surveillance and Control, Public Health England, London, UK; <sup>3</sup>International Organization for Migration, International Organization for Migration, Manila, Philippines.  
e-mail: rob.aldridge@gmail.com

**Background:** The Enhanced Matching System (EMS) is probabilistic record linkage software developed by Public Health England. EMS allows linkage of pre-entry screening data to the UK national tuberculosis register to assess the quality of screening and improve understanding of non-UK tuberculosis notifications in the UK. This study investigated the accuracy of EMS and presents preliminary findings of its use to link screening data to the national register.

**Design/Methods:** To examine the accuracy of EMS, two UK public health tuberculosis databases were matched deterministically using National Health Service (NHS) number as the unique identifier (gold standard) followed by probabilistic matching on the same two datasets without inclusion of NHS number to assess the accuracy of matching. Migrant pre-entry screening data collected

by International Organization for Migration (IOM) in 2012 were then linked to the national tuberculosis register using EMS to identify cases of disease notified in individuals after arrival in the UK.

**Results:** The sensitivity of EMS probabilistic matching was estimated as 99.3%, specificity as 99.6%, positive predictive value as 99.6%, and the negative predictive value as 99.9%. Using EMS to match pre-entry screening and national tuberculosis data, seven cases of tuberculosis (in individuals screened pre-entry) were identified in the UK national tuberculosis register. All except one of these cases occurred after more than seven months of having been screened pre-entry. The remaining case (notified 43 days after screening by IOM) was in an individual with extra-pulmonary disease and would not have been picked up by the CXR-based pre-entry screening.

**Conclusion:** EMS was found to have high accuracy for linkage between public health datasets. This study demonstrates the feasibility of using probabilistic record linkage for quality assurance purposes by identifying cases arising in individuals recently migrating to the UK having been screened pre-entry, and for further studies aimed at understanding and improving the health of these migrants.

**PD-656-30 Poor admissions of TB screening tool resulting in low TB case finding in Swaziland**

K Sibandze,<sup>1</sup> E Phiri,<sup>1</sup> E Nhlengetfwa.<sup>1</sup> <sup>1</sup>Infection Control, National Tuberculosis Control Programme, Mbabane, Swaziland. Fax: (+268) 24047199.  
e-mail: nompumelelon@urc-sa.com

**Background and challenges to implementation:** Tuberculosis (TB) screening is conducted in over 130 health facilities in Swaziland as one of the active TB case finding strategies. An average of 20 cough officers are deployed in each of the TB decentralized service points and use a highly sensitive TB screening tool which was introduced in 2010 to identify TB presumptive cases. The tool asks questions on major symptoms including; cough of any duration, fever, night sweats and weight loss and if a patient answers yes on any of these, they are documented as presumptive TB cases and investigated.

**Intervention or response:** A retrospective study of TB screening reports from all the implementing health facilities was conducted. The reports were reviewed by following the cascade of events from TB screening to diagnosis and eventually initiation of treatment. The findings were compared with annual TB case notifications documented in the National TB Control Programme's (NTCP) annual reports for the years 2010 to 2013 and the respective World Health Organization estimates for annual TB case notifications in Swaziland.

**Results and lessons learnt:** An increase in patients screened for TB was observed in health facilities countrywide from 29,634 in 2010; 175,787 in 2011; and 294,611 in 2012. The 2012 results indicate that of the total screened, 16,140 (6%) screened positive, 10 % (1,671/16,140) were diagnosed with TB disease and 86%

(1,428/1,671) were initiated into TB treatment. Despite the increase in patients screened annually, the National TB Control Program (NTCP) annual reports show an overall decline in annual notifications of TB cases of all forms from (11565 TB cases) in 2010; (9180 TB cases) 2011; (7741 TB cases) 2012 and (6565 TB cases) in 2013.

**Conclusions and key recommendations:** The high volume of patients turning up for consumption of health services compared to a small number of deployed cough officers resulted to the poor admission of the TB screening tool. There is a need for retraining of cough officers to effectively utilize the TB screening tool and also inclusion of other healthcare workers to improve human resource.

### **PD-657-30 A global study of IFN- $\gamma$ release assay (IGRA) reversions in low-risk health-care workers: which cut offs minimise reversions and predict stable results?**

W Thanassi,<sup>1,2</sup> A Noda,<sup>2</sup> J Yesavage,<sup>1,2</sup> D Marder,<sup>3</sup> D Tripodi,<sup>4</sup> J Torres-Costa,<sup>5</sup> A Nienhaus.<sup>6</sup> <sup>1</sup>Medicine, MIRECC, or WRIISC, Veterans Administration Health Care System, Palo Alto, CA, <sup>2</sup>Emergency Medicine or Psychiatry, Stanford University Hospital and Medical Center, Stanford, CA, <sup>3</sup>University Health Services, University of Illinois, Chicago, IL, USA; <sup>4</sup>Occupational Medicine, Nantes University Hospital, Nantes, France; <sup>5</sup>Pneumology, Hospital CUF Porto, Lisbon, Portugal; <sup>6</sup>Competence Centre for Epidemiology and Health Service Research for Healthcare Workers (CVcare), University Medical Centre Hamburg-Eppendorf (UKE), Hamburg, Germany. e-mail: wendy.thanassi@gmail.com

**Background:** Tuberculosis (TB) is recognized as an occupational disease in healthcare workers (HCW) and serial TB screening is performed on HCWs even in low risk settings. The IGRA can replace the tuberculin skin test for these screenings especially in populations with BCG vaccination. However, interpretation of IGRA results of HCW in low risk settings remains challenging. Despite improved specificity, reversion rates for IGRAs in HCW is high and not all HCW with a single positive IGRA might profit from chemoprevention. Therefore it is useful to identify a borderline or retesting zone for IGRA interpretation which minimizes the number of reversions and maximizes the number of stable positive results. In a global multi-center study comprising HCW from the United States, France, Germany and Portugal we used receiver operation characteristic analysis (ROC) for deriving such retesting zones or new cut-offs.

**Methods:** Serial test results from 33,578 HCW from 4 countries were included. In 1094 US HCW and 628 HCW from France, Germany and Portugal had a positive QuantiFERON Gold in Tube (QFT) (INF- $\gamma$ >0.35 IU/ml) and a 2nd QFT was run. Average time between first and second QFT was 13 months. The second QFT was done either due to known new contact to a patient with TB or for general risk assessment in Europe, and as part of mandatory serial screening in the US.

**Results:** Reversion in QFT occurred in 201 of 628 European HCW (32%) and in 602 of 1094 US HCW

(55%). In the US, 3 distinct geographic regions all had ROC-derived reversion zones at <1.1 IU/ml. In Germany 28 of 74 (38%), in France 53 of 142 (37%) and in Portugal 120 of 412 HCWs (29%) reverted. For both Germany and France the ROC identifies the same cut-off (<0.81 IU/ml,  $p$ <0.001). In Portugal the incidence of TB is higher than in France and Germany and the cut-off found by ROC was lower at <0.73 IU/ml ( $p$ <0.001). For a combined European population the cut-off for QFT proposed by employing ROC is <0.79 IU/ml ( $p$ <0.001) (See Table 1).

**Conclusion:** Using a higher cut-off, or employing a retesting zone, above the current 0.35 IU/ml will reduce the number of reversions in HCW. The optimal cut-off seems to depend on the background risk for TB infection as the cut-off proposed is lower in Portugal than in Germany and France, which are in turn lower than for the US. As the TB incidence in the US is lower than in Germany or France this further corroborates the hypothesis that the cut-off of the QFT in serial testing of HCW should be chosen depending on the background risk for TB infection.

### **PD-658-30 Analysis of and lessons from the UK's tuberculosis pre-entry screening programme: January 2006-December 2013**

M Muzyamba,<sup>1</sup> R Aldridge,<sup>1,2</sup> P Dhavan,<sup>3</sup> D Zenner.<sup>1,2</sup>

<sup>1</sup>Centre for Infectious Disease Surveillance and Control, Public Health England, London, <sup>2</sup>Research Department of Infection and Population Health, University College London, London, UK; <sup>3</sup>IOM Office, Manila, International Office for Migration, Manila, Philippines. Fax: (+44) 208 327 6112. e-mail: morris.muzyamba@phe.gov.uk

**Background:** The incidence of tuberculosis (TB) in the UK (UK) has been increasing over the last decade and the majority (73%) of UK TB cases are diagnosed amongst individuals, who were born in high incidence countries. The UK has a CXR-based pre-entry TB screening programme for long-term migrants from high incidence countries ( $\geq 40$  cases/100,000). The aim of this study was to analyse the demographic distribution and case yield amongst participants of this screening scheme.

**Methods:** We used data from a global web-based system, recording details on all screening participants accessing clinics from the International Organisation of Migration between 2006 and 2013. Descriptive analysis and logistic regression was carried out using Stata 13.

**Results:** A total of 709,933 applicants were screened. About 64.5% were male and the median age was 24 years. Almost all applicants (98.7%) had chest X-Rays (CXR). A total of 32,832 applicants (4.6%) had CXR lesions consistent with TB and submitted sputum for testing. Of these, 585 were positive for TB. In addition there were 48 were clinically diagnosed with TB. In total of 633 cases were found (yield 89.2 per 100,000). TB yields have increased significantly over time (from 44.8 to 166.3 per 100,000 between 2006 and 2013, Chi square test for trend  $p$ <0.001). Logistic regression analysis indicated that risk factors for being screened positive for TB included age group, sex (female 1.5 more

likely than males), screening year and having a family TB contact. A TB family contact was the strongest risk factor (OR 16.27, 95% CI 10.79-24.54) and its effects remained even after adjusting for confounders (OR 13.96, 95% CI 9.23-21.11).

**Conclusion:** The majority of UK-bound migrants were from the Indian subcontinent reflecting both the timeline for clinic establishment and migration trends. Whilst the overall yield is lower than expected, more detailed analysis shows that yields vary significantly between countries, age, visa type and year of screening and family TB contact. We present the first results of the UK pre-entry screening programme demonstrating an insight into which groups have higher yields than others, and demonstrating that screening is feasible and yields are increasing as programme improves.

Table1: Risk factors for active pulmonary TB at pre-entry screening

Factor	Crude Odds Ratio	95% CI	P-value	Adjusted Odds ratio	95% CI	P-value
<b>Age group</b>						
0-15	1.00	-	-	1.00	-	-
16-35	2.41	1.33-4.38	0.003	2.88	1.63-5.43	<0.001
35-64	3.73	1.98-7.03	<0.001	4.43	2.25-8.91	<0.001
≥65	18.37	9.13-36.98	<0.001	17.49	8.88-35.11	<0.001
<b>Sex</b>						
Female	1.00	-	-	1.00	-	-
Male	1.59	1.28-1.75	<0.001	1.37	1.16-1.60	<0.001
<b>Screening year</b>						
2006	0.49	0.26-0.88	0.012	0.47	0.27-0.81	0.007
2007	0.71	0.52-0.96	0.025	0.70	0.51-0.95	0.021
2008	0.83	0.63-1.10	0.194	0.81	0.61-1.07	0.129
2009	1.00	-	-	1.00	-	-
2010	0.83	0.63-1.10	0.220	0.81	0.61-1.07	0.145
2011	0.98	0.74-1.29	0.885	0.95	0.72-1.25	0.715
2012	1.18	0.88-1.59	0.278	1.08	0.80-1.47	0.595
2013	1.83	1.42-2.36	<0.001	1.64	1.26-2.14	<0.001
<b>Family TB contact</b>						
No	1.00	-	-	1.000	-	-
Yes	16.27	10.79-24.54	<0.001	13.958	9.23-21.11	<0.001

## PD-659-30 Who should be investigated for TB among people attending for HIV care?

Y Hanifa,<sup>1</sup> K Fielding,<sup>2</sup> S Jawad,<sup>2</sup> V Chihota,<sup>3,4</sup> a Karstaedt,<sup>5,6</sup> L Adonis,<sup>7</sup> G Churchyard,<sup>1,3,4</sup> A Grant.<sup>1</sup>

<sup>1</sup>Clinical Research, and <sup>2</sup>Infectious Disease Epidemiology, London School of Hygiene & Tropical Medicine, London, UK;

<sup>3</sup>Research - Epidemiology, The Aurum Institute, Johannesburg, <sup>4</sup>School of Public Health, University of the Witwatersrand, Johannesburg, <sup>5</sup>Medicine, Division of Infectious Diseases, Chris Hani Baragwanath Hospital, Johannesburg, <sup>6</sup>Clinical Medicine, University of the Witwatersrand, Johannesburg, <sup>7</sup>Medicine, Mamelodi Hospital, Tshwane, South Africa.

e-mail: yhanifa@hotmail.com

**Background:** WHO recommends screening people with HIV for TB at every clinical encounter using a tool comprising any cough, weight loss, fever or night sweats, with further evaluation of those screening positive. In the context of the XPHACTOR study, which is evaluating a novel algorithm to determine priority for TB investigation, we assessed risk factors for undiagnosed active TB in adults enrolled in HIV care in South Africa.

**Methods:** A systematic sample of adult clinic attendees were screened for TB using the WHO tool and Xpert was requested if high priority for TB according to XPHACTOR algorithm (any of: cough, BMI<18.5, CD4<100, weight loss ≥10%). All were reviewed monthly, with reinvestigation if indicated, to 3 months when sputum and blood were taken from all for TB culture. We defined

TB cases as: Xpert+ or culture+ for *M. tuberculosis* at any point.

**Results:** Among 1889 participants, 1491 (79%) were on antiretroviral therapy (ART) at enrolment, of whom 70% were female, median age 42 years, median CD4 count 421 cells/mm<sup>3</sup>, and median duration on ART 50 months. Among 398 pre-ART participants, 71% were female; median age 35 years, median CD4 453 cells/mm<sup>3</sup> and median duration since HIV diagnosis 17 months. The prevalence of TB in on-ART and pre-ART groups, respectively, was 49/1491 (3.3%, 95% confidence interval [CI] 2.4%, 4.3%) and 18/398 (4.5%, 95% CI 2.7%, 7.1%). In multivariable analysis (Table) prevalent TB was associated with CD4<100 cells/mm<sup>3</sup> (aOR 4.7, 95% CI 2.5–8.9), BMI <18.5kg/m<sup>2</sup> (aOR 2.5, 95% CI 1.2–5.3), WHO tool positive (aOR 3.8, 95% CI 2.1–6.8), history of chronic obstructive pulmonary disease (aOR 5.3, 95% CI 1.6–17.4), and previous isoniazid preventive therapy (aOR 0.23, 95% CI 0.05-0.98) which was protective. Among participants with CD4<100, those pre-ART had a much greater risk of TB than those on-ART, OR 31.96 (95% CI 9.6–106.5) vs. OR 3.37 (95% CI 1.4–7.8).

**Conclusions:** Individuals enrolled in HIV care with CD4<100 cells/mm<sup>3</sup>, particularly those who are ART-naïve with CD4<100; or those who are underweight (BMI<18.5kg/m<sup>2</sup>) require investigation for TB irrespective of WHO tool screen result. Although smoking is an established risk factor for TB, the association we describe between COPD and risk of TB is novel in this setting.

Table: Factors associated with prevalent TB among adult clinic attendees with HIV in South Africa

Characteristic	Total (N=1889) n (%)	Active TB prevalence (n=67/1889) n (%)	Unadjusted OR (95% CI)	Adjusted OR (95% CI) <sup>1</sup> (n=1715)
Participant category				
On-ART	1491 (78.9)	49/1491 (3.3)	0.72 (0.41-1.25)	1
Pre-ART	398 (21.1)	18/398 (4.5)		
WHO screening tool (N=1788)				
Positive <sup>2</sup>	623 (34.8)	47/623 (7.5)	5.19 (2.99-9.03)	3.81 (2.14-6.76)
Negative	1165 (65.2)	18/1165 (1.6)		
Sex				
Female	1325 (70.1)	39/1325 (2.9)	0.58 (0.35-0.95)	0.78 (0.44-1.38)
Male	561 (29.9)	28/561 (5.0)		
Age category, years				
≥35	1407 (74.5)	49/1407 (3.5)	0.93 (0.54-1.61)	1
<35	482 (25.5)	18/482 (3.7)		
Socioeconomic status <sup>3</sup> (N=1801)				
High	617 (34.3)	22/617 (3.6)	1.10 (0.59-2.03)	1
Medium	571 (31.7)	20/571 (3.5)	1.08 (0.57-2.02)	
Low	613 (34.0)	20/613 (3.3)		
History of mine work (N=1839)				
Yes	40 (2.2)	4/40 (10)	3.17 (1.09-9.17)	2.83 (0.84-9.50)
No	1799 (97.8)	61/1799 (3.4)		
Smoking status (pack years)				
≥30	19 (1.0)	3/19 (15.8)	5.31 (1.51-18.69)	1.88 (0.45-7.77)
Never or <30	1817 (99.0)	62/1817 (3.4)		
Alcohol status <sup>4</sup> (N=1825)				
≥ twice per month	172 (9.4)	10/172 (5.8)	1.83 (0.91-3.66)	1
≤ once per month	1653 (90.6)	54/1653 (3.3)		
History of TB (N=1775)				
Yes	600 (33.8)	20/600 (3.3)	0.86 (0.51-1.48)	1
No	1175 (66.2)	45/1175 (3.8)		
Reported history of COPD (N=1842)				
Yes	23 (1.3)	4/23 (17.4)	6.07 (2.0-18.37)	5.34 (1.64-17.38)
No	1819 (98.9)	61/1819 (3.4)		
Duration since HIV diagnosed, years (N=1752)				
≥1	1501 (85.7)	48/1501 (3.2)	0.56 (0.30-1.03)	1
<1	251 (14.3)	14/251 (5.6)		
History of IPT (N=1779)				
Yes	242 (13.6)	2/242 (0.8)	0.19 (0.05-0.80)	0.23 (0.05-0.98)
No / don't know	1537 (86.4)	63/1537 (4.1)		
History of CPT (N=1779)				
Yes	1289 (73.0)	42/1289 (3.2)	0.66 (0.39-1.12)	1
No / don't know	480 (27.0)	23/480 (4.8)		
BMI at enrolment kg/m <sup>2</sup> (N=1767)				
<18.5	97 (5.5)	11/97 (11.3)	3.83 (1.93-7.58)	2.53 (1.20-5.34)
≥18.5	1670 (94.5)	54/1670 (3.2)		
CD4 at enrolment cells/mm <sup>3</sup> (N=1773)				
<100	97 (5.5)	17/97 (17.5)	7.21 (3.97-13.09)	4.71 (2.50-8.89)
≥100	1676 (94.5)	48/1676 (2.9)		

<sup>1</sup> adjusted for all variables shown

<sup>2</sup> defined as self-report of any of cough, fever, night sweats or unintentional weight loss

<sup>3</sup> Socioeconomic position was defined using a principal component analysis with five determinants of wealth and categorised into low, medium and high positions using the 33% and 86% percentile.

<sup>4</sup> defined by frequency of alcohol consumption in previous 1 year

BMI = Body mass index; COPD = Chronic obstructive pulmonary disease; CPT = Cotrimoxazole preventive therapy; IPT = Isoniazid Preventive Therapy



## 15. MOLECULAR EPIDEMIOLOGY: FROM BEIJING TO BRAZIL AND POINTS IN BETWEEN

### PD-660-30 Molecular characterisation of *Mycobacterium tuberculosis* in Benishangul Gumuz region, western Ethiopia

K Tulu,<sup>1</sup> A Shana,<sup>2</sup> G Chimdi,<sup>3</sup> H Marru.<sup>4</sup> <sup>1</sup>Microbiology, Armauer Hansen Research Institute, Addis Ababa, <sup>2</sup>Tropical and Infectious Disease, Addis Ababa University, Addis Ababa, <sup>3</sup>Microbiology, Addis Ababa University, Addis Ababa, <sup>4</sup>Medical and Health Science, Wollega University, Nekemte, Ethiopia. Fax: (+251) 0576617980. e-mail: haimadis2012@gmail.com

**Background:** The knowledge of genetic diversity of *Mycobacterium tuberculosis* in certain geographic region is needed for a better understanding of epidemiology of TB and could have implications for development of new diagnostics, drugs, and vaccines. The aim of this study was to provide preliminary information on the strains of *M. tuberculosis* circulating in Benishangul Gumuz Region.

**Design/Methods:** Cross-sectional study was conducted in order to generate a preliminary data on the genetic diversity of *Mycobacterium tuberculosis* between November 2012 and April, 2013. *M. tuberculosis* isolates were characterized using region of difference 9 (RD9) and spoligotyping. The patterns of strains identified by spoligotyping were compared with the patterns registered in the SpolDB4 database of the Pasteur Institute.

**Results:** From a total of 53 smear positive samples, 34 (64.15%) were culture positive, of which, 33 samples were confirmed to be *M. tuberculosis* by RD9 deletion typing. Further characterization of these 33 isolates using spoligotyping lead to the identification of 24 individual spoligotype patterns, among which, 18 were unique while the remaining six were found in clusters containing two to four isolates. Of the 24 patterns identified by the present study, only six patterns were registered in SpolDB4 international database, while 18 patterns were not previously registered in the database. Grouping of the 33 isolates into the lineages showed that 19 (57.6%) isolates were members of Euro-American, 6 (18.2%) isolates were Indo-Oceanic while the remaining 8 (24.2%) could not be categorized to the presently known lineages.

**Conclusion:** Characterization of the *M. tuberculosis* strains showed the identification of new strains and lineages which could not match with the existing strains and lineages suggesting the localization of these strains and lineages in this Region. Hence, further research is required to identify and document the strains and lineages circulating in the Region.

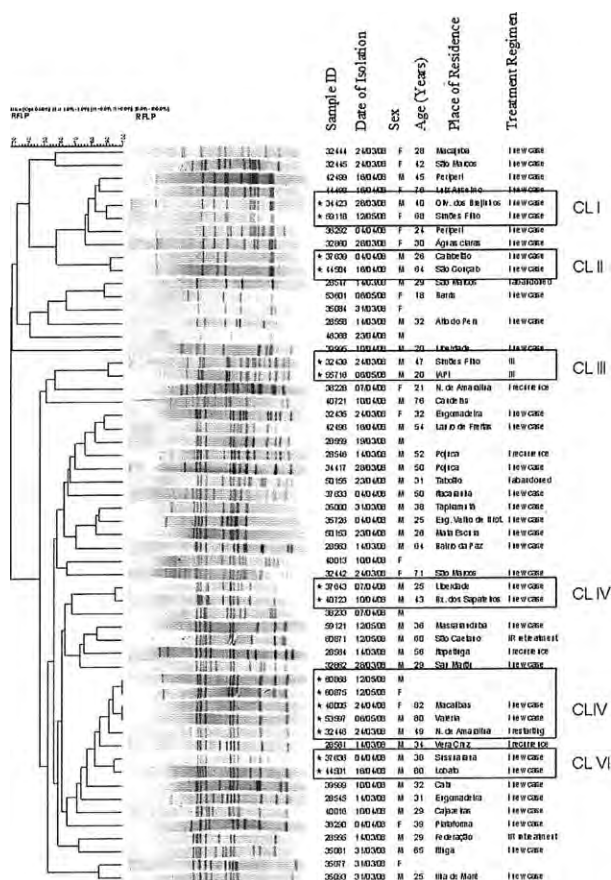
### PD-661-30 Genetic diversity of *Mycobacterium tuberculosis* strains in salvador, Brazil: needs for further research and implications for regional policy

A Silva,<sup>1</sup> E Mota,<sup>2</sup> S Pereira,<sup>2</sup> M Reis,<sup>1</sup> J Pedreira.<sup>1</sup>

<sup>1</sup>Laboratório de Biologia e Patologia Molecular, Centro de Pesquisa Gonçalo Muniz, Fundação Oswaldo Cruz, Salvador, BA, <sup>2</sup>Instituto de Saúde Coletiva, Universidade Federal da Bahia, Salvador, BA, Brazil. Fax: (+71) 31762289. e-mail: aidanasci@hotmail.com

**Background:** Little is known about transmission dynamics and genetic diversity of tuberculosis (TB) in Salvador, Bahia State, in which the incidence of this disease is high. The aim of the present study was to describe the genetic population structure of *M. tuberculosis* circulating in Salvador.

**Design/Methods:** Molecular typing of *M. tuberculosis* isolates is a efficient tool for studying the dynamics of TB transmission. The current standardized strain typing method is based on Southern blot analysis of the restriction fragment length polymorphisms (RFLP) associated with the insertion sequence IS6110, in accordance with the standardized protocol of van Embden et al (1993). The genetic profile of each strain was analyzed and visualized with GelCompar II version 4.0 (Applied Maths, Kortrijk, Belgium) using *M. tuberculosis* 14323 as the reference strain. A total of 56 confirmed cases of pulmonary tuberculosis, identified between March and June 2011, were analyzed using restriction fragment length polymorphism (IS6110-RFLP).



**Results:** The study population was characterized by a predominance of males (71.43%) over 30 years of age (68.75%). Forty-one isolates were found to belong to a single pattern (73.2%), while 15 (26.7%) were found in group patterns, forming six clusters.

**Conclusion:** In recent research in the Brasil, and as the first study conducted in Bahia, was observed higher level of diversity much more suggestive of endogenous reactivation than recent transmission among TB patients in referral hospital of the Salvador City. And the approach can support public health policies in the definition of preventive and control TB program in health services, the dynamics of disease transmission in high risk subgroups, even when performed at the institutional level.

### PD-662-30 Genetic diversity of MDR-TB in Nepal

B Maharjan,<sup>1</sup> B Shrestha,<sup>1</sup> P Rajendra,<sup>2</sup> G Mezzabotta,<sup>3</sup> H Hoffmann,<sup>4</sup> A. Beneke,<sup>4</sup> C Nakajima,<sup>5</sup> Y Suzuki.<sup>5</sup>

<sup>1</sup>Laboratory, German Nepal TB Project (GENETUP), Kalimati Kathmandu, <sup>2</sup>Administration, National Tuberculosis Center, Thimi Bhaktapur, <sup>3</sup>Administration, World Health Organization, Pulchok, Nepal; <sup>4</sup>Laboratory, KuratoriumTuberkulose in der Welt e.V. Germany, München-Gauting, Germany; <sup>5</sup>Laboratory, Hokkaido University, Research Center for Zoonosis Control, Sapporo, Japan. Fax: (+977) 01-270019.

e-mail: bthagwan.maharjan@yahoo.com

**Background:** Multi-drug resistant tuberculosis (MDR-TB) is a major threat for successful TB control in Nepal. Genotype of MDR-TB is important for suspected outbreak and tracing transmission chain. Nonetheless, the genetic diversity of MDR-TB strains has so far not been systematically studied in Nepal.

**Design/Methods:** A total of 601 MDR-TB identified isolates of 12 main cities from five development region of Nepal (April 2008 to March 2013) were selected. DNA had been extracted following the instructions provided in GenoType MTB DR plus manual (Hain Lifescience, Germany). An in house made Japanese array spoligotype was used to determine the spoligotypes of the isolates to identify the respective genotypes by comparing the patterns with the international spolDB4.0 database.

**Results:** Out of 601 MDR-TB isolates, 58 distinct spoligotype patterns were obtained. Among them, 541 (90%) were found shared type and 60 (10%) were orphan. Of those 601 isolates, 294 (48.9%), 182 (30.3%), 90 (15%) and 35(5.8%) belonged to in lineage 2 (East Asian includes Beijing strain), lineage 3 (East-African Indian), lineage 4 (Euro American) and lineage 1 (Indo-Oceanic) respectively. Regionally, lineage 2 Beijing genotype which is known as more pathogenic, more virulent and develops drug resistant rapidly was 69% in Eastern Region, 54% in Central Region, 46% in Western region, 30% in Mid-Western Region and 24% in Far Western Region.

**Conclusion:** Beijing genotype is the predominant (49%) among MDR-TB in Nepal. The result also shows a clear cut variance in prevalence among Eastern, Central to Western Region in Nepal. The high rate of Beijing strain

in Eastern and Central Regions of Nepal is unknown and needs further investigation.



### PD-663-30 *Mycobacterium tuberculosis* isolated from pulmonary TB patients with previous treatment history in Makassar, Indonesia

S Wahyuni,<sup>1,2</sup> H Saleh,<sup>3</sup> M Massi,<sup>4,5</sup> S Phyu,<sup>6</sup> I Yusuf,<sup>7</sup> P Bifani.<sup>8</sup>

<sup>1</sup>Epidemiology, Novartis Institute of Tropical Diseases-Hasanuddin Clinical Research (NHCR), Makassar, <sup>2</sup>Parasitology, Faculty of Medicine, Hasanuddin University, Makassar, <sup>3</sup>Molecular Biology, Novartis Institute of Tropical Diseases-Hasanuddin Clinical Research (NHCR), Makassar, <sup>4</sup>TB unit, Novartis Institute of Tropical Diseases-Hasanuddin Clinical Research (NHCR), Makassar, <sup>5</sup>Microbiology, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia; <sup>6</sup>Bacteriology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore; <sup>7</sup>Physiology, Faculty of Medicine, Hasanuddin University, Makassar, Indonesia; <sup>8</sup>TB unit, Novartis Institute for Tropical Diseases, Singapore, Singapore. Fax: (+62) 411586297. e-mail: wahyunim@indosat.net.id

**Background:** The rising numbers of multi-drug resistant (MDR) TB and extensively drug resistant (XDR) TB threaten TB control strategies and management. Our previous study on pulmonary TB patients in Makassar, Indonesia revealed more than 30% of the cases had a history of anti-tuberculosis therapy; while 19% of them were infected with multi-drug resistant (MDR) strains. Here we set-out to determine the phenotypic and genotypic characteristics of the isolates in order to identify the factors responsible for this increase.

**Design/Methods:** Previously treated TB patient from collaborating hospitals in Makassar were enrolled in this study. Information on the history of previous treatment was recorded and sputum samples were collected for smear and culture analysis. Culture positive isolates were tested for drug susceptibility and for DNA sequence analysis.

**Results:** Forty four percent (451/1035) of sputum samples collected from patients were culture positive by either Lowenstein Jensen- or liquid-culture media or both. Drug susceptibility testing (DST) was performed on

401 isolates, 50/451 were discarded due to contamination in the sub-culture. DST using Mycobacteria Growth Indicator Tube (MGIT) revealed 40.9% (164/401) and 24% (98/401) Mtb isolates were resistant to at least one first-line anti TB drugs and to both INH and Rifampicin (MDR-TB), respectively. Out of 98 MDR-TB isolates, 2% (2/98) were XDR-TB (also resistant to ofloxacin and kanamycin/amikacin). DNA sequence analysis of *rpoB* and *katG* genes indicated substitutions of S531L and S315T are being predominant mutations for RIF and INH resistance, respectively

**Conclusion:** Extensive drug resistant TB (XDR-TB) is now present in Makassar. The increased number of MDR-TB from 19% (2008) to 25% (2012) among previously treated TB patients is alarming. There is an urgent need to determine whether this increase is associated with treatment failure, reactivation, transmission or emergence of new drug-resistant cases. Improvement of TB management needs to be prioritized.

#### PD-664-30 Whole genome sequencing of *Mycobacterium tuberculosis* strains obtained from patients with pulmonary and extrapulmonary tuberculosis

E Chernyaeva,<sup>1,2</sup> M Rotkevich,<sup>1</sup> V Zhuravlev,<sup>2</sup> N Solovieva,<sup>2</sup> M Shulgina,<sup>2</sup> A Lapidus,<sup>1,3</sup> SJ O'Brien.<sup>1</sup>

<sup>1</sup>Dobzhansky Center for Genome Bioinformatics, St. Petersburg State University, St. Petersburg, <sup>2</sup>St. Petersburg Research Institute of Phthisiopulmonology, St. Petersburg, <sup>3</sup>St. Petersburg Academic University, St. Petersburg, Russian Federation. e-mail: echernya@gmail.com

**Background:** The aim of our work is to study the genetic diversity of *M. tuberculosis* strains, collected in different regions of the Russian Federation from patients with pulmonary and extrapulmonary tuberculosis (TB).

**Design/Methods:** Genomic DNA of 30 *M. tuberculosis* strains was sequenced using Illumina MiSeq platform. Sequencing data for *M. tuberculosis* sequenced genomes were deposited in the NCBI Sequence Read Archive under accession number PRJNA218508. *Mycobacterium tuberculosis* H37Rv reference genome (NC\_000962.3) was used for SNP and Indel calling using bowtie2 and samtools packages. R-package and Fisher's exact test was used for statistical analysis.

**Results:** Studied *M. tuberculosis* isolates were collected in St. Petersburg, Leningrad Region, Volgograd, Kalmykiya, Buryatia, Arkhangelsk Oblast, Chelyabinsk Oblast, Kaliningrad Oblast, Novgorod Oblast, Nizhniy Novgorod Oblast, Ulyanovsk Oblast and Zabaykalsky Krai. Information about drug susceptibility, diagnosis and HIV-status of patients was collected for genome association analysis. Twelve strains were isolated from patients with extrapulmonary TB, 15 from patients with pulmonary TB and three from patients with both forms of the disease. Genetic clades were identified based on SNP analysis. We identified 5472 SNPs and 657 Indels in protein-coding regions of sequenced strains. Single nucleotide mutations were compared in different groups of bacteria. Following nonsynonymous mutations were associated with extrapulmonary TB: PEPGRS9 T320A

( $p=0.008$ ) and T445A ( $p=0.008$ ); mce3F A396E ( $p=0.02$ ); PEPGRS6 D227G ( $p=0.04$ ); PEPGRS56 I306T ( $p=0.04$ ); lppB G47D ( $p=0.007$ ). Mutation PEPGRS55 N396D ( $p=0.02$ ) is associated with pulmonary TB.

**Results** are represented in Genome-wide *Mycobacterium tuberculosis* Variation (GMTV) database, (<http://mtb.dobzhanskycenter.org>) that catalogues genome variations of *M. tuberculosis* strains collected across Russia. **Conclusion:** Obtained data should be proved by further large-scale study. Identified mutations might be used as a prognostic marker for TB outcome.

#### PD-665-30 TB lineages and association with patients' demography and co-morbidities in Ghana

D Yeboah-Manu,<sup>1</sup> A Asante-Poku,<sup>1</sup> ID Otchere,<sup>1</sup> S Osei-Wusu,<sup>1</sup> A Forson,<sup>2</sup> H Ganiyu,<sup>1</sup> A Baddoo,<sup>2</sup> S Gagneux.<sup>3</sup> <sup>1</sup>Bacteriology, Noguchi Memorial Institute for Medical Research, University of Ghana, Legon, <sup>2</sup>Chest Clinic, College of Health Sciences, University of Ghana, Korle-Bu, Ghana; <sup>3</sup>Tuberculosis Unit, Swiss Tropical and Public Health Institute, Basel, Switzerland. Fax: (+233) 3021 502 182. e-mail: dyeboah-manu@noguchi.mimcom.org

**Background:** *Mycobacterium africanum* (MafriC) has been identified as an important TB pathogen in West-Africa. The objective of our work was to use molecular methods to study the prevalence in Ghana and interactions with forces such as pathogen drug resistance, and host factors including demography, co-morbidities: HIV and diabetes.

**Design/Methods:** We collected samples from sputum smear positive cases and obtained isolates were characterized by large sequence polymorphism (LSP), spoligotyping and Single Nucleotide Polymorphic (SNP) markers specific for the six published MTBC lineages. We also collected data on patients' demography, HIV and diabetic status. The association between isolate lineage and patients' demographic characteristics, comorbidity was determined using multivariate analysis.

**Results:** Among 613 retrospective isolates collected between 2007 and 2011 we identified 508 (80.25%) as *Mycobacterium tuberculosis sensu stricto* (MTBss) with the remaining 105 classified as *M. africanum* (MafriC) subdivided into, Lineage 5 (N= 86, 82% and Lineage 6 (N=19, 18%). Apart from Cameroon sub lineage (N=313, 61.6%), spoligotyping identified 10 additional sub-lineages among the MTBss. Among the patients' demographic parameters analyzed we found individuals of Ewe ethnicity more likely to present disease caused by MafriC than MTBss. ( $P < 0.01$ ). In an on-going prospective study, out of the 1140 (N= 849, 74.47%) characterized isolates are L4; Lineage 6 (N=105, 9.21%), Lineage 5 (N=139, 12.19%), Lineage 2 (36, 3.16%), Lineage 1 (N=15, 1.31%) and Lineage 3 (N=12, 1.05%) and 6 (0.50%) *M. bovis* with 16% (N=160) co-infected with HIV. There was no difference in the rate of MTB (N=753, 16.33%) patients co-infected with HIV and those infected with *M. africanum* (N=246, 15.04%) ( $p=0.0559$ ). However,



Lineage 5 (N=139, 19.42%) was significantly associated with HIV compared to Lineage 6 (N=105, 9.52%) ( $p=0.033$ ). In terms of gender, females were significantly co infected than males [OR = 0.56; 95% CI: 0.51-0.94;  $P = 0.02$ ]. Of the 413 cases screened for diabetes, fifty (12%) were co infected were diabetes. MTB was significantly associated with TB/DM (N=30, 73%) and males than *M. africanum* (N=3, 7%) and females ( $P<0.000$ ).

**Conclusion:** Our findings confirm the importance of *M. africanum* in Ghana, and also co-morbidity of TB with HIV and diabetes.

#### PD-666-30 Beijing and H4/Ural genotypes of *M. tuberculosis* are predominating among M-/XDR-TB patients in Moldova

V Crudu,<sup>1</sup> E Romancenco,<sup>2</sup> E Noroc,<sup>2</sup> S Alexandru,<sup>2</sup> S Niemann,<sup>3</sup> C Lange,<sup>3</sup> R Garfein,<sup>4</sup> A Catanzaro.<sup>4</sup>

<sup>1</sup>Tuberculosis, Center for Public Health and Studies, Chisinau,

<sup>2</sup>Microbiology, Phthisiopneumology Institute, Chisinau,

Moldova; <sup>3</sup>Microbiology, Research Center Borstel, Borstel, Germany; <sup>4</sup>GCDD, University of California, San-Diego, CA, USA. Fax: (+373) 22- 226387.

e-mail: valeriu.crudu@gmail.com

**Background:** Beijing genotype strains of *Mycobacterium tuberculosis* (Mtb) are associated with drug resistance, particularly multidrug resistance and their prevalence is increasing worldwide. However, other genotypes of Mtb also seem to be significantly associated with multidrug (MDR-TB) and extensively resistant tuberculosis (XDR-TB) cases. The objective of this study was to determine the genetic diversity of Mtb related to drug sensitive and drug resistant strains among TB patients in Moldova, a high burden country for MDR-TB.

**Design/Methods:** A total of 222 Mtb strains isolated over a period of more than four years were genotyped, using IS6110-RFLP, spoligotyping and MIRU-VNTRs. 74 of isolated were sensitive to first line drugs and 148 samples were resistant to at least isoniazid and rifampin (MDR-TB or XDR-TB).

**Results:** Among the 74 sensitive strains, the genotypes identified were: 29.7% (n=22) Beijing, 17.6% (n=13) LAM, 16.2% (n=12) H4/Ural, 8.1% (n=6) Haarlem, T1&T3 6.8% (n=5), and types X, H1, and Cameroon were 1.4% (n=1) each. Thirteen (17.6%) strains could not be classified based on their spoligotype pattern and were labeled as "indeterminate" (was named "Moldova like H37Rv"). Among 148 MDR-TB strains, the genotypes identified were: H4/Ural - 50.7% (n=75), Beijing - 43.2% (n=64), LAM - 1.4% (n=2), X - 0.7% (n=1) and "indeterminate" - 4.1% (n=6). From 148 MDR-TB strains, 71 strains were also resistant to second line drugs (XDRTB), among which 49.0% (n=35) were Beijing and 35% (n=25) were H4/Ural genotypes

**Conclusion:** Beijing and H4/Ural genotypes of Mtb are predominating among MDRTB patients and significantly are associated with XDRTB ( $P<0.001$ ).

#### PD-667-30 A six-year spoligotyping analysis of *Mycobacterium tuberculosis* (MTB) isolated from a multi-ethnic population in Brescia, northern Italy

A C Carvalho,<sup>1</sup> F Bernoni D'aversa,<sup>2</sup> A Matteelli,<sup>2</sup> G Pinsi,<sup>3</sup> TM Silva,<sup>4</sup> F Castelli,<sup>2</sup> ACB Santos,<sup>4</sup> MH Saad.<sup>4</sup>

<sup>1</sup>Laboratory of Innovations in Therapies, Education and Bioproducts (LITEB), Oswaldo Cruz Institute (IOC), FioCruz, Rio de Janeiro, RJ, Brazil; <sup>2</sup>Clinic of Infectious and Tropical

Diseases, Università degli Studi di Brescia, Brescia, <sup>3</sup>UO Microbiology and Virology, Spedali Civili di Brescia, Brescia, Italy; <sup>4</sup>Laboratory of Cellular Microbiology, Oswaldo Cruz

Institute (IOC), FioCruz, Rio de Janeiro, RJ, Brazil. Fax: (+55) 21 2562 14 32. e-mail: a.carvalho@libero.it

**Background:** Spoligotyping remains a highly informative genotyping method to the identification of family-specific MTB signatures. Immigrants represent 19% of Brescia's population and account for about 70% of TB cases diagnosed in the city.

**Design/Methods:** Objective: to determine the MTB structure population isolated from multi-ethnic TB patients from the Clinic of Infectious and Tropical Diseases of Brescia.

**Methods:** MTB strains isolated from patients treated for TB from 2007 to 2013 were included in the analysis. Samples were cultured in liquid medium and tested for drug susceptibility to first-line drugs. Thereafter, DNA was extracted and genotyped by spoligotyping.

**Results:** 402 strains from patients with complete sociodemographic information were included in the analysis. Fifty-nine percent were male, the median age was 36 years (IQR 26 – 47) and 76% were foreign-born. Forty-one percent had pulmonary TB disease, 32% extrapulmonary and 27% pulmonary plus extrapulmonary disease. Among foreign-born, 47% were from Indian subcontinent, 23% were from Sub-Saharan Africa and 15% from Eastern Europe. The most represented clades were LAM (25%), T (22%), CAS (17%) and H (14%); 10% were classified as Orphans and 11% had no identified signature. Beijing family was identified in 12 patients (3%). Resistance to at least one drug was detected in 15% of cases (56/361), 21% of them were MDR (1 of Beijing family), representing 3% of total. LAM and H clades were inversely associated with being foreign born (OR= 0.57; 95% CI 0.33 – 0.97 and OR= 0.37; 95% CI 0.20– 0.68, respectively). On the other hand, CAS and EAI clades were almost exclusively found among immigrants (just 1 case among Italians), mainly from Indian sub-continent (90% of cases). CAS strains were also significantly associated with extrapulmonary forms of TB (OR=2.81; 95% CI 1.51 – 5.25;  $p=0.001$ ). There was no statistically significant association between clades and drug resistance, HIV infection, age or time of arrival in Italy. Beijing strain was associated with recent transmission involving a seven months old baby, born in Italy from an immigrant family.

**Conclusion:** our results seem to indicate that MTB infection in immigrants was acquired in the country of origin, without intensive transmission to Italians.

However, periodic molecular studies are necessary to identify the introduction of new clades, mainly those with higher virulence and risk for MDR such as Beijing strains.

**PD-668-30 Using molecular epidemiological data to estimate the extent of recent transmission in a multi-ethnic, high incidence setting in England, 2007–2011**

A Keen,<sup>1</sup> J Evans,<sup>2</sup> S Khanom,<sup>2</sup> R White,<sup>1</sup> P Hawkey,<sup>2</sup> I Abubakar,<sup>3,4</sup> G Smith,<sup>2</sup> E Vynnycky.<sup>1,5</sup> <sup>1</sup>Infectious Disease Epidemiology, TB Centre, TB Modelling Group, London School of Hygiene & Tropical Medicine, London, <sup>2</sup>PHE West Midlands Public Health Laboratory, Heart of England NHS Foundation Trust, Birmingham, <sup>3</sup>TB section, Public Health England, London, <sup>4</sup>Research Department of Infection and Population Health, University College London, London, <sup>5</sup>Public Health England, Statistics, Modelling and Economics, London, UK. e-mail: emilia.vynnycky@phe.gov.uk

**Background** The proportion of tuberculosis incidence that is attributable to recent transmission in England is currently poorly understood. Studies to date measuring “clustering” of M tuberculosis isolates may have underestimated this proportion by considering a short (1 year) period or settings with high levels of migration. We analysed cases in the West Midlands region as it has one of the highest TB notification rates in England (18 per 100,000 in 2011), with much ethnic diversity, aiming to calculate the amount of “clustering” of M tuberculosis isolates and estimate the extent of recent transmission.

**Methods** Isolates from culture-confirmed tuberculosis cases in the West Midlands received between 1<sup>st</sup> January 2007 and 31<sup>st</sup> December 2011 were typed using 24 locus MIRU-VNTR. Isolates were considered to be “clustered” if their genotype profile matched that of another isolate in the study period, with less than 2 missing loci (the “n” method). The proportion of disease attributable to recent transmission was calculated using the “n-1” method and a retrospective approach (the proportion of cases whose isolates matched that of a case during the preceding two years).

**Results** Genotype profiles were available for 84% (2311/2749) of the culture-confirmed tuberculosis cases over the study period. Of these, 46% were clustered, based on the “n” method, with 35% attributed to recent transmission, based on both the “n-1” method and the retrospective approach. The proportion clustered decreased with age from 71% (28/39 patients) for 0–14 year olds to 38% (53/139 patients) for those aged ≥65 years. Over 40% of the White, Black Caribbean, Black African and Black Other and South Asian groups were “clustered”. The levels of clustering was significantly higher for those who had arrived 5–9 years previously than for recent immigrants (OR: 1.6, 95% CI: 1.2–2.3), but it is unclear if differences in clustering by time since arrival reflect genuine differences in the amount of disease attributable to recent transmission.

**Conclusions** The levels of clustering in this region are comparable to those seen nationally elsewhere in Western populations and about a third of disease may

be attributable to recent transmission. This is the first time that the area with the highest tuberculosis incidence outside London has been studied in this way. The findings will be relevant for future studies both using data collected through the national strain-typing service, introduced in 2010 and NGS.

**PD-669-30 Reverse zoonosis occurred in dairy cows of Bangladesh by *Mycobacterium orygis*: a new causative agent of tuberculosis**

M Rahim.<sup>1</sup> <sup>1</sup>Mycobacteriology Laboratory, icddr,b, Dhaka, Bangladesh. Fax: (+880) 2 881 2529. e-mail: zeaur@icddr.org

**Background:** Bangladesh is one of the Tuberculosis (TB) endemic countries of the world. Various initiatives are in progress to control human TB without considering TB of animals and their role as reservoir of human TB. In this study, vital organs of the dead cows were analyzed after postmortem to (a) isolate and identify *Mycobacterium* from the vital organs of the dead cows, (b) perform drug susceptibility testing and (c) genotyping of isolates.

**Design/Methods:** After post-mortem, granulated part of the lung, liver, and kidney of dead cows were studied to assess TB infestation. Part of the tissue sample was processed for histopathological examination. For culture, tissue homogenate samples were inoculated on Lowenstein-Jensen (L-J) slants (with sodium pyruvate but without glycerol). Characteristic colonies were confirmed *Mycobacterium* by acid-fast staining, colony morphology. Sensitivity testing was performed following proportion susceptibility testing method. For molecular characterization, DNA was extracted from the culture of *Mycobacterium* for RD analysis was performed for *cfp32*, RD1, RD4, RD9, and RD12; single nucleotide polymorphism for the *gyrB*, *mmlp6*, *TbD1* and *PPE55* genes. Genotyping was performed by standard spoligo- and VNTR MIRU typing.

**Results:** In this study, lungs, livers and kidneys of 21 dead cows were studied for TB infection after postmortem. These organs had prominent nodulation. Histopathological examination, demonstrated prominent granuloma, caseation necrosis, and calcification as proof of TB infestation. *Mycobacterium* grew from the vital organs of 18 dead cattle. AFB staining, sensitivity to PNB indicated that the strains belong to *M. tuberculosis* complex. Molecular characterization indicated that these strains belong to *M. orygis*. Isolated strains were sensitive to all first line anti-TB drugs. It indicated that these strains were not challenged with anti-TB drugs.

**Conclusion:** Strains of *Mycobacterium* isolated from the vital organs of dead cows were identified as *M. africanum* based on spoligotyping. Further molecular characterization of these strains identified these strains into *M. orygis*. Further epidemiological studies needs to be conducted to identify the possible reservoir of this species and its mode of transmission to dairy cattle. Since *M. africanum* is a human pathogen, its infestation with dead cow indicates that the cows possibly acquired TB

infection from Human TB patients, which is reverse zoonosis.

#### PD-670-30 Prevalence of Beijing genotype among clinical isolates of *M. tuberculosis* from different regions of Kazakhstan

A Akhmetova,<sup>1,2</sup> U Kozhamkulov,<sup>1,2</sup> V Bismilda,<sup>3</sup> L Chingisova,<sup>3</sup> E Ramanculov.<sup>2</sup> <sup>1</sup>Genomic and Personalized Medicine, Nazarbayev University, Astana, <sup>2</sup>National laboratory of Biotechnology, National Center for Biotechnology of the Republic of Kazakhstan, Astana, <sup>3</sup>Bacteriology, National Center for Tuberculosis Problems, Almaty, Kazakhstan. e-mail: ainur.akhmetova2@nu.edu.kz

##### Background:

**Methods** of genotyping of *M. tuberculosis* play important role in tuberculosis (TB) infection control. These techniques are used to detect or exclude laboratory errors, control recurrent cases and determine ways of TB transmission. Today, there are more than 10 methods of genotyping, MIRU-VNTR is one of the widely used method in the world. Aim: Estimation of biological diversity of clinical isolates of *M. tuberculosis* from different regions of Kazakhstan based on MIRU-VNTR analysis.

**Design/Methods:** MIRU-VNTR genotyping of 134 clinical isolates of *M. tuberculosis* isolated from new cases and recurrent cases of TB from different regions of Kazakhstan was carried out in this study. Amplification was done using 15 MIRU-VNTR loci. Determination of the number of tandem repeats in corresponding locus was performed via Quantity One v.4.4.0 (BioRad, USA) software. H37Rv (NC\_000962) reference strain was used as a positive control.

**Results:** Phylogenetic tree was built using www.miru-vntr.org web-resource based on the results of MIRU-VNTR analysis. Beijing family strains associated with drug resistance to antituberculosis drugs prevail among all isolates of *M. tuberculosis* circulating in Kazakhstan. Strains of Beijing genotype prevail both in new cases and recurrent cases of tuberculosis showing 65% and 89,4%, respectively. The second meaningful genotype that is spread in the territory of Kazakhstan is LAM, the frequency of distribution is 7,3% and 4,5%, respectively. Other families of *M. tuberculosis* such as Ural, Haarlem, CAS, NEW-1, S were found in less than 4% cases.

**Conclusion:** Prevalence of Beijing family strains among all isolates of *M. tuberculosis* from different regions of Kazakhstan was shown (65% and 89,4%). Strains of this family prevail among young people. The genotype is responsible for ongoing TB transmission in the present time. Genotype is more virulent, that is why investigation of epidemiology of Beijing genotype plays crucial role in monitoring of tuberculosis.

#### 16. TB PUBLIC PRIVATE MIX IN COUNTRIES OTHER THAN INDIA

##### PD-671-30 Cost-effectiveness of TB health services in Sana'a city, Yemen: a comparison between different types of health care providers

N A A Thabit,<sup>1</sup> A Al-shamiry.<sup>1</sup> <sup>1</sup>National Tuberculosis Program, Ministry of Health, Sana'a, Yemen. Fax: (+967) 777918339. e-mail: najeb\_aziz@yahoo.com

**Background:** Since 2010 there has been an engagement of private health services as per the Public Private Mix intervention initiative in Yemen. Therefore this cross-sectional study was conducted at Sana'a city to assess the cost-effectiveness of government/co-operative(Go/co-op) and private providers to evaluate the new model with increased engagement of private sector.

**Design/Methods:** 451 newly registered TB patients attending TB treatment centers in Sana'a city were enrolled during a period from Augustus 2012 to September 2013. Data about the patient costs and treatment supporter costs of the different provider was collected by interview using a pre-structured questionnaire.

**Results:** This study found the treatment success of TB patients in the Go/co-op sector (Go) was 83.2 % (227/273) comparing with 84.3% (150/178) in the private sector,  $p < 0.754$ . Cost of DOT visits was 71.4\$, in Go/co-op sector comparing with 54.1\$ in private sector,  $p < 0.076$ . Cost of follow up tests and hospitalization was 25.4\$, 0.8\$ in Go/co-op sector comparing with 17.7\$,0.5\$ in private sector,  $p < 0.167$ , 0.828 respectively. Cost of treatment supporter was 7.2\$ in Go/co-op sector comparing with 6.6\$ in private sector,  $p < 0.0001$ . Total cost was 104.8\$ in Go/co-op sector comparing with 78.8\$ in private sector,  $p < 0.004$ . Cost-effectiveness of TB health services in Go/co-op sector was 126.04\$ comparing with 93.5\$ in private sector.

**Conclusion:** This study found no statistically significant difference between the effectiveness of Go/co-op and private sectors. Treatment in private sector reduce cost to 25.8% comparing with Go/co-op sector in Yemen. NTP Yemen can expand the role of the private sector in the roll out of NTP program.

##### PD-672-30 Involvement of informal health care providers, pharmacies, in population services international Myanmar's TB control activities

P Swe,<sup>1</sup> S Zarni,<sup>1</sup> K Win.<sup>1</sup> <sup>1</sup>Program Management Division, Population Services International Myanmar, Yangon, Myanmar. Fax: (+95) 1 527 668. e-mail: ppswe@psimyanmar.org

**Background** TB is a major public health problem in Myanmar. A national TB prevalence survey conducted in 2009–2010 highlighted that passive case finding alone is inadequate for TB control. According to survey data, the majority (41%) of people with chronic cough were self-medicating with drugs purchased from pharmacies. In



2004, Population Services International Myanmar (PSI/M) started TB control programming through a franchised network of private clinics, branded Sun Quality Health (SQH). In 2012, PSI/M implemented TB active case finding activities (ACF) through pharmacies in urban slum areas with the support of TB REACH Wave 2 funding.

**Intervention** The ACF project was implemented in 30 townships in the Yangon region where urban slum dwellers are located. 480 registered pharmacies interested in ACF were recruited and their staffs were trained in symptomatic screening of TB and referral to labs and SQH clinics where free diagnostic and treatment services are provided. Pharmacies were provided IEC materials for TB education, as well as tools for screening and referral. Trained sales staff screened clients for presumptive TB symptoms and those with symptoms were provided with a sputum collection cup, instructions on sample collection and referral to the nearest lab and SQH clinic.

**Results** 263 out of 480 recruited pharmacies (55%) participated in TB ACF activities. From July 2012 to December 2013, active pharmacies referred 2,335 presumptive TB patients to diagnosis and treatment centers. 86% (2013) of referred clients underwent diagnosis and of those, 19.6% (395) had bacteriologically confirmed TB. 18.9% (306) clients that were smear negative underwent further investigation and 179 of those were clinically diagnosed with TB. 521 out of 574 diagnosed TB patients were registered at SQH clinics for treatment.

**Conclusions** The prevalence of bacteriologically confirmed TB among patients with presumptive TB was higher in pharmacies (19.6%) than SQH clinics (11% in 2013). This suggests that pharmacy engagement is crucial for TB control. The low participation of pharmacies was driven by social stigma and time constraints. Loss to follow-up among referred patients was attributed to poor knowledge of TB among patients and inadequate diagnostic facilities. Despite these barriers, the program was highly successful and concentrated efforts should address the remaining barriers to further the success of pharmacy engagement to increase TB case finding in Myanmar.

#### PD-673-30 BRAC's experience in engaging different healthcare providers in TB control programme

R Amzad,<sup>1</sup> K Fatema,<sup>1</sup> S Islam,<sup>1</sup> G Raihan,<sup>1</sup> M Akramul Islam,<sup>1</sup> MA Husain,<sup>2</sup> M Hossain.<sup>3</sup> <sup>1</sup>HNPP, BRAC, Dhaka, <sup>2</sup>TB, NTP, Dhaka, <sup>3</sup>TB, URC, Dhaka, Bangladesh.  
e-mail: shayla.dhaka@gmail.com

**Background and challenges to implementation:** Tuberculosis (TB) is one of the greatest killers worldwide due to a single infectious agent. Bangladesh faces considerable difficulties in providing TB services till 1980s. To address this problem, BRAC initiated a pilot community based TB control program in 1984 in Manikganj. BRAC signed a MoU with government in 1994 and expanded

the GO-NGO collaboration in TB control. BRAC is now the largest NGO partner of National Tuberculosis Control Program (NTP) which covers 297 sub-districts in 42 districts with a population of 93 million.

**Intervention or response:** BRAC conducts networking meetings with the graduate private practitioners (GPP) and non-GPP to engage them in identifying TB patients, proper referral and treatment adherence. To increase the accessibility of diagnostic facilities, outreach sputum collection centers have been established by involving the community clinics (CC). CC staffs are oriented to mobilize and refer TB symptomatic. The coordinated linkage efforts is expected to increase overall case notification and smear negative (NSN), extra pulmonary (EP) case notification in the 12 districts with the support of URC. Program organizers of BRAC do outreach centers for sputum collection in the CC. However, due to heavy patients flow, often it is inconvenient to arrange outreach center in clinic premises. So, these centers were held at the nearest places of respective clinics.

**Results and lessons learnt:** From Apr'2012-Mar'2013, BRAC conducted 505 networking meetings with GPP and non-GPPs and reached 7,995 of them. Total 8,317 of smearing centers have been established in the CC and 1,178 CC staffs were oriented. A total of 24,830 TB symptomatic were referred by GPP and non-GPPs. Total number of symptomatic examined were 32,001 in Apr'12-Mar'13, whereas it was 26,207 in the previous year. NSP increased to 23,265 in one year, and NSN and EP in total increased to 12,888 from 8,300 in Apr'11 to Mar'13.

**Conclusions and key recommendations:** Detection of TB symptomatic has increased after implementation of the project in the 12 districts. Detection of NSN and EP also increased significantly. Introduction of better networking might play a role in this increasing number of cases. This finding substantiates, that proper networking and linkage plays an important role in increasing accessibility of TB services.

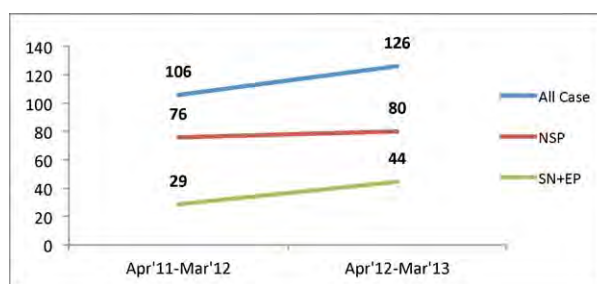


Figure1: Increased trend of case detection

### PD-674-30 Strengthening the Public-Private Mix (PPM) initiative in Dhaka, Bangladesh using systematic screening for active pulmonary tuberculosis and GeneXpert

MT Rahman,<sup>1</sup> A Mahmud,<sup>2</sup> A Nahar,<sup>1</sup> S Ahmed,<sup>1</sup> R Ahmed,<sup>1</sup> M.M. Rahman,<sup>3</sup> MA Husain,<sup>3</sup> S Banu.<sup>1</sup>

<sup>1</sup>Centre for Communicable Diseases, International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka,

<sup>2</sup>Respiratory Medicine, Institute of Epidemiology, Disease Control & Research, Dhaka, <sup>3</sup>Directorate General of Health Services, National TB Control Program, Dhaka, Bangladesh. Fax: (+880) 2 9827062. e-mail: sbanu@icddr.org

**Background** In order to identify the missing three million, systematic screening for active tuberculosis (TB) is needed to supplement the current passive case finding approaches in place by the National TB Control Programs (NTPs) in high TB burden limited resource countries like Bangladesh. Private healthcare sector is accessed primarily by majority of patients and can be targeted to improve the standard of TB care and also to address the gap in notification as part of strengthening the public private mix (PPM) initiative.

**Intervention** Systematic screening for active TB was conducted focusing on 23 high volume physicians' (specialists and general practitioners) practice places in the private sector of Dhaka city through a well designed diagnostic algorithm from September, 2013 to March 2014. Patients along with attendants visiting these physicians were verbally screened by the Community Screeners placed at the patient waiting areas for any TB symptoms (cough of any duration, haemoptysis, weight loss, fever or night sweats) to identify presumptive pulmonary TB cases. Single, good quality, spot sputum specimen was collected from presumptive cases after providing sputum submission instruction. Collected sputum specimens were then tested with GeneXpert (GXP) to identify bacteriologically confirmed (B+) TB cases. Confirmed cases were enrolled for TB treatment under the referring physician in the private sector or registered for free treatment with DOTS centre following the NTP guidelines. All patient identification and case management documentation were recorded and reported to the NTP using standardized format.

**Results** Over the period 91,998 individuals were actively screened for pulmonary TB and 14,254 presumptive cases were identified. Sputum specimens from 14,161 (99%) presumptive cases were collected and GXP tests were performed in 14,020 (98%). A total of 871 (6% of 14,020) B+ pulmonary TB cases were identified through GXP and 799 (92%) enrolled for anti-TB treatment. The number needed to screen to detect a B+ case was 105.

**Conclusions** A large number of undiagnosed active TB cases can be identified at the earliest through systematic screening thereby limiting TB transmission and improving the disease outcomes. Innovative initiatives can improve the TB notification from private sector leading to stronger PPM linkages.

### PD-675-30 Peer meetings to increase engagement of pulmonologists in private practice

F Putri,<sup>1</sup> E Burhan,<sup>2,3</sup> M A Nawas,<sup>2,3</sup> D Kusumo Sutoyo,<sup>2,3</sup> F Yunus,<sup>2,3</sup> B Djojonegoro,<sup>4</sup> P Hopewell,<sup>4</sup>

DE Mustikawati.<sup>5</sup> <sup>1</sup>Indonesia, KNCV Tuberculosis

Foundation, Jakarta, <sup>2</sup>PDPI, Indonesian Society of Respiriology, Jakarta, <sup>3</sup>Pulmonology and Respiratory Medicine, Faculty of Medicine, University of Indonesia, Jakarta, Indonesia; <sup>4</sup>UCSF, Curry International Tuberculosis Center, San Francisco, CA, USA, <sup>5</sup>National TB Program, Ministry of Health, Jakarta, Indonesia.

e-mail: baby.djojonegoro@ucsf.edu

**Background:** Based on assessments of antituberculosis drugs sales to the private sector in Indonesia, nearly 50% of tuberculosis (TB) patients are managed outside of the national TB control program (NTP) and not notified. As an approach to systematic engagement of the private sector, the Indonesian Society of Respiriology (PDPI) in collaboration with the NTP developed a project to engage private pulmonologists in national TB control activities, following the International Standards of Tuberculosis Care (ISTC) and NTP guidelines.

**Intervention:** Pulmonologists were recruited based for their TB patient case load and interest in participating. Ninety-seven pulmonologists and their staff from 61 private hospitals have been recruited in a stepwise fashion from 10 districts in and around Jakarta. Participants received a 2-day ISTC-based training course before enrolling patients. PDPI provided staff members for data collection; data are used for performance feedback to participants in biannual monitoring and evaluation meetings. Participants take an active role in the discussions with guidance from PDPI and other experts. Identified issues were discussed among peers, NTP/MOH, and hospital administrators, and well-performing participants shared experiences and provided suggestions to others facing similar difficulties. **Result:** From project initiation in October 2010 through December 2012, 22 pulmonologists in 17 private hospitals have managed 3,386 pulmonary and extrapulmonary TB patients. The performance trend of the pulmonologists started with 77% sputum smear for diagnosis, 48% sputum smear for monitoring, 63% success rate, and 20% default rate for the first cohort of patient. Their patient cohort from the fourth quarter of 2012 has 80% sputum smear for diagnosis, 48% sputum smear for monitoring, 76 % success rate, and 15% default rate.

**Conclusion:** The first recruited group of private pulmonologists has shown improvements in the success and default rates of their patients over the two years of the project. Regular monitoring and evaluation meetings with them have sustained the pulmonologists' commitment to provide quality care to their patients. Although resource intensive, active feedback of participants' performance has been effective for engaging pulmonologists practicing in private hospitals in national TB control activities and improving overall care of TB patients.

### PD-676-30 Increase in TB case detection through a PPM partnership: community health worker symptomatic screening at a high-volume government hospital in Karachi

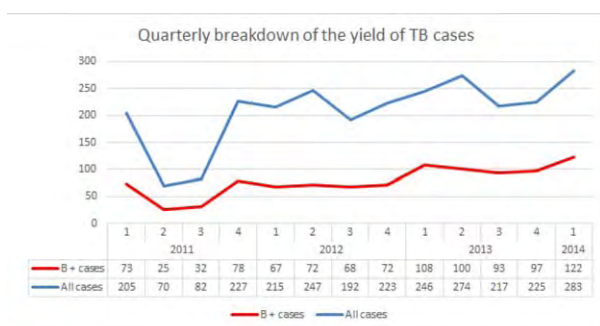
N Khalid,<sup>1</sup> N Masood,<sup>2</sup> A Malik,<sup>1</sup> A Zaidi,<sup>1</sup> S Khowaja,<sup>1</sup> R Jawaid,<sup>3</sup> N Rizvi,<sup>3</sup> A Khan.<sup>1</sup> <sup>1</sup>Community Health Solutions, Interactive Research & Development, Karachi, <sup>2</sup>Zonal TB Coordinator, Provincial TB Control Program, Karachi, <sup>3</sup>Chest Medicine, Jinnah Post Graduate Medical Centre, Karachi, Pakistan.  
e-mail: nashwa.khalid@irdresearch.org

**Background:** Pakistan's TB case detection rate (all forms) of 65%, in 2012 was 65%, below internationally established targets in high-burden countries, and has a consistent issue with under-diagnosis and missed cases. Screening at private practitioner clinics and outpatient department of private hospitals has proven to be an effective way of increasing the case detection and notification in urban settings in the past.

**Objective:** To evaluate the effectiveness of screening at the outpatient chest department of a tertiary care public hospital at increasing the case notification of TB.

**Methods:** A public-private mix project (PPM) initiative was launched late November 2013 in Karachi. Lay screeners were provided training on an interactive algorithm on cellphones to assess patients and visitors at the outpatient chest department of a large public sector hospital. If the individuals screened exhibited symptoms of TB they were indicated for a GeneXpert MTB/RIF test and asked to provide a sputum sample. Doctors additionally referred inpatients suspected for tuberculosis for a GeneXpert MTB/RIF test. The outcome of interest was the change in TB case notification to the Provincial TB Program from the intervention hospital from October 2012 to March 2014.

**Findings:** Screeners assessed 5,807 individuals at the Chest OPD over 5 months (November 2013 – March 2014). 1911 (33%) presumptive tuberculosis cases were detected of which 388 (20%) individuals were tested on GeneXpert MTB/RIF. 70 (18%) were MTB+ve, including 5 (7%) that were RIF resistant. An increased number of sputum smear positive cases were found in the intervention period, a 35% increase when comparing Q4 2012 with Q4 2013 and a 13% increase in Q1 2013 when compared to Q1 2014. Similarly for all forms of tuberculosis, a 1% increase was observed when Q4 2012 was compared to Q4 2013 and a 15% increase in all forms of tuberculosis cases was observed when Q1 2013 was compared to Q1 2014.



**Conclusions:** Active screening for tuberculosis at public sector hospitals by lay community screeners using mobile phone software can reduce the number of missed cases.

### PD-677-30 Comprehensive tuberculosis control through joint effort by the private, civil society and public sectors

C Thamsuwan,<sup>1</sup> Y Kasetjaroen.<sup>2</sup> <sup>1</sup>The Global Fund project, World Vision Foundation of Thailand, Bangkok, <sup>2</sup>Department of Disease Control, Bureau of Tuberculosis, Bangkok, Thailand. Fax: (+66) 023814923.  
e-mail: chin\_tham@hotmail.com

**Background:** TB is still an important public health challenge in Thailand, especially among the more vulnerable populations. Quality and efficient TB control requires support from a variety of organizations and sectors to facilitate early detection and treatment of cases. There is a need to improve the quality of DOTS by creating networks among public and private agencies under the Stop TB Strategy and expand implementation according to TB control guidance to improve coverage of services.

**Interventions:** Private agencies and CSO have received grants from the Global Fund to implement activities for TB control including raising awareness of the challenge, promoting reduced risk behavior, and conducting social advocacy to reduce stigma. Promote TB screening and counseling, home visiting, and improving access to diagnosis, for example, by collecting sputum and transferring these to diagnostic facilities, accompanying people with suspicious symptoms to public health facilities, care and monitoring during the course of treatment, observation of TB systems and co-infections, support for continuous adherence to the treatment regimen, providing TB education, and following up the results of therapy. The activities are tailored to the local context.

**Results and lessons learnt:** This collaborative program, funded by the GF, in risk populations, over the past 2 years (2011-13). The project has screened a total of 1,031,616 persons, and referred 5,318 persons with symptoms indicative of TB for diagnosis. Of these, a total of 424 TB cases were confirmed (All TB case notified = 41%). The treatment success rate was 97%. Success is also attributed to the collaboration of the Pharmacists Association and 83 drug store members in Bangkok who helped in the screening of cases with suspicious symptoms who appeared at the drug store for cough medicine and referring them for formal diagnosis and care. Despite this success, there remain challenges of how to be accelerated recruit, test, treatment and retain.

**Conclusion:** Collaborative implementation of TB control in Thailand has helped filled gaps in coverage, but there remains a need to improve and provide continuing support to create sustainability of interventions and a consistent standard of implementation. There needs to be improved acceptance of this collaborative model by the



public sector which emphasizes integrating community-based tuberculosis activities into the work of NGO and other CSOs.

### **PD-678-30 The contribution of private practitioners on tuberculosis suspects and cases finding In Denpasar, Bali, Indonesia, 2013**

IWG Artawan Eka Putra,<sup>1</sup> A Swandewi,<sup>1</sup>  
Pase Kardiwinata,<sup>1</sup> CISC Astiti,<sup>2</sup> IM Sutarga,<sup>1</sup>  
C Umbul Wahyuni,<sup>3</sup> A Probandari,<sup>4</sup> P Riono.<sup>5</sup>

<sup>1</sup>Epidemiology, School of Public Health, Faculty of Medicine, Udayana University, Denpasar, <sup>2</sup>Disease Control, Health Office of Bali Province, Denpasar, <sup>3</sup>Epidemiology, Faculty of Public Health, Airlangga University, Surabaya, <sup>4</sup>Public Health, Faculty of Medicine, Sebelas Maret University, Solo, <sup>5</sup>Biostatistic, Faculty of Public Health, University of Indonesia, Depok, Indonesia. Fax: (+62) 3617448773.  
e-mail: gedartawan@unud.ac.id

**Background:** Partnership with private practitioners (PPs) is important on Tuberculosis (TB) control acceleration. An agreement had been made between the Governor of Bali and the Chairman of the Indonesian Medical Doctors Association (IMDA) to encourage the PPs on TB control program. We aimed to assess the PPs knowledge regarding international standards for TB care (ISTC), potency and the effect of agreement to their contribution on TB suspects and cases finding.

**Design/Methods:** This is a descriptive cross-sectional study, conducted from April to September 2013. Populations were all PPs (general practitioners and specialists) in Denpasar City. Samples are all PPs that visited at the practice site when the agreement was disseminated. Data collection using self-administered questionnaire and analysed descriptively. PPs contribution assessment conducted per quarter during 2013 through the routine data of TB program (secondary data).

**Results:** 473 Of 724 (65.3%) registered PPs were successfully visited. Most of them are general practitioners (71.9%), mean age of 42 years old and 59.2% are male. 74.4% of PPs have good knowledge regarding standards for diagnosis, 91.1% have good knowledge regarding standards for therapy and only 42.7% have good knowledge regarding standards for public health responsibility. PPs have high potency on TB suspects and cases finding, 35.1% of them have found TB suspects at the last 3 months and mostly (91.2%) have been willing to contribute. The effect of agreement to PPs contributions on TB suspect finding are still low, the average only 1.1%. While the effect on TB cases finding are significant, reaching 7.1%. These are shows that they were too selective in recruiting suspects (positive rate above 15%).

**Conclusion:** Since the PPs potency are high, improving their knowledge regarding ISTC through continuous training and refreshing especially on standards for diagnosis and public health responsibility is needed.

### **PD-679-30 Compliance to national TB treatment guidelines on diagnosis, treatment, and reporting by physicians in the Namibian private health sector**

H Mungunda,<sup>1</sup> F Mavhunga,<sup>1</sup> R Amutenya,<sup>1</sup>  
T N. Shilongo,<sup>1</sup> V Mogotsi,<sup>1</sup> A Thomas.<sup>1</sup> <sup>1</sup>Directorate  
Special Programmes, Ministry of Health and Social Services,  
Windhoek, Namibia. Fax: (+264) 61252740.  
e-mail: mungundah@gmail.com

**Background:** Namibia has a high per capita TB burden, with a case notification rate of 487/100,000 in 2013. In 2012 Namibia had 341 registered private physicians, catering for about 15% of the population. Not much is known of TB related services provided by the private sector in Namibia. This study was therefore carried out to determine the proportion of physicians working in the Namibian private health sector providing TB related services, characterize their compliance to the national TB treatment guidelines and identify the reasons for non-compliance to national guidelines.

**Design/Methods:** The study comprised data analysis from the 2009 Namibia Health facilities Census; an interviewer administered questionnaire assessing private practitioners' knowledge and practice on TB diagnosis, treatment and case management; and using mystery clients who presented themselves for consultation at the private practitioner with symptoms of TB. OpenEpi was used to determine sample size of 180 for the questionnaire using a confidence level of 95% for a population of 341. Mystery clients were used for 70% (randomly selected) of the respondents to the questionnaire

**Results:** A total of 341 private practices are registered in Namibia. Of these, 161 were interviewed; while mystery patients were attended to by 126 practitioners. 90 (56%) of the respondents had received training on the National Guidelines for the Management of Tuberculosis, 156 (98%) of them were knowledgeable of the signs and symptoms of TB, with no significant difference between those recently trained and those not trained. However regarding treatment regimens, 11 (26%) of the practitioners trained on TB who did not refer patients to other facilities were aware of the correct the new patient regimen, compared to none (0%) of those not trained on TB. Only 9% of the practitioners knew treatment for previously treated patients. Only trained respondents knew regimens for EPTB (2.5%) and MDR-TB (1.25%).

**Conclusion:** Awareness of the clinical features of TB is high among private practitioners in Namibia, even among those who have not received specific training on the guidelines. There are however gaps and inconsistencies in the treatment regimens and treatment approach, with the potential for suboptimal therapy.

**Interventions** should thus focus on educating private practitioners on the management of TB and creating linkages to government health facilities.

### PD-680-30 Issues and challenges in the Public-Private mix model for tuberculosis treatment in Sindh, Pakistan

J Hasnain,<sup>1</sup> S Bhutkiya.<sup>1</sup> <sup>1</sup>Research, Bridge Consultants Foundation, Karachi, Pakistan.  
e-mail: drjhasnain@gmail.com

**Introduction:** In developing countries a large proportion of the population utilize the private sector for their health care needs because of it easy access and affordability. As a result in 2007 in Pakistan the concept of public-private mix model (PPM) for the management and control of tuberculosis (TB) emerged to integrate the services of the private healthcare providers and the expertise of the public sector. Although this partnership received attention in terms of TB control in many districts of Pakistan but this model has several operational issues which need to be identified and documented. In this regard a study was conducted to identify the issues and challenges in PPM model in Sindh, Pakistan.

**Methods:** We conducted desk review, focus group discussions (FGDs) and in-depth interviews (IDIs) in Karachi, Hyderabad, Sukkur and Sanghar districts of Sindh Province. Data were obtained from: (1) systemic literature search using PubMed and (2) "grey" literature on TB and PPM related topics in Pakistan. FGDs and IDIs were conducted with TB patients, their treatment supporters, general physicians (GPs), paramedics, NGO members and field officers working in the PPM project. Data were transcribed and analyzed through coding, categorizing, and identifying of themes.

**Results:** Six main themes emerged from the data: (1) most GPs find the recording and reporting tools (TB forms and cards) very tedious; (2) increased distance between treatment centers and diagnostic facilities in some districts is a reason for primary default; (3) lack of incentives (cash/kind) for the GPs and paramedics in the PPM project de-motivates these professionals; (4) high turnover of trained staff is a particular problem in a few districts; (5) low salary packages and temporary employment were the main issues of the PPM field officers; and (6) interruptions in TB awareness sessions because of delays in disbursement of funds was also highlighted by the PPM team members as a major issue.

**Conclusion:** This study highlights the importance to motivating the PPM staff and the PPM partners to strengthen the existing program. Further it emphasizes the need of simplifying the processes and the documentation in the program so that the activities are conducted uninterrupted and the implementing members may find the execution uncomplicated.

### PD-681-30 Role of private practitioners in TB case detection and treatment, challenges and lesson learnt

M Rafique Mangi,<sup>1</sup> S Shah,<sup>2</sup> S Soomro,<sup>3</sup> G Nabi.<sup>4</sup>

<sup>1</sup>Tuberculosis/HIV, Bridge Consultants Foundation, Karachi, <sup>2</sup>Public health, Bridge Consultants Foundation, Karachi, Sindh, <sup>3</sup>Tuberculosis, Bridge Consultants Foundation, Karachi, Sindh, <sup>4</sup>TB/HIV, Bridge Consultants Foundation, Karachi, Sindh, Pakistan. Fax: (+92) 21-5683106.  
e-mail: rafiquemangi2@gmail.com

**Background and challenges to implementation:** Tuberculosis remains a major cause of death and disability across the globe. Pakistan ranks 5<sup>th</sup> among 22 high TB burden countries in the world. Incidence of TB is 231/100000, prevalence is 371/100000, and still 60000 TB patients die every year in the country.<sup>2</sup> Sindh province, the second most populated province of Pakistan with population of 55245497, there are 60000 new TB cases reported annually, 55000 cases remained undiagnosed yearly, and 18000 deaths attributable to TB<sup>1</sup> In Pakistan 70% population has limited access to public health facilities, so only 30% population is seeking health care at private sector, National Tuberculosis control Program Pakistan implanted Public private Mix (PPM) strategy to involve private practitioners under Global Fund grant Round-9 in 2011

#### Intervention or response:

**Objective;** To provide TB DOTs services through private practitioners in three districts of Sindh. Mapping was conducted in three district (Umerkot, Badin & Naushero Feroz) All those who were short listed as per defined criteria were given six days TB-DOTs training and three days training given to one paramedic of each private doctor, ten private laboratories were strengthened for sputum AFB smear microscopy & technician were provided ten days basic Microscopy training, all the recording and reporting tools, weighing scale and Anti TB drugs, IEC material was made available at the clinics.

**Results and lessons learnt:** In last two years, total 1409 all types of TB cases registered in three districts (Male 844, females 565) In Umerkot the Case Detection Rate (CDR) of NSS+ve cases was 91%, of all types was 85% Treatment success Rate was 82%, Default Rate was 7% after PPM

**Intervention** CDR of NSS+ve cases has been increased from 91% to 106%, TSR has been increased 82% to 87%, Default rate has been decreased from 7% to 3%. PPM Contribution in Badin is > 5% CDR of all types, In Naushero Feroz > 4% CDR of all types. 58 Doctors, 58 paramedics and 10 lab technicians were trained for TB-DOTs.

**Conclusions and key recommendations:** It is feasible to implement PPM in three districts of Sindh, majority of private practitioners are willing to work, they signed MOU, attended the trainings, they are treating the patients at their private clinics. PPM is an effective strategy and more effectively it can be replicated throughout the country, Incentive should be given to paramedics and lab technicians to decrease the turnover of trained

TB case registered in Three PPM Districts

District	Year	NSS+ve	All Types	Male	Female
Umerkot	2012	94	313	195	118
Badin	2012	17	45	36	9
N. Feroze	2012	10	19	12	7
Umerkot	2013	204	727	432	295
Badin	2013	66	160	94	66
N. Feroze	2013	66	145	84	61
Total		457	1409	853	556

### PD-682-30 Private-Public Mix (PPM) of referral of TB symptomatic by drug sellers in four townships of Myanmar

TT Nwe,<sup>1</sup> K Tin Min Min,<sup>1</sup> S Thein,<sup>1</sup> H G,<sup>2</sup> H Nishiyama,<sup>2,3</sup> K Okada,<sup>2,3</sup> N Yamada.<sup>2,3</sup> <sup>1</sup>National TB Programme, Ministry of Health, Nay Pyi Taw, <sup>2</sup>Major Infectious Disease Control Project, JICA, Yangon, Myanmar; <sup>3</sup>Centre for International Cooperation and Global TB Information, Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association (RIT/JATA), Tokyo, Japan. Fax: (+81) 42 492 8258. e-mail: nyamada@jata.or.jp

**Background:** Prevalence survey in 2009 shows 22% of TB cases with chronic cough visited traditional medicine and drug sellers. NTP and JICA project introduced a model of PPM program of drug sellers' referral of presumptive TB who visited them to TB diagnostic centres. After successful implementation in one township (Hlaing), the program was expanded to other 4 townships (South Dagon, South Okalapa, Mahaangmyae, Chanmyathazi) in July 2013 to assess applicability of the program to other areas in Myanmar. The preliminary assessment of the program during the initial phase in the 4 townships is carried out.

**Methods:** Training on identifying presumptive TB was given prior to commence of this program in each township. No monetary incentive is given to drug sellers. The referred presumptive TB received smear-examination at the township health facilities. When AFB is negative, transportation fare for chest X-ray examination was provided. Supervisors visited the participating drug sellers monthly to collect data. Activity results during first 6 months (July-December of 2013) were reviewed. Limitations and challenges were also identified by discussion with drug sellers in the review workshops.

**Results:** Out of 365 registered drug sellers in total, 212 (average 62%) participated in the program. Out of 212, 71 drug sellers (average: 34%) referred at least one presumptive TB to diagnostic facilities. 251 presumptive TB visited township health facilities through the referral by the drug sellers. Out of them, 53 smear-positive cases (average: 20%) were detected and 77 (average: 31%) in total were treated as TB. According to drug sellers, one of experienced problems is that some presumptive TB didn't visit diagnostic centres due to time and cost of transportation.

**Conclusion:** While there is some variation in degree of engagement of drug sellers by area, such as participation rates (range: 41% - 78%), efficiency of detecting TB cases from the referred presumptive TB is generally good. Because drug sellers are existing resources in communities, inputs required for this program could be limited to

initial training and regular monitoring/evaluation. Solutions for the experienced difficulties, such as involvement of community volunteers in collecting sputum, may need to be explored. Considering health seeking behavior found by the survey, the feasibility and efficiency of case detection, this program is recommended to be utilized widely in the country.

### PD-683-30 Promoting tuberculosis case findings in the community through Public-Private partnership

I Asieba,<sup>1</sup> O Omeh,<sup>1</sup> D Oqua,<sup>1</sup> A Adesina,<sup>1</sup> P Agada,<sup>1</sup> O Adeboga,<sup>1</sup> A Wutoh,<sup>1</sup> m Odo.<sup>2</sup> <sup>1</sup>Strengthening Integrated Delivery of HIV/AIDS Services (SIDHAS) project, Howard University, Pharmacists and Continuing Education, Abuja, <sup>2</sup>SIDHAS, FHI360, Abuja, Nigeria. e-mail: iyeseunasieba@yahoo.com

**Background:** The Stop TB strategy envisions a TB free world and the goal is to dramatically reduce the global burden of TB by 2015. One component of the strategy involves engaging all care providers. WHO advocates for the engagement of all relevant health care providers in TB care and control through a public private partnership. WHO further highlighted possible support of the strategy by pharmacists through case detection, standardized treatment supervision and an effective drug supply management system. Community pharmacists (CPs) are trained health professionals who operate their private pharmacies within the communities. They are generally open for long hours, well trusted and the first port of call for community health care needs. Howard University-PACE (HU-PACE) is the implementing partner responsible for strengthening pharmacy services within the FHI360 led project, SIDHAS, funded by USAID. Drawing on the Stop TB Strategy, CPs were engaged by the HU-PACE to provide TB services in 4 selected Local Government Areas (Calabar Municipal, Ikom, Surulere and Lagos Island) in Nigeria.

**Intervention:** In collaboration with the Association of Community Pharmacists of Nigeria, interested CPs were engaged and trained on Community TB care. The CPs carried out routine TB screening (using a designed checklist) in their pharmacies for clients who complained of cough and referred the TB suspects a government AFB laboratory for diagnosis. They also engaged in community outreaches where TB sensitization and referrals were made. Sputum positive clients were linked to treatment at TB DOTS providing facilities. CPs also provided treatment support including adherence counseling and screening for adverse drug reactions.

**Results:** Within a six month period, 63 CPs were enrolled in the program, 1758 referrals for TB made, 298 smear positive clients detected and placed on TB therapy and 112 persons were supported on treatment. The TB sputum positivity rate among referred clients was 5.9%. The participating pharmacists offered their services and time without charge as part of their commitment to improving public health.

**Conclusions:** The involvement of community pharmacists in TB case detection has been demonstrated to be viable



and increase access and entry into TB care. CPs have sustainable systems to support TB services within the community. Community pharmacist's role in TB should be expanded to include the routine provision of TB DOTS.

## 17. TB INFECTION CONTROL

### PD-684-30 Assessment of impact of FAST strategy on tuberculosis case finding, time to diagnosis and treatment in Abia State, south-eastern Nigeria

O Okorie,<sup>1</sup> M Gidado,<sup>2</sup> Fada Omoniyi,<sup>3</sup> E Ubochioma.<sup>3,4</sup>

<sup>1</sup>Public Health Department, Ministry of Health, Abia,

<sup>2</sup>TBCARE 1, KNCV Nigeria, Abuja, <sup>3</sup>WHO/TBCARE 1, WHO, Abuja, <sup>4</sup>Public health, NTBLCP, Abuja, Nigeria.

e-mail: onphil200@yahoo.co.uk

**Background and challenges to implementation:** Nigeria started implementing TB/HIV collaborative activities in 2006. Though progress has been made in most of the key TB/HIV collaborative interventions, the implementation of TB infection control in the country is still suboptimal. It was observed that infection control implementation was slow, a FAST strategy was introduced which stands for Finding TB cases Actively, Separating safely, and treating effectively. FAST focuses on the most important administrative TB transmission control intervention. The FAST strategy is built on a renewed appreciation of evidence showing that effective TB treatment reduces TB spread rapidly, even before sputum smear and culture turn negative. This is a descriptive study to assess the impact of FAST strategy on Tuberculosis case finding, time to diagnosis and treatment. The study was piloted in two tertiary institutions in Abia State.

**Results and lessons learnt:** Within the pilot facilities, it was found that the strategy improved the quality of health care services. There was a remarkable increase in the tracked presumptive and DR TB cases notified in the facilities. There was also 10% increase in number of cases registered and managed in the two facilities. The average time to diagnosis and treatment reduced from 4 days to 2 days and 7 days to 2 days respectively.

**Conclusions and key recommendations:** FAST strategy has shown significant impact on both early case detection and reduction of nosocomial infection. This should be adopted and scaled up in TB control program.

### PD-685-30 Expérience de riposte à une épidémie de tuberculose dans une prison du Burkina Faso.

A Ouedraogo,<sup>1</sup> A Combarry,<sup>1</sup> T L Sawadogo,<sup>1</sup>

T Ouedraogo,<sup>2</sup> G Konseimbo,<sup>1</sup> A Roggi,<sup>1,3</sup> Y Moyenga.<sup>1</sup>

<sup>1</sup>Coordination, Programme national tuberculose, Ouagadougou, Burkina Faso, <sup>2</sup>Sahel, Direction régionale de la santé du Sahel, Dori, Burkina Faso; <sup>3</sup>Maladie infectieuse, Université de Brescia, Brescia, Italy. Fax: (+226) 50317979.

e-mail: adamaouedraogo68@yahoo.fr

**Contexte** La prison de Djibo est l'une des 25 prisons collaborant avec le Programme national tuberculose (PNT). Elle compte 7 cellules de détention réparties en 3

quartiers (hommes, femmes et mineurs), fermées de 18 heures à 6 heures, insuffisamment ventilées. L'effectif des détenus à la date de l'investigation était de 114 pour une capacité 120. La prison dispose d'une infirmerie. Un seul cas de tuberculose a été dépisté de 2010 à 2012. Une épidémie de tuberculose a été suspectée suite à deux collectes actives de crachats (11 juin et 28 juillet 2013) dans cette prison. Réponse Deux missions urgentes (investigation des cas et suivi de la mise en œuvre des recommandations) d'une équipe multidisciplinaire du PNT ont été effectuées dans la prison du 10 au 12 septembre et du 30 au 31 octobre 2013. Résultats et leçons apprises L'épidémie de tuberculose a été confirmée. Au total, 17 nouveaux cas de tuberculose pulmonaire à microscopie positive ont été confirmés après contrôle de qualité externe des lames. Tous étaient de sexe masculin, d'âge compris entre 18 et 57 ans, provenant de cellules de détention différentes. La densité bacillaire au dépistage était connue pour 16/17 cas: <<1-9 BAAR/100 champs>>: 9 cas; <<+>>: 2 cas; <<++>>: 5 cas. La durée moyenne de détention était de 11 mois. Seize tuberculeux sur 17 (94,1%) ont été testés au VIH, tous négatifs. Le temps écoulé entre l'identification du cas index et le lancement de la recherche active d'autres cas était de 46 jours. Celui entre le dépistage des cas et le début du traitement variait entre 10 et 29 jours. La collaboration entre l'administration pénitentiaire et les agents de santé était insatisfaisante. Le screening systématique des détenus à la recherche de suspects de tuberculose à l'admission dans la prison n'était pas effectif. Les recommandations issues de l'investigation ont été mises en œuvre: traitement directement observé, réalisation des contrôles bacilloscopiques selon les directives. Tous les tuberculeux ont été guéris et le screening systématique des détenus à l'admission est désormais effectif.

**Conclusion** L'épidémie a été rapidement contrôlée. Des mesures de surveillance épidémiologique rigoureuses ont été prises. Aussi, une évaluation de la lutte contre la tuberculose dans toutes les prisons du pays a été réalisée au dernier trimestre de 2013 et les résultats sont en cours d'exploitation.

### PD-686-30 Facility risk assessment and tuberculosis infection control measures in five hospitals in Cambodia

S Saint,<sup>1</sup> S Kien,<sup>1</sup> T E Mao.<sup>1</sup>

<sup>1</sup>National Center For

Tuberculosis and Leprosy Control, Ministry of Health,

Cambodia, Phnom Penh, Cambodia. Fax: (+855) 23218090.

e-mail: saint.saly@yahoo.com

**Background:** Inadequate infection control (IC) poses risk for the emergence and transmission of tuberculosis (TB) in healthcare facility, especially in the high TB burden countries like Cambodia. In 2012, a national scale review documented insufficiently implemented TB IC measures among Cambodian hospitals. As a follow-up of this report; the National Center for Tuberculosis and Leprosy (CENAT), in collaboration with U.S/CDC, systematically assessed TB IC measures in five hospitals (CENAT, Pursat, Battambang, Banteay Meanchey, and Pailin).

**Methods:** A cross-sectional assessment was conducted in March 2014 to evaluate TB infection risk level and IC practices. Data were collected by interviewing and observing staff, observing patients, and reviewing available documents. When applicable, direct measurement of area's configuration, airflow, and UVGI was conducted. Areas assessed were out-patient department (OPD), wards, X-Ray unit, intensive care unit, and TB laboratory/culture center.

**Results:** TB IC in five hospitals appeared inadequate with IC committees established, but not actively or routinely providing an oversight for TB IC matter. At policy level, neither operational facility plan for TB IC nor annual TB screening program for staff was in place, but all hospitals screened people living with HIV/AIDS for TB disease. Screening and separation of TB suspects/patients was insufficient at OPDs, but good separation of patients was observed in most in-patient wards. Most areas were naturally ventilated, some with air change per hour below recommendations. UVGI use was available; however, regular maintenance was lacking. Respirator fit testing program did not exist in all hospitals; a shortage or inaccessibility of the respirators to staff was commonly reported

**Conclusion and recommendation:** Practices of TB IC in these five hospitals should be strengthened, including revitalization of IC committees and institution of operational TB IC plan at facility level, annual TB screening program among staff, and respirator fit testing program. A plan for regular maintenance of facility to optimize ventilation as well as of the UVGI should be established.

### **PD-687-30 Tuberculosis infection control and prevention in Mozambique: a gap between daily practice and the guidelines**

M Brouwer,<sup>1,2</sup> E Coelho,<sup>3</sup> C Das Does Mosse,<sup>4</sup> L Brondi,<sup>5</sup> F Van Leth.<sup>6</sup> <sup>1</sup>Consulting, PHTB Consult, Tilburg, Netherlands; <sup>2</sup>Technical Advise, Health Alliance International, Maputo, <sup>3</sup>National TB Programme, Ministry of Health, Maputo, <sup>4</sup>Provincial Health Directorate Tete, Ministry of Health, Tete, Mozambique; <sup>5</sup>Centre for Population Health Sciences, The University of Edinburgh, Medical School, Edinburgh, UK; <sup>6</sup>Global Health, Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands.  
e-mail: mbrouwer@phtbconsult.org

**Background:** Health Care Workers (HCWs) are, through their work, more exposed to Tuberculosis (TB) than the general population. Infection prevention and control (IPC) measures aim to reduce the transmission of TB in health care settings. HCWs at all levels of the healthcare system are crucial in the implementation of these measures. We assessed the level of implementation of IC measures in Mozambican healthcare facilities, and identified barriers and facilitators for HCWs to IPC implementation.

**Design/Methods:** Quantitative assessment of 29 healthcare facilities, and focus group discussion (FGDs) with four categories of HCWs: auxiliary workers, medical staff, nurses and TB program staff.

**Results:** A written TBIPC plan was present in 48% of the facilities. Ninety per cent provided educational TB activities for health staff and 58% did this at least monthly. All facilities had guidelines for treatment of diagnosed TB patients, but only 66% had guidelines for identification of (presumptive) TB patients. Separation of (presumptive) TB patients occurred in 11% of laboratories, out patient departments and medicine wards. 91% of health staff instructed patients on sputum collection, but only 4% observed production of a sample. Just 52% of the departments had adequate ventilation, which could increase to 76% if all doors and windows would be opened. Three-quarters of the departments had respirators available. Only 36% of the staff used it correctly. Participants of the FGDs were well aware of their occupational TB risk and used various measures to reduce it. The main barriers they faced using the measures were lack of clear guidelines, windows that don't open, and insufficient respirators. Patient behaviour was a barrier if patients were not willing to comply with measures such as prioritization those with cough. Health education for health facility users and training on TB and TBIPC facilitated use of TBIPC measures.

**Conclusion:** State the implications of the results and key recommendations. Present specific findings on how the research addressed the study, question and challenge. Highlight opportunities for future research as well as implications for further research or TB prevention and control programmes.

### **PD-688-30 Uniting for tuberculosis control: experiences from a collaborative effort in the copperbelt province prisons of Zambia**

L Lochting,<sup>1</sup> O Simooya,<sup>2</sup> N Sanjobo,<sup>2</sup> R Mwilu,<sup>3</sup> B Chikumbi.<sup>3</sup> <sup>1</sup>International Cooperation, Norwegian Heart and Lung Patient Organisation (LHL), Oslo, Norway, <sup>2</sup>Programmes, In But Free Prisons Project, Kitwe, Zambia, <sup>3</sup>Directorate, Copperbelt Health Project, Kitwe, Zambia.  
e-mail: nsanjobo@cbru.ac.zm

**Background and challenges to implementation:** Tuberculosis (TB) and Human Immunodeficiency Virus (HIV) are major public health challenges affecting prison populations. Studies show higher rates of TB and HIV infection in prison settings than outside. Because most prisoners are in jail for a short period, protecting them from infectious diseases provides public health benefits to the greater community outside. Measures to prevent the transmission of infectious diseases inside prisons are needed urgently.

**Intervention or response:** Beginning 2012, IN BUT FREE Prisons Project entered into collaboration with the Copperbelt Health Education Programme with financial support from the Norwegian Heart and Lung Patient Organisation to implement a tuberculosis awareness programme targeting 3,000 inmates and 350 prison officers in 8 prisons. The objective of the collaboration is to build capacity of inmates and officers in TB and HIV using guidelines developed by the Ministry of Health. The programme uses volunteer inmates and officers trained as Treatment Supporters. Sensitization cam-

paings are carried out through drama performances, cell teachings, edu-sport, poems, distribution of Information, Education and Communication (IEC) materials.

**Results and lessons learnt:** 300 Inmates and 60 Prison Officers have been trained. IEC materials in form of TB Booklets, Brochures and Posters on TB/HIV have been printed and distributed. Mentoring visits and Command meetings are conducted quarterly. Drama Groups have been established. Health education and TB case detection has become a regular feature. Patient referral system has been developed and follow up is regularly conducted. At the beginning of the collaboration in 2012, there were 64 TB Patients while currently there are 30 patients. Despite these positive developments, lack of adequate medical facilities, conflicts between infection control measures and inmate segregation and lack of facilities in some prisons to isolate TB patients with smear positive are still some challenges to effective TB control.

**Conclusions and key recommendations:** The use of prisoners and prison officers as key players in TB control is an initiative we find promising to demonstrate community commitment and drive. Prison authorities should seek ways of providing isolation bays. Prison health systems should be linked to district health systems.

#### PD-689-30 Resistance to disinfectants of *Mycobacterium tuberculosis* parallels antibiotic resistance

M Acurio,<sup>1</sup> E Pacheco,<sup>1</sup> Z Puyen,<sup>1</sup> J Sagripanti.<sup>2</sup> <sup>1</sup>Public Health, National Institute of Health, Lima, Peru; <sup>2</sup>Public Health, Edgewood Chemical Biological Center, Edgewood, MD, USA. e-mail: eacuriou@yahoo.com

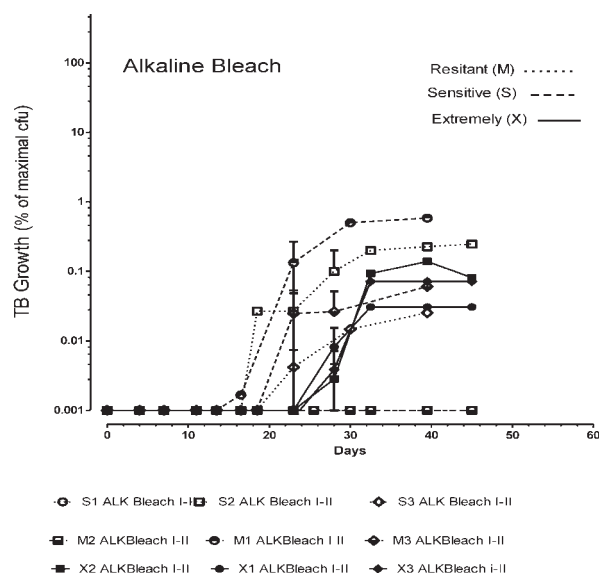
**Background:** The prevalence of tuberculosis acquired in hospitals and laboratories of Peru highlights the need for improving current disinfection. The microbiocidal effect of common disinfecting agents such as phenol, ethanol, and chlorine has been studied in the past. However, the efficacy of these disinfectants on an increasing number of emerging strains of *M. tuberculosis* (MTB) that are resistant to antibiotics has yet to be established. Thus, the objective of our study was determining whether disinfectants previously found to inactivate sensitive strains of MTB are also effective against multi-drug resistant (MDR) and extremely resistant strains (XDR).

**Methods:** We quantitatively compared in parallel experiments, the relative efficiency of reagents commonly used for disinfection of hospitals and laboratories in Peru against sensitive, MDR and XDR strains of MTB. We exposed every strain to each disinfectant (or to sterile water as control) for 30 minutes at 21°C and then, survival kinetics of every combination was determined by enumerating every two days the colonies that appeared in Lowenstein Jensen culture medium up to 60 days post treatment.

**Results:** Phenol 5%, ethanol 70% and 1% commercial chlorine (bleach, sodium hypochlorite) without adjusting its pH (pH 12.3 out of the commercial bottle), all produced a partial inactivation of MTB that correlated with the respective resistance of strains to antibiotics.

Interestingly, the same hypochlorite (bleach) was able to inactivate each strain below the detection limit of our method (5 Log10) when its alkalinity was neutralized to pH 7. In addition, two commercial products (containing quaternary-ammonium-salts) with tuberculocidal claims were found ineffective.

**Conclusions:** These findings indicate that resistance of *M. tuberculosis* strains to disinfection parallels their antibiotic resistance. Thus, reagents commonly used to inactivate sensitive strains may fail to disinfect MDR and XDR strains. The data also suggests that neutralized hypochlorite is an effective disinfectant while the use of phenol, commercial bleach at alkaline pH, quaternary ammonium salts and ethanol is discouraged in environments potentially exposed to all types of *M. tuberculosis* strains (sensitive, MDR and XDR). These results should contribute to increased biosecurity in Peru as well as in other countries with similar conditions.



**Figure 1. Survival kinetics of TB treated with alkaline bleach.** Three sensitive strains (S) of TB alkaline bleach and seeded into LJ culture. Similarly, resistant (M, half dark symbols) and extremely resistant strains (X, dark symbols), three of each were exposed to disinfectant. At various times indicated in the X-axis, the number of colonies was counted and the growth curves for each strain represented in the graph by either dotted line (S), dashed lines (M), or solid lines (X). In each experiment, each strain was independently exposed to sterile distilled water as control and the colonies obtained considered as 100% survival. The effect of disinfectants is expressed as a percentage of the maximal colony number obtained in the water treated controls. Standard deviation is indicated by growth kinetics above the mean of two independent experiments with duplicated data points each.

#### PD-690-30 Improving HIV screening of inmates with suspicion of active TB disease through a cough surveillance team in Cipinang detention center

YN Sumarli,<sup>1</sup> N Tandirerung,<sup>2</sup> M Samsuri,<sup>3</sup> MR Christian,<sup>4</sup> H Al-darraj.<sup>5</sup> <sup>1</sup>Clinic, Cipinang Detention Center, Jakarta, <sup>2</sup>National TB Program, Ministry of Health, Jakarta, <sup>3</sup>Clinical Services Unit, Family Health International 360, Jakarta, <sup>4</sup>Tuberculosis unit, World Health Organization, Jakarta, Indonesia; <sup>5</sup>Centre of Excellence for Research in AIDS, University of Malaya, Kuala Lumpur, Malaysia. e-mail: regina.loprang@gmail.com

**Background and challenges to implementation:** Despite the detrimental convergence of HIV and TB, particularly in correctional systems, screening for HIV infection



among active TB cases is limited in Indonesia (0.8% of incident TB cases reported in 2012 in Indonesia had known HIV status). Cipinang detention centre is currently housing around 3,500 inmates; a 300% of its actual capacity of 1,136 inmates. There is no routine HIV testing in the facility. This overcrowding facilitates TB and HIV transmission among inmates and to the community in large. We developed a cough surveillance model, where educated inmates were chosen to define fellow inmates with current cough to be screened for active TB disease. We investigated the effect of such an intervention on improving screening for HIV among inmates suspected with TB disease

**Intervention or response:** Thirty inmates were trained to be cough officers and were assigned to 4 blocks in the DC and their work was divided into 3 shifts. Their tasks were to identify inmates with any duration of cough, to provide them with surgical masks and to refer suspects to the detention centre clinic for further TB and HIV investigation.

**Results and lessons learnt:** From December 2012 to August 2013, of the total number of 581 inmates who were surveyed, 257 were identified with cough for any duration. 136 (53%) were identified as TB suspects and 20 (14.7%) were AFB microscopy smear positive and were prescribed anti-TB medications. All of the 136 inmates suspected with active TB disease were counseled for HIV testing and 32 were HIV co-infected: 19 (95%) of active TB cases and 12 (10.4%) of the rest.

**Conclusions and key recommendations:** Empowering inmates as cough officers is one of promising methods to intensify HIV and TB case finding in detention center with limited resources. Early detection and prompt linkage to timely healthcare services are expected to reduce TB and HIV transmission in similar settings.

### PD-691-30 Interventions improve TB infection control at hundreds of health facilities in Ethiopia, 2012–2013

B Negash,<sup>1</sup> B Girma,<sup>2</sup> Y Molla,<sup>2</sup> T Anteneh,<sup>2</sup> D Jerene,<sup>2</sup> M Melese,<sup>2</sup> P Suarez.<sup>3</sup> <sup>1</sup>Federal Ministry of Health, Disease Prevention & Control Directorate, Addis Ababa, <sup>2</sup>Help Ethiopia Address Low TB Performance (HEAL TB) project, Management Sciences for Health (MSH), Addis Ababa, Ethiopia; <sup>3</sup>Management Sciences for Health (MSH), Arlington, VA, USA. e-mail: bgirma@msh.org

**Background:** TB infection control (TB IC) is necessary to control the spread of TB and multidrug resistant TB (MDR-TB). Although Ethiopia has developed and disseminated national guidelines for TB IC in health care settings, implementation of these guidelines has not been monitored and health facilities have not systematically documented or reported their TB IC activities.

**Interventions:** In 2012 and 2013, the Amhara and Oromia Regional Health Bureaus (RHBs), with assistance from the USAID-funded Help Ethiopia Address Low TB Performance (HEAL TB) project, supported the systematic implementation and documentation of TB IC measures at 691 health facilities in the Amhara and Oromia regions. The partners first conducted a TB IC

baseline assessment and then used the assessment results to inform their interventions. The RHBs and HEAL TB helped each facility establish or strengthen its TB IC committee, develop a TB IC plan, and monitor implementation of their plan. All facilities' TB IC plans included regular TB screening among health workers. The partners also encouraged facilities to establish a system for promptly screening all patients in out-patient departments to prevent TB transmission within the facilities. The RHBs and HEAL TB defined a set of key TB IC indicators and developed checklists to monitor the facilities' performance against the indicators.

**Results:** At baseline out of 9264 health workers, 50 (539/100,000 (95% CI=405.1, 705.5) had developed TB in one year. As compared to the case notification rate, health workers had 3 times higher risk of infection. At baseline only 9% of the health facilities had TB IC plans. After implementing a TB infection plan, by June of 2013, 32% had TB IC plans. Similarly, at baseline, only 22% of the health facilities prioritized care for presumptive TB patients, but by June of 2013, 59% of the facilities were prioritizing care for presumptive TB patients. The number of facilities with functional TB IC committees increased by 46% and the number of facilities with standalone TB clinic increased by 21%.

**Conclusion:** The magnitude of TB among health workers is high and the TB infection measures are required. Stronger implementation, monitoring and evaluation mechanisms should be instituted at all levels of the health care system so that TB IC measures can be regularly examined and enhanced.

indicator	Baseline %	Post intervention%
TB IC plan	9	32
TB IC committee	25	71
Prioritize presumptive cases	22	59
Standalone TB clinic	68	89

### PD-692-30 Survey of the implementation of tuberculosis infection control at healthcare facilities in four districts in Malawi

D Garone,<sup>1</sup> O Jalon,<sup>1</sup> T Beyene,<sup>2</sup> M Van Lettow,<sup>2,3</sup> J Van Oosterhout,<sup>2</sup> F Cataldo,<sup>2</sup> M Matchaya,<sup>4</sup> M Murowa.<sup>5</sup> <sup>1</sup>Medical, Médecins Sans Frontières-Belgium, Thyolo, <sup>2</sup>Medical and Research, Dignitas International, Zomba, Malawi; <sup>3</sup>Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada; <sup>4</sup>Nsanje District Hospital, Ministry of Health Malawi, Nsanje, <sup>5</sup>Thyolo District Hospital, Ministry of Health Malawi, Thyolo, Malawi. e-mail: msfocb-blantyre-opr@brussels.msf.org

**Background:** Tuberculosis infection control (TB IC) is rarely implemented in the health facilities (HF's) in resource limited settings and is a crucial component of HIV and TB services integration. The study aim was to assess TBIC plans, practices and potential barriers to implementation in Malawi.

**Design/Methods:** As part of a cross-sectional study aiming to measure and analyse the level of HIV and TB service integration, the implementation of TBIC policies

was assessed in 95 HF's (5 district hospitals and 90 Health centres) within Thyolo, Nsanje, Zomba and Balaka districts, Malawi. A survey tool that included a scoring system was used to explore the facility-level managerial, administrative, environmental and personal protection and infection control measures

**Results:** 53 (56%) HF's had infection prevention and control committees and 55 (58%) had a designated person in charge of IC, however only 28% of HF's had a meeting convened in the last month. 26 (27%) HF's had a displayed TBIC plan. In the majority of HF's (93%), health talks given in the waiting areas included TB awareness messages. 44 (47%) HF's were screening patients for cough and education of cough hygiene was provided as they enter the facility. However, only 10/94 (11%) of the facilities reported providing masks to patients with cough. Ventilation in the waiting areas was adequate for TBIC in all HF's; however in half of the consultations rooms windows could not be opened. Despite availability of N95 masks in most (97%) HF's, only 11% of the staff working in high risk areas was wearing masks. Only 3% of HF's achieved > 70% of the personal protection observations with only 32% routinely screening health staff for TB. 8% of the HIV staff and 40% of the TB staff were trained in TBIC.

**Conclusion:** Our study shows that substantial barriers to full implementation of national TBIC measures exist in Malawi, in particular defective administrative measures, lack of personal protection measures and insufficient TBIC training. Successful implementation of HIV/TB services integration requires incorporation of effective TB infection-control strategies.

#### **PD-693-30 Improving infection control practices for TB through consistent mentorship and training of health-care workers in an HIV treatment programme**

P Nahirya-Ntege,<sup>1</sup> C Sekimpi,<sup>1</sup> D Nangendo,<sup>1</sup> P Ikongit,<sup>1</sup> R Ogwang,<sup>1</sup> J Bitarabeho.<sup>1</sup> <sup>1</sup>New Hope Project, Children's AIDS Fund-Uganda, Kampala, Uganda.  
e-mail: pnahirya.caf@gmail.com

**Background and challenges to implementation:** Infection control (IC) practices by healthcare workers are important in reducing transmission of Tuberculosis in HIV clinics. Children's AIDS Fund Uganda provides comprehensive HIV/AIDS Care services to about 25,000 clients in 7 health facilities. Quality is assured through support supervision, mentorships, training for health workers and facility based quality improvement activities. Children's AIDS Fund(CAFU) evaluated the contribution of training and mentorship on infection control practices in the 7 health facilities.

**Intervention or response:** In February 2013, an initial assessment to establish level of appropriate IC practices using a guide was done by a CAFU technical quality assurance(TA) team. The broad areas of IC assessed were availability of written policies for IC, active practice of these policies and procedures for handling medical and non-medical waste. Based on the findings, 30 health-

workers were trained in infection control practices one month later. This was followed by support supervision and mentorship by the CAFU TA team. A second assessment was done in August 2013 to review any improvements in infection control practice. The results are described using summary statistics.

**Results and lessons learnt:** All 7 sites improved in availability of written policies for infection control, active practice of these policies according to guidelines and procedures for handling medical and non-medical waste by 56.5%( $p<0.003$ ), 30%( $p<0.001$ ) and 33%( $p<0.064$ ) respectively. There was complete improvement in using surgical masks for TB suspects in the clinic, using the TB screening tool at every patient visit, use of sputum to screen for TB, fast tracking all TB patients, establishing a TB focal person, using sterile gloves and ensuring potential waste is incinerated off-site in all sites. Other improvements in policies for IC were use of IC documents by staff from 0–71%; while in active practice of guidelines were use of N95 masks by staff from 29–71%, hand washing between patients from 57–86%, isolation of TB suspects from 43–71%, creating a TB day in the clinic from 43–71%; and in handling waste were use of separate waste disposal containers including sharps from 43–86% and a written & displayed procedure for medical waste from 29–71%. Formal training as an intervention reinforced by ongoing /real-time on-site mentorships and support supervision resulted in application of acquired knowledge for improved infection control practices.

**Conclusions and key recommendations:** In addition to mentorship, HIV programmes should focus resources towards in-service training of staff to improve health services especially TB infection control.

#### **PD-694-30 A baseline assessment of TB infection control practices in health facilities in Kenya**

E Masini,<sup>1</sup> J Kioko,<sup>1</sup> R Muthoka.<sup>1</sup> <sup>1</sup>Tuberculosis, Leprosy and Lung Disease Unit, Ministry of Health, Nairobi, Kenya.  
Fax: (+254) 6824003. e-mail: emasini32@gmail.com

**Background:** Kenya has a high TB and HIV burden, with TB case notification of 338/100,000 (2012). The country has successfully implemented TB-HIV collaborative activities including integration of TB-HIV services, testing for HIV and provision of antiretroviral therapy to co-infected patients. We present the findings of a baseline assessment of TB infection control practices conducted in 254 health facilities from across the country by the Kenya national Tuberculosis Program in 2012-13.

**Design/Methods:** In 2011, the National TB program developed a health facility TB infection control roll-out plan. Consequently, the national TB infection control policy guidelines and a national training curriculum including a health facility TB infection control assessment tool were developed. Trainings on TB infection control of selected members of hospital staff from 254 health facilities drawn from across the county was then done. The trained staff conducted the TB infection

control assessment in their facilities using the standard TB infection control assessment tool. We conducted a descriptive analysis of the data collected from this assessment.

**Results:** A total of 254 facilities were assessed comprising 47 County hospitals, 61 sub-County hospitals and 146 health centres. None of these health facilities had ever conducted a prior TB infection control risk assessment. Though 56 facilities (22.0%) had a general infection control plan, only 5 (1.9%) had TB component incorporated in it. 16 (6.3%) of the health facilities provided screening for cough among general out-patient department attendees. However, only 9 (3.5%) provided separation for patients with presumptive TB from those who were not including providing priority service to those with presumptive TB to ensure shorter waiting times. In 94.9% (241) of the facilities, patients collected sputum in an open space. The median laboratory turn around-time for sputum microscopy was 2 days (range 1–5 days). None of the health facilities provided systematic TB screening for hospital staff. In 53(20.8%) of health facilities at least one member of the hospital staff had been diagnosed with TB disease one year prior to the assessment.

**Conclusion:** This data suggests sub-optimal TB infection control practises in health facilities in Kenya with likely ongoing nosocomial transmission. It provides a baseline for future measurement of the impact of the ongoing implementation of TB infection control practises in the country.

## 18. MDR-TB MANAGEMENT

### PD-695-30 Use of genetic analysis of multidrug-resistant TB strains for rapid diagnosis in comparison with conventional technique

**MK Munir.**<sup>1</sup> <sup>1</sup>PMRC TB Research Centre, Pakistan Medical Research Council, Lahore, Pakistan.  
e-mail: munir\_gemini81@yahoo.com

**Background:** Tuberculosis is a contagious disease that is caused by a bacterium called *Mycobacterium tuberculosis*. World Health Organization has estimated that eight million people are infected with TB every year, out of those 95% live in developing countries. Nearly one-third of the global population, that is more than two billion people are infected with M. tb and are at risk of developing the disease. Impact of TB on socioeconomic status is substantial in Pakistan as it harbors 5.1% of total national disease burden. Aim of this study was to amplify katG and rpoB genes by PCR for using these genes as markers for the rapid diagnosis of isoniazid and rifampicin resistant strains in smear positive pulmonary TB patients and to compare it with drug susceptibility testing on Lowenstein Jensen medium.

**Design/Methods:** The descriptive study was carried out in the Institute of Molecular Biology and Biotechnology, The University of Lahore, Lahore in collaboration with Pakistan Medical Research Council, TB Research Centre

and Department of Chest Medicine, Mayo Hospital, Lahore during January 2012 to August 2012. A total of 50 Ziehl Neelsen smear positive sputum specimens were included in this study. Convenient purposive sampling technique which is non probability sampling technique was used in this study.

**Results:** A total of 40 (80%) were resistant to at least one of the four 1<sup>st</sup> line anti TB drugs. Among 40 resistant cases 60% was of MDR TB of which 64% had acquired MDR TB while 50% had primary MDR TB. Phenotypically 56% out of 50 cases were resistant to isoniazid, 64% were resistant to rifampicin. Out of 32 strains which were rifampicin resistant by drug proportion method on LJ medium, 78.2% had mutation of which 23 isolates had mutations affecting four amino acid codons of rpoB gene; 531 (60%), 516 (20%), 526 (8%) and 512 (4%) within the rifampicin resistance determining region (RRDR) while 8% had mutations outside RRDR. Out of 28 isoniazid resistant strains 68% had S315T mutation in katG while 32% of resistant isolates had no mutation in this region. In diagnosis of MDR there is insignificant difference (P Value >0.05) showing the technique is valid however rate of diagnosis is 25% lower as compared to drug proportion method.

**Conclusion:** it is suggested that gene amplification technique could only be used as supportive tool for early diagnosis where available with standard proportion method as 75% agreement was shown with gold standard.

### PD-696-30 Comparison of tuberculosis drug activity and minimum inhibitory concentration among MDR-TB patients at Kibong'oto Hospital

**R Kinyaha,<sup>1</sup> S Mpagama.<sup>2</sup>** <sup>1</sup>Laboratory, Kibong'oto Infectious Diseases Hospital, Kilimanjaro, <sup>2</sup>Research, Kibong'oto Infectious Disease Hospital, Kilimanjaro, United Republic of Tanzania. e-mail: r.kinyaha@kcrc.ac.tz

**Background** Plasma Inhibitory Activity Assay (Plasma Bactericidal Assay) is an assay that gives a quantitative estimates of effectiveness of the bactericidal effect in patients who are on anti-tuberculosis therapy. The assay involves the use of pre-isolated organisms and blood (plasma) from the same patient on treatment. Minimum Inhibitory Concentration (MIC), the minimum concentration of drug that will kill/inhibit the growth of micro-organism. This is the quantitative estimation of Drug Susceptibility of an organism to tested drugs. It involves the use of pre-isolated organisms from the patient before the start of treatment.

**Design/Methods:** The study was cross-sectional study. It involved participants who were diagnosed and confirmed to have MDR-TB, who agreed to sign the consent form. Prior to the start of MDR-TB treatment, sputum was collected from each participant, processed and cultured on solid and liquid media. Three weeks after the initiation of MDR-TB treatment, blood was collected from each participant and plasma separated. Plasma was used to test pre-isolated organisms in a liquid culture and



Time to Positivity (TTP) was recorded. Drug Susceptibility Test (DST) using Minimum Inhibitory Concentration (MIC) was done on trek plates (Sensititre® MYCOTB MIC plates) using the pre-isolated organisms from solid media. Tuberculosis Drug Activity (TDA) calculated from TTP was correlated with MIC.

**Results:** The mean TDA among fourteen (14) participants was  $2.19 \pm 0.62$  for those who were treated with Capreomycin, Ofloxacin, Ethionamide, and Pyrazinamide. Among 14 participants, seven (7) participants were treated with Kanamycin, Ethionamide, Levofloxacin, Pyrazinamide and Cycloserine later showed the mean TDA of  $2.19 \pm 1.0$ . MIC and TDA showed inverse relationship (i.e the increased Drug Activity showed the lower concentration that inhibited/killed the organisms' growth).

**Conclusion:** Drug activity was found to correlate with Minimum Inhibitory Concentration during treatment of pulmonary TB. This indicates that, this marker (TDA) assay have a role and can be used in monitoring the treatment outcome which includes prediction of drug resistance in early stages of treatment.

#### **PD-697-30 Decentralisation of programmatic management of drug-resistant tuberculosis (PMDT) services in Nigeria: lessons learnt**

M Gidado,<sup>1</sup> J Obasanya,<sup>2</sup> R Eneogu,<sup>2</sup> G Akang,<sup>2</sup> O Emmanuel,<sup>3</sup> J Onazi,<sup>1</sup> T Odusote,<sup>4</sup> O Fabiyi.<sup>5</sup> <sup>1</sup>TB Project, KNCV/TB CARE I Project, Abuja, <sup>2</sup>Public Health, National TB & Leprosy Control Program, Abuja, <sup>3</sup>TB project, MSH/TB CARE I Project, Abuja, <sup>4</sup>TB/HIV unit, USAID, Abuja, <sup>5</sup>Clinical, Sacred Heart Hospital Abeokuta, Abeoguta, Nigeria. e-mail: gidadom@kncvnigeria.org

**Introduction:** With MDR-TB prevalence of 2.9% among new TB cases and 14.3% among previously treated TB cases; Nigeria is among the high drug-resistant TB (DR-TB) burden countries.. The introduction of GeneXpert MTB Rif machines has led to an increase in the number of Rifampicin-resistant TB cases requiring treatment for DR-TB. There are only 10 DR-TB treatment sites with less than 300-bed capacity resulting in waiting list and patient's refusal for admissions in facilities outside their states. The objective of the paper is to describe the lessons learnt from PMDT decentralization.

**Methodology:** The national PMDT guideline was revised to adapt a mix model of care with clear criteria for: 1) A 3-month hospitalization during the intensive phase; 2) Enrolment on treatment within the community; 3) An 8-month hospitalization throughout the intensive phase. Capacity building for State teams on all the 3 models was done in 8 selected states for phased implementation.

**Results:** A total of 91 health care providers were trained from the 8 States. 72 DR-TB patients were admitted under the mix model for a shorter duration of 3 months intensive phase (M:51; F: 21) in 2 batches 47 and 25 patients respectively. 61.6% of the patients were in the age group 25–44 years; 87.7% had documented HIV status, of which 78.6 % are HIV negative. All 47 in the first batch were discharged after 3 months of the intensive phase with negative sputum smear results & the

25 patients awaiting discharge. Currently, 24 patients have been enrolled for treatment at the community.

**Challenge:** Delay in completion of all the base-line investigations for patients primarily enrolled at community level; documentation of follow-up lab results & drug intake and ensuring TB IC.

**Conclusion:** Ambulatory/community PMDT is feasible. Capacity building and logistic support for patient's daily transport for DOT and sample movement are important for success.

#### **PD-698-30 Tuberculosis multidrug-resistance (MDR) patterns among patients attending public health facilities in Nairobi, Kenya, February-August, 2012**

J Limo,<sup>1,2</sup> W Boru,<sup>1,2</sup> T Galgalo.<sup>1</sup> <sup>1</sup>National Public Health Laboratories Services, Field Epidemiology and Laboratory Training Program, Nairobi, <sup>2</sup>National Public Health Laboratories Services, Ministry of Health, Nairobi, Kenya. e-mail: jacqmaru@gmail.com

**Background:** Tuberculosis (TB) is a bacterial infection caused by *Mycobacterium tuberculosis* (MTB) complex. TB caused by Mycobacterium Drug Resistant (MDR) bacilli is a growing concern with an estimated 0.5 million cases worldwide and 40,000 in Africa. In Kenya about 3000MDR TB cases were reported in 2011. The objective of this study was to determine the burden of drug resistance to first line anti TB drugs among MTB patients attending public health facilities in Nairobi.

**Methods:** A retrospective laboratory records review of all drug resistant TB patients from selected facilities was done. Information including age, drug resistance, HIV status, new and retreatment cases were extracted using line listing form. A case was defined as any patient who was resistant to at least both isoniazid and rifampicin during the study period. Data was analyzed using Epi Info and Excel.

**Results:** A total of 605 TB isolates had their MTB strains diagnosed for drug susceptibility testing. 590 isolates had complete data for analysis, 390 were new patients and 200 previously treated. Majority of the cases were from the age group between 25–34 at 30% (n=180) and with the highest TB-HIV co-infection rate of 33% (n=200) with in the same age group. About 82 % and 77% of the strains from new patients and previously treated were fully sensitive to all the drugs tested respectively. Among new patients resistance to isoniazid, streptomycin, ethambutol and rifampicin was 10.3%, 1.02%, 5.1% and 4.6% respectively while among previously treated patients resistance was 19.5%, 10%, 9% and 10% respectively. Most of the TB cases were from Kamukunji district 30% (177) while Westlands had the least at 4% (n=24). The prevalence of MDRTB was 0.77% and 13.5% among newly and previously treated patients respectively.

**Conclusion:** The study found high levels of multi drug resistant TB and high TB-HIV co-infection rate. Concerted efforts are therefore required to prevent drug resistance and effectively treat patients with MDR-TB as

a crucial protection of public health and TB control. The DOTS strategy developed in 1970s and 1980s can prevent MDR TB from becoming a serious problem in a population and also reduce MDR TB once it has occurred. We call for strengthened efforts on the implementation of the comprehensive framework of DOTS-Plus strategy that add components for MDR-TB diagnosis, management and treatment integrated within the DOTS program.

### PD-699-30 Are all eligible tuberculosis patients in national tuberculosis programme screened for drug resistance in Puducherry, India?

H Shewade,<sup>1</sup> S Burugina Nagaraja,<sup>2</sup> J Tripathy,<sup>3</sup> S Govindarajan,<sup>4</sup> P Chinnakali,<sup>5</sup> A Kumar,<sup>6</sup> AK Paulraj,<sup>7</sup> G Roy.<sup>5</sup> <sup>1</sup>Community Medicine, Mahatma Gandhi Institute of Medical Sciences (MGIMS), Sevagram, Wardha, <sup>2</sup>Community Medicine, ESIC Medical College, Bengaluru, <sup>3</sup>Community Medicine, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, Chandigarh, <sup>4</sup>State TB cell, Directorate of Health Services, Puducherry, <sup>5</sup>Preventive and Social Medicine, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry, Puducherry, <sup>6</sup>South East Asia Office, The Union, New Delhi, <sup>7</sup>Country Office in India, World Health Organization, New Delhi, India.  
e-mail: hemantjipmer@gmail.com

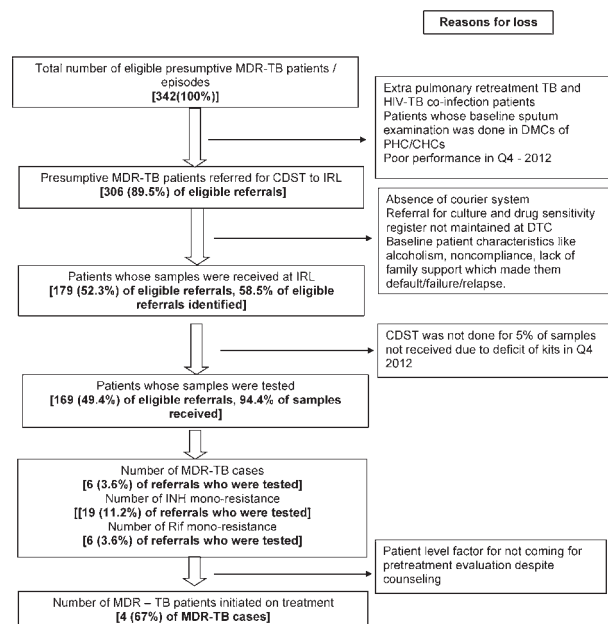
**Background:** Previous studies from India and elsewhere globally have documented high pre-diagnostic and pre-treatment attrition among multi-drug resistant tuberculosis (MDR-TB) patients. In this study, we aimed to assess the proportion of eligible presumptive MDR-TB patients referred, tested, diagnosed and initiated on MDR-TB treatment and assess the factors associated with failure to complete the diagnostic pathway.

**Methods:** The study was conducted in Puducherry district (population~1 million), South India. 'Presumptive MDR-TB patients' (all retreatment TB; any follow up smear positive; new pulmonary TB who were contacts of known MDR-TB patients; and all HIV-TB co-infected cases at diagnosis) were referred to the laboratory for culture and drug-susceptibility testing using Line Probe Assay and those diagnosed with MDR-TB patients were offered treatment. The study had two components. The quantitative component consisted of retrospective cohort analysis, through record review, of all the eligible presumptive MDR-TB patients identified by investigators between October 2012 and September 2013. The qualitative component included in-depth interviews of key informants involved in the implementation and monitoring of programmatic management of drug-resistant TB services. Data were double entered, validated and analyzed using EpiData.

**Results:** Of 342 eligible presumptive MDR-TB patients/episodes identified by the investigators, 306 (90%) were identified and referred. Of them, 127 (42%) did not reach the laboratory; 10 (6%) did not get tested even after reaching the lab. Of 169 tested, 6 (4%) were diagnosed as MDR-TB of whom four were started on treatment. Patients, with extra pulmonary retreatment

tuberculosis (RR=2), HIV/TB co-infection (RR=1.5), identified in quarter 4 of 2012 (RR=1.4) and identified at primary/secondary health centres (RR=1.7) were less likely to be tested. During in depth interviews, failure to maintain referral for culture and drug sensitivity testing register at district TB centre, absence of courier service to transport sputum and patient noncompliance (related to alcohol abuse and lack of family support), shortage of diagnostic kits were the key operational issues identified. **Conclusion:** There was high attrition at every stage of the diagnostic pathway. Urgent measures including a mechanism of sputum collection and transport and continuous supply of test kits are required to fill the gap.

Figure 1: Flow of presumptive MDR-TB patients identified from Oct 2012-Sept 2013 in Puducherry, India.



### PD-700-30 Validation of genotype MTB-DR plus assay for rifampicin and isoniazid resistance detection on sputum samples in Cote D'Ivoire

K N'guessan,<sup>1</sup> A Tehe,<sup>2</sup> M-S Keita Sow,<sup>3</sup> C Adje-toure,<sup>4</sup> J Kouakou,<sup>5</sup> M Dosso.<sup>6</sup> <sup>1</sup>Bactériologie-Virologie, Institut Pasteur de Côte d'Ivoire, Abidjan, <sup>2</sup>Laboratory Branch, RetroCI/CI, Abidjan, Côte D'Ivoire; <sup>3</sup>Laboratory Branch, American Society for Microbiology, New York, NY, USA; <sup>4</sup>Laboratory Branch, RetroCI, Abidjan, <sup>5</sup>Direction, Programme National de Lutte contre la Tuberculose, Abidjan, <sup>6</sup>Bactériologie-Virologie, Institut Pasteur de Côte d'Ivoire, Abidjan, Côte D'Ivoire. e-mail: kouassinguessan@pasteur.ci

**Background:** In 2012, with the help of international and national partners, laboratories of culture for Tuberculosis in Côte d'Ivoire were renovated and equipped. The laboratory of Pasteur Institute Côte d'Ivoire serves as the national TB reference laboratory (NTRL). In addition, CeDReS, a central laboratory has developed the capacity to diagnose and identify Multi-Drug Resistant-TB. The NRTL developed MDR-TB diagnostic algorithms which

include different assays such as the GenoType MTBDRplus. Objective: We conducted an evaluation study on the GenoTypeMTBDRplus assay's ability to detect mutations conferring resistance to Rifampin and Isoniazid directly from sputum.

**Methods:** In Ivorian tuberculosis centers, 120 smear positive pulmonary patients' suspects of MDR-TB were recruited. The sputum were collected and transported in an icebox at 4°C to the National Reference Laboratory for Tuberculosis at Institut Pasteur de Côte d'Ivoire. Sputa were decontaminated by NALC and comparatively analyzed with the MTBDRplus assay version 2.0 and the Bactec MGIT 960 automated Drug Susceptibility Testing (MGIT-DST). The GeneXpert MTB/RIF assay was performed for 21 sputa with absence of hybridization for at least one *rpoB* wild-type probes. Four and seven respectively discordant and concordant results were also analyzed.

**Results** The mutations in the *rpoB* gene were 21 (17.5%), 20 (16.7%), 7 (5.8%), 10 (8.3%), respectively for D516V, H526Y, H526D, S531L. S315T mutation in *katG* gene associated or not with mutation in promoter of *inhA* was detected in 76 (63.3%) of the sputum. Compared to MGIT-DST, the sensitivity and specificity of the MTBDRplus for Rifampin resistance detection were 100% (75–100%) and 73.2% (61.3–84%) respectively. For Isoniazid resistance detection, the sensitivity and specificity were respectively 95% (90–99) and 95.1% (88.5–100%). Interpretation of 16 sputa without hybridization of *rpoB* wild-type probe 8 compared to those obtained with MGIT-DST and GeneXpert MTB/RIF were discordant and concordant respectively for 11 and 5.

**Conclusion** For Rifampin and Isoniazid resistance detection directly with sputum, the MTBDRplus assay is an excellent tool for rapid diagnostic of MDR-TB. However, interpretation of absence of hybridization of *rpoB* wild-type 8 without specific protein detected needs to be confirmed. Furthermore, due to possible differences noted in results in different environments, operational research is key when introducing a new assay.

#### PD-701-30 Evaluation of the impact of line probe assay on time to treatment initiation for MDR-TB patients in Archangelsk region of Russia

P Eliseev,<sup>1</sup> G Balantsev,<sup>2</sup> E Nikishova,<sup>1</sup> DA Enarson,<sup>3</sup> A Detjen,<sup>3</sup> P Phillips,<sup>4</sup> S Squire,<sup>5</sup> A Maryandyshev.<sup>1</sup>

<sup>1</sup>Tuberculosis, Northern State Medical University, Arkhangelsk, <sup>2</sup>Tuberculosis, Northern Arctic Federal University, Arkhangelsk, Russian Federation; <sup>3</sup>Tuberculosis, The International Union Against Tuberculosis and Lung Disease, Paris, France; <sup>4</sup>Tuberculosis, MRC Clinical Trials Unit at UCL, London, <sup>5</sup>Tuberculosis, Liverpool School of Tropical Medicine, Liverpool, UK. e-mail: pediatrics@yandex.ru

**Background:** In Archangelsk region of Northern Russia, MDR-TB rates among new cases are amongst the highest in the world. In 2013, MDR TB rates reached 35.4% among new cases and relapses. The development of new diagnostic tools allows for faster detection of both TB and MDR TB and should lead to reduced transmission by

earlier initiation of anti TB therapy. The PROVE-IT Russia study aimed to assess the impact of the implementation of LPA as part of a new diagnostic algorithm for MDR suspects on the time from sputum sample collection to the initiation of MDR TB treatment as the primary outcome, as well as patient outcomes in both the civil sector and the penitentiary system.

**Design/Methods:** To assess the 'time from sputum collection to MDR treatment initiation', we compared the 'culture-based' diagnostic algorithm used prior to LPA implementation to a 'LPA-based' algorithm where LPA replaced BacTAlert and Löwenstein Jensen (LJ) for drug sensitivity testing.

**Results:** A total of 295 MDR TB patients were included in the study, 163 diagnosed with the 'culture-based' algorithm, 132 with the 'LPA-based' algorithm. The implementation of a the 'LPA-based' algorithm in the civil sector led to a mean decrease of the time to MDR TB treatment initiation of 58 days in 'smear positive' and 49 days in 'smear negative' patients. The mean reduction in time to treatment initiation for 'smear positive' patients in the penitentiary system was 14 days, for 'smear negative' patients 13.5 days. Cure rates were higher ( $p < 0.05$ ) in patients diagnosed with the 'LPA-based' algorithm (65%) compared to those diagnosed with the 'culture-based' algorithm (44.8%). All-cause mortality (7.5 %) and lost to follow up (18.2 %) rates were lower ( $p < 0.05$ ) in those diagnosed using the 'LPA-based' algorithm compared to the 'culture-based algorithm' (all-cause mortality – 15.9%, lost to follow up – 32.5 %). There was no statistically significant difference in treatment failure and amplification of XDR TB, as well as in smear and culture conversion rates between the two algorithms.

**Conclusion:** The implementation of LPA results in earlier treatment initiation for MDR TB patients and improves treatment outcomes.

#### PD-702-30 Assessing GenoType MTBDRplus and sequencing methodologies for detecting resistance in clinical isolates of *Mycobacterium tuberculosis*

X Montes-Rincon,<sup>1</sup> M Orduz,<sup>1</sup> W Ribon.<sup>1</sup> <sup>1</sup>Grupo de Inmunología y Epidemiología molecular, Universidad Industrial de Santander, Bucaramanga, Colombia. e-mail: wellmanribon@yahoo.es

**Introduction:** in recent years, cases of multidrug-resistant TB (MDR-TB) have been increasing and representing a high percentage of total TB cases in the world. Nowadays, they are considered as a challenge to control the disease. The objective of this study is to evaluate the GenoType MTBDRplus and sequencing method for determining drug resistance in clinical isolates of *M. tuberculosis* in the Department of Santander, Colombia.

**Materials and methods:** We included 25 clinical isolates of *M. tuberculosis* from Department of Santander, previously characterized by Spoligotyping. The isolates were evaluated with GenoType MTBDRplus (Hain Life Science) and amplification of the *rpoB*, *katG*, *inhA*-ORE,



inhA-REG and oxyR-ahpC genes for subsequent automated DNA sequencing capillary electrophoresis.

**Results:** the most common lineages were LAM9, H1, U, H3 and X1. GenoType MTBDRplus assay identified 6 MDR isolates and 8 isoniazid (INH) mono resistant isolates. Most rpoB mutations were located between codons 526–529 (6/8) and two strains showed characteristic double mutation at codon S531W/Q and between 526–529 codons (2/8) in rpoB gene. All mutations in katG correspond to S315T (14/14), 3 of which were presented in conjunction with the inhA C15T mutation. This resistance patterns were confirmed by sequencing method, however, it accurately identified rpoB mutations H526L, H526N and S3531W. Furthermore, due to the sequencing of inhAORF and oxyR-ahpC intergenic region, two isolates could be identified with the mutation inhAORF S94A and no mutations were found in the oxyR-ahpC gene.

**Conclusion:** it is important that each country carry out the identification of mutations associated with drug resistance in *M. tuberculosis* to determine whether the use of commercial methodologies is suitable. In our tested clinical isolates, it was found a concordance of 100% between GenoType MTBDRplus and sequencing method. However, the most common mutation associated with rifampicin resistance (rpoB 526) in our study and the inhAORF S94A mutation, couldn't be directly identified by the commercial method, that is because it is necessary to include more drug resistance *M. tuberculosis* isolates to determine if this is behavior of mutations in the Department of Santander.

#### PD-703-30 Management of rifampicin resistant TB in the Xpert MTB/RIF era: experiences from South Africa

L Scott,<sup>1</sup> Y De Lima,<sup>1</sup> MP Da Silva,<sup>2</sup> T Wojno,<sup>3</sup> C Hayes,<sup>4</sup> W Stevens,<sup>1,5</sup> M Patel,<sup>6</sup> A Van Rie.<sup>6</sup> <sup>1</sup>Molecular Medicine and Haematology, University of the Witwatersrand, Johannesburg, <sup>2</sup>Microbiology, National Health Laboratory Service, Johannesburg, <sup>3</sup>Microbiology, National Health Laboratory Service, Bloemfontein, <sup>4</sup>Microbiology, National Health Laboratory Service, Port Elizabeth, <sup>5</sup>National Priority Program, National Health Laboratory service, Johannesburg, South Africa; <sup>6</sup>Epidemiology, University of North Carolina, Chapel Hill, NC, USA. e-mail: lesley.scott@nhls.ac.za

**Background:** Xpert MTB/RIF (Xpert) allows rapid diagnosis of rifampicin (RIF) resistant tuberculosis (TB), a marker of multi-drug resistant (MDR) TB. Translation of a RIF-resistant result into appropriate patient management depends on correct implementation of testing and treatment algorithms.

**Design/Methods:** Observational cohort study (EXIT-RIF) of patients diagnosed with RIF resistance by Xpert in 3 South African provinces (Gauteng, Free State and Eastern Cape). We evaluated adherence to the Department of Health (DOH) Xpert diagnostic algorithm, which recommends MDR-TB treatment for patients with RIF resistance on Xpert and collection of a specimen for culture and drug susceptibility tests (DST) for RIF, isoniazid, fluoroquinolones and aminoglycosides.

**Results:** Of 278 RIF-resistant patients, 223 (80%) started MDR-TB treatment after a median 10 days (IQR:6–20), 24 started first-line TB treatment, 16 lost to follow-up, 14 died prior to treatment, and 1 refused treatment. A follow-up sputum specimen was collected in 203 (73%) patients after a median of 7 days. Smear microscopy was requested in 188 (68%) patients; 100 were smear-positive. Culture was requested in 193 (69%) patients: *M. tuberculosis* complex isolated in 144 cultures, was negative in 36, non-tuberculous mycobacteria isolated in 5, and 8 contaminated. HAIN line probe assay (LPA) was performed in 158 (57%) patients directly on sputum (n=65) or culture (n=93). LPA confirmed RIF resistance in 130 patients: 42 were RIF resistant and 88 MDR-TB. Indeterminate RIF resistance result occurred in 7. Phenotypic DST for RIF and isoniazid was performed in 18 patients and confirmed RIF resistance in 5 and MDR-TB in 2 patients in whom LPA was not done or indeterminate. In total, RIF-resistance was confirmed in 137 of the 278 (49%) patients. Phenotypic second-line DST was performed in 76 (27%) patients. Based on all available results, 45 (16%) were diagnosed with RIF-mono resistant TB, 61 (22%) patients were diagnosed with MDR-TB, 14 (5%) with pre-XDR and 17 (6%) with XDR-TB. The resistance profile of the remaining 141 (51%) patients could not be determined.

**Conclusion:** Adherence to the diagnostic algorithm was poor. While 80% of patients initiated MDR-TB treatment, MDR-TB was only confirmed in 33% and assessment for XDR-TB was completed in 27%. To ensure a positive impact of Xpert on outcomes of RIF-resistant TB patients, attention needs to be paid to confirmatory testing of RIF resistance and assessment of XDR-TB.

#### PD-704-30 Resistance to first- and second-line drugs amongst MTB strains resistant to isoniazid and/or rifampicin by the MODS assay in Peru

A Mendoza,<sup>1</sup> D Moore,<sup>2</sup> E Castillo,<sup>3</sup> A San Miguel,<sup>4</sup> M Perea,<sup>5</sup> E Leo,<sup>6</sup> N Quispe,<sup>6</sup> A Alarcon.<sup>1</sup> <sup>1</sup>Estrategia Sanitaria Nacional de Prevencion y Control de la TB, Lima, Peru; <sup>2</sup>Clinical Research, London School of Hygiene and Tropical Medicine, London, UK; <sup>3</sup>Direccion de Salud de Callao, Callao, <sup>4</sup>Direccion de Salud Lima Sur, Lima, <sup>5</sup>Direccion de Salud de Arequipa, Arequipa, <sup>6</sup>Instituto Nacional de Salud, Lima, Peru. e-mail: mendozalberto@hotmail.com

**Background:** As a part of programmatic activities to control TB in Peru, all TB cases deemed resistant to isoniazid (H) and/or rifampicin (R) by MODS commence treatment with standardized regimens whilst conventional indirect DST for first and second line drugs is performed to determine whether an individualized regimen is needed.

**Objective:** To determine the prevalence of resistance to first and second line drugs in strains determined to be resistant to H or R and H (MDR) by the MODS assay (to guide standardized regimens).

**Methods:** We analyzed routinely recorded data from the Peruvian National Network of Public Health Laborato-

ries to describe the results of agar proportion method DST and pyrazinamidase method for strains resistant to H and susceptible to R, and for MDR-TB strains detected by MODS.

**Results:** During 2010, first and second line DST results for 103 strains deemed resistant to H and susceptible to R and 123 MDR-TB by MODS were obtained. The MODS-proportion method concordance for H resistant and R susceptible strains and MDR strains was 78% (80/103) and 94% (115/123), respectively. The prevalence of resistance to extended first line and second line agents (as defined by agar proportion method or pyrazinamidase) for these strains is presented in the table. For the H resistant strains, (non-MDR) replacement of H with a fluoroquinolone is appropriate. For MDR strains, replacement of H and R by a fluoroquinolone, plus an injectable drug with cycloserine and ethionamide remains a reasonable and logical standardized regimen.

**Conclusion:** These results support the policy to initiate immediate empiric standardized regimens according to the results of rapid DST to H and R in Peru, and guide their elaboration. Due to high resistance to R in H-resistant (non MDR) strains, and high resistance to first line drugs in MDR strains it is mandatory to extend the DST to first and second drugs in all strain resistant to H or R by rapid tests.

Drugs evaluated by referent methods	H-resistant and R susceptible by MODS		MDR – TB strains by MODS	
	No resistant/No Tested, Percentage (95%CI) resistant by referent method		No resistant/No Tested, Percentage (95%CI) resistant by referent method	
Isoniazid (H)	96/103	93.2% (87.0 – 96.9)	116/123	94.3% (89.1 – 97.5)
H high level*	90/103	87.4% (79.9 – 92.8)	114/123	92.7% (87.0 – 96.4)
Rifampicin (R)	17/103	16.5% (10.3 – 24.6)	120/123	97.6% (93.5 – 99.4)
Ethambutol (E)	7/103	6.8% (3.0 – 12.9)	35/123	28.5% (21.0 – 36.9)
Pyrazinamide (Z)	4/101	4.0% (1.2 – 9.1)	39/121	32.2% (24.4 – 40.9)
E&Z	1/101	1.0% (0.04– 4.8)	17/121	14.0% (8.7 – 21.1)
Streptomycin	51/103	49.5% (39.9 – 59.1)	59/123	48.0% (29.2 – 56.8)
Ciprofloxacin	0/103	0.0% (0.0 – 2.9 )	0/123	0.0% (0.0 – 2.4)
Kanamycin	7/103	6.8% (3.0 – 12.9)	14/123	11.4% (6.6 – 17.9)
Capremoycin	0/103	0.0% (0.0 – 2.9)	3/123	2.4% (0.6 – 6.5)
Ethionamide	15/103	14.6% (8.7 – 22.4)	11/123	8.9% (4.8 – 15.0)
Cycloserine	0/103	0.0% (0.0 – 2.9)	0/123	0.0% (0.0 – 2.4)
PAS	2/103	1.9% (0.3 – 6.3)	0/123	0.0% (0.0 – 2.4)

\* H concentration 1.0 ug/ml

## PD-705-30 Impact of rapid diagnosis of rifampicin resistance by Xpert MTB/RIF on mortality among patients with rifampicin-resistant TB

A Van Rie,<sup>1</sup> P Da Silva,<sup>2</sup> Y Voss De Lima,<sup>3</sup> J Wojno,<sup>2</sup> M Patel,<sup>1</sup> C Hayes,<sup>2</sup> W Stevens,<sup>2,4</sup> L Scott.<sup>2,4</sup>

<sup>1</sup>Epidemiology, University of North Carolina, Chapel Hill, NC, USA; <sup>2</sup>Tuberculosis, National Health Laboratory Services, Johannesburg, <sup>3</sup>CHRU, University of the Witwatersrand, Johannesburg, <sup>4</sup>Haematology and Molecular Medicine, University of the Witwatersrand, Johannesburg, South Africa. Fax: (+1) 919 966 2089. e-mail: vanrie@email.unc.edu

**Background:** Xpert MTB/RIF (Xpert) has the potential to revolutionize the management of multidrug-resistant tuberculosis (MDR-TB). The impact of a rapid diagnosis of rifampicin resistance (RR) on survival of patients with RR-TB is not yet known.

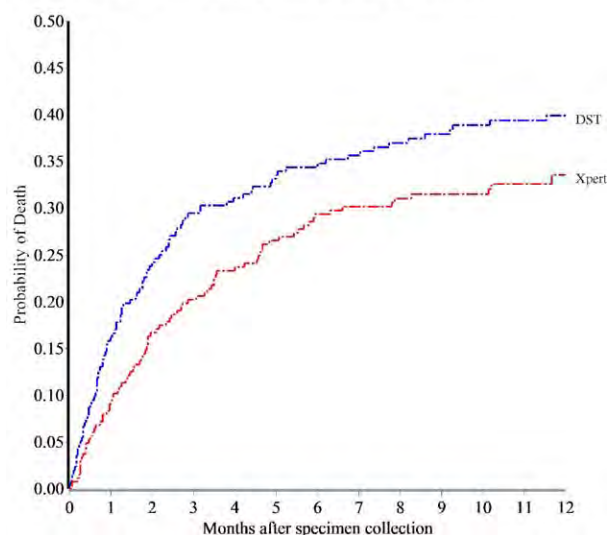
**Design/Methods:** Prospective observational cohort study (EXIT-RIF) embedded in the Xpert roll-out in three provinces of South Africa (Eastern Cape, Free State and Gauteng). Cases of RR pulmonary TB were identified by review of all RR specimens at laboratories between January 2012 and March 2013. Individuals with RR-TB were eligible if not on TB treatment at time of sputum collection. Before November 2012, RR was diagnosed by line probe assay (LPA) or phenotypic drug susceptibility test (DST). After November 2012, RR was diagnosed by Xpert. Management of RR-TB was performed by routine clinic or hospital staff. Survival in the first year following sputum collection was examined using Kaplan Meier method and Cox proportional hazards model.

**Results:** Of 542 individuals enrolled, 231 resided in the Eastern Cape Province, 164 in Gauteng, and 147 in the Free State Province. Half (51.5%) were female, median age was 36 years and 75.8% were HIV positive. In each of the 3 provinces, 51% to 53% of participants were diagnosed with RR TB by Xpert. There were no differences in gender, age or HIV status by diagnostic method. Median time from sputum collection to RR diagnosis was faster for Xpert compared to LPA/DST: 0 vs. 43 days ( $p<0.0001$ ). More patients started MDR-TB treatment when RR was diagnosed by Xpert compared to LPA/DST (83.5% vs. 70.1%,  $p<0.0002$ ) and medium time to treatment initiation was shorter (11 vs. 43 days,  $p<0.0001$ ). Overall, mortality tended to be lower in those with RR TB diagnosed by Xpert (30.6% vs. 37.5%,  $p=0.10$ , log-rank test  $p=0.077$ , HR 0.77, 95% CI: 0.57-1.03). Difference in mortality was only statistically significant among HIV negative individuals (2.4% v. 26.7%,  $p=0.002$ ), not among those living with HIV (34.1% v. 38.3%,  $p=0.38$ ). Among those alive, loss to follow up in the first year was higher in those diagnosed with RR TB by Xpert than LPA/DST (21.8% vs 14.6%,  $p=0.08$ ).

**Conclusion:** Access to Xpert resulted in higher treatment rates and faster MDR-TB treatment initiation in people diagnosed with RR TB. Diagnosis by Xpert resulted in a 10-fold reduction in mortality among HIV-negative individuals. Mortality among people living with HIV

remained high and did not decrease after the introduction of Xpert.

**Figure 1: Cumulative Probability of Death in the first 12 Months following Specimen Collection by diagnostic basis for rifampicin resistance (line probe assay or phenotypic culture-based drug susceptibility test versus Xpert MTB/RIF)**



### PD-706-30 High prevalence of *inhA* promoter mutations among patients with drug-resistant tuberculosis in KwaZulu-Natal, South Africa

J Brust,<sup>1</sup> A Niehaus,<sup>2</sup> N Gandhi,<sup>3</sup> B Mathema,<sup>4</sup> K Mlisana.<sup>2</sup> <sup>1</sup>Medicine, Albert Einstein College of Medicine & Montefiore Medical Center, Bronx, NY, USA; <sup>2</sup>Medical Microbiology, National Health Laboratory Services & University of KwaZulu Natal, Durban, South Africa; <sup>3</sup>Epidemiology, Global Health & Infectious Diseases, Rollins School of Public Health, Emory University, Atlanta, GA, <sup>4</sup>Epidemiology, Columbia University Mailman School of Public Health, New York, NY, USA. Fax: (+1) 718 944 3841. e-mail: jcb26@columbia.edu

**Background:** South Africa has one of the world's worst epidemics of multidrug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis (TB). Typically, resistance to isoniazid (INH) is caused by mutations in one of two genes: *katG* and *inhA*. Mutations in *inhA* (unlike *katG*) confer cross-resistance to ethionamide (Eth), and only low-level resistance to INH. MDR and XDR TB patients with *inhA* mutations may benefit from the addition of high-dose INH in their treatment regimens but would not benefit from Eth. Eth is empirically included in MDR and XDR TB regimens, because phenotypic susceptibility testing to Eth is not routinely available in South Africa. Line Probe Assays (LPAs) that detect mutations in *katG* and *inhA* are currently performed on all positive TB cultures in KwaZulu-Natal province; however, the frequency of *inhA* mutations in drug-resistant TB patients has not been examined.

**Methods:** We reviewed a representative sample of LPA (Hain MTBDRplus®) results between 2012–2013 at the TB reference laboratory in KwaZulu-Natal to determine the proportion of isolates with *inhA* and/or *katG* mutations. Samples were included in the analysis if they

had genotypic resistance to INH, rifampin, or both. We determined the proportion of isolates with only an *inhA* mutation without a *katG* mutation (ie, low-level INH resistance) as well as those with an *inhA* mutation regardless of *katG* (ie, Eth resistance). We stratified these results by overall drug-resistance category, using results of phenotypic drug-susceptibility tests (ie, mono-resistant, MDR, pre-XDR, or XDR TB). Duplicate isolates from the same patient were excluded.

**Results:** Among the 994 unique isolates, all 11 districts of the province were represented. 694 (69.8%) were MDR, 72 (7.2%) were pre-XDR, and 29 (2.9%) were XDR (Table). In each group, the prevalence of *inhA* mutations without a concurrent *katG* mutation was 14.8%, 4.2%, and 10.3% respectively. The prevalence of an *inhA* mutation with OR without a *katG* mutation in each group was 30.2%, 47.2%, and 79.3%, respectively.

**Conclusions:** More than 10% of patients with MDR and XDR TB could potentially benefit from treatment with high-dose INH. Furthermore, nearly a third of MDR TB patients and a majority of XDR TB patients are likely resistant to Eth. Routine reporting of LPA INH mutation data may avoid unnecessary Eth toxicity and identify candidates for high-dose INH. The efficacy of high-dose INH for those with *inhA* mutations should be studied further.

		LPA Results							TOTAL	
		INH Mono-Resistance		RIF Mono-Resistance						INH and RIF resistance
				Mutations in:						
		inhA	katG	inhA & katG	rpoB	rpoB & inhA	rpoB & katG	rpoB & inhA & katG		
Culture DST Results	INH Mono-Resistance	21	89	15	1	1	2	0	129	
	RIF Mono-Resistance	0	1	0	68	1	0	0	70	
	MDR-TB (INH & RIF resistance)	4	28	38	21	99	435	69	694	
	Pre-XDR TB	0	3	6	0	3	35	25	72	
	XR-TB	0	1	11	0	3	4	10	29	
TOTAL		25	122	70	90	107	476	104	994	

## 19. EPIDEMIOLOGY: TUBERCULOSIS MANAGEMENT AND CONTROL

### PD-707-30 Patterns and direct costs of health service utilisation by tuberculosis patients in Quebec, Canada: a population-based study

L Ronald,<sup>1,2</sup> JM Fitzgerald,<sup>2,3</sup> K Schwartzman,<sup>1,4</sup> A Benedetti,<sup>1,4</sup> G Bartlett-Esquilant,<sup>5</sup> JF Boivin,<sup>1</sup> R Menzies.<sup>1,4</sup> <sup>1</sup>Epidemiology, Biostatistics, and Occupational Health, McGill University, Montreal, QC, <sup>2</sup>Centre for Clinical Epidemiology and Evaluation, Vancouver Coastal Health Research Institute, Vancouver, BC, <sup>3</sup>Institute for Heart and Lung Health, University of BC, Vancouver, BC, <sup>4</sup>Respiratory Epidemiology and Clinical Research Unit, Montreal Chest Institute, Montreal, QC, <sup>5</sup>Family Medicine, McGill University, Montreal, QC, Canada. e-mail: ronaldal@shaw.ca

**Background:** Understanding the rates, timing, and costs of health service use by TB patients is important for policy makers to predict resource needs, and to evaluate the cost-effectiveness of TB prevention and control programs. The study objective was to describe patterns



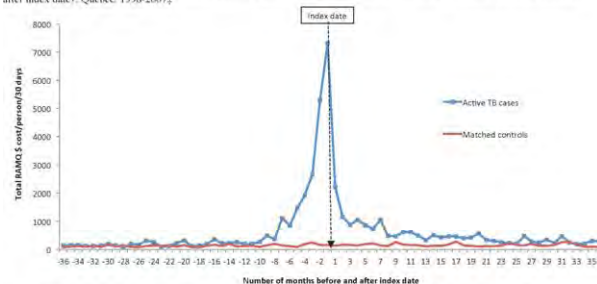
and direct costs of health service use by patients with active TB over a 10-year period in the Canadian province of Quebec.

**Design/Methods:** Data were extracted from the provincial health administrative database, which has near complete capture of all health service use for Quebec residents. A matched cohort design was used to estimate health service use rates and direct costs of all active TB patients starting treatment in Quebec between January 1, 1998 and December 31, 2007. Controls (patients without TB treatment) were matched 2:1 to TB patients on age, sex, residential postal area, treatment start year, and follow-up time. Total direct health system costs included the sum of emergency department (ED) visits, hospitalizations, physician inpatient and outpatient visits, hospital day procedures, and drugs dispensed. TB-attributable costs were estimated as the difference in mean costs between active TB patients and controls.

**Results:** The study included 1776 active TB patients and 3415 controls. More than half (59%) of active TB patients had at least one hospitalization within the three months before and during TB treatment. Half (49%) of TB patients had at least one ED visit, with most visits (79%) occurring in the three months before treatment start. Direct costs of active TB cases were almost seven times higher in the month before treatment start than they had been twelve months prior. After subtracting costs of matched controls, the total mean estimated health system cost (2011 Canadian dollars) for an active TB patient was \$22,649 (95% CI: \$21,333–23,966). Hospitalizations accounted for more than 80% of all direct costs.

**Conclusion:** This study found high rates and costs of health service use among active TB patients at the time of treatment initiation and an increase in costs in the months leading up to treatment start. Future studies should investigate the impacts of diagnostic delay and long-term sequelae of active TB on disease costs.

Figure 1. Estimated health resource use costs for active TB patients and matched controls\*, stratified by number of months before and after index date†, Quebec, 1998–2007‡



\*Controls were patients with no first-time TB drugs and matched to active TB patients at a ratio of 2:1 by index date, age, sex, and postal code area (first 3 digits of postal code) and follow-up time.  
†Index date = start date of first drug dispensation record in the provincial health administrative database for a first-time TB drug.  
‡Total RAMQ cost = Estimated government (RAMQ) paid costs of hospitalizations + emergency department (ED) visits + hospital day procedures + outpatient physician visits + inpatient physician visits + drugs dispensed (in 2011 Canadian dollars). Note: not costs assigned to hospitalization (\$1408/day), ED visits (\$183.08/visit) and hospital day procedure (\$183.08). Actual billed costs used for physician visits and drugs dispensed, adjusted to 2011 dollars using the Consumer Price Index.

## PD-708-30 Profile of pulmonary tuberculosis patients associated with poor treatment outcome in Douala, Cameroon

A Nana Yakam,<sup>1</sup> J Noeske.<sup>2</sup> <sup>1</sup>Faculty of Economic and Applied Management, University of Douala, Douala, <sup>2</sup>Independant Consultant, HS, Yaoundé, Cameroon.  
e-mail: nanayakam@yahoo.com

**Objective:** To identify the Demographic and socio-cultural characteristics of smear positive pulmonary tuberculosis patients (PTB+) with unsuccessful treatment outcome in Douala, Cameroon, and identify possible risk factors.

**Design:** Analysis of a cohort of PTB+ patients registered between 1<sup>st</sup> of May 2011 and 30<sup>th</sup> of April 2012 in TB Diagnosis and treatment centres, based on semi-structured interviews at base-line collecting data and on subsequent analysis of treatment registers.

**Methods:** During the study period, a network of twenty health facilities were functioning as diagnosis and treatment centers (DTC) for tuberculosis. A cohort of 1589 (62% of total notification cases) adult ( $\geq 15$  years old) randomly selected among the 2545 patients consecutively diagnosed with PTB+ in any one of the 20 DTCs during the study period, permanently residing in Douala ( $\geq 3$  months), and consenting to participate to the study, were followed up until the end of their treatment. The outcomes of their treatment were classified according to the WHO definition as successful (for cured or completed treatment patients) and unsuccessful (for lost-to-follow-up, failed treatment or death patients). The association between the treatment outcomes and potential risks factors were accessed using bivariate test statistics and multivariate logistic regression analysis. Ethics clearance and administrative authorization were given for the study.

**Results:** Among the PTB+ patients (n=1589) enrolled in this study, 38.9% (618) were female and 61.1% (971) were male. 20.9% (332) were between 15 and 24 years old, 71% (1129) between 25 and 54 years old. The outcomes of their treatment were as follow: 66.2% (1052) were cured, 18.9% (300) had completed treatment, 8.7% (138) were lost-to-follow-up, 2.4 % (38) failed treatment and 3.8 % (61) died. Overall, 1352 (85.1%) patients had a successful treatment outcome. In bivariate and multivariate analysis, unsuccessful treatment outcome of the remaining 237 (14.9%) patients was associated with history of previous treatment (OR = 1.39; 95% CI: 1.06-2.00), HIV positive status (OR = 1.86; 95% CI: 1.38-2.52), tobacco smoking (OR= 2.05; 95% CI: 1.30-3.22), ignorance of TB being a curable disease (OR = 1.86; 95% CI: 1.06-3.26), and a high number of person sharing the same bedroom (OR = 1.23; 95% CI: 1.02-1.48)

**Conclusion:** Newly presenting PTB+ patients – if presenting possible risk factors – should be followed-up with particular attention and additional measures.

### PD-709-30 Does level of access to tuberculosis treatment predict default patterns? a multilevel analysis

S Driver,<sup>1,2</sup> L J Podewils,<sup>1</sup> M Kramer,<sup>2</sup> C Heidebrecht,<sup>1</sup> C Samuel,<sup>3</sup> J Ngozo.<sup>4</sup> <sup>1</sup>Tuberculosis Elimination, Centers for Disease Control and Prevention, Atlanta, GA, <sup>2</sup>Epidemiology, Emory University, Atlanta, GA, USA; <sup>3</sup>GIS, KwaZulu-Natal Department of Health, Pietermaritzburg, , <sup>4</sup>TB Control Programme, KwaZulu-Natal Department of Health, Pietermaritzburg, South Africa.  
e-mail: SteviDriver@gmail.com

**Background:** KwaZulu-Natal (KZN) province in South Africa has one of the highest prevalence rates of tuberculosis (TB) and multidrug-resistant TB in the world. Poor TB treatment outcomes such as treatment default, increase the risk for morbidity, mortality, acquisition of drug resistance, and continued community transmission. An aspect of TB control that has been understudied is patient access to care. Relevant studies have found various metrics of access to be associated with default, but have been limited by small sample sizes, qualitative designs, and evaluation of factors operating solely at the patient level. We evaluated the association between measures of access to care at the individual and population level and risk for treatment default among persons diagnosed with TB.

**Methods:** We conducted a multilevel analysis of existing surveillance and administrative data for patients with active TB and an available treatment outcome in KZN from 2010–2011. The primary outcome was treatment default: outcomes were dichotomized as default or other (cured, completed, died or failed treatment). Metrics used for access to care included directly-observed therapy (DOT; individual level), density of health facilities (population level), and health quality score (population level).

**Results:** A total of 28,875 TB patients were included; 3,261 (11.3%) defaulted from treatment. Patients who received DOT throughout the entire treatment course and who lived in an area with a high density of facilities were significantly less likely to default than persons without DOT or who lived in areas with a lower concentration of facilities (RR=0.3, 95% CI=0.2-0.3 and RR=0.4, 95% CI=0.3-0.5, respectively). There was no significant association between health quality score and treatment default.

**Conclusions:** By linking existing data, we demonstrated that consistent provision of DOT and residing in an area with a greater concentration of health facilities decreased the risk for TB treatment default. Program managers may consider actions that aim to ensure patients receive DOT throughout the treatment course and novel methods to bring care in closer proximity to communities (e.g., mobile clinics, outreach) as an approach to improve TB treatment outcomes.

### PD-710-30 Mathematical model of HIV among TB patients using sentinel site surveillance information

B N Jnawali,<sup>1</sup> LR Paudel.<sup>2</sup> <sup>1</sup>Department of Health Services, Kathmandu, <sup>2</sup>Ministry of Health and Population, Kathmandu, Nepal. Fax: (+977) 016634379.  
e-mail: bngyawali@hotmail.com

**Rational:** The relationship between human immune deficiency virus (HIV) and TB is well known. Increasing numbers of HIV-related TB cases can be expected as the prevalence of HIV increases in Nepal. The National TB programme has conducted eight rounds of surveillance of HIV in TB patients since 1993 till to date. From five sentinel sites, eight periodic surveys and around one thousands samples were tested in around six diagnostic centers of tuberculosis in Nepal.

**Objectives:** The study aim is to find out the overall trends of HIV and its estimate in TB patients using regular sentinel site surveillance secondary information.

**Methods:** Nepal has been doing periodic sentinel site surveillance of HIV prevalence survey of all newly registered TB cases above 15 year old to provide point estimate of HIV among TB. These eight surveys was carried out since 1993/94 to 2011/12 under five major diagnostic centers. The calculated sample size in each surveillance was around 1000. A descriptive study of HIV among TB in different time periods and different sentinel sites was done with trained health workers. By using regression, a mathematical model was developed for future projection. SPSS package was used for data analysis. **Analysis:** Total 5528 TB patients were tested in different diagnostic centers of tuberculosis and found 118 HIV patients during the 8 study periods with average percentage was around 2.14. During the study period, reported HIV percentage (%) was 0 in 1993/93 while 2.444% was found in 2001/02.

SNo	Years	Sentinel Sites	Sample tested	HIV Positive	HIV Percentage
1	1993/94	5	300	0	0
2	1995/96	5	1000	9	0.9
3	1998/99	5	1221	23	1.88
4	1999/00	5	938	13	1.39
5	2001/02	5	1023	25	2.44
6	2006/07	5	1000	24	2.4
7	2011/12	6	1000	24	2.4

Overall increasing trend of HIV percentage was 0.461 by representing an equation: HIV Positive % = 0.461 \* Year - 0.1111 (P<0.001).

**Conclusion:** The result can provide future information working in TB and HIV field to guide programme planning and management in order to achieve programme goal and targets. **Recommendations:** To obtain more information about the trend of the HIV among TB patients in Nepal the surveillance needs to be repeated more over the years.

### PD-711-30 Trends and causes of pulmonary TB defaulting in Talasea district, west New Britain Province, Papua New Guinea, 2010–2012

B Peni,<sup>1</sup> H Yapen,<sup>1</sup> M O'Reilly.<sup>2</sup> <sup>1</sup>Disease Control, West New Britain Health Authority, Kimbe, <sup>2</sup>National Dept. of Health, Field Epidemiology Training Program Papua New Guinea, Port Moresby, Papua New Guinea.  
e-mail: moreilly24@yahoo.com

**Background and challenges:** West New Britain has an estimated tuberculosis prevalence of 430/100,000. Defaulters from treatment for pulmonary tuberculosis (PTB) are at high risk of poor outcomes, including multi drug resistant tuberculosis, first isolated from Papua New Guinea in 2000. A retrospective review of program monitoring data from 2010–2012 indicated that in Talasea district more than 300 patients had defaulted from PTB treatment, with default rates of 30%–60% in its four sub-districts. Diagnostic practice was not optimal: in 2012, only 30.1% of PTB cases were diagnosed by identification of acid-fast bacilli on sputum examination. Treatment outcomes were limited: only 25% of patients converted to a negative sputum. A survey of 100 consecutive defaulters revealed that 42% of males and 29% of females stated that feeling better in the first few months of treatment contributed to cessation of PTB medications. Among females, 33% stated that moving place of residence led to lapses in treatment. Among males, 24% said a belief that TB was caused by sorcery led them to cease drug therapy.

**Intervention:** An active contact tracing and follow up program was instituted, along with intensive education of patients on the importance of compliance to drug therapy. Training on the importance of obtaining sputum specimens for each patient suspected of PTB was conducted for area health care workers.

**Results:** After interventions, sputum diagnosis increased to over 60%. Post intervention, 55% of sputum positive PTB patients converted to a negative sputum. Defaulter and cure rates will be analysed after 2 quarters (6 months) of post-intervention program experience.

**Conclusions:** A small number of basic evidence-based interventions were able to substantially change program outcomes, including an increase in conversion rates. Trends in longer-term outcomes – defaulter and cure rates – will be closely scrutinized. Follow up surveys will help to quantify the impact of our intensive education on maintaining compliance with therapy. These evidence-based interventions could be used as a model to improve PTB care in other resource-constrained settings.

### PD-712-30 Association of gender with successful TB treatment in Kitwe, Zambia

M Kapambwe,<sup>1</sup> S Siziya.<sup>1</sup> <sup>1</sup>School of Medicine, Copperbelt University, Ndola, Zambia.  
e-mail: michimuka2002@yahoo.co.uk

**Background:** Gender may influence how a patient perceives the symptoms, receive the diagnosis, accept the treatment and adheres to it. This may be so because males and females usually have different occupations as

well as social habits. On the Copperbelt Province and Kitwe town in particular, most males are miners and engage in alcohol drinking. Therefore, these factors are important determinants of successful tuberculosis (TB) treatment. The objective of the study was to determine the association between gender and successful TB treatment.

**Design/Methods:** A retrospective study of all patients diagnosed, treated and completed treatment in Kitwe district was conducted. The patients' data was captured from paper-based facility TB registers in Kitwe for the period 2006–2010. Multivariate logistic regression analysis was used to determine the association between gender and successful TB treatment, while adjusting for patient type, Human Immunodeficiency Virus (HIV) status and type of Directly Observed Therapy short-course (DOTs) plan. Adjusted odds ratio and 95% confidence interval are reported.

**Results:** A total of 13,124 records of TB patients over a period of 5 years (2006–2010) were abstracted for this study. Overall, 12,223 out of the 13,124 study population had a known sex of which the majority, 60.4% were males. Male TB patients were 11% (AOR=0.89; 95% CI [0.82, 0.97]) less likely to have a successful treatment compared to female patients after adjusting for patient type, HIV status and type of DOTs plan.

**Conclusion:** From the findings that males were less likely to have a successful treatment outcome than females, it can be concluded that this may be so because males may continue with their habits of smoking and drinking of alcohol despite being on TB treatment. Alcohol intake may lead to the patient forgetting to take their daily intake of TB medication. In future, it can be recommended that gender-sensitive interventions of TB treatment should be designed to enhance successful TB treatment in the entire TB population.

Table 1: Association of gender with successful TB treatment in Kitwe, Zambia

Factor	Adjusted odds ratio (95% Confidence Interval)
<b>Sex</b>	
Male	0.89 (0.82, 0.97)
Female	1
<b>Patient type</b>	
New	1.31 (1.09, 1.57)
Relapse	1.23 (1.00*, 1.51)
Treatment resumed after interruption	1
<b>HIV result</b>	
Positive	0.80 (0.72, 0.89)
Negative	1
<b>DOT plan</b>	
Clinic DOT	1.08 (0.99, 1.18)
Relative DOT	1

\*AOR=Adjusted Odds Ratio

\*p=0.054



### PD-713-30 How to achieve sustained reductions in the burden of tuberculosis: examples from two Pacific islands

K Viney.<sup>1</sup> <sup>1</sup>National Centre for Epidemiology and Population Health, Australian National University, Canberra, ACT, Australia. e-mail: kerri.viney@hotmail.com

**Background and challenges to implementation:** Sustainable reductions in tuberculosis (TB) have been difficult to achieve in many countries. In other countries the rate of TB is declining at a slow rate. In countries where rates have decreased and where this decline has been large and or sustained, it is imperative that we note what interventions were put in place to achieve this decline. The reasons behind the decline may include dedicated public health interventions and / or wider socio-economic changes. Our aim was to assess regional and national TB data to assess where TB has declined in the Pacific Islands and to examine reasons behind the decline in countries with a large and sustained reduction in TB.

**Intervention or response:** We undertook a descriptive analysis of routinely collected TB data to determine changes in TB case notification rates and other programmatic parameters for the period 2000–2012, for the Pacific Island countries and territories. We also surveyed national TB programme managers in the Pacific.

**Results and lessons learnt:** TB rates have been increasing in the Pacific since the year 2000, when the Directly Observed Strategy short-course was introduced. This partly reflects efforts to increase TB case detection. Despite the fact that TB rates have been increasing across the region; two Pacific Island countries have observed large and sustained reduction in TB rates. These countries are New Caledonia and the Commonwealth of the Northern Mariana Islands (CNMI). The TB case notification rate has decreased by 66% in New Caledonia for the period 2000–2012. Similarly in the CNMI the TB case notification rate has decreased by 52% (in the same time period). During this time (and also preceding it) both countries implemented a number of public health interventions designed to control TB including very active TB case finding efforts and treatment of both active and latent TB. Both countries have also undergone socio-demographic and economic changes which will be discussed.

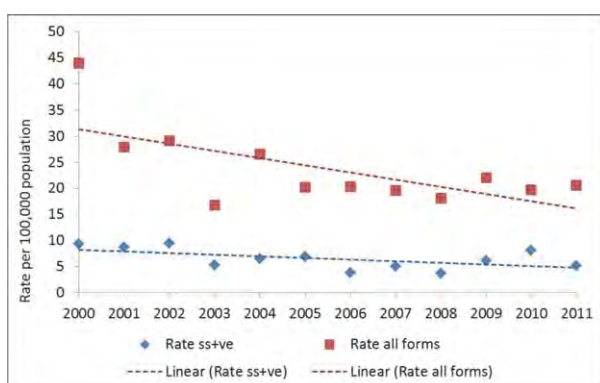


Figure 1: Impact of TB control in New Caledonia: a sustained reduction in TB case notification rates from 2000 to 2011

**Conclusions and key recommendations:** Large and sustained reductions in the TB burden can be achieved. There is a role for dedicated public health interventions in reducing the burden of TB such as active TB case finding and treatment of latent TB. This can feasibly be achieved in small countries with sufficient resources for TB management. Lessons from these countries can be applied to other countries in similar settings.

### PD-714-30 Increased initial defaulter density in urban as compared to rural areas in Maharashtra, India: epidemiological trend analysis, 2011–2013

B Pawar,<sup>1</sup> O Bera,<sup>2</sup> S Chadha,<sup>2</sup> P Banuru Muralidhara.<sup>2</sup>

<sup>1</sup>State Tuberculosis Control Society, ADHS, Pune, Maharashtra, <sup>2</sup>Union South East Asia Office, International Union Against Tuberculosis and Lung Disease, New Delhi, India. e-mail: oprakash@theunion.org

**Background and challenges to implementation:** Diagnosing a tuberculosis (TB) patient without assurance of a full course of treatment and cure is public health issue. Under Revised National TB Control Programme (RNTCP) smear-positive (SP) TB patients not confirmed as initiated on treatment are reported as 'Initial defaulters'. Limited research has been done to assess burden of initial defaulters within RNTCP. The objective of the study was to assess magnitude and establish pattern of initial defaulters in rural and urban areas of RNTCP, Maharashtra, India

**Intervention or response:** Using district wise quarterly performance reports of January 2011 to December 2013 retrospective epidemiological analysis was done of all 78 RNTCP reporting units in Maharashtra. 45 are categorized as urban units and 33 as rural units. Total population in Maharashtra is 115.3 million and that of urban and rural areas are 34.8 million and 80.5 million respectively. Performance reports are generated from all reporting units and are aggregated and validated at state level on quarterly basis. The quarterly reports were aggregated to form state annual report. Percentage of initial defaulter was calculated out of the total smear positive (SP) cases diagnosed annually.

**Results and lessons learnt:** Total number of initial defaulters recorded from Jan 2011 to Dec 2013 was 10016. Total number of SP - TB patients diagnosed in this period were 231558. Out of the total, 96157 SP cases were reported from urban areas and 135401 NSP cases were reported from rural areas. Around 6% of SP patients from urban areas and 3.2% from rural areas are confirmed as not having initiated treatment. Out of total initial defaulters, 5700(57%) cases were from urban area and 4316(43%) from rural areas. Density of initial defaulters per million in urban areas is 163.7 whereas it is 53.6 in rural areas.

**Conclusions and key recommendations:** Three fold density of initial defaulters in urban area calls for exclusive strategy to be inked out for containing the situation. With diverse issues ranging from increased seasonal migration from rural to urban areas, mismatch

of health facility timings to that of work timings of patients, follow-up, monitoring and supervision issues from health staff and trend of patients reaching out to private practitioners has posed a serious challenge for the managers of the TB programme to contain the proportion of initial defaulters in urban areas.

### PD-715-30 National population-based survey of tuberculosis prevalence in Thailand

T Thailand Ntp.<sup>1</sup> <sup>1</sup>Disease Control, TB Bureau, Bangkok, Thailand. e-mail: sxj47@yahoo.com

**Background:** As one of 22 TB high-burden countries, Thailand government and its partners have implemented financial and policy efforts since 1996 to prevent and control the disease. A prevalence survey was conducted to measure progress toward a 50% reduction in TB prevalence set for 2015.

**Design/Methods:** A stratified, multi-stage cluster sampling survey was conducted to assess the prevalence of bacteriologically positive cases of pulmonary TB in Thailand in the adult population. The sample size estimate of 76,311 based on WHO-recommended equations was inflated by 17% to ensure a valid national estimate excluding the city of Bangkok because the participation rate in Bangkok was expected to be low. Eligible populations were 15 years of age and above and sleeping in the selected location for  $\geq 14$  days. Field work started in February to September 2012 for 83 non-Bangkok clusters and April to July 2013 for 17 Bangkok clusters. Survey operation included household census and X-ray activities with TB symptom interviews. X-ray images were read by local physicians on site. Participants were eligible for two sputum samples if they had abnormal CXR and/or TB symptom score  $> 3$ . Ziehl-Neelsen staining and 2% Ogawa method were used for sputum microscopy and culture respectively. The analysis was done by logistic model with robust standard errors, with missing value imputation in participants with positive CXR or symptom screening but missing smear and/or culture and field CXR results. Due to 26% participation rate in Bangkok, national results excluding Bangkok are presented here.

**Results:** Out of 78,840 eligible populations, 79% attended CXR screening. CXR positive, symptom positive as well as both CXR and symptom positive were reported in 3,767 participants, 1,713 participants, and 526 participants, respectively. The survey detected 58 smear-positive cases and 84 culture-positive cases, totaling 142 bacteriologically positive pulmonary TB cases. Preliminary results based on the logistic model with adjustment for census population, smear-positive TB prevalence was 110.1 (54.1–223.8) /100,000 adult population. Bacteriologically positive TB prevalence was 253.3 (187.5–342.0) /100,000 adult population.

**Conclusion:** Thailand is likely to meet the target for reduction in prevalence. When compared to the national survey in 1991, smear-positive TB prevalence was reduced (203/100,000 in 1991), while bacteriologically

positive TB prevalence showed a slow decline (281/100,000 in 1991).

### PD-716-30 Tuberculosis retreatment: profile and factors associated with successful treatment outcomes in the Free State Province, South Africa (2003–2012)

G Kigozi,<sup>1</sup> S Van Der Merwe,<sup>2</sup> P Chikobvu,<sup>3,4</sup> J Heunis.<sup>1</sup>

<sup>1</sup>Center for Health Systems Research & Development, University of the Free State, Bloemfontein, <sup>2</sup>TB Directorate, Free State Department of Health, Bloemfontein,

<sup>3</sup>Department of Community Health, University of the Free State, Bloemfontein, <sup>4</sup>Strategic Information Management, Free State Department of Health, Bloemfontein, South Africa. Fax: (+27) 4445011. e-mail: kigozi@ufs.ac.za

**Background:** Retreatment for tuberculosis (TB) contributes substantially to the global disease burden. In South Africa, ranked first among the 22 high-burden countries, 15% of all reported TB patients were classified as retreatment cases in 2012. Treatment outcomes of retreatment cases in South Africa are suboptimal; success ranged from 52% in 2003 to 66% in 2011, with 61.8% in the Free State Province in 2012. Varying outcomes have been established amongst subgroups of retreatment cases, respectively classified as relapse, retreatment after failure, retreatment after default, and 'other'. This study sought to ascertain retreatment TB patient characteristics and factors associated with successful treatment outcomes in the Free State.

**Methods:** A retrospective record review of TB patients registered in the electronic TB register between 2003 and 2012 was conducted. The study population was defined as all retreatment TB cases registered in the database. Extracted data was described using percentage for categorical variables and mean for continuous variables. Pearson's  $\chi^2$  test was used to establish any association between independent variables and the outcome variable 'treatment success', defined as patients who were cured or had completed treatment. The data was also subjected to logistic regression analysis using Stata version 12.

**Results:** Retreatment TB cases comprised 16.5% ( $n = 43\ 666$ ) of the 264 653 records reviewed. The mean age of retreatment cases was 38.6 ( $\pm 11.5$ ) years, with just over one-third (33.5%) aged between 33 and 44 years. The majority of these were classified as relapsed pulmonary TB cases (70.1%) receiving Regimen 2 (2HRZES 1HRZE 5HRE) therapy (95.5%). HIV status was unknown in 61.1% of the retreatment cases. While age, HIV status and smear category were risk factors, being on antiretroviral therapy (ART) (OR: 1.3; CI: 1.2–1.4), having a CD4 count between 201–350 cells/mm<sup>3</sup> (OR: 1.6; CI: 1.3–1.8) or more than 350 cells/mm<sup>3</sup> (OR: 1.8; CI: 1.5–2.1) and sputum smear conversion at three months (OR: 3.7; CI: 3.6–3.9) increased the likelihood of treatment success. Subjection of cases to cotrimoxazole prophylaxis did not significantly influence treatment success.

#### Conclusion:

**Results** showed that being on ART, having a high CD4 count and smear conversion had a significant positive

influence on treatment outcomes among retreatment patients. It is thus important to provide HIV counselling and testing and ART to TB-HIV co-infected retreatment patients.

### PD-717-30 Effectiveness of a structured network of specialist reference units for tuberculosis control

I Barrabeig,<sup>1</sup> MA Tarres,<sup>1</sup> M Boldu,<sup>1</sup> M Santin.<sup>1,2</sup>

<sup>1</sup>Barcelona-South Health Region, CN-SHR TB Network, Barcelona, <sup>2</sup>Clinical Sciences, University of Barcelona, Barcelona, Spain. e-mail: msantin@bellvitgehospital.cat

**Background:** It is widely accepted that care for tuberculosis (TB) should be provided by specialist teams to optimize prescription, adherence and management of adverse events, and to improve the global outcome of TB patients. A reorganization of the assistance and control of TB was conducted in the Barcelona-South Health Region (BCN-SHR) along the 2004. The operative programme was based on the implementation of a network of 9 hospital TB Units (TBU) in the health area. The TBUs offer a comprehensive programme of diagnosis and treatment of all cases of TB and their contacts. Patients and contacts direct referral between paediatric and adult TBUs was established. Regular meetings for management of cases among TBUs health professionals, DOTS therapists, epidemiological surveillance professionals and community health workers were introduced. Furthermore, every TB cases detected at the primary care are referred to the corresponding TBU for further evaluation and management. DOTS coverage is universally available for all TB patients. The aim of our study was to evaluate the trends in the TB indicators in the health area since the implementation of this operative programme (2005 to 2012).

**Design/Methods:** Descriptive study of TB indicators trends in the BCN-SHR. The study included the TB cases reported to the Epidemiological Surveillance Unit, and prospectively registered in a database, between 2002 and 2012. Five major TB indicators were assessed: rates of new childhood TB, rates of new smear-positive pulmonary TB (PTB), treatment success rates, % of TB patients treated under DOT if needed and % of TB patients with smear-positive PTB who had contacts studied. For the purpose of the analysis, we compared two periods (pre-Operative Programme (pre-OP; 2002–2003), and during the Operative Programme (OP; 2005–2012) periods respectively); and results of the OP period were also compared with the WHO standards.

**Results:** During the study period, 923 new smear-positive PTB cases were reported (203 and 720 during the pre-OP and the OP periods respectively). In children < 5 years, 110 new TB cases were notified (21 and 89 during the pre-OP and the OP periods respectively), a rate of 18/10,000 persons-year and 14,9/100,000 persons-year in the pre-OP and OP periods respectively. Overall, there was an improvement of all indicators after de implementation of the OP, and most of them achieved the standards established by the WHO. Comparison of the

4 major TB indicators between the two periods is given in the table (attached).

**Conclusion:** The implementation of an Operative Programme based on a structured network of Reference TB Units improved the TB indicators in our health area. Improvement of contact-tracing among foreign-born people deserves specific attention, such as reinforcement of the role of community health workers.

Table. Outcome Indicators.

TB Indicator	Aim	Pre-OP (2002-03)	OP (2005-12)	Outcome Median (range)
New smear (+) PTB cases	<10%	9/100,000 (203)	7/100,000 (720)	–8% (–2.4%–15%) Achieved
Median rate (n)				
- % of Autochthonous people		83%	56%	
- % of Foreign-born people		17%	44%	
Treatment success (smear + cases)	85%	84% (178)	88.5% (637)	Achieved
% (number)				
-Autochthonous		85.70%	87.80%	
-Foreign-born		77.80%	89.50%	
-Children < 5 years		90%	96.60%	
Smear (+) PTB patients treated under DOT if needed	100%	70%	87.50%	Improved
Smear (+) PTB patients who had contacts studied	95%		87.50%	Improved
-Autochthonous		74%	93.20%	
-Foreign-born		80%	81%	

### PD-718-30 Risk factors for tuberculosis death in the Province of Alberta, Canada, 1996–2012

A Parhar,<sup>1</sup> Z Gao,<sup>1</sup> C Heffernan,<sup>1</sup> R Ahmed,<sup>1</sup> V Gallant,<sup>2</sup> R Long.<sup>1</sup>

<sup>1</sup>TB Program Evaluation and Research Unit, University of Alberta, Edmonton, AB, <sup>2</sup>Public Health Agency of Canada, Surveillance and Epidemiology Division, Centre for Communicable Disease and Infection Control, Ottawa, ON, Canada. e-mail: aparhar@ualberta.ca

**Background:** Although the incidence and mortality from tuberculosis (TB) in high-income countries is declining, the proportion of incident cases that are TB deaths is relatively constant. In this study, we set out to determine risk factors for TB death in the Province of Alberta, Canada between 1996 and 2012. A TB death is defined as a TB case that died before or during the period of active treatment of TB, with TB being either the primary or a contributory cause of death.

**Methods:** Demographic, clinical, laboratory and treatment outcome information was abstracted from the Provincial TB Registry (Alberta Health Services). The proportions of TB cases, not including those whose death was unrelated to TB or who had other outcomes (see below) were compared by characteristics including age, sex, population group, disease type, disease site, drug



resistance, and HIV. The study period (1996–2012) reflects availability of data regarding mortality and other outcomes from TB. Death rates by population group were age and sex adjusted using all TB cases in Canada between 2008 and 2012 as the reference.

**Results:** In Alberta, there were 2432 TB cases reported in 1996–2012; 160 (6.6%) TB deaths; 2041 (83.9%) cure/treatment complete and 231 (9.5%) with other outcomes (death unrelated to TB, treatment failure, transferred out, absconded, ongoing or unclassified). The proportion (mean  $\pm$  SD) of TB cases that were TB deaths (TB deaths/TB death plus cure/treatment complete) averaged 7.5  $\pm$  3.4%. TB deaths were more common in those  $>64$  years of age (17.4% vs 2.8% in those  $<64$  years), Canadian-born Aboriginal (9.3% vs 4.4% vs 5.2% in Canadian-born non Aboriginal and foreign-born, respectively), combined respiratory and non-respiratory cases (10.3% vs 5.4% in those with respiratory or non-respiratory disease alone) and HIV co-infected cases (9.8% vs 3.5% in those that were HIV negative).

**Conclusions:** Not surprisingly, TB death in Alberta was more common in older cases, combined respiratory and non-respiratory cases and HIV co-infected cases. Most notably, Canadian-born Aboriginals had an increased risk TB death, presenting an opportunity for targeted strategies by TB programs to address underlying causes of death in this population group – be they addressing underlying social determinants of health, co-morbidities or delayed diagnosis.

## 20. MDR-TB: TREATMENT AND ADVERSE REACTIONS

### PD-719-30 Spectrum of further drug resistance in multidrug-resistant tuberculosis patients from 9 countries in regards to bedaquiline implementation

E Kurbatova,<sup>1</sup> T Dalton,<sup>1</sup> J Ershova,<sup>1</sup> P Cegielski,<sup>1</sup> and Global Petts Investigators. <sup>1</sup>Division of TB Elimination, CDC, Atlanta, GA, USA. Fax: (+1) 404-639-1566. e-mail: ies3@cdc.gov

**Background.** For the treatment of multidrug-resistant (MDR) tuberculosis (TB), The World Health Organization's interim policy guidance recommends adding the new drug, bedaquiline (BDQ) when an effective regimen (containing at least four effective second-line drugs (SLDs) plus pyrazinamide) cannot be designed because of resistance to fluoroquinolones (FQ), second-line injectable (SLI) agents, or drug toxicity. To simulate the potential use of BDQ in the treatment of a large cohort of MDR TB patients, we analyzed data from the "Preserving Effective TB Treatment Study".

**Methods.** Drug susceptibility testing (DST) of locally confirmed MDR isolates was done at the U.S. Centers for Disease Control (CDC) by the indirect agar proportion method on Middlebrook 7H10 agar. For analysis purposes, ciprofloxacin and ofloxacin were counted as the same drug (a fluoroquinolone) and kanamycin and

amikacin were counted as the same drug (an aminoglycoside). DST results were analyzed for 7 drugs: high-dose isoniazid, ethambutol, FQ, aminoglycoside, capreomycin, ethionamide, and para-aminosalicylic acid.

**Results.** Among 1,254 patients, 73 (5.8%) had resistance to a FQ, but not an SLI, at the start of MDR-TB treatment, 155 (12.4%) had resistance to SLI, but not a FQ, and 74 (5.9%) had resistance to both, i.e. extensive drug resistance (XDR). Thus, 302 (24.1%) of 1,254 patients with resistance to a FQ and/or SLI would qualify for a BDQ-containing regimen based on the drug resistance indication. The proportion of patients with baseline resistance to a FQ and/or SLI varied between countries from 7.5% to 52.8%. Among 302 cases with FQ and/or SLI resistance, the median number of drugs that remained susceptible was 3 (range 0–4), including high-dose isoniazid. In XDR cases the median was 2 (range 0–4), and in pre-XDR it was 4 (range 1–6) ( $p<.001$ ). Susceptibility to  $<3$  drugs was noted in 26% (79/302) overall, a majority of XDR patients (77.0%, 57/74) had susceptibility to  $<3$  drugs compared to 9.7% (22/228) of pre-XDR patients ( $p<.001$ ).

**Conclusion.** Cases with FQ and/or SLI resistance commonly have resistance to other first- and second-line drugs. Countries planning to implement BDQ should include plans to procure third-line drugs, such as linezolid, clofazimine, etc. These additional drugs will be required to build effective regimens because of the extent of resistance to other SLDs among patients who may be candidates for BDQ.

### PD-720-30 Analysis of the work of the MDR-TB councilium in a region with a high level of drug resistance and HIV prevalence

D Ruzanau,<sup>1</sup> A. Khailiukin,<sup>2</sup> A. Demidova,<sup>3</sup> S. Zhevnyak,<sup>3</sup> N Juravleva,<sup>4</sup> M. Uranova.<sup>1</sup> <sup>1</sup>TB and Pulmonology Department, Gomel State Medical University, Gomel, <sup>2</sup>Office Expertise, Gomel Regional Clinical Hospital, Gomel, <sup>3</sup>Department of MDR-TB, Gomel Regional Clinical Hospital, Gomel, <sup>4</sup>Clinical department, Gomel Regional Clinical Hospital, Gomel, Belarus. Fax: (+103) 75232749831. e-mail: druzanoff@mail.ru

The worst epidemic situation about multidrug-resistant tuberculosis (MDR TB) in the Belarus is Gomel region, the southern part of Belarus (38.5% of newly recorded TB cases are MDR cases), affected by the Chernobyl disaster, where 55.8 % of HIV-positive patients of the country live. The DOTS strategy was launched in the country only in 2008. To unify diagnosis and adequate treatment under DOTS-Plus, they had to organize a MDR TB councilium in 2009. The main objectives of the councilium in 2009 were diagnosis and prescription of treatment. Later on the functions significantly expanded: cohort analysis and MDR register, pharmaceutical management of second-line antituberculosis drugs (TBD) and means to reduce side-effects (SE), definition of indicators and volume of surgery, training of medical personnel, infection control (IC) over placing of MDR patients, promotion of adherence in patients refusing to undergo treatment or stopping it. Within the period of its

work, the number of treatment failures due to the impossibility to find an effective treatment scheme has 4.6 times decreased, the waiting list reduced to 8–12 people (schemes with Linezolid). The effectiveness of the treatment (the illness was cured) in the cohort over 2009 - I quarter 2012, when the councilium worked, increased from 24.7% to 55.8% (within 24 months). Although the average terms to diagnose MDR decreased from 109.3 days in 2009 to 42.7 days in 2013, they are still long. The duration of in-patient treatment decreased from 293.6 to 118.5 days, which made it possible to improve the effectiveness of IC. The objectives until the end of 2015 are: to increase application of Rapid diagnosis (RD) up to 95%, to ensure regular supply of test-systems for RD, to use the whole spectrum of all existing TBD (Clofazimine, Terizidone, Bedaquiline, more common – Linezolid) in the treatment for XDR (the ratio of XDR in MDR was 11.2%), 100% provision with necessary SE arresting drugs, decrease of the number of stopped treatment cases to 10%, death rate to 16%, ineffective treatment to 12%. The regulations of the councilium have been formulated, the typical errors in the work of the councilium having affected the effectiveness of MDR treatment (prescription of ineffective treatment schemes due to the TBD deficiency or disregard to SE treatment) have been analyzed and ranged. The MDR TB councilium is a necessary condition for successful MDR management in the region.

#### **PD-721-30 Emergence of fluoroquinolone resistance amongst multidrug-resistant tuberculosis suspects at a tertiary care facility in Karachi**

N Khalid,<sup>1</sup> A Zaidi,<sup>1</sup> N Rizvi,<sup>2</sup> A Haseeb,<sup>2</sup> A Malik,<sup>1</sup> S Khawaja,<sup>1</sup> N Saifullah,<sup>2</sup> A Mohiuddin.<sup>1</sup> <sup>1</sup>International Health, Interactive Research & Development, Karachi, <sup>2</sup>Chest Medicine, Jinnah Post Graduate Medical Centre, Karachi, Pakistan. e-mail: nashwa.khalid@irdresearch.org

**Background:** Pakistan is a high burden tuberculosis (TB) country with large numbers of multi-drug resistant TB (MDR-TB) cases and reports of extensively-drug resistant disease. Over-prescription and self-medication of antibiotics is common and has important implications for empirical management of multi-drug resistant TB, particularly with increased availability of GeneXpert MTB/Rif testing. A large and poorly regulated private sector has accentuated this problem as patients receive various antibiotic medication before reaching a TB facility. The aim of this study was to investigate antimicrobial resistance patterns amongst MDR-TB suspects in Karachi.

**Methods:** A total of 132 patients with suspected MDR-TB presenting to the TB clinic at Jinnah Postgraduate Medical Institute, Karachi's largest public sector hospital were recruited into the study. Suspects included cases with history of treatment failure, treatment default, relapse and household contacts of patients with MDR-TB. Sputum samples were collected for liquid culture and drug susceptibility testing. Resistance patterns for first-

line and second-line anti-tuberculous drugs were assessed. Frequency analyses for resistance patterns and associations with demographic variables and clinical history were assessed.

**Results:** Median age of the patients was 16 (IQR: 10 – 26) and 51.5% were male. Fifty-two percent of individuals had history of Category I treatment and 48% had history of Category II treatment. One reported case was of an MDR failure and one case had contact history with an MDR-TB case. Within first-line drugs, resistance to Isoniazid and Rifampicin was reported in 97% of cases followed by Pyrazinamide (86%), Ethambutol (69%) and Streptomycin (64%). Within second-line drugs, Ofloxacin resistance was observed in 34.6% of cases. Resistance to Ethionamide and Amikacin was 2.3% and 1.6%, respectively. Ofloxacin resistance was more commonly observed in Category I failures (50%) compared to Category II (34.8%). Age and gender were not significantly associated with resistance to second-line drugs.

**Conclusion:** Fluoroquinolone resistance was observed in an alarmingly high proportion of MDR-TB cases. Our results suggest caution in their use for empirical management of MDR-TB cases. Further drug-susceptibility patterns need to be urgently assessed by other centers in Pakistan. Engaging private sector providers and stringent pharmacy regulations are required to prevent an XDR epidemic.

#### **PD-722-30 Verapamil potentiates the activity of Bedaquiline (BDQ) in the mouse TB model: a strategy to reduce BDQ toxicity**

S Gupta,<sup>1,2</sup> S Tyagi,<sup>1</sup> K Winglee,<sup>1</sup> M Maiga,<sup>1</sup> W Bishai.<sup>1,2</sup>

<sup>1</sup>Center for TB Research, Johns Hopkins School of Medicine, Baltimore, MD, <sup>2</sup>Howard Hughes Medical Institute, Chevy Chase, MD, USA. e-mail: wbishai@gmail.com

**Background:** Bedaquiline (BDQ) is a promising new drug for TB. However, its current label carries a black box warning, and there are concerns that its toxicities, particularly QTc prolongation might limit its use.

**Design/Methods:** We observed that the addition of verapamil, which is an FDA-approved efflux pump inhibitor, enhances BDQ killing of *M. tuberculosis* in vitro. In the present study, we investigated the effect of verapamil on the antimicrobial activity of BDQ and clofazimine in a mouse model of tuberculosis infection.

**Results:** Verapamil yielded an 8- to 16-fold decrease in the bedaquiline MIC of drug-susceptible and drug-resistant clinical isolates of *M. tuberculosis*. We also found that the MIC of clofazimine against *M. tuberculosis* decreases by 8-fold in the presence of 50 mg/ml verapamil. In vivo studies showed that verapamil could also potentiate sub-inhibitory doses of bedaquiline to its full anti-microbial effects in the mouse model. In BALB/c mice using the acute infection model, we found that co-administration of verapamil with 12.5 mg/kg of BDQ gave the same bactericidal effect as 25 mg/kg of BDQ alone. Similar results were obtained for clofazimine.

**Conclusion:** Our results indicate that verapamil potentiates the activity of bedaquiline and clofazimine against *M. tuberculosis* in both an in vivo and in vitro model. This may be due to efflux pump inhibition by verapamil resulting in higher intracellular anti-mycobacterial drug levels and enhanced drug activity. These studies suggest that adjunctive use of verapamil may permit lower doses of BDQ and thereby reduce dose-related toxicities of BDQ.

### PD-723-30 Conditions affecting the minimal inhibitory concentration (MIC) of bedaquiline against *Mycobacterium tuberculosis*

N Lounis,<sup>1</sup> L Vranckx,<sup>1</sup> T Gevers,<sup>1</sup> K Kaniga,<sup>2</sup> K Andries.<sup>1</sup>

<sup>1</sup>Research & Development, Janssen, Beerse, Belgium;

<sup>2</sup>Research & Development LLC, Janssen, Titusville, NJ, USA. e-mail: nlounis@its.jnj.com

**Background:** Bedaquiline (BDQ, TMC207) is a diarylquinoline that exhibits potent in vitro activity against several mycobacterial species. BDQ has potent in vitro activity against drug-sensitive and drug-resistant strains of *M. tuberculosis* with MICs equal to or lower than that of approved anti-mycobacterial agents. The aim of the studies was to determine the impact of different testing conditions on BDQ's in vitro activity against *Mycobacterium tuberculosis* H37Rv.

**Design/Methods:** Since no critical concentration was defined for BDQ, the activity of BDQ was assessed by determining the MIC of BDQ on 7H11 agar defined as the lowest concentration of BDQ (in mg/L) that prevents growth of *M. tuberculosis* by at least 99%. The MIC of BDQ was also performed using the 7H9 broth medium and was defined as the lowest concentration of BDQ that prevented a visual growth. A 4-fold change in the MIC value of BDQ in the presence of the condition in question was considered to be significant. The following conditions were assessed: inoculum size ( $10^5$ ,  $10^6$  and  $10^7$  CFU/ml); pH (pH 6, pH 7 and pH 8); incubation temperature (33 °C, 37 °C and 41 °C); concentration of Tween 80 (0.02% and 0.2%); phase of the inoculum culture (log phase and stationary phase); concentration of proteins (5% bovine serum albumin in 7H11 agar; and the use of egg-based Lowenstein Jensen medium) and type of plastic ware (polystyrene and polypropylene).

**Results:** An inoculum higher than  $10^6$  CFU/ml ( $10^5$  CFU plated) resulted in at least 4-fold increased MICs in solid and liquid media. pH had no discernable effect on solid medium, but both acidic and alkaline conditions resulted in increased MICs in liquid medium. Incubation temperatures of 33 °C and 37 °C had no impact on the activity of BDQ. *M. tuberculosis* did not grow at 41 °C. Tween 80 had no impact at 0.02% but increased the MICs at 0.2% in both media. The phase of the inoculated culture had no impact on BDQ's activity. The addition of proteins to liquid or solid media significantly increased the BDQ MICs. BDQ MICs were increased when the tests were performed in polypropylene ware compared to tests performed in polystyrene ware.

**Conclusion:** In order to obtain reproducible MIC results, the activity of BDQ against *M. tuberculosis* isolates should be assessed in polystyrene plates or tubes with an inoculum size of  $10^6$  CFU/ml ( $10^5$  CFU plated) on 7H11 agar or with  $10^5$  CFU/ml in 7H9 broth, at pH 7, with a Tween 80 concentration of 0.02%, and without protein enrichment.

### PD-724-30 Trend of fluoroquinolone resistance in Thai new pulmonary tuberculosis patients

C Chuchottaworn.<sup>1</sup> <sup>1</sup>Respiratory Medicine, Central Chest Institute of Thailand, Nonthaburi, Thailand. Fax: (+66) 25919252. e-mail: charojnj@hotmail.com

**Background:** Fluoroquinolones are broad spectrum antibiotics which have activities against most respiratory pathogens including tuberculosis. The widely use of fluoroquinolones in respiratory tract infections made it unavoidable for undiagnosed tuberculosis (TB) patients to expose against fluoroquinolones. So it is likely for tuberculosis to develop increasing resistance when fluoroquinolones were used for long period of time. The aim of this study was to determine trend of fluoroquinolone resistant tuberculosis in Thai pulmonary tuberculosis patients for planning of appropriated use of fluoroquinolones in treatment of drug resistant tuberculosis.

**Method:** Study was conducted at TB laboratory, Department of Pathology, Central Chest Institute of Thailand (CCIT). The log books of TB drug susceptibility test (DST) were reviewed. Only first DST results of every new TB patients were included in the study and classified according to calendar year. Because TB laboratory of CCIT had included ofloxacin and kanamycin in panel of first line drugs since 1997, but in this study was considered results only in the past 10 years.

**Result:** Trend of fluoroquinolone resistance in new Thai tuberculosis patients was not increasing and MDR-TB had a declining trend in this study.

Rate of resistance against each anti-tuberculosis drug ( % )

Year	No.	INH	RMP	MDR	FQ	KM
2004	1341	12.00	13.34	7.68	2.68	1.04
2005	1143	12.68	9.45	5.69	1.22	1.14
2006	1172	15.70	9.56	5.29	1.11	0.68
2007	995	15.88	8.54	5.43	1.41	0.0
2008	751	15.98	9.32	8.12	2.53	1.60
2009	812	13.79	8.74	7.64	3.08	1.85
2010	891	6.40	7.18	3.48	6.73	1.23
2011	910	6.15	5.82	1.65	3.19	2.31
2012	944	11.55	8.16	4.66	1.48	1.06
2013	837	14.81	7.17	4.06	2.39	1.55

INH = isoniazid, RMP = rifampicin, MDR = Multidrug resistant, FQ = Fluoroquinolone; KM = kanamycin

**Conclusionns:** There was not increasing trend of fluoroquinolone resistant TB in Thai pulmonary tuberculosis patients. Initial resistant rate of kanamycin was low. So fluoroquinolones and kanamycin can be used as empiric treatment for MDR.



**PD-725-30 Hypokalaemia and elevation of serum creatinine in patients with rifampicin resistant TB treated with kanamycin and capreomycin in Khayelitsha**

S Moyo,<sup>1</sup> P Patient,<sup>1</sup> V Cox,<sup>1</sup> J Daniels,<sup>1</sup> O Muller,<sup>1</sup> G Van Cutsem,<sup>1</sup> H Cox.<sup>2</sup> <sup>1</sup>Khayelitsha DR-TB, Medecins Sans Frontieres, Cape Town, <sup>2</sup>Medical Microbiology, University of Cape Town, Cape Town, South Africa.  
e-mail: sizulumoyo@gmail.com

**Background:** Injectable agents; capreomycin and the aminoglycosides have been considered key agents in the treatment of rifampicin-resistant TB (RR-TB). In South Africa, kanamycin is the injectable of choice in the standard RR-TB regimen, with capreomycin reserved for demonstrated kanamycin-resistant cases. While both drugs are reportedly associated with significant side effects, capreomycin is assumed to have a higher risk of renal toxicity. There is, however, limited data comparing adverse events associated with these drugs in South Africa, and among HIV-infected RR-TB patients.

**Objective:** To compare the occurrence of serum creatinine elevation (renal toxicity) and hypokalemia (electrolyte imbalance) in RR-TB patients treated with capreomycin and kanamycin in Khayelitsha.

**Methods:** A retrospective analysis among patients treated for RR-TB over the period 2010 to 2012 was conducted. Data was extracted from routine DR-TB program data. Serum creatinine elevation was defined as serum creatinine >100mIU/L, and hypokalaemia as serum potassium < 3.4mmol/L.

**Results:** Among 649 patients (438, 67% HIV positive), serum creatinine and potassium results were available for 604 (93%) and 500(77%) patients respectively. Creatinine elevation at some point during treatment occurred in 50% (25/50) of those treated with capreomycin and 33% (185/554) of those treated with kanamycin (R 2.0, 95%CI 1.12-3.58). Similarly hypokalemia was higher among those treated with capreomycin, 56% (28/50) vs 30% (134/450) for kanamycin, OR 3.0 (95%CI 1.67-5.40). HIV infection was associated with increased renal toxicity (OR 1.59, 95%CI 1.07-2.39) and hypokalemia among patients treated with kanamycin. These figures were similar, although non-significant for the smaller number of patients treated with capreomycin; renal toxicity (OR 1.23, 95%CI 0.33-4.60) and hypokalemia (OR 2.06, 95%CI 0.58-7.68).

**Conclusion:** DR-TB patients treated with kanamycin or capreomycin in Khayelitsha experience a high burden of electrolyte imbalance and renal toxicity overall, with a significantly greater risk in those treated with capreomycin. HIV infection is associated with increased adverse events, particularly hypokalemia with kanamycin use. Given high levels of cross-resistance between capreomycin and kanamycin in this setting, our results suggest restriction of capreomycin to only those with demonstrated susceptibility. These data highlight the need for modified regimens that remove the reliance on the injectable agents.

**PD-726-30 Quantitative second-line drug susceptibility in patients treated for multidrug-resistant tuberculosis in Bangladesh: implications for regimen choice**

S Heysell,<sup>1</sup> S Ahmed,<sup>2</sup> s Rahman,<sup>2</sup> A Mahmud,<sup>3</sup> E Houpt,<sup>1</sup> S Banu.<sup>2</sup> <sup>1</sup>Infectious Diseases and International Health, University of Virginia, Charlottesville, VA, USA; <sup>2</sup>Mycobacteriology, icddr,b, Dhaka, <sup>3</sup>IEDCR, Institute of Epidemiology, Disease Control and Research, Dhaka, Bangladesh. e-mail: scott.heysell@gmail.com

**Background:** Regimens used to treat multidrug-resistant tuberculosis (MDR-TB) in endemic areas are often designed without individual susceptibility testing, or based on limited qualitative methods performed at reference laboratories. Such qualitative drug-susceptibility testing (DST) is performed by comparative growth in culture media with and without a single drug concentration and does not provide the quantitative DST range present with minimum inhibitory concentration (MIC) testing using multiple dilutions.

**Design/Methods:** Adult patients that were referred throughout Bangladesh during the period of 2011–2013 for planned initiation on a regimen for MDR-TB with an available pretreatment *M. tuberculosis* isolate were enrolled. MIC testing for 12 first and second-line anti-TB drugs were performed on the Sensititre MYCOTB plate.

**Results:** Sixty-six patients met inclusion criteria with a mean age of 35 ±15 years, and 44 (67%), were men. Nearly all, 65 (99%) had been previously treated for TB. Despite alternative DST report of MDR-TB in the field prior to referral, 12% of isolates retained susceptibility to isoniazid, and 11% for rifampin. Seven (88%) of the isolates susceptible to isoniazid were within the borderline susceptible range, and all 7 had MTBDRplus results that revealed inhA mutation only in 3, katG mutation only in 2, and the remaining 2 were wildtype for both regions. Five (71%) of the isolates susceptible to rifampin were of borderline susceptibility (all with rifampin MIC of 1.0 µg/ml) and of those, 4 had Xpert MTB/RIF results that revealed rpoB mutation in 3. Of 57 isolates with rifampin resistance (rifampin MIC >1.0 µg/ml), 12 (21%) were susceptible to rifabutin (rifabutin MIC ≤0.5 µg/ml). Amikacin retained full susceptibility in 65 isolates (98%), whereas kanamycin was fully susceptible in only 49 (74%) (p<0.001). Ofloxacin was borderline susceptible in 60%, and fully susceptible in only 13 (20%) compared to 54 (81%) of isolates for moxifloxacin (p<0.001).

**Conclusion:** MIC testing in patients referred for MDR-TB treatment in Bangladesh found the majority of isolates with borderline susceptibility or resistance to ofloxacin, lower within class MICs and an absence of borderline susceptibility for amikacin compared to kanamycin, and a surprisingly high number of isolates with fully susceptible or borderline susceptible MICs to isoniazid, rifampin and rifabutin. MIC testing can impact regimen choice.

### PD-727-30 What is the prevalence of adverse drug reactions among multidrug-resistant TB patients in a DR-TB centre of India in last four years?

S Sarkar,<sup>1</sup> T Quazi,<sup>1</sup> A Sen,<sup>2</sup> B Pradhan,<sup>2</sup> S Haldar,<sup>3</sup> B Bishnu,<sup>1</sup> N Paty,<sup>3</sup> S Chattopadhyay.<sup>3</sup> <sup>1</sup>Tuberculosis, WHO Country Office India, Kolkata, <sup>2</sup>DRTB Site, KS Roy TB Hospital, Kolkata, <sup>3</sup>Tuberculosis Cell, Department of health and family welfare, West Bengal, Kolkata, India.  
e-mail: sarkars@rntcp.org

**Background:** Though India is the second-most populous country in the world one fourth of the global incident TB cases occur in India annually. MDRTB (Multidrug resistant Tuberculosis) is an emerging threat to the successful control of TB in India. MDRTB among notified pulmonary TB patients is 0.064 million (0.049-.079 CI). The notified patients are provided with free good quality second-line drugs (SLD). One of the challenges facing patients treated with these drugs is its toxic nature. This study will help managers of RNTCP (Revised National Tuberculosis Programme) and clinicians in similar epidemiologic settings in making evidence-based decisions for optimizing treatment for DR-TB patients.

**OBJECTIVES:** To determine the types and frequency of adverse events associated with the use of second-line anti-TB medicines in a selected DR-TB treatment facility in Kolkata, India during January 2010- 2014.

**Design/Methods:** The study was conducted in a DRTB centre in Kolkata, India. This is a cross-sectional descriptive study; the study population included all patients treated with second-line anti-TB medicines at this DR-TB treatment facility from January 2010 –2014. All patient records were reviewed and entered in a structured data collection form. Data were single-entered into Epi Info version 3.5.3 and accuracy of entry verified against the original paper forms. The data were analysed using descriptive statistics.

**Results:** 1074 patients were treated for MDR-TB during the study period. The patients were treated with Kanamycin, levofloxacin, Ethionamide, Cycloserine, pyrazinamide and Ethambutol. 500 patients i.e. 47% experienced at least one adverse drug reactions during the course of their treatment and 78% of them had Gastrointestinal symptoms, 10% had peripheral neuritis, 9% were restless, 8% had joint pain, 5% had CNS symptoms and giddiness, 3% were found hypothyroid, 2% had deafness and rash, 1.4% suffered from hepatitis and dimness of vision.

**Conclusion:** The study found that nearly half of the patients treated had at least one ADRs. Deafness, skin rashes, CNS symptoms is quite low among the patients. Gastrointestinal symptoms are the predominant adverse reactions. It can help the program managers to feel confident in continuing with the present policy of early ambulatory treatment among MDRTB patients and mobilize efforts to control ADRs at local level. Unnecessary hospital admission and wage loss on the part of the patients can be avoided.



**Study site, KOLKATA**

### PD-728-30 Laboratory monitored drug adverse events in patients undergoing treatment for drug resistant tuberculosis in Khayelitsha, South Africa

S Moyo,<sup>1</sup> P Patient,<sup>1</sup> V Cox,<sup>1</sup> J Daniels,<sup>1</sup> O Muller,<sup>1</sup> G Van Cutsem,<sup>1</sup> H Cox.<sup>2</sup> <sup>1</sup>DR-TB, Khayelitsha, Medecins sans Frontieres, Cape Town, <sup>2</sup>Medical Microbiology, University of Cape Town, Cape Town, South Africa.  
e-mail: sizulumoyo@gmail.com

**Background:** Treatment regimens for drug resistant tuberculosis (DR-TB) are associated with a wide range of side effects. While some side effects are readily reported by patients, early detection of more occult side effects requires close monitoring of laboratory parameters. We describe the occurrence of selected laboratory monitored adverse events among patients treated for DR-TB in a decentralised DR-TB programme in South Africa, in 2010.

**Methods:** A retrospective analysis of selected laboratory parameters of patients treated for DR-TB in Khayelitsha in 2010 was conducted. Patient details were extracted from routine DR-TB program data. Laboratory data was extracted from a regional laboratory database. The proportion of patients experiencing each adverse event is presented.

**Results:** 211 patients were started on treatment for DR-TB in Khayelitsha, in 2010. Serum potassium, magnesium, creatinine, alanine aminotransferases (ALT), and thyroid stimulating hormone (TSH) results were available for 136, 74, 179, 122 and 156 patients respectively. Among these 36 (26%), 38 (51%), 63 (35%) and 27 (22%) and 23 (14%) experienced hypokalemia (serum potassium <3.4mmol/L), hypomagnesaemia (magnesium < 0.70mmol/L), and elevated serum creatinine (creatinine >100mIU/L, ALT (ALT>1.25xULN) and TSH (TSH>5.6 mIU/L levels) respectively. Parameters were persistently abnormal in 2/36 (6%) patients with hypokalaemia, 4/38(11%) with hypomagnesaemia, 4/63 (6%) with elevated creatinine, 5/27 (19%) with elevated ALT, and 3/23(13%) with elevated TSH levels. Overall

36 patients experienced extremely severe levels of laboratory parameters; elevated serum TSH ( $>10\text{mIU/L}$ ) 21/23 (91%); elevated serum creatinine ( $>3.5\text{xULN}$ ) 9/63 (14%); hypokalaemia (potassium  $<2.0\text{mmol/L}$ ) 4/36 (11%); hypomagnesaemia (magnesium  $<0.30\text{mmol/L}$ ) 3/38 (8%); and elevated serum ALT (ALT  $>10.0\text{xULN}$ ) 1/27(4%). Two patients had more than one laboratory parameter reaching extremely severe levels.

**Conclusion:** Although the majority of laboratory parameters had normalized at the end of observation, adverse events were frequent among DR-TB patients in Khayelitsha, with some patients experiencing life threatening levels of the parameters analysed. Treatment regimens with lower adverse event profiles are needed for DR-TB.

### PD-729-30 Prevalence of XDR, ofloxacin- and aminoglycosid-resistance among different MDR tuberculosis cases

N. Lytvynenko,<sup>1</sup> S. Cherenko.<sup>1</sup> <sup>1</sup>MDR TB, National Institute of Phthisiology and Pulmonology "F.G. Yanovsky" National Academy of Medical Sciences of Ukraine, Kyiv, Ukraine. e-mail: litvinenko@ifp.kiev.ua

**Background:** Emergence of extensively drug-resistant (XDR) tuberculosis (TB) in Ukraine has increased as a result of the inadequate management of TB-infected individuals. Aim: to study the prevalence of ofloxacin- and aminoglycosid-resistance among different MDR tuberculosis cases

**Design/Methods:** 575 patients with new cases of bacteriologically confirmed MDR TB were examined. Drug susceptibility test to II line TB drug was performed on liquid media in national reference laboratory with external control from supranational laboratory. Men were 356 (61.0%), average age of patients was (34,1  $\pm$  2,5) years. Patients were divided on 2 groups based to history of previous TB treatment: new cases were 100 (17.4 %) patients, rest of them were previously treated.

**Results:** in new patients with MDR TB XDR was revealed in 13 (13%) cases, ofloxacin-resistance – in 12 (12%) cases, aminoglycoside-resistance – in 19 (19%) cases; overall resistance to ofloxacin (with XDR cases) were determined in 25% new patients, aminoglycosid-resistance – in 32 (32%). In previously treated patients with MDR TB (relapses, treatment after failure, treatment after loss to follow up patients) XDR was revealed in 132 (27,8%) cases ( $p < 0,05$  in comparison with new cases), ofloxacin-resistance – in 48 (10,1%) cases, aminoglycoside-resistance – in 102 (21,5%) cases; overall resistance to ofloxacin (with XDR cases) were determined in 180 (37,9%) previously treated patient with MDR TB cases, aminoglycosid-resistance – in 234 (49,3%) cases of them,  $p < 0,05$  in comparison with new cases.

**Conclusion:** Prevalence of ofloxacin-resistance and aminoglycosid resistance including XDR resistance is high as in new patients with MDR TB as in previously treated patients (respectively – in 27,8–37,9% cases and 32–49,0%), that is great challenge to treatment and demand using moxifloxacin and capreomycin in standard regimen. The prevalence of XDR and ofloxacin-, amino-

glycosid resistant TB in previously treated patients of MDR TB was significantly higher than in new cases.

### PD-730-30 DNA methylation and its role in the resistance of *Mycobacterium tuberculosis* to levofloxacin

A Nataly,<sup>1,2</sup> J Robledo,<sup>1,2</sup> F Rouzaud.<sup>1,3</sup> <sup>1</sup>Bacteriology and Micobacteriology Unit, Corporación para Investigaciones Biológicas, Medellín, <sup>2</sup>Health Sciences, Univesidad Pontificia Bolivariana, Medellín, Colombia; <sup>3</sup>Equal Opportunity Life Sciences, Rockville, MD, USA. e-mail: nalvarez@cib.org.co

**Backgown:** In bacteria the most common epigenetic event is the DNA methylation and studies on gram negative bacilli have determined associations between the epigenetic inheritance and low levels of antibiotic resistance. It has been suggested that the evolution of bacterial antibiotics resistance can be mediated by epigenetic inheritance due to the variations in the gene expression patterns. Levofloxacin is a second-line fluoroquinolone recommended by the WHO to treat MDR tuberculosis. However the use of suboptimal doses of the antibiotic prolonged treatments as well as the use of the drug without a medical prescription have induced the emergence of increased levels of levofloxacin resistance. Epigenetics events such as DNA methylations have been largely unexplored in *Mycobacterium tuberculosis* and it is important to investigate their possible contributions to the resistance mechanisms used by the pathogen to evade levofloxacin treatment. The complete understanding of the mechanisms displayed by MTB LVX-R isolates is a condition for the design and development of new therapeutics targets.

**Objective:** To determine a correlation between DNA methylations and levofloxacin resistant phenotypes in MTB LVX-R isolates.

**Methodology:** We studied a set of 3MTB-XDR LVX-R isolates in parallel with another set of 3MTB-MDR; all isolated from pulmonary TB patients in Medellín, Colombia between 2006–2010. Each group was cultivated in liquid medium Middlebrook 7H9 with and without levofloxacin. The LVX concentrations used during 5 days exposure were 1  $\mu\text{g/mL}$  and 2  $\mu\text{g/mL}$  for MTB-MDR and MTB-XDR LVX-R respectively. Total DNA was subsequently extracted and purified before proceeding to methyl-sequencing, using SMRT technology. DNA 5-methylcytosine (5mC) modifications were analyzed.

**Results:** Significant quantitative differences were found in the genome wide methylation (5mC) status of MTB isolates exposed and non-exposed to levofloxacin. Differentially methylated genes were annotated and grouped by functional families for further studies.

**Conclusion:** Our results support the hypothesis that DNA methylation is involved in the early stages of the emergence of levofloxacin resistance in MTB. However further studies are necessary to correlate methylation levels with those of gene expression for a deeper better understanding of this mechanism.



## 21. TB IN VULNERABLE POPULATIONS

### PD-731-30 Active screening of pulmonary tuberculosis in migratory nomadic population: a missing link in Iran's national tuberculosis plan

B Honarvar,<sup>1</sup> A Farahbakhsh,<sup>2</sup> A Hosseini,<sup>3</sup> S Mazarej,<sup>3</sup> F Jamshidi,<sup>2</sup> M Karimi,<sup>1</sup> H Bagherpour Haghighi,<sup>3</sup> k.B Lankarani.<sup>1</sup> <sup>1</sup>Shiraz University of Medical Sciences, Health Policy Research Center, Shiraz, <sup>2</sup>Shiraz University of Medical Sciences, Shiraz -Enghelab Health Center, Shiraz, <sup>3</sup>Shiraz University of Medical Sciences, Farashband City Health Center, Farashband, Iran. Fax: (+98) 7112309615. e-mail: honarvarbh32@yahoo.com

**Background** Seasonal migratory nomadic populations are at risk for developing tuberculosis (TB) and may remain undiagnosed for a long time. The delay results in increasing severity, mortality and disease spread.

**Methods** This community-based cross-sectional study was performed from October 2012 to March 2013, during the migration season of migratory nomads to summering pastures in Fars province, southern Iran.

**Results** In this study, 5506 (82.8%) of a total nomad population of 6650 from 1337 tents were screened for pulmonary TB. Their mean of age was  $27.4 \pm 18.2$  with range from 1 to 109 years. Considering cough and other symptoms, 141 of 5506 (2.6 %) individuals were identified as TB suspects. Mean age of TB suspects was  $44.87 \pm 20.12$ . One male adult and three female adult new cases of smear-positive pulmonary TB were detected, for an incidence rate of 0.7 per 1000 population and 28.4 per 1000 TB suspects. The incidence of smear-positive pulmonary TB among nomads was about 0.7 per 1000 compared to 0.08 per 1000 in the general population of same region. Median time to onset of symptoms in detected cases was 82.5 days. Tribal stigma toward female TB patients was one of the main barriers to appropriate health-seeking behaviors.

**Conclusion** The incidence of smear-positive pulmonary TB among migratory nomads is about nine-fold as high as in the general population. Active screening of TB in migratory nomads should be integrated in the national TB plan of Iran. However, destigmatization, especially toward female TB patients, should also be addressed.



### PD-732-30 Associated factors with prevalence and annual risk infection of tuberculosis among indigenous population from Brazilian Amazon

P Basta,<sup>1</sup> J Malacarne.<sup>1</sup> <sup>1</sup>National Scholl of Public Heath, Oswaldo Cruz Foundation, Rio de Janeiro, RJ, Brazil. Fax: (+55) 2125982610. e-mail: paulobasta@gmail.com

**Background:** Recent studies had shown high incidence and prevalence of infection by *Mycobacterium tuberculosis* (MTB) and the emergence of drug resistance in indigenous populations around the world. However, little is known about the factors that contribute to maintenance of the disease in communities. **Objective:** To estimate the prevalence and annual risk of infection (ARI) by MTB and identify associated factors with transmission of the disease among the Wari'/Pakaanóva indigenous population from Brazilian Amazon.

Table 1: *Poisson* Model (Prevalence Ratio - PR) to assess the associated factors to TT  $\geq$  5mm, Indigenous Land of Igarape Ribeirao, Rondonia, Amazonia, Brazil, 2011.

Variables	n	PR Crude	CI	PR Adjusted	CI
<b>Sex</b>					
Female	122	1		1	
Male	141	1.19	(0.92-1.54)	1.137	(0.94- 1.37)
<b>Age</b>					
< 15 years	124	1		1	
$\geq$ 15 years	139	5.72	(3.65-8.97)	5.488	(3.48- 8.63)
<b>Monthly Income</b>					
$\geq$ U\$ 250.00	111	1			
< U\$ 250.00	122	0.92	(0.71-1,21)	-	
<b>Schooling of head of house</b>					
1 to 4 years	97	1			
No schooling	186	0.69	(0.54-0.89)	-	-
<b>Number of persons per house</b>					
1 to 4	55	1			
5 to 9	202	0.68	(0.53-0.88)	-	-
> 10	26	0.53	(0.29-0.95)	-	-
<b>Previous TB</b>					
No	212	1		1	
Yes	47	2.18	(1.79-2.65)	1.431	(1.19- 1.71)
<b>Contact with TB patient &lt; 2 years</b>					
No	254	1		1	
Yes	5	1.67	(1.06-2.63)	3.803	(1.21- 11.88)
<b>BCG scar</b>					
No	15	1		1	
Yes	242	0.62	(0.44-0.87)	1.35	(0.89- 2.03)
Doubtful	6	1.14	(0.71-1.82)	1.852	(1.18- 2.88)
<b>Chest radiographs result</b>					
Normal	81	1			
Sequelae	29	0.85	(0.67-1.08)	-	-
Active TB	6	0.98	(0.68-1.42)	-	-
Other disease	4	0.59	(0.22-1.57)	-	-

**Design/Methods:** We conducted a cross-sectional study in the Indigenous Land (IL) Igarapé Ribeirão, in February 2011. During house visits we applied Tuberculin test (TT) in the resident population. Moreover we offered smear and culture of sputum and chest X-ray to people who reported respiratory symptoms (RS). We conducted analysis of socio-demographic, and clinical-epidemiological characteristics to the population and RS, respectively. We used Poisson regression with robust variance to assess the associated factors with TT  $\geq$  5mm. Prevalence ratio (PR) was used as association parameter.

**Results:** We examined 263 Indians, of whom 9.1% reported RS and 18.6% previous history of TB. The prevalence of MTB infection was 40.3 % and ARI 2.4%. The variables age  $\geq$  15 years old (PR=5.5, 95%CI:3.5–8.6), contact with TB patient (PR=3.8, 95%CI:1.2–11.9), previous TB (PR=1.4, 95%CI:1.2-1.7) and BCG scar (PR=1.9, 95% CI:1.2-2.9 ) were associated with TT  $\geq$  5 mm (Table 1).

**Conclusion:** The prevalence of infection and ARI summarize the factors, which influence the transmission dynamics of TB, in a specific area, and its trend reflects the impact of control measures employed. In comparative analysis, it was found that in a decade, there were virtually no changes in these indicators. Moreover, previous TB and the recent contact with TB patients reported indicate that control measures have no had positive impacts on control disease, revealing that IL Igarapé Ribeirão constitutes an area of high risk of transmission.

#### PD-733-30 Active detection of tuberculosis among miners in Mererani, Tanzania

A Mbuya.<sup>1</sup> <sup>1</sup>Community Health, Kibong'oto Infectious Diseases Hospital, Kilimanjaro, United Republic of Tanzania. Fax: (+255) 272758883. e-mail: kiletsa@hotmail.com

**Objective:** To conduct active detection for tuberculosis among miners in Mererani, Tanzania.

**Challenge:** Kibong'oto Infectious Diseases Hospital (KIDH) located in Kilimanjaro – Tanzania is a specialized referral hospital for infectious diseases. For more than 10years about 15% of attendees are noted to come from Mererani, most are miners and are commonly diagnosed with TB, HIV/AIDS, silicosis or their combination. To the best of our knowledge, the true burden of TB among this population is not known.

**Design/Methods:** The study deployed a cross-sectional design. Mererani mines constitute a small, densely populated area, in the north-eastern Tanzania. The mines are notorious for huge numbers of miners, among them are children. Miners spend a 12hours shift per day underground where the general environment is extremely poor (congestion, poor ventilation and dust). The area is estimated to be more than 15,000 miners (Bratveit M, et al, 2003). Under financial support from LHL International–Norway, KIDH conducted active detection of TB among miners in Mererani from 4<sup>th</sup> to 23<sup>rd</sup> November

2013. Consent was sought from authorities and individual miners. Miners with TB related symptoms were evaluated by smear microscopy and some by chest X-rays. Data were documented in registers, summarized in Microsoft Office-Excel and analysed online using 'Social Sciences Statistics' page. The intended outcome was to document the burden of TB among the miners.

**Results:** Of investigated clients (602), 26 (4.3%) were bacteriologically diagnosed to have TB. This is well above (14X higher) than in general community (0.3%) as per National Tuberculosis and Leprosy Programme, 2013 (p<0.00001, 95%CI: 2.68%-5.92%). In addition, 14 clients were diagnosed to have TB based on X-ray findings, making the total TB cases 40 (6.6%) and 64 (10.6%) had radiological features suggestive of TB, silicosis or malignancy, hence put under close follow up.

**Conclusion:** Miners in Mererani carries very high burden of TB. This may be the source of TB infection to the surrounding communities. Joint efforts to seek solution are urgently needed. We need to strengthen the already started efforts on ensuring sustainable preventive measures, including provision of extensive education and improving miners' working condition. For sustainable solution, involvement of mines owners is a must.

#### PD-734-30 Mortality due to tuberculosis in the indigenous population Brazil, 2010

T Magalhães,<sup>1</sup> A De Paula Lobo,<sup>1</sup> A Torrens,<sup>1</sup> D Chaves Kühleis,<sup>1</sup> M Jacobs,<sup>1</sup> V Camargo Da Costa,<sup>1</sup> D Barreira.<sup>1</sup> <sup>1</sup>National Tuberculosis Control Program, Brazilian Ministry of Health, Brasília, DF, Brazil. e-mail: tatiana.magalhaes@saude.gov.br

**Background:** In Brazil, mortality due to infectious and parasitic diseases accounts as the fifth cause of death in indigenous population, tuberculosis included as the main diagnosis. The aim of this study was to describe mortality due to tuberculosis in indigenous population in Brazil, in 2010.

**Design/Methods:** It was conducted a descriptive study. Data were obtained from the Mortality Information Systems during 2010. Codes A15.0 to A19.0 of the X International Statistical Classification of Disease and Related Health Problems 10<sup>TH</sup> Revision (ICD-10) were considered. Mortality coefficients (MC) per 100.000 indigenous inhabitants were calculated according to sex, age and household. Stata 9 and Epiinfo 3.5.1. were used to data analysis.

**Results:** A total of 44 TB-related deaths occurred during the period. Of these, 29 (65.9%) were male, 18 (40.9%) individuals aged 20–59 years old and 20 (45.5%) inhabited in the North Region. Pulmonary tuberculosis (with neither bacilloscopy nor histological confirmation) accounted for 84.1% of all TB-related deaths. As associate cause, it was registered a total of 10 deaths, an increment of 22.7% number of deaths amongst patients with tuberculosis. Amongst the cases that had tuberculosis as an associated cause, 3 (30%) were coinfecting with HIV. Tuberculosis mortality rate in the indigenous population was of 5.4/100.000 inhabitants, twice as higher when compared to the general population

(2.4/100.000 inhabitants). Male sex (7.1/100.000 inhabitants) and individuals aged 60 years (24.2/100.000 inhabitants) or more had the highest mortality rates. Individuals from the Central Western Region had a higher risk to tuberculosis-related death (16 deaths, mortality rate 12.3/100.000 inhabitants).

**Conclusion:** Mortality due to tuberculosis is an indicator that shows effectiveness of public health policies to reduce clinical worsening.

**Results** supports the importance of tuberculosis follow up in the indigenous population to reduce its mortality.

### **PD-735-30 Fate is the main reason for tuberculosis? Knowledge about TB among women in Kerala, India**

S Gadala,<sup>1</sup> M Krithika,<sup>1</sup> T Thomas,<sup>1</sup> H Corrie,<sup>1</sup> J Jabun,<sup>1</sup> P Banuru Muralidhara.<sup>2</sup> <sup>1</sup>Project Axshya, Catholic Health Association of India, Hyderabad, <sup>2</sup>Project Axshya, Union Against Tuberculosis & Lung Diseases, New Delhi, India. Fax: (+91) 40-27811982. e-mail: srinivasa-rao@chai-india.org

**Background:** Worldwide, women carry a disproportionate burden of poverty, ill-health, malnutrition and disease. Gender and culture barriers inhibit women from seeking health-care, leading to poor diagnosis rates, yet higher susceptibility to TB and greater mortality rates. Tuberculosis causes more deaths among women than all causes of maternal mortality combined and women of reproductive age are more susceptible to developing TB than men of same age. Increased knowledge is related to treatment seeking behavior. Through project Axshya even the most vulnerable and marginalized groups were reached and women are sensitized and awareness activities among such groups helped in bringing awareness and treating the entire family.

**Method:** A pilot study was conducted to understand the knowledge, attitudes and practice about tuberculosis among women. All women respondents of the 11 communities of Vilvattam district were listed and 80 women were selected through stratified sampling method. Women were interviewed about knowledge, attitudes and practice relating TB care and control.

**Result:** About 77.5% of the respondents were unemployed leading to backwardness of respondent's treatment seeking behavior. Only about 50% of them participated in awareness programs but 75% of the respondents had knowledge of the transmission of TB. 47.5% knew about the DOTS treatment and around 41% did not know the duration of the treatment. 71.3% did not know the possibility to get infected with TB. For 58.8% responded TB does not need care and 88.8% responded that TB can be cured without treatment. About 82.5% believe that fate is the main reason for TB.

**Conclusion and recommendation:** Addressing TB among women in conjunction with the community, there would be greater success in achieving the goals as women are integral change makers within the family units. Awareness programs for kudumbasree units (women self help

groups), other women's group and continuous evaluation of Axshya programs to reach out for more vulnerable groups is recommended.

### **PD-736-30 Supporting the appropriate management of TB in small mining companies of South Africa**

M T Mbatha,<sup>1</sup> S Thamaga,<sup>1</sup> G Baloyi,<sup>2</sup> D Moleba.<sup>1</sup> <sup>1</sup>PPM, URC, Pretoria, <sup>2</sup>TB, Provincial Department of Health, Polokwane, South Africa. e-mail: thulanim@urc-sa.com

**Background and challenges to implementation:** There is currently a significant focus on management of TB in the mining sector in Southern Africa. This focus is mostly limited to the large, principal mining companies. Small- and medium-sized mines, many of which are locally run and less regulated, also face considerable challenges related to workplace TB exposure but frequently do not have in-house TB or HIV workplace programmes. There are over 100 small and medium sized mines located in Limpopo Province. Limpopo Province has a population of 5,404,868, and has two of the six districts that have been identified by the National Department of Health (NDOH) for immediate support as part of addressing TB in the mines in peri-mining communities. The two districts are Waterberg which has a total TB cases of 980 and Sekhukhune with a total TB cases of 894.

**Intervention or response:** To help prepare for an inclusive and harmonized response, the USAID TB Program South Africa conducted a rapid situational analysis in 12 small mines from key peri-mining communities identified by the NDOH. These were platinum, uranium and coal producing mining companies. The situational analysis was aimed at identifying critical gaps in the management of TB and HIV in mines, and provide a roadmap for prioritizing gaps and areas of technical support for these mines.

**Results and lessons learnt:** Out of the 12 mining companies that were assessed, only 4 had a workplace policy on TB and HIV. Eight of the mines had a HIV workplace but no workplace policies on TB. Only 2 of the mines have an on-site health service facility for employees. The rest of the mines outsourced their health services. In 8 of the mines that had a HIV workplace policy, the health care workers did not have knowledge and information about NTP guidelines and policies on TB management. All 12 mining companies did not have industry specific information, education and communication materials on TB.

**Conclusions and key recommendations:** Improving the management of TB care, prevention and treatment in small and medium sized mines remains an important challenges. It is essential to scale up the effort of addressing TB in small and medium sized mines. Capacity building on TB management to health care workers in small and medium sized mines and to their outsourced health care service providers is critical.



**PD-737-30 Early detection of tuberculosis in NGOs working with vulnerable groups in Ukraine**

Z Islam,<sup>1</sup> S Filippovych,<sup>1</sup> O Smetanina,<sup>1</sup> I Zharuk,<sup>1</sup> S Liudmyla.<sup>1</sup> <sup>1</sup>Treatment and Procurement, International HIV/AIDS Alliance in Ukraine, Kiev, Ukraine. Fax: (+38) 444905489. e-mail: zislam@aidsalliance.org.ua

**Background and challenges to implementation:** Over the past years, the incidence of tuberculosis (TB) in Ukraine among general population decreased, however, the number of TB cases among PWID and PLHA remains very high. In 2013, TB was diagnosed among 55,8 % of the total number of AIDS patients who have dispensary registration. Percentage of deaths that are caused by TB/HIV, among the total number of AIDS deaths was 62.7 %. Level of TB/HIV continues to grow each year from 4.3 per 100,000 populations in 2006 to 10.5 in 2013. Implementation of active methods for early detection of TB among vulnerable groups is one of the key interventions in reducing the burden of TB in Ukraine.

**Intervention or response:** In 2013 Alliance Ukraine, introduced services for the early detection of tuberculosis as a pilot among risk groups in the HIV "harm reduction" program. 36 NGOs were included to implement the pilot. Partnerships were established between TB services and NGOs to create a service delivery mechanism for TB detection and diagnosis. Screening questionnaires for active questioning of clients at risk for TB symptoms, referral of sputum for TB microscopy was introduced and referral systems were developed to support the patients navigate through this complicated health care system. NGO staff has been trained on identification of TB, its prevention methods and infection control measures including supply of sputum containers.

**Results and lessons learnt:** In 2013, 36 local NGOs conducted active TB screening questionnaire for 55,549 clients; 12,305 clients (22.2%) had suspected TB; 5698 clients (46.3%) were screened for TB; 626 cases of tuberculosis (11%) were diagnosed.

**Conclusions and key recommendations:** Organization and implementation of a screening questionnaire for early and active TB case findings have shown their effectiveness and exceeded the overall level of TB detection. Cooperation in the field of TB detection at an early stage between health care and NGOs allowed the most vulnerable groups to improve access to TB services. Expansion of active TB detection based on NGOs will lead to prevention of new cases of the disease and reduce mortality among the most vulnerable groups at risk of TB. Stigma for TB remains high thus its crucial to support clients to motivate to undergo further diagnosis of TB following the case detection.

**PD-738-30 Social inclusion framework for TB risk management in the marginalised population of Delhi, India**

Ashw Khanna,<sup>1</sup> S Chandra,<sup>2</sup> N Sharma,<sup>3</sup> K Ashok,<sup>4</sup> A K Vasisht,<sup>5</sup> A Narnoliya,<sup>6</sup> B Neeti.<sup>1</sup> <sup>1</sup>State TB Control Office, Directorate of Health Services, New Delhi, <sup>2</sup>Revised National Tuberculosis Control Program, WHO Country Office for India, New Delhi, <sup>3</sup>Community Medicine, Maulana Azad Medical College, New Delhi, <sup>4</sup>Chest Clinic, Deen Dayal Upadhyay Hospital, Directorate of Health Services, New Delhi, <sup>5</sup>Chest Clinic, Moti Nagar TB Hospital, Municipal Corporation of Delhi, New Delhi, <sup>6</sup>Chest Clinic, Choudhary Desraj Hospital, Municipal Corporation of Delhi, New Delhi, India. e-mail: chandras@rntcp.org

**Background and challenges to implementation:** The converging interest over universal access to TB care highlights the importance of early and timely treatment initiation for all the eligible patients especially the vulnerable group of marginalized population. As a risk management strategy, the model of Homeless resource centres (HRC) was rolled out by Government of Delhi for the care of marginalized groups like homeless population, drug addicts, daily laborers and pavement dwellers. Each HRC has 15–20 night shelters which houses around 70 inmates each. Under the aegis of a mother NGO, these HRC's are supervised for the care they offer to the night shelter inmates regarding nutrition, education, health and rehabilitation. Each night shelter acts as an interface wherein the relevant government departments collaborate to provide basic amenities to the marginalized groups.

**Intervention or response:** Analysis of the contribution of one HRC towards TB care in North and North West Delhi in urban slum settings was undertaken. In 2013, all the community mobilisers and livelihood coordinators employed at each night shelter by the HRC were sensitized. Early morning sputum was collected and transported to the nearby diagnostic centre. Once diagnosed, treatment was started through the attached area DOT centre. Based on the knowledge gleaned, the study proposed a decentralized risk management model for TB management in all night shelters across Delhi.

**Results and lessons learnt:** During the study period (July-Dec 2013) there were monthly 1100 inmates residing in each of the 16 night shelters of North and North West Delhi. An additional yield of 55 new TB cases was notified by the attached Chest Clinics from the referrals of the linked night shelters. In the corresponding quarters, the North and North West Delhi Chest Clinics reported a 19 % increase of suspect examinations and total case notification rates when compared with same quarters previous year. Till December 2013, two patients were lost to follow up and HIV positive found in 5 inmates.

**Conclusions and key recommendations:** The unreached shelter less population residing in pavements would have gone unserved had they not been embraced in the formal health system under the HRC framework. The proposed model of intersectoral collaboration promotes social inclusion and provides equitable health services for the

marginalized population residing in high risk urban slum settings.

### PD-739-30 TB among mining populations: risk perceptions on TB infection: views among Mozambique mining population

A Mataruse,<sup>1</sup> S Machevo Chilundo,<sup>2</sup> D Sacur,<sup>1</sup> S Essama-bibi,<sup>3</sup> E Oliveras,<sup>2</sup> A Abdula,<sup>1</sup> C Juliana.<sup>1</sup>

<sup>1</sup>Community Health, Family Health International, Maputo,

<sup>2</sup>Strategic Planning, Family Health International, Maputo, Mozambique; <sup>3</sup>Global Health, Family Health International, Washington, DC, USA. e-mail: amataruse@fhi360.org

**Background:** Mozambique now ranks 11<sup>th</sup> among the 22 high burden tuberculosis (TB) countries (STOPTB Partnership, 2012) but the recent gains can be easily eroded if TB mitigation efforts are not put in place given the recent boom in mining activities in Central Mozambique, where over 100,000 immigrants have settled resulting in overcrowding - favorable for TB. Despite regional interest in addressing TB in mining populations, within Mozambique little has been done to understand and mitigate TB infection resulting from mining activities

**Design/Methods:** An operational research study was designed to explore individual and sociocultural constraints to seeking TB care in order to inform the design of communication and advocacy strategies for TB control. The study was conducted in 3 regions and the study population comprised health professionals, TB patients, community health workers, community members (including miners) and leaders. Among the 157 in-depth interviews (IDI) and 27 focus groups discussion (FGD) conducted, 2 FGDs were conducted with ex-miners from South Africa and 5 miners on TB treatment were interviewed. Recordings of IDIs and FGDs were transcribed verbatim and coded using codes derived from the data as well as codes based on the research objectives

**Results:** While most of the risk factors for TB that were raised were related to individual and sociocultural factors, miners also raised occupational risks. A majority of the minors discussed poor working conditions and lack of work hygiene as influential to TB infection "...the coughing I'm referring to here is that we get due to the work in South Africa. The mine dust results in TB infection." (FGD, Ex-mine worker, Magude) Among miners who were TB patients, they associated infection with mining conditions, use of alcohol and risk behavior but clearly indicated the need to use personal protection equipment to reduce infection. Despite knowledge of risks, miners acknowledged defaulting treatment and returning to work which increases the odds of transmission to others and the risk of drug resistant TB. Miners linked their drop out to the failure of employers to provide support during sickness

**Conclusion:** These results highlight the need to better understand and address TB among miners. Practical solutions are needed improve TB control among labor sharing countries in SADC especially for effective cross-border medical referral systems and adequately create legal frameworks to protect rights of mine workers for TB

### PD-740-30 Intensified case finding and supportive treatment among vulnerable groups in Thailand: achievement of two-year implementation of the Global Fund Project

J Rattanadilok Na Bhuket,<sup>1</sup> P Pungrassami.<sup>1</sup> <sup>1</sup>Department of Disease Control, Ministry of Public Health, Bureau of Tuberculosis, Bangkok, Thailand. Fax: (+66).

e-mail: petchawanp@yahoo.com

**Background and challenges to implementation:** Addressing prisoners, refugees and other high-risk groups is one of the main objectives of the Global Fund project during 2012–2014 (SSF-PhaseI). Implementation areas are 41 prisons, 1 refugee camp at Thailand-Myanmar border, 5 Northern provinces, 3 unrest Southernmost provinces, and 35 shelters. The project is monitored through meetings, quarterly reports, and periodic supervision visits.

**Intervention or response:** Bureau of Tuberculosis (BTB) works with GOs and NGOs for TB awareness raising, early detection and successful treatment for the vulnerable. Routine practices in prisons include symptom screening for all new inmates, all who stayed >6 months, and all PLWHA; sputum AFB examination for all with presumptive TB; and chest radiograph for those with smear negative. Working with prison & hospital staff; NGO1 volunteers make rapport with TB patients and support them to continue the treatment after their release. For refugee camp; interventions operated by NGO2 include training volunteers and health care staff, health dissemination and mass campaign, treatment with referral to outside hospital, patient supervision and support in TB village. For Northern ethnics, intensified case finding (ICF) activities are implemented by NGO3 and NGO4 volunteers and networks. For migrants in the South, 3 provincial health offices are responsible for ICF. BTB coordinates with the Ministry of Social Development and Human Security for training the care-takers and nurses in the shelters. Chest radiography before entry and referral to hospital are shelter routine.

Results of intensified case finding and supportive treatment activities among 5 vulnerable groups in Thailand during October 2011 – September 2013<sup>1</sup>.

Target group	Project Area (Targeted population <sup>2</sup> )	Tested for TB	Diagnosed as TB <sup>3</sup> (%)	Outcome Evaluated <sup>4</sup>	Treatment Success (%)
Prisoners	41 prisons in 22 provinces (107,725-121,058)	21,501	854 (4.0)	762	652 (85.6)
Refugees	1 camp (78,835)	495	10 (2.0)	2	2 (100)
Ethnics	15-19 districts, 5 provinces (106,719-132,919)	1,594	24 (1.5)	10	10 (100)
Unrest	33 districts in 3 provinces (>64,000)	338	32 (9.5)	3	2 (66.7)
Homeless	35 shelters in 25 provinces (6,911)	3,409	0 (0)	-	-
Total		27,337	920 (3.4)	777	666 (85.7)

<sup>1</sup> Except for unrest areas and shelters where the activities were started in 2013.

<sup>2</sup> The exact numbers are changeable over time.

<sup>3</sup> Smear positive or negative pulmonary TB.

<sup>4</sup> New smear positive cases registered during October 2011- January 2013.

**Results and lessons learnt:** During 2-year implementation, 27,337 vulnerable people were tested for TB and 920 TB cases (3.4%) were detected. The case detection rates vary between 0–9.5%. The highest numbers of TB test and diagnosis were among prisoners whereas the highest case detection rate was among migrants in the

unrest area (see Table). Eleven TB cases were detected before entry the shelters or outside ICF period, but no additional cases were found by project ICF. Among 777 new smear-positive cases, 666 (85.7%) were cured or completed the treatment. Increased success rates were observed among prisoners (data not shown).

**Conclusions and key recommendations:** The highest numbers of TB test, diagnosis and treatment were achieved among prisoners; with >85% success rate. Given the much limited budget of the New Funding Model for Thailand, prioritized program and budgeting should be considered.

#### **PD-741-30 Molecular characterisation of strains of the *Mycobacterium tuberculosis* in the indigenous and non-indigenous population of Mato Grosso do Sul**

E Cunha,<sup>1</sup> L Ferrazoli,<sup>2</sup> L Lempke,<sup>1</sup> M Marques,<sup>3</sup> F Munhoz,<sup>4</sup> R Maia,<sup>5</sup> I Costa.<sup>6</sup> <sup>1</sup>Mycobacteriology, Central Laboratory of Public Health of Mato Grosso do Sul, Campo Grande, MS, <sup>2</sup>Nucleus of Tuberculosis and Mycobacteriosis, Adolfo Lutz Institute, Campo Grande, MS, <sup>3</sup>State Program For Tuberculosis Control, State Department of Health of Mato Grosso do Sul, Campo Grande, MS, <sup>4</sup>Program of Post Graduation in Applied Computing, Federal University of Mato Grosso do Sul, Campo Grande, MS, <sup>5</sup>National Tuberculosis Control Program, Ministry of Health, Campo Grande, MS, <sup>6</sup>College of Medicine, Federal University of Mato Grosso do Sul, Campo Grande, MS, Brazil.  
e-mail: euniceatsuko@uol.com.br

**Background:** Tuberculosis, a contagious infectious disease, has been diagnosed by laboratory methods for over 100 years. Despite the availability of treatments that ensure complete recovery in nearly 100% of cases, the disease remains a major public health issue worldwide. In Mato Grosso do Sul state, in West-Central Brazil, its incidence is similar to the national average of 37.9 per 100 000 population, whereas in the indigenous population it reached 199.8 per 100000 in 2010.

**Design/Methods:** This study investigated antituberculosis drug resistance in isolates collected from indigenous and non-indigenous patients in Mato Grosso do Sul in the period 2000–2008. The standard procedure for collecting samples included smear fast (bacilloscopy, by Ziehl-Neelsen culture method), culture (Lowenstein-Jensen, Ogawa-Kudoh and MGIT960 methods), and investigation for antituberculosis drug resistance (proportions method and MGIT960) in the isolates. Also, a research was done using RFLP (Molecular Biology) Analysis.

**Results:** Resistance was found in 17.4% of cases and multidrug resistance in 3.7%. The latter percentage was higher than that estimated for Brazil (1.4%). Drug-resistant isolates accounted for 4.63% of indigenous patients and multidrug resistance for less than 1%. Restriction fragment length polymorphism (RFLP) analysis allowed recent transmission to be distinguished from endogenous infection. A total of 149 samples were analyzed. Three isolates were excluded for showing less than six bands; another 18 were excluded for being

repeated. Clusters between profiles of indigenous and nonindigenous samples encompassed 77 isolates (59.6%); 29 isolates were found to be non-clustered. Unique profiles accounted for 22 samples. Two families of isolates clustered over 12 years were identified, all of them from Amambai county, whose indigenous population is around 12 000.

**Conclusion:** The results obtained revealed the occurrence of recent transmission, as well as endogenous infection, emphasizing the importance of early diagnosis and continuous chemoprophylaxis.

#### **PD-742-30 Tuberculosis incidence among immigrants to the United States compared with WHO estimates in country of origin**

S Jonnalagadda,<sup>1</sup> Z Wang,<sup>1</sup> W Zhou,<sup>1</sup> J Painter.<sup>1</sup> <sup>1</sup>Division of Global Migration and Quarantine, Immigrant Refugee and Migrant Health Branch, Centers for Disease Control and Prevention, Atlanta, GA, USA. e-mail: wau4@cdc.gov

**Background:** Prior to arrival in the United States, immigrants undergo a mandatory overseas medical examination for tuberculosis (TB) and a recommended re-examination following arrival. We compared crude TB prevalence estimates (per 100,000) from the pre-departure and post-arrival exams among immigrants who arrived in the United States in 2012 with corresponding country-specific WHO 2012 TB prevalence estimates (per 100,000).

**Methods:** During the pre-departure immigrant exam, individuals  $\geq 15$  years undergo chest radiography (CXR); those with findings suggestive of TB undergo smear and culture testing on three sputum samples. Those with laboratory-confirmed TB complete treatment prior to arrival in the United States and undergo post-arrival screening involving three sputum smears and cultures. Individuals with CXR suggestive of TB but negative smears and cultures during the overseas exam and contacts of overseas laboratory-confirmed TB cases also undergo post-arrival screening in the United States. TB prevalence was estimated using laboratory-confirmed TB cases diagnosed during pre-departure and post-arrival exams and arriving in the United States in 2012 as numerator and newly arriving immigrants  $\geq 15$  years in 2012 as denominator, stratified by country of birth. We selected 10 countries with the greatest number of TB cases diagnosed among 2012 arrivals.

**Results:** Prevalence of TB among immigrants (numbers of TB cases diagnosed per the numbers of immigrant arrivals in 2012) was: Philippines 1310 (391/29,842), Viet Nam 1575 (313/19,867), China 138 (44/31,813), Mexico 28 (17/60,750), Haiti 125 (16/12,758), Cambodia 866 (14/1616), the Dominican Republic (DR) 46 (11/23,780), India 36 (8/21,970), Nepal 262 (8/3055) and Peru 137 (6/4361). TB prevalence among immigrants was significantly greater compared to the WHO estimate for Philippines (461) and Viet Nam (218) but not significantly different for China (99), Mexico (33), Haiti (296), Cambodia (764), DR (98), Nepal (241) and Peru (121) (Figure). The TB prevalence among immigrants



from India was significantly lower than the WHO estimate (230).

**Conclusion:** TB prevalence among immigrants is based on a highly sensitive method of TB diagnosis (active case-finding and use of culture). While immigrants might differ from the general population in a country, and the estimates from the immigrant exam might not be generalizable, data from immigrant screening could serve as a resource when estimating country-specific TB burden.

#### PD-743-30 Gender and tuberculosis: a prospective study exploring risk factors for higher notification of tuberculosis (TB) in adult women in Khyber Pakhtunkhwa

M Aziz,<sup>1</sup> S Campbell,<sup>1</sup> A Esmail.<sup>1</sup> <sup>1</sup>Primary Care, University of Manchester, Manchester, UK.  
e-mail: dr Aziz@hotmail.co.uk

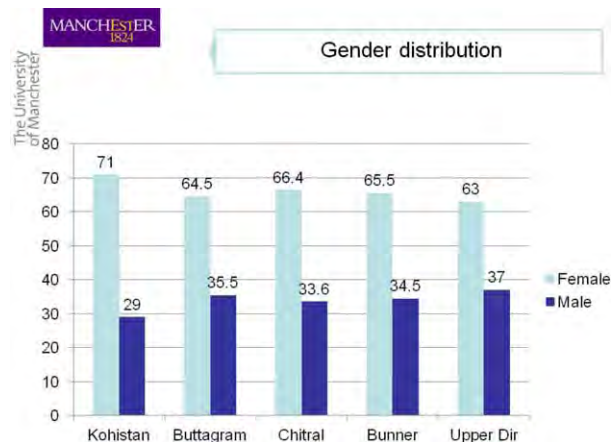
**Background:** Tuberculosis (TB) remains continue to be major killer disease of adult females in Pakistan, which ranks fifth highest country with TB burden globally<sup>1</sup>. There is emerging evidence of the differential impact of risk of infection, progression of disease, case fatality and access to treatment which is mediated by gender differences in TB<sup>2</sup>. There is dearth of relevant research and data on gender aspects of TB<sup>3</sup>. This study, therefore, aims to explore the risk factors associated with higher notification of TB in women in KPK Province in North West Pakistan, with a view to identifying areas where supplementary action could be provided for the strengthening of the planning, administration and implementation of the National TB Control Programme. Aim: To explore the causes of higher notification of TB in adult Females in the province of Khyber Pakhtunkhwa, Pakistan. Objective: To determine risk factors for newly diagnosed laboratory confirmed TB disease in all adult females in Khyber Pakhtunkhwa from Jun 2013 to September 2013.

**Design/Methods:** We collected information regarding potential risk factor by an administered questionnaire targeting new TB patients. For this purpose ten districts, five from higher (Kohistan, Buttagram, Chitral, Buner and Lower Dir) and five from lower notification area (Karak, Kohat, Mardan, Nawshehra and Malakand) were selected. These districts were identified as higher and lower TB occurrence regions through the earlier descriptive study using the National Tuberculosis Control Programme data from 2001 to 2010, in respect of gender difference of TB in Khyber Pakhtunkhwa. Five TB diagnostic centres from each district were randomly selected for the recruitment of study subjects. All confirmed adult TB patients presented to each centre between 1st June 2013 and 30th September 2013 were included in the study. Epi info 7 was used for data entry and calculation of logistic regression with 95% confidence interval.

**Results:** A Total of 914 new TB patients were reported in the data set, with a prevalence of TB 62% female and 38% male. Significant risk factors were low literacy level

(OR 0.33 95% CL 0.12-1.20), low income status (OR 0.54 95% CI 1.62-3.73), and overcrowding (OR 0.56 95% CI 1.13-2.87). Female patients were 4 and six times more likely have TB with BMI <18.5 (95% CI 5.53-21.52) and anaemia ( $p=0.008$ ; 95% CI 1.12-1.99) than male respectively.

**Conclusion:** This study concludes that the cause of higher notification of TB in adult females of KPK is not medical but mainly socioeconomic. Due to low literacy level unemployment is more come in the females of KPK, particularly in the higher notification districts.



## 22. TOBACCO USE IN WOMEN AND CHILDREN: A WORRYING TREND

#### PD-744-30 Influence of social environment on adolescents smoking behaviour: a risk factor and protective factor study from a hilly state of north India

A Gupta.<sup>1</sup> <sup>1</sup> Community Medicine, Indira Gandhi Medical College, Shimla, India. Fax: (+91) 0177 265 8339.  
e-mail: dranmol1964@gmail.com

**Background:** Cigarettes smoking is a common mode of consuming tobacco in India. This evil habit usually starts in adolescence and tracks across the life course.

**Interventions** like building decision making skills and resisting negative influences are effective in reducing the initiation and level of tobacco use.

**Aims and objectives:** To assess the prevalence of cigarette use and its risk and protective factors among adolescent school students in North India.

**Methodology:** A cross-sectional study was conducted among 720 school going adolescents in schools located in Shimla town of North India. The study was conducted from September 2012 to Nov2013. Data was collected using a standardized pretested questionnaire.

**Results:** The overall prevalence of current smokers was 11.8% (1% females and 22% males). Protective factors for smoking were parents knowing about free time activity, sharing problems with parents and helpful classmates. Risk factors included male gender, smoking

family member, friends, matters of worry in family, feeling sad and falling grades. The multiple logistic regression model revealed that male gender (OR=11.9; CI=4.5–31.4), family member smoking (AOR=1.9, CI 1.1–3.5) and friends smoking (3.6, CI=2.0–6.5) were significant risk factors associated with adolescent's smoking behaviour. Parents knowing free time activity of the adolescent (AOR=0.3, CI=0.2–0.6) was a significant protective factor.

**Conclusion:** A high proportion of school adolescents in Shimla town of North India were current cigarette smokers. Family and peers influence were identified as factors affecting cigarette smoking behaviour. The smoke free policies in India should focus on designing interventions that promote family involvement and promote peer group activities; so as to accelerate efforts in tackling the adolescent smoking epidemic in India.

#### **PD-745-30 Translation and validation of the Malay version of the second-hand smoker (SHS) questionnaire among pregnant women at hospital Sungai Buloh, Selangor**

B Muadz,<sup>1</sup> MN Norizal,<sup>1</sup> N Ismail,<sup>2</sup> B Abdullah,<sup>3</sup> H Halilah.<sup>4</sup> <sup>1</sup>Pathology and Laboratory Medicine, <sup>2</sup>Population Health and Preventive Medicine, <sup>3</sup>Women and Child Health, and <sup>4</sup>Statistic and Decisional Sciences, University of Technology, MARA, Shah Alam, Malaysia. e-mail: muadz\_liverpool@yahoo.com

**Background:** This study was conducted to assess the reliability and construct validity of the Malay version of questionnaire from International Agency for Research on Cancer, WHO among pregnant women in Hospital Sungai Buloh, Selangor.

**Design/Methods:** A total of 200 pregnant women consented to participate in the study and were administered the Malay version of the questionnaire. Reliability test was determined using Cronbach's alpha for internal consistency while construct validity was assessed using factor analysis. Thirty randomly selected pregnant women were asked to complete the questionnaire for the second time three month later for test-retest reliability.

**Results:** The mean (SD) age of the participants was 27.9 (5.01) years. The results indicated that Cronbach's alpha coefficients revealed decision household SHS exposure (0.812), knowledge (0.733), attitude (0.799) and avoidance of SHS exposure (0.902). Factor analysis showed self avoidance, self feeling and social exposure as three meaningful common factors that could explain the construct of avoidance of SHS exposure. For test retest test the value ranged from 0.957 to 0.993 which indicates excellent test-retest reliability.

**Conclusions:** The SHS questionnaire from International Agency for Research on Cancer WHO, was successfully translated and adapted into Bahasa Melayu. It was successfully tested for internal consistency, test-retest reliability, and construct validity. We strongly recommend the SHS questionnaire and can be applied in the future studies in Malaysia.

#### **PD-746-30 The reasons for violations of the Russian Federal Law No. 15 (as of 23/02/2013) on protecting people from second hand tobacco smoking in Krasnoyarsk**

O Kutumova,<sup>1</sup> L Kononova,<sup>1</sup> D Trufanov.<sup>2</sup> <sup>1</sup>Regional Center for Medical Prevention, Krasnoyarsk, <sup>2</sup>Siberian Federal University, Krasnoyarsk, Russian Federation. e-mail: bg1960@yandex.ru

**Objectives:** In the frame of the Agreement with International Union against tuberculosis and lung diseases the sociological study to identify the reasons of the Smoke Free Law violation among adult population in Krasnoyarsk region was conducted in 2013. Also, one of the study objectives was to determine the smoking prevalence among adult population.

**Methods:** Telephone interviews of 1286 respondents aged 18 to 64 with interviewer-administrated questionnaires were performed (44,7% men and 55,3% women) using random selection.

**Results:** The incidence of adult smokers was found to be 33,1%, which is lower compared to GATS data of 2009 for Russia (39,1%). However, the prevalence of smoking among men compared to that of GATS data appeared to be lower (44,3% and 60,2% respectively), while prevalence of smoking among women in comparison with same from GATS report were higher (23,9% and 21,2% respectively). The most of the citizens (85,3%) are informed about the Smoke Free Law, but 43,8% of the smokers admitted violating the Law and continue smoking in public places. The reasons for violation of the law proved to be subjective - stress, habitual smoking, as well as the absence of places for smoking, the absence of signs forbidding smoking and the absence of fines for smoking. However, in 2013 the number of citizens who applied for medical help on smoking refusal, has increased and makes up 13800 (in 2012 it was 6780).

**Conclusion:** Thus, smoking among men tends to decrease, though it increases amongst women. However, the positive trend and growing number of those who looks for counseling and treatment services proves that The adoption of the Federal Law No15 promoted refusal from smoking. For Smoke Free Law to be observed, it is necessary to improve the system of State enforcement and to develop instruments for compliance monitoring and public control as well as access to tobacco dependence treatment.

#### **PD-747-30 Quitting smokeless tobacco use among low SES women in a community counselling set-up**

M Aghi.<sup>1</sup> <sup>1</sup>Behavioral Science, Advocacy Forum for Tobacco Control, New Delhi, India. e-mail: mirabaghi@gmail.com

**Background:** In India, intervention to promote quitting tobacco use among lower SES strata has been successfully carried out in a project mode. The present intervention was conducted in an urban area in a community setting to help low SES women to quit the use of smokeless tobacco. Low SES women feel more comfortable discussing health in a group. Eight women

domestic servants in South Delhi formed the sample for this study. They were between 25 and 35 years of age and had been consuming smokeless tobacco (ST) for over five years. They each made their own quid, except for one, who consumed Gutka.

**Intervention:** After listening to a discussion on the harms of smokeless tobacco use in a neighbourhood school over four consecutive days, women showed interest in quitting. They were prepared for Cessation over a three-day period where they got to know what to expect and what to do. The counsellor met with them three times on Day 1 and Day 2 of the Cessation, and gave them detailed instructions. On Day 3 the counsellor met with them twice, and for four more days just once a day. The total time scheduled for Cessation was 11 days, the 11th day being optional. Each session lasted 30–45 minutes unless someone wanted private time. Sessions were largely interactions meant to solve their daily discords at home or at work, and then discussing its impact on their ST use. At no point of time were they made to feel deprived of tobacco forever. They were coached to postpone its use up to a particular time until they felt they could not do without it. The discomfort reported was highest on Day 2 and 3, while Day 4 was fine for all of them. Day 5 was bad for two, but when the other women talked to them they felt better. They got lozenges and rock sugar to suck on if they felt uncomfortable. Two of them did not use anything. One also used black peppercorns to relieve her discomfort a couple of times. They were encouraged to drink plenty of water, do head and neck relaxation, keep busy and avoid friends who chew tobacco.

**Results:** By the 15<sup>th</sup> day, seven of the eight women had not used ST the entire time. The eighth had gotten sick on the last day and had ended up using Gutka. However, she wanted to try it all over again.

**Conclusion:** This demonstrates the use of community set-up to help urban women of lower socio-economic status to quit ST use.

#### **PD-748-30 Youth initiatives against tobacco: a milestone in Bangladesh**

A Bakul,<sup>1</sup> I Chowdhury.<sup>2</sup> <sup>1</sup>NGO, Action In Development - AID, Dhaka, <sup>2</sup>Technical Advisor, International Union Against Tuberculosis and Lung Disease (The Union), Dhaka, Bangladesh. Fax: (+880) 45161189(105).  
e-mail: aminulislambakul@gmail.com

**Background and challenges to implementation:** SUBASH is an organized young group those are fighting against the tobacco using in the different educational institution across the Khulna division of Bangladesh. This group has developed with the initiative of Action In Development- AID by the implementing the project 'Smoke Free Khulna Division through Effective Enforcement of Smoke-Free Provision of Tobacco Control Law'. The main objectives of SUBASH are develop awareness against the tobacco using among the young students and strengthening the students voice against the tobacco at colleges and universities and Control the aggression of the tobacco companies at the colleges and

universities. The main challenges of the SUBASH activities were; some administrative personnel's were smokers and they created some barriers to implement the activities. Similarly the peer effects for the smoking were the challenge for the implementation of SUBASH activities.

**Intervention or Response:** As the part of the different activities SUBASH has developed awareness among the 25000 students in the 14 education institutions of the Khulna division in Bangladesh including the covering area of institution campus, students residential halls and hostels for the part of the social campaign SUBASH organized the rally, campaign, sticker and sign provision, celebration of the world no tobacco day in last years. At present SUBASH is planning to organize a national student conference against tobacco using with the participation of the students in the different institution. Similarly SUBASH has developed the awareness among the institutions administration, small shop keepers in the campus area on the bad impact of tobacco using. Similarly for the reduction of the aggression of the tobacco producing companies SUBASH formed the committee in the each institution.

**Results and lessons learnt:** By the effective action of the SUBASH team in different educational institutions of Khulna division it has reduced 75 % of smoking in campus area and the frequency of the tobacco using among the students in the colleges and university reduce drastically in the Khulna division the tobacco producing companies aggression in the different institution based shops and advertisement are reduced and the attractive attitude on tobacco using has changed for the activities of SUBASH by this process it has learned that collective and dedicated youths can change the world.

#### **PD-749-30 Prevalence of tobacco use among women: a cross sectional survey from a squatter settlement of Karachi, Pakistan**

M Irfan,<sup>1</sup> N Iqbal,<sup>1</sup> N Ashraf,<sup>1</sup> S Awan,<sup>1</sup> J Khan.<sup>1</sup>

<sup>1</sup>Pulmonary Section, Department of Medicine, Aga Khan University, Karachi, Pakistan. Fax: (+92) 2134934294.  
e-mail: muhammad.irfan@aku.edu

**Background:** While the prevalence of tobacco use has been slowly declining in the developed countries over the past 20 years, it has been steadily increasing in developing countries especially in women. This has led to a rapid rise in lung diseases among women. Objective: To determine the prevalence of tobacco use (both smoking and smokeless tobacco) among women in an urban squatter settlement in Karachi, Pakistan.

**Methods:** A cross-sectional survey was conducted from 1<sup>st</sup> July 2012 to 31 December 2012 on near 19,325 females of aged 15 - 80 years in Orangi Town, an urban squatter settlement in Karachi, Pakistan. The approximate population is near 2 million. A total of 16,987 women responded. Modified questionnaire, developed by WHO, was used in Urdu.

**Results:** The mean age was  $37.3 \pm 9.8$  years and 15,255 (89.80%) were married. 9143 (53.82%) admitted that at



least one person uses tobacco in some form in their homes. The prevalence of smokeless tobacco use was 47.08% while cigarette smoking was 2262 (13.31%) among women. Among smokers 1927(85.19%) admitted that they have tried to quit smoking during last 12 months but failed and 1658 (73.29%) mentioned that they have received their doctor advice for quitting. Almost all smokers mentioned that they think of quitting after seeing warning on cigarette pack. 99.5 % promise to quite this habit during interview.

**Conclusion:** Tobacco use among women in an urban squatter settlement is very high and alarming. Preventive and control measures against tobacco use are required in these communities.

### PD-750-30 Tobacco threatens Indonesian child right: a policy review

R Fauzi.<sup>1</sup> <sup>1</sup>Tobacco Control Support Center, Indonesian Public Health Association, Jakarta, Indonesia.  
e-mail: ridwan@tcsc-indonesia.org

**Background:** Child right is the right which has been recognized by international convention, and also national constitution of Indonesia. This right encompasses rights to life, and the survival and development of the child. Therefore, the government is obliged to fulfill these rights, including protecting against harmful effects of smoking. This paper will elaborate current situation of tobacco problem among children, and evaluate current policies related to tobacco control and children.

**Design/Methods:** Reviewed on all tobacco control regulation in both national and sub-national level, and supported by several household survey conducted from 2004–2013. We used WHO Framework Convention on Tobacco Control as protocol of compliance.

**Results:** Analysis revealed that 18.3% of adolescent (15–19 years old) were smoker. Smoker started smoking at 5–9 years old were 2.2% which was increased fivefold in the last decade. 78.1% teenagers (13–15 years old) exposed to tobacco smoke outside their homes. This high tobacco epidemic was related to lack of tobacco control regulation. Cigarette price in Indonesia is one of the lowest among ASEAN country. Cigarette is accessible and unrestricted on selling it to children. Only Fifteen cities have already protected by 100% smoke free regulation whose population is about 30 million. In addition, many tobacco industry activities remain unrestricted.

**Conclusion:** Indonesian children have not fully enjoyed their right due to strong challenge from tobacco industry. Therefore, we recommend following set policies: Raise cigarette tax to increase its prices, develop special smoking cessation service, implement comprehensive smoke free area in public places to reduce secondhand smoke, ban tobacco advertising, promotion, and sponsorship to denormalize tobacco industry, and restrict tobacco selling to children.

### PD-751-30 A study on compliance to prohibition of sale of tobacco products to children in Mizoram, India

J Ralte,<sup>1</sup> R J Singh,<sup>2</sup> Zo Chhakchhuak,<sup>3</sup> L Lalnuntluangi,<sup>4</sup> H Renthlei.<sup>5</sup> <sup>1</sup>Health & Family Welfare, Mizoram State Tobacco Control Society, Aizawl, <sup>2</sup>The Union South-East Asia, New Delhi, <sup>3</sup>Health & Family Welfare, Mizoram State AIDS Control Society, Aizawl, <sup>4</sup>Health & Family Welfare, NPCDCS, Aizawl, <sup>5</sup>Management, Mizoram University, Aizawl, India.  
e-mail: tluangtlei@gmail.com

**Background:** Mizoram, a tiny northeast Indian state has the highest prevalence of tobacco consumption in India (67% of all adults, GATS 2009-10). With low quit rates among current users, an important public strategy is to prevent young children from exposure, experimentation and regular consumption of tobacco. Section 6 of The Cigarettes and Other Tobacco Products Act (COTPA) deals with this aspect through Section 6a prohibiting sale of any tobacco product to minors under 18 years of age. Section 6b prohibits sale of tobacco products within 100 yards of educational institutions. These are important interventions considering cultural acceptance and encouragement even in certain circumstances of tobacco consumption where children are frequently asked to buy tobacco products for their relatives. Widespread dissemination of information regarding these prohibitions has been undertaken through public awareness utilizing various forms of media by the Mizoram State Tobacco Control Society (MSTCS).

**Design/Methods:** Observational survey was conducted across 8 districts in the state in which 1271 tobacco vendors were visited in 2011 and 1583 in 2013. Since it is impossible to observe vendors for long periods of time, they were evaluated based on the presence of signage prohibiting sale to minors. In relation to Section 6b, 314 vendors were visited in 2011 and 322 in 2013. Schools were surveyed for the presence of Section 6b signage. Researchers also surveyed area within 100 yards of educational institutions for any vendor selling tobacco products.

**Results:** In 2011, 42% of the tobacco vendors visited had Section 6a signage put up. In 2013 this figure was up to 73.53% across the state. 28.6% and 69.9% of the schools visited in 2011 and 2013 respectively had Section 6b signage put up. 46.8% of the schools visited in 2011 had vendors within 100 yards radius of the school selling tobacco products. In 2013, this figure was down to 16.46%.

**Conclusions:** Significant improvements have been seen regarding putting up of signage prohibiting sale of tobacco products to minors in vendors and in areas within 100 yards of an educational institutions. This indicates that the various interventions implemented towards fulfillment of Section 6a and 6b have been instrumental in reducing ready and widespread exposure of children to tobacco products in Mizoram. Further research is needed regarding the various other sources of exposure of children to tobacco products in the state.

### PD-752-30 Social economic determinant of youth smokers in Indonesia

N Kusumawardani,<sup>1</sup> E Rahajeng.<sup>1</sup> <sup>1</sup>Ministry of Health, National Institute of Health Research and Development, Jakarta, Indonesia. e-mail: nunikk@gmail.com

**Background:** Smoking among youth in Indonesia is one of the major public health issues in Indonesia. Adolescents who smoke regularly are exposed to the addictive effect of tobacco, which most likely will continue into adulthood. A school-based survey for grade 7 to 9, in different provinces in Indonesia in 2004 showed relatively high proportion of smoking in adolescents, particularly males. A survey in 2005 showed that the prevalence of smoking among adolescents aged 13 to 15 was 67.4% in Medan city and 67.1% in Surakarta city in Indonesia. It is important to understand issues on youth smokers as inputs for decision and policy making for smoking prevention among youth.

**Objective:** This study aims to describe social and economic determinant of youth smokers in Indonesia.

**Design/Methods:** this study uses data from a cross sectional population based survey (Indonesia national health survey) in 2013. Total number of sample is 262,027 people (127,775 females and 134,272 males) aged 10 to 24 years. Data were collected by questionnaire based interview. Data was analysed using statistical test for testing the difference and correlations of smoking and social determinant variables (economic, education, age group, sex and location).

**Results:** smoking prevalence is higher among male youth aged 19 – 24 years (59.2%) compare to the younger age groups 16 – 18 years (34.2%), 13 – 15 years (8.6%) and 10 – 12 years (0.7%). Female youth smokers shows relative low in Indonesia (0.5%). Youth male smokers are higher among those who completed high school and higher education (48.7% and 41.8%) and among those who has occupation (62.8%), living in rural areas (54.2%) and has lower economic quintile (29%). Smoker youth have higher proportion of having mental disorders.

**Conclusion:** Prevention of youth smokers need to focusing more on lower social economic group, rural setting, higher education and among those who earn money. Further research on smoking prevention strategy among youth need to be developed.

### PD-753-30 Gender-specific health warning on tobacco packaging: an emergent need in India

T Soni,<sup>1</sup> P Lal,<sup>1</sup> R J Singh.<sup>1</sup> <sup>1</sup> Tobacco, International Union Against Tuberculosis and Lung Disease, New Delhi, India. e-mail: tanusoni.86@gmail.com

**Background:** In India, 47% of males and 20% of females age above 15yrs use tobacco in some form. Among the 20.3 per cent of female tobacco users, 18.4 % use tobacco in smokeless form. As per National Family Health Survey (NFHS) 2005–2006, 8.5% of antenatal mothers and 10.8% of breastfeeding women use tobacco. Majority of them are unaware of the negative reproductive consequences of the effects of the tobacco

use like low birth weight babies and still births. Present health warning on tobacco packaging in India were implemented in 2009 and little is known about effect of same on motivation to quit as per the gender.

**Objective:** The study aims to see the significance of the gender differences in association to the motivation to quit tobacco usage by noticing present health warning labels on tobacco packaging.

**Methodology:** Nationally representative data from the India Global Adult Tobacco Survey (GATS) conducted in 2009–2010 was analyzed. SPSS- 19 was used to analyze data. Chi square test was used to analyze the significant gender differences in motivation to quit tobacco use by noticing health warning labels on tobacco packaging for both smoked and smokeless tobacco products.

**Result:** A significant ( $p=0.00$ , chi square value=2.91) difference was seen among male and female smoking tobacco users who noticed health warning on the cigarette packages 30 days prior to the survey. Among current daily tobacco smokers, 1% of female noticed health warning as compared to male (19.9 %). In not daily tobacco smokers only 0.4% noticed health warning as compared to males (5%). A significant difference ( $p=0.00$ ) was seen among both genders who were motivated to quit smoking after noticing the health warning. Among smokeless tobacco users ( $p=0.00$ , chi square value=3.87) a significant difference was seen among both genders where only one third (7%) of female noticed health warning and thought of quitting the same.

**Conclusion:** Despite slow implementation of the health warning on tobacco packaging in India, it is imperative to consider the differential impact of tobacco usage in respect to gender. Till now no research has been done to integrate gender analysis into tobacco control strategies like health warning on tobacco packaging. It is required that more in-depth research on both quantitative and qualitative dimension be done on the same aspect so as to explore the gender dimension of tobacco cessation initiatives in respect to tobacco control.

### PD-754-30 Dependence among daily smoking youth: cross sectional study from India's first smokefree city, Chandigarh

O Bera,<sup>1</sup> S Goel,<sup>2</sup> P Lal.<sup>1</sup> <sup>1</sup>The Union South East Asia Office, International Union Against Tuberculosis and Lung Disease, New Delhi, <sup>2</sup>Public Health, PGIMER, Chandigarh, India. e-mail: oprakash@theunion.org

**Background and challenges to implementation:** Nicotine dependence is the main determinant for regular tobacco use, especially smoking, and significantly important among youth. Global evidence suggests that earlier the initiation to tobacco use, stronger is the addiction, and lower is the probability to quit at a later age. The objective of the study was to describe prevalence and extent of nicotine dependence among daily smokers (15–25 yrs).

**Intervention or response:** An ethically reviewed, cross-sectional study was done using pre-tested Fagerstrom Test of Nicotine Dependence (FTND) based question-

naire study among school and college attending students of Chandigarh. Using stratified random sampling, 12 schools and 6 colleges were selected randomly and 1320 students (1032 from urban area, 162 from slums, and 132 students from rural area) were selected using proportionate population sampling. Data entry and analysis was done using SPSS (Version 16)

**Results and lessons learnt:** Out of 1320 students, 57.6% were males and 42.4% were females. Of the 216 (16.29%) daily smokers, 26.6% were male and 2.3% were female. 96.3% (N=208) of these daily smokers had mild dependence (urban-79.6%, rural-9.7% and slum-6.9%) and only 3.7% (N=8) had moderate dependence. 54.2% youth in the age group of 16–18 years have mild dependence followed by youth in the age group of 19–24 years (26.39%) and  $\leq 15$  years (15.74%). Males have higher dependence level both at mild and moderate level as compared to females. Association of dependence is significant ( $p < .05$ ) with increased duration of smoking, but not with age group, gender, alcohol use or locality.

**Conclusions and key recommendations:** It was observed that most of the school leaving youth (16–18 years) had mild dependence. This age group can potentially quit tobacco with little effort and therefore counseling and cessation services must be offered to them at earliest. Tobacco cessation strategies should be targeted to youth so as to reduce future adult tobacco use prevalence, and in effect avert future deaths. Its high time to customize the cessation strategies especially for youth by identifying the dependence level and designing quitting programs accordingly.

### PD-755-30 Modeling the health impact of cigarette smoking by pregnant women in Brazil

A Szklo,<sup>1</sup> D Levy,<sup>2</sup> L Almeida.<sup>1</sup> <sup>1</sup>Epidemiology, Brazilian National Cancer Institute, Rio de Janeiro, RJ, Brazil; <sup>2</sup>Cancer Control, Georgetown University, Washington, DC, USA. e-mail: andreszk@hotmail.com

**Background:** The United Nation's Millennium Development Goals included a goal of improving maternal and child health outcomes as an important step for economic development and reducing poverty in Low-Middle income countries. This study aimed at evaluating the effect of strong tobacco control policies on low-birth weight babies in Brazil

**Design/Methods:** We use a previously developed Brazil SimSmoke simulation model. Data on population and births, the prevalence of maternal smoking and selected adverse MCH outcome (Low-Birth weight), relative risk, are from existing Brazilian studies, or surveys conducted in Brazil. Standard attribution measures are used to calculate the number of adverse MCH outcomes.

**Results:** Current policies (cigarette taxation, smoke-free air laws, marketing bans, health warnings, media and educational campaigns, cessation treatment, and youth access restrictions) are estimated to reduce a cumulative total of 704,976 low-birth weight babies by 2050, as compared to no policies. With more comprehensive tobacco control policies, the number of smoking-

attributable low-birth weight babies may fall to 383,907 by 2050, far less than predicted 562,852 with current policies in place from 2011 forward.

**Conclusion:** Brazil is an example of a low- and middle-income country where tobacco control has reduced pregnant women's smoking prevalence, and as a result, adverse maternal and child health outcomes. The benefits for maternal and child health outcomes are often overlooked in discussions of tobacco control.

### PD-757-30 Prevalence and associated factors of tobacco consumption among secondary and higher secondary school students in Morocco

B Zarrouq,<sup>1,2</sup> K Bendaou,<sup>1,2</sup> Adil Najdi,<sup>1</sup> I Rammouz,<sup>3</sup> K Elrhazi,<sup>1</sup> C Nejari.<sup>1</sup> <sup>1</sup>Laboratory of Epidemiology, Clinical Research, and Community Health, Faculty of Medicine and Pharmacy of Fez, University Sidi Mohammed Ben Abdallah, Fez, <sup>2</sup>Laboratory of Physiology-Pharmacology and Environmental Health, Faculty of Sciences Dhar El Mahraz, University Sidi Mohammed Ben Abdallah, Fez, <sup>3</sup>Service of Psychiatry, Ibn Al Hassan Hospital, CHU Hassan II, Faculty of Medicine and Pharmacy of Fez, University Sidi Mohammed Ben Abdallah, Fez, Morocco. e-mail: b.ensfes@gmail.com

**Background:** To estimate the prevalence of tobacco use and its correlates among secondary and higher secondary students of North Central Region of Morocco.

**Design/Methods:** A cross-sectional study was conducted from April 2012 to November 2013 in public secondary and higher secondary school of two regions in the North-Center of Morocco. An anonymous self-administered questionnaire was used to assess tobacco use among a representative sample of students from grades 7 to 12, aged 11–23 years, selected by stratified cluster random sampling. Factors associated with smoking were identified by using binary logistic regression analysis.

**Results:** Among the 3020 students included in the study, the mean age was 16.09 years (SD = 2.16) with 53% male students. The overall prevalence of current smoking was 9.12% (95% CI: 8.12% - 10.21%). The mean age of initiating smoking for males was 13.76 years (SD=2.56), and 14.58 years (SD = 2.42) for females; ( $p < 0.05$ ). The average daily use was 6.48 cigarettes (SD = 6.15) and 70.59% (95% CI: 64.11% - 76.51%) of the current smokers reported the use of water pipe also. In the univariate analysis, smoking prevalence increased with age (4.2% in [11–14 years], 17.90% in [15–18 years], 32.20% in [19–23 years],  $p < 0.001$ ). It was statistically associated with gender (boys 15.10%, girls 2.50%,  $p < 0.00$ ), high educational level of father (17.80% vs 13.60% when father is illiterate,  $p < 0.05$ ), high educational level of mother (23.5% vs 15.90% when mother is illiterate,  $p < 0.02$ ), and feeling insecure in family (22.80% vs 15% among students with security sensation,  $p < 0.00$ ). After adjustments on different cofactors, tobacco use was statistically associated with male gender (OR 7.29; 95% CI: 5.49 – 9.70), age (OR 1.36; 95% CI: 1.30 – 1.44), high educational level of father (OR 1.66; 95% CI: 1.15 – 2.40), and feeling insecure in family (OR 2.12; 95% CI: 1.55 – 2.91).



**Conclusion:** Antismoking education must be further promoted to Moroccan school students, by implementation of an educational program against smoking and parents should be involved in school anti-smoking efforts to achieve the objectives.

## ORAL ABSTRACT PRESENTATION SESSIONS

### 01. PAEDIATRIC AND ADOLESCENT TB: EPIDEMIOLOGY, OUTCOMES AND MDR

#### OAP-200-30 TB incidence and risk factors in HIV co-infected children in Africa: an analysis of the ARROW trial

A Crook,<sup>1</sup> V Musiime,<sup>2</sup> M Bwakura-Dangarembizi,<sup>3</sup> A Kekitiinwa,<sup>4</sup> P Nahirya-Ntege,<sup>5</sup> A Turkova,<sup>1</sup> A Prendergast,<sup>6</sup> D Gibb.<sup>1</sup> <sup>1</sup>MRC Clinical Trials Unit, UCL, London, UK, <sup>2</sup>Joint Clinical Research Centre, Joint Clinical Research Centre, Kampala, Uganda; <sup>3</sup>Paediatrics and Child Health, University of Zimbabwe Medical School, Harare, Zimbabwe; <sup>4</sup>Baylor College of Medicine, Baylor College of Medicine Children's Foundation, Kampala, <sup>5</sup>Research Unit, MRC/UVRI, Entebbe, Uganda; <sup>6</sup>Maternal Child Health, Zvitambo Institute, Harare, Zimbabwe.  
e-mail: acr@ctu.mrc.ac.uk

**Background:** The incidence of TB in HIV co-infected children on antiretroviral therapy(ART) over time remains uncertain. The ARROW trial was a large paediatric HIV trial with long-term follow-up and provides the opportunity to (i) estimate the incidence of TB in children over time following initiation of ART and (ii) to investigate the potential role of stopping cotrimoxazole(CTX) prophylaxis on the risk of developing TB in this population as this was one of the randomisations in the trial.

**Methods:** 969 ART naïve children with no previous history of TB, enrolled between March 2007 and November 2008, from 4 centres from Uganda and Zimbabwe were included in the analysis. Children were randomised to initial 3-drug ART or to 4-drug ART induction, reducing to 3 drugs after 36 weeks. After 96 weeks children over 3 years were randomised to stop or continue CTX prophylaxis. Crude incidence rates of TB before and after CTX randomisation were estimated. Multivariable Cox PH models were fitted to estimate the adjusted effect of this randomisation on the risk of TB and explore other potential risk factors:age, sex, centre, CD4, weight, time on ART and initial ART strategy. Endpoints including TB were adjudicated blind to randomisation by an independent Endpoint review committee.

**Results:** By end of follow-up (median 4 years), 87 children had a TB diagnosis recorded (3632 person-years). The overall incidence of TB was 2.4/100 py,(95% CI 1.9-3.0) and was highest in the first 3 months following ART initiation:11.5/100 py,(95% CI 7.8-16.7)

compared to after 3 months, 1.8/100 py, (95% CI 1.4-2.3). Before the CTX randomisation, TB incidence in the whole cohort was 2.5/100 py, (95% CI 1.8-3.5); after randomisation, TB incidence remained similar in those stopping CTX (2.5/100 py,(95% CI 1.5-4.1) ), but declined in those randomised to continue CTX (0.9/100 py,(95% CI 0.4-2.1) ). This effect of prolonged use of CTX (compared to stopping) remained after multi-variable adjustment: hazard ratio (HR) for risk of TB =2.7(95% CI 1.0-7.4), p=0.04. A higher risk of TB was also independently associated with a lower weight for age Z-score and CD4 percent within the first 3 months of initiating ART.

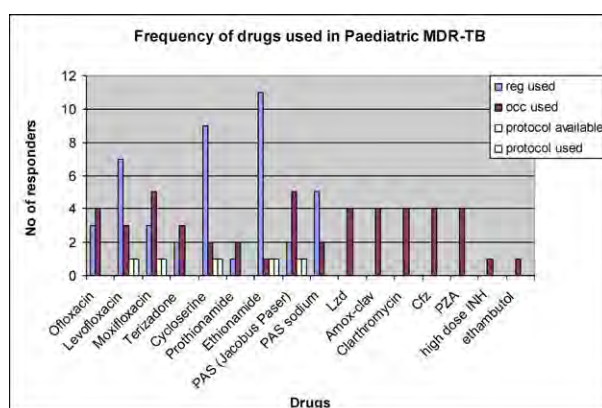
**Conclusion:** These findings suggest TB incidence varies over time following ART initiation and that children continuing cotrimoxazole prophylaxis beyond 96 weeks are diagnosed with TB less frequently. This emphasises the importance of screening for TB prior to ART initiation.

#### OAP-201-30 Issues administering oral second-line medications to children with multi-drug resistant TB (MDR-TB)

G Brigden,<sup>1,2</sup> J Furin,<sup>2</sup> E Lessem,<sup>2,3</sup> C Zen Ruffinen,<sup>1</sup> L McKenna.<sup>2,3</sup> <sup>1</sup>Access Campaign, medecins sans Frontieres, Geneva, Switzerland; <sup>2</sup>TB, The Sentinel Project on Pediatric Drug-Resistant Tuberculosis, Boston, MA, <sup>3</sup>TB/HIV, Treatment Action Group, New York, NY, USA.  
e-mail: Grania.BRIGDEN@geneva.msf.org

In 2010 an estimated 31,000 children developed MDR-TB. True numbers remain unknown due in part to the lack of appropriate diagnostics and the perception that children do not transmit TB. Children with MDR-TB who are actually diagnosed and put on treatment face the same two year regimen of toxic drugs as adults. While children often experience better treatment outcomes, there are few paediatric formulations available and most second-line drugs (SLD) lack evidence of safety and effectiveness in children. Caregivers are left with the difficult and burdensome task of manipulating adult medications and an increase risk of inappropriately dosing children. The Sentinel project surveyed its global network of members to characterize common practices in treating paediatric MDR-TB and challenges in administering appropriate doses of SLD. A questionnaire was sent via Survey Monkey to all Sentinel group members in July 2012 with a response period of 2 months. Sentinel group members received 2 reminder emails. The questionnaire consisted of 9 questions, the majority were free text responses with one tick box question. A total of 21 Sentinel group members started the questionnaire, although due to different levels of clinical involvement, not all questions on all surveys were answered. 477 children were reported to be on treatment, with the largest patient numbers reported by respondents in India (58 patients) and South Africa (75 patients). USAID reported 280 patients on treatment. Figure 1 shows the response of 14 participants on which drugs they use to treat MDR-TB in children, how frequently they use them and if there is a protocol on

how to prepare them. 50% of respondents reported problems administering appropriate doses of cycloserine, with 35% and 29% reporting issues administering PAS and ethionamide, respectively. Challenges in appropriately dosing second line injectables were noted in the free text section of the questionnaire. The survey shows that for some of the most commonly used SLD there is no standardised protocol for preparation, increasing the chances of drug errors and administration of incorrect dosages in children. The range of drugs used was broad and included a number of group 5 drugs. Despite the recent development of paediatric dosing spoons for PAS, providers still struggle to prepare this medication. While there is an urgent need for child-friendly formulations of SLD, there may be cause to prioritise development of those used most frequently.



### OAP-202-30 Treatment outcomes of childhood tuberculous meningitis: a systematic review and meta-analysis

S Chiang,<sup>1</sup> F Ahmad Khan,<sup>2</sup> M Milstein,<sup>2</sup> A Tolman,<sup>2</sup> A Benedetti,<sup>3,4,5</sup> J Starke,<sup>1</sup> M Becerra.<sup>2</sup> <sup>1</sup>Pediatrics, Section of Infectious Diseases, Baylor College of Medicine, Houston, TX, <sup>2</sup>Global Health and Social Medicine, Harvard Medical School, Boston, MA, USA; <sup>3</sup>Epidemiology, Biostatistics & Occupational Health, McGill University, Montreal, QC, <sup>4</sup>Medicine, McGill University, Montreal, QC, <sup>5</sup>Respiratory Epidemiology and Clinical Research Unit, Montreal Chest Institute, Montreal, QC, Canada.  
e-mail: schiang@alummi.stanford.edu

**Background:** Tuberculous meningitis (TBM), which disproportionately strikes young children, is the deadliest form of tuberculosis. Though numerous studies have described childhood TBM, questions remain about the frequency of symptoms and diagnostic findings at presentation, optimal management, and treatment outcomes.

**Methods:** To address these uncertainties, we performed a systematic review and meta-analysis of childhood TBM studies published through October 12, 2012. Included studies applied rigorous diagnostic criteria and described treatment regimens and outcomes. For our primary objective, we used random effects models to estimate pooled risks of death during treatment and neurological

sequelae among survivors. As secondary objectives, we evaluated study-level and treatment characteristics as sources of heterogeneity and pooled frequencies of symptoms and diagnostic findings at presentation.

**Results:** From 1870 citations, we identified 19 eligible observational studies, which included 1636 children treated for TBM in 10 countries between 1952–2005. Diagnostic criteria, patient characteristics, and treatment approaches varied widely. Among treated patients, 19% (95% confidence interval: 14–26%) died, and 37% (28–46%) survived without neurological sequelae. Among survivors, risk of neurological sequelae was 54% (43–65%). Diagnosis in stage III, the most advanced stage, was common (46% of patients) and associated with worse outcomes. Risk of death was 34% (22–49%) in stage III versus 10% (5–21%) in stage II and 1% (0–13%) in stage I. Risk of sequelae was 71% (51–84%) in stage III versus 41% (28–55%) in stage II and 27% (9–59%) in stage I. Between-study heterogeneity was significant for all outcomes and partially explained by numerous study-level characteristics. The most common findings at presentation were fever (90% [80–95%]), hydrocephalus (86% [69–95%]), and cerebrospinal fluid (CSF) leukocytosis (97% [92–99%]), but between-study heterogeneity was significant for these findings. CSF was smear-positive in 9% (5–15%) and culture-positive in 35% (17–59%) of patients.

**Conclusions:** Childhood TBM has poor outcomes despite treatment. The unfavorable prognosis and frequent late diagnosis highlight the importance of contact investigation and preventive therapy. Implementation of consensus clinical definitions, standardized reporting of outcomes, and high-quality clinical trials are urgently needed to facilitate early diagnosis and optimize therapy.

### OAP-203-30 High HIV-TB co-infection among young children in rural Mozambique

A Lima-chedas,<sup>1</sup> E López-Varela,<sup>1,2</sup> A García-basteiro,<sup>1,2</sup> O Augusto,<sup>1</sup> M Rupérez,<sup>1,2</sup> L Madrid,<sup>1,2</sup> J Sacarlal,<sup>1,3</sup> P Alonso.<sup>1,2</sup> <sup>1</sup>Tuberculosis, Manhica Health Research Centre (CISM), Manhica, Mozambique; <sup>2</sup>Barcelona Centre for International Health Research (CRESIB) Hospital Clinic-Universitat de Barcelona, ISGLOBAL, Barcelona, Spain; <sup>3</sup>Medical School, Eduardo Mondlane University, Maputo, Mozambique. e-mail: elisa.lopez@cresib.cat

**Background:** HIV infected children are at highest risk of developing TB disease following infection. The increased diagnostic challenge in this population frequently result in higher morbidity and mortality attributable to under- or delayed diagnosis. We aimed to describe the prevalence of HIV among presumptive childhood TB cases <3yr and to analyze the clinical characteristics and outcomes of TB-HIV coinfection.

**Methods:** This study was nested in a prospective one-year study to determine the minimum community incidence rate of TB among children <3years in a rural district. We enrolled presumptive TB cases identified through passive and active case detection who were investigated through HIV testing, Chest X Ray (CXR), tuberculin skin testing (TST) as well as gastric aspirate

and induced sputum sampling. Samples were processed for AFB smear, culture, and mycobacterial molecular identification. Participants were followed up for an additional 7 months for disease classification purposes. TB and/or HIV cases were managed according to national guidelines. HIV and outcome data was retrieved retrospectively 12 months after study completion.

**Results:** Out of the 789 enrolled presumptive cases, 45 were classified as TB, with an HIV prevalence of 13% (N=104) and 44% (N=20) among presumptive and TB cases respectively, being the strongest predictor of TB in multivariate analysis (OR 5.4,  $p < 0.001$ ). Almost 40% of all HIV infected children did not received any PMTCT services and only 35.4% were diagnosed before 12 months of age. HAART treatment was initiated in 78%, the overall coverage for cotrimoxazole and isoniazide preventive treatment was 87% and 22% respectively. Among co-infected cases, median age of HIV and TB diagnosis was 13 and 19 months respectively, 14 had evidence of BCG scar, 4 reported a TB contact, 8 had a positive TST, 16 % had an abnormal CXR and 9 were undernourished at enrolment. No statistically significant predictors for TB disease among HIV were detected. Seventeen % of HIV infected children died, with a significantly higher mortality rate as compared to HIV uninfected (174 vs 36/1000py, RR 18,  $p < 0.001$ ).

**Conclusions:** This prospective study demonstrated a high TB-HIV incidence among children <3years. The risk of death was significantly higher for HIV infected presumptive TB cases. This data highlights the importance of preventive measures in HIV positive children as well as the need for intensified efforts in TB diagnosis in high burden HIV settings.

### OAP-204-30 Characteristics of TB-HIV co-infected Nigerian children enrolled in an HIV-TB treatment programme

N Sam-Agudu,<sup>1,2</sup> N Otubu,<sup>1</sup> O Olupitan,<sup>1</sup> S Dutt,<sup>1</sup> V Ibeziako,<sup>1</sup> O Ogbanufe,<sup>1</sup> E Ekong,<sup>1,2</sup> P Dakum.<sup>1,2</sup> <sup>1</sup>Clinical Programs, Institute of Human Virology-Nigeria, Abuja, Nigeria; <sup>2</sup>Epidemiology, Institute of Human Virology, University of Maryland-Baltimore, Baltimore, MD, USA. e-mail: nsamagudu@ihvnigeria.org

**Background:** Globally, Nigeria bears the highest pediatric HIV burden and is also a TB/DR-TB high-burden country. In 2012, an estimated 1.4% of HIV-positive Nigerians developed incident TB. There is a paucity of clinical and epidemiological data on TB/HIV co-infected children in Nigeria. We describe baseline characteristics of HIV-positive children diagnosed with incident TB in a large HIV/TB treatment program.

**Design/Methods:** This retrospective chart review examined data from all HIV-positive children < 15 years old diagnosed with TB infection during the 12-month review period (October 2012 to September 2013). All patients were on first-line TB regimens (Isoniazid, Rifampin, Pyrazinamide and Ethambutol). Data including demographics and TB/HIV treatment duration were compiled and analyzed. Descriptive statistics were applied, and

two-tailed t test compared proportions between independent samples.

**Results:** Data was collected from 23 healthcare facilities in 18 of Nigeria's 37 states. Out of 4,640 HIV-positive children in HIV care, 297 (6.4%) were diagnosed with active TB, and this was significantly higher than expectation based on national estimates (6.4% vs 1.4%,  $p < 0.0002$ ). The proportion of females in the TB/HIV vs HIV-positive pediatric group was significantly higher (55.6% vs 47.5%,  $p = 0.0071$ ). Further results are displayed in Table 1.

**Conclusion:** Incident TB infection rate in this HIV-positive pediatric cohort was higher than the national estimate, and TB diagnosis was greater in girls than boys. The majority of TB/HIV+ children were on ART, and for at least 1 year, at the time of TB diagnosis. Most children had fair CD4 counts and were still on 1st line ART at initiation of, and during TB treatment, suggesting environmental TB exposure rather than ART failure as the single major risk factor for TB infection in this cohort. TB contact investigation, especially in HIV-affected households, should emphasize identification of exposed, at-risk HIV-positive children for preventive measures. Baseline viral load at TB diagnosis would be useful for more accurate determination of ART failure for co-infected children.

Table 1. Characteristics of TB/HIV Co-Infected Children

Characteristic	N evaluated	Median (IQR) or N (%)
Gender	297	Female 165 (55.6%)
<b>HIV treatment</b>		
Age at ART initiation (Years)	245	5.3 (2.4–8.5)
On ART at TB diagnosis	297	262 (88.2%)
ART Regimen (at least 3 drugs)	256	NNRTI-based 234 (91.4%) PI-based 13 (5.1%) NRTI-only 4 (1.6%) Others (2 <sup>nd</sup> line) 5 (1.9%)
Duration of ART at TB treatment initiation (Months)	246	14.3 (4.9–36.4)
Duration of ART at end of review period (Months)	246	21.5 (10.9–39.2)
CD4 count at TB diagnosis (cells/mm <sup>3</sup> )	229	435 (176–783)
<b>TB treatment</b>		
Age at TB treatment initiation (Years)	297	7.1 (4.3–10.5)
Duration on TB treatment at end of review period (Months)	297	5.1 (2.9–8.4)



### OAP-205-30 Magnitude of tuberculosis among mal-nourished children in Afghanistan

A Momand,<sup>1</sup> M Rashidi,<sup>1</sup> Ghul Qader,<sup>1</sup> V Veeda,<sup>2</sup> A Malikzai,<sup>2</sup> M Shah,<sup>3</sup> P Suarez,<sup>1</sup> A Ahmadi.<sup>3</sup> <sup>1</sup>TB CARE I, Managment science for Health (MSH), Kabul, <sup>2</sup>Health, Afghan Health and Development Services (AHDS), Kandahar, <sup>3</sup>Health, Health Net Transcultural Psychosocial Organization (HNTPO), Gardiz, Paktia, Afghanistan.  
e-mail: amomand@msh.org

**Background:** To improve TB control in Afghanistan, the Ministry of Public Health integrated TB services into the general health system and subcontracted primary health care service delivery to non-governmental organization (NGOs) in 31 of Afghanistan's 34 provinces. Unfortunately, the NGOs have found TB control among children to be challenging due to poor pediatric diagnostic capacity, particularly among malnourished children. Malnourished children are vulnerable to infectious diseases, including TB, because a lack of nutrition weakens their immune system.

**Intervention:** To address this challenge, the National TB Program (NTP) and the USAID-funded TB CARE I helped the NGOs conduct an assessment to determine the prevalence of TB among malnourished children under the age of five at 73 health facilities in the Kandahar, Paktyia, and Khost provinces. The NTP and TB CARE I designed this study to help NGOs increase TB screening, testing, and treatment among malnourished children.

**Results:** In 2013, the 73 facilities diagnosed 19,202 children with severe, acute malnutrition (SAM). Among these children, the facilities identified 1,009 (5.3%) children as TB suspects and found that 63 of the suspects (6.2%) had active pulmonary TB. The facilities also diagnosed 22,984 children with moderate, acute malnutrition (MAM), and among these, identified TB symptoms in 423 children (1.8%) and diagnosed 12 of these suspects (2.8%) with active pulmonary TB. In summary, health facilities diagnosed 42,186 children under five with either SAM or MAM, screened 1,432 of these children for TB, and diagnosed 75 (5.2%) children with active pulmonary TB. This study revealed that there was a TB prevalence rate of 5.2% among SAM and MAM children at the 73 facilities. The TB annual incidence rate among the general population of Afghanistan is significantly lower, at just 0.358% (358/100,000 population).

**Conclusions:** This study discovered that the prevalence of pulmonary TB among malnourished children under the age of five at 73 health facilities was significantly higher than the prevalence of pulmonary TB among the general population. The study also found that the prevalence of TB among SAM was six times higher than TB prevalence among MAM children at the 73 facilities. The NTP should strengthen TB screening among severely and moderately malnourished children under the age of five using advanced technology, such as GeneXpert.

Children under five years old with severe, acute malnutrition (SAM) or moderate, acute malnutrition (MAM), who were screened, diagnosed, and treated for TB at 73 health facilities in three provinces of Afghanistan

Provinces	Type of mal-nutrition	Number mal-nourished children under 5	Number of mal-nourished children under 5 screened for TB	Number mal-nourished children under 5 diagnosed with TB	TB positivity rate among mal-nourished children under 5
Kandahar	Severe, acute mal-nutrition (SAM)	8,460	210	11	5.2%
	Moderate, acute mal-nutrition (MAM)	7,768	67	2	2.9%
	Total	16,228	277	13	4.6%
Khost	SAM	6,281	490	29	5.9%
	MAM	8,971	167	4	2.4%
	Total	15,252	657	33	5%
Paktia	SAM	4,461	309	23	7.4%
	MAM	6,245	189	6	3.2%
	Total	10,706	498	29	5.8%
Total	SAM	19,202	1,009	63	6.2%
	MAM	22,984	423	12	2.8%
	Total	42,186	1,432	75	5.2%

### OAP-206-30 Evaluation of healthcare providers knowledge of childhood tuberculosis

S Chiang,<sup>1</sup> A Cruz,<sup>1,2</sup> H Del Castillo Barrientos,<sup>3</sup> C C Contreras,<sup>4</sup> M Becerra,<sup>4,5</sup> L Lecca.<sup>4</sup> <sup>1</sup>Pediatrics, Section of Infectious Diseases, Baylor College of Medicine, Houston, TX, <sup>2</sup>Pediatrics, Section of Emergency Medicine, Baylor College of Medicine, Houston, TX, USA; <sup>3</sup>Pulmonary Medicine, Instituto Nacional de Salud del Niño, Lima, <sup>4</sup>Socios En Salud/Partners In Health, Lima, Peru; <sup>5</sup>Global Health and Social Medicine, Harvard Medical School, Boston, MA, USA.  
e-mail: schiang@alumni.stanford.edu

**Background:** Most national tuberculosis programs (NTPs) focus on adult tuberculosis (TB). Consequently, healthcare providers may not appreciate differences in the natural history and clinical presentation of childhood TB.

**Methods:** We invited Peruvian NTP physicians, nurses, and nursing technicians to complete surveys designed to evaluate their knowledge of childhood TB. These providers all worked in areas of Lima with TB incidences of 175–225 per 100,000 per year (data from Peru's Ministry of Health, 2010). Surveys consisted of multiple-choice and true-false questions grouped into five sections: transmission, symptoms, diagnosis, prevention, and treatment. The surveys also asked about previous TB training and experience. For content questions, each provider group received overall and separate section scores. Demographic data were expressed as percentages, and pair-wise comparisons between groups were evaluated using the chi-square test.

**Results:** A total of 310 providers—103 physicians, 106 nurses, and 101 nursing technicians—participated in the study. Amount of time working in TB control was

associated with improved overall score for nurses but not for physicians or technicians. Recent pediatric TB training and personal/family TB history were not associated with test performance in any group; however, few providers had these characteristics. Scores revealed knowledge gaps in three areas: extrapulmonary TB, diagnosis, and prevention. Only 57% of physicians and fewer than 50% of nurses and technicians recognized that young children have a higher risk of extrapulmonary TB than adults. Only 23% of physicians knew the sensitivity of gastric aspirate culture, and only 42% correctly identified all radiograph findings consistent with pulmonary TB. Fewer than half of providers who interpreted tuberculin skin tests (TSTs) recognized causes of false negative TSTs. No more than two-thirds of each provider type correctly defined latent TB infection (LTBI), recognized young children's high risk of progression from LTBI to disease, or knew to administer isoniazid preventive therapy to any household contact under age five without TB disease.

**Conclusions:** Providers at the front line of Peru's TB control efforts demonstrated childhood TB knowledge gaps, which likely result in delayed or missed diagnoses, particularly of extrapulmonary disease, and lost opportunities for prevention. Educational interventions targeting NTP personnel could improve childhood TB care and outcomes.

Survey Section Scores (as Percentage of Correct Responses) by Provider Type

Section	Physician (n=103)	Nurse (n=106)	Nursing technician (n=101)
Transmission	98%	97%	99%
Symptoms	66%	52%	51%
Diagnosis	63%	45%	26%
Prevention	54%	54%	50%
Treatment	85%	84%	83%
Overall	66%	60%	58%

### OAP-207-30 The missing cohort: adolescents in tuberculosis research

L McKenna,<sup>1</sup> B J Seaworth,<sup>2</sup> M Theunissen,<sup>3</sup> M Frick,<sup>1</sup> S Nachman,<sup>4</sup> J Furin.<sup>5</sup> <sup>1</sup>TB/HIV Project, Treatment Action Group (TAG), New York, NY, <sup>2</sup>Tuberculosis, Heartland National TB Center, San Antonio, TX, USA; <sup>3</sup>Famcru Research Unit, Tygerberg Hospital, University of Stellenbosch, Stellenbosch, South Africa; <sup>4</sup>Pediatrics, HSC SUNY Stony Brook, Stony Brook, NY, <sup>5</sup>Division of Infectious Diseases and HIV Medicine, Case Western Reserve University, Cleveland, OH, USA.  
e-mail: lindsay.mckenna@treatmentactiongroup.org

**Background** Despite increased visibility, children remain an afterthought and adolescents the missing cohort in tuberculosis (TB) research. Clinical trials of TB drugs typically exclude participants younger than 18 years, even when safety has been demonstrated. Limited data have shown outcomes in adolescents may be worse than in adults with HIV, and given most adolescent doses are extrapolated from those of adults, data on this group is urgently needed. The rationale behind excluding adoles-

cents warrants closer scrutiny and reexamination given their physiological maturity and ability to tolerate adult formulations.

**Methods** We conducted 3 searches on clinicaltrials.gov to determine the number of phase 3 TB trials that included adolescents. The first search looked at open trials, the second at completed trials, and the third at active, non-recruiting trials. Our analysis only includes trials that evaluated existing or novel drugs for TB treatment or prevention. In the first (criteria: tuberculosis; open studies; interventional studies; adult; phase 3), second (criteria: tuberculosis; completed; interventional studies; adult; phase 3; received from 01/01/2001 to 04/16/2014), and third search (criteria: tuberculosis; active, not recruiting; interventional studies; adult; phase 3), 6 of 29, 6 of 34, and 7 of 14 studies, respectively, were included in the analysis.

**Results** Of the 6 open trials, just 1 included persons younger than 18. Of the 6 completed trials, 0 included participants younger than 18. And of the 7 active, non-recruiting trials, 3 allowed for inclusion of participants younger than 18. Among the 4 trials that included adolescents, 3 looked at TB preventive therapy and 1 looked at treatment of drug-susceptible TB.

**Conclusions** Adolescents are excluded from a majority of late stage TB trials. To address the neglect of this vulnerable population, communities and researchers must advocate for their inclusion where safety has been demonstrated. A number of strategies can be used such as: community consultations; community advisory board (CAB) protocol reviews; establishment of adolescent CABs, as has been done in HIV; and both consortium and local level advocacy with Institutional Review Boards. Researchers and advocates must also be prepared to address barriers to enrollment such as balancing the need for parental informed consent with honoring the privacy and autonomy of the adolescent and potential issues with the recruitment and retention of young people.

Study Title	Adolescent Inclusion	ClinicalTrials.gov Identifier
Tuberculosis; open studies; interventional studies; adult; phase 3		
Latency in Pulmonary TB	N	NCT01154959
Evaluating the Safety and Effectiveness of Short-Course Rifapentine/Isoniazid for the Prevention of Active TB in HIV-Infected Individuals With LTBI	Y (13+ years)	NCT01404312
Efficacy and Safety of Levofloxacin vs INH in LTBI in Liver Transplant Patients	N	NCT01761201
A Controlled Trial of a 4-Month Quinolone-Containing Regimen for the Treatment of Pulmonary TB	N	NCT00216385
Randomized Clinical Trial Comparing 4RIF vs. 9INH for LTBI Treatment-effectiveness	N	NCT00931736

Comparing Daily vs Intermittent Regimen of ATT in HIV With Pulmonary TB	N	NCT00933790
<b>Tuberculosis; completed; interventional studies; adult; phase 3; Received from 01/01/2001 to 04/16/2014</b>		
TB Treatment Shortening Trial	N	NCT00130247
High-Dose INH Adjuvant Therapy for Multidrug Resistant TB	N	NCT00513396
Efficacy of Thrice Weekly Directly Observed Treatment, Short-course (DOTS) in HIV-associated TB	N	NCT00698334
TBTC Study 22: Efficacy of Once-Weekly Rifapentine and INH in Treatment of TB	N	NCT00023335
TBTC Study 23A: Pharmacokinetics of Intermittent INH and Rifabutin in HIV-TB	N	NCT00023348
TB Prevention for HIV Infected Adults	N	NCT00057122
<b>Tuberculosis; active, not recruiting; interventional studies; adult; phase 3</b>		
Comparing Two Preventive Regimens for LTBI	N	NCT01398618
Preventive Therapy for TB in HIV Infected Persons	Y (15+ years)	NCT00351702
Short Course Intermittent Regimens for the Treatment of HIV-Associated TB	Y (15+ years)	NCT00376012
Safety and Efficacy Trial of Delamanid for 6 Months in Patients With Multidrug Resistant TB	N	NCT01424670
Controlled Comparison of Two Moxifloxacin Containing Treatment Shortening Regimens in Pulmonary TB (REMoxTB)	N	NCT00864383
Early Antiretroviral Treatment and/or Early INH Prophylaxis Against TB in HIV-infected Adults (ANRS 12136 TEMPRANO)	N	NCT00495651
Three Months of Weekly Rifapentine and INH for M. TB Infection (PREVENT TB)	Y (2+ years)	NCT00023452

## 02. SCREENING / TESTING / DIAGNOSTICS IN TB-HIV

### OAP-208-30 Point-of-care testing for tuberculous meningitis in HIV-co-infected adults

J Cox,<sup>1,2</sup> R. Lukande,<sup>3</sup> S. Kalungi,<sup>4</sup> R Colebunders,<sup>1,5</sup> Y Manabe.<sup>2,6</sup> <sup>1</sup>Clinical Sciences, Institute of Tropical Medicine, Antwerp, Belgium; <sup>2</sup>Research, Infectious Diseases Institute, Kampala, <sup>3</sup>Pathology, Makerere University, Kampala, <sup>4</sup>Pathology, Mulago Hospital Complex, Kampala, Uganda; <sup>5</sup>Epidemiology and Social Medicine, University of Antwerp, Antwerp, Belgium; <sup>6</sup>Infectious Diseases, Johns Hopkins University School of Medicine, Baltimore, MD, USA. e-mail: jannekecox@xs4all.nl

**Background:** HIV-TB co-infection increases the incidence of TB meningitis (TBM). TBM has a high mortality and requires prompt treatment. Current diagnostics are slow or not sufficiently sensitive. Point-of-care diagnostics for TBM are urgently needed. We compared the outcomes of lateral flow lipoarabinomannan (LFA-LAM), ELISA LAM and Xpert MTB/RIF testing in cerebrospinal fluid (CSF) to autopsy findings in deceased HIV-infected Ugandan adults.

**Design/Methods:** We included HIV-infected adults that died during hospitalization in a tertiary hospital. CSF was collected postmortem from the fourth ventricle and stored at -20°C. A complete autopsy was performed including routine sampling of the brain stem, left- and right cerebrum and cerebellum. TBM was diagnosed using an algorithm including clinical symptoms, macro- and microscopic findings and the diagnosis of TB elsewhere. The following categories were distinguished: definite, probable, possible, non-TBM and meningitis of unknown origin. For Xpert MTB/RIF, 1 mls thawed CSF was mixed with 2 mls reagent after which 2 mls were transferred to the cartridge. The LAM-LFA was performed twice, using thawed CSF and supernatant that was obtained after boiling and spinning the CSF. The ELISA-LAM was performed according to the manufacturer's guidelines.

**Results:** We collected adequate CSF samples for 91 patients. Their median CD4 cell count was 47 cells/mm<sup>3</sup> (21-165), 30% were on anti-TB treatment for a median duration of 30 days (IQR8-60). We identified 8 (9%) definite, 6 (7%) probable, 8 (9%) possible and 62 (68%) non-TBM. Meningitis of unknown origin was identified in 7 (8%) cases, which were excluded from analysis. Xpert MTB/RIF had the highest sensitivity, 100% for definite TBM and 86% for definite and probable TBM and a specificity of 85% (Table 1). All false positive results for the Xpert MTB/RIF and the TB-ELISA assay were patients with disseminated TB without clinical, macro- or microscopic signs of meningitis who were classified non-TBM. Diagnostic accuracy of LAM testing was moderate. LFA sensitivity increased when using CSF supernatant after boiling, however this was only significant for definite TBM when using +2 cut-off (P=0.04). LFA specificity did not benefit from increasing the LFA cut-off point.



**Conclusion:** Of the studied test modalities, Xpert MTB/RIF had the highest diagnostic accuracy on CSF to diagnose HIV-TBM co-infected patients.

**Table 1** Test performance in TBM (define and definite + probable)

	Sensitivity % (95%CI) n/N	Specificity % (95%CI) n/N	PPV % (95%CI) n/N	NPV % (95%CI) n/N
<b>TBM (definite)</b>				
Xpert MTB/RIF	100 (63–100)	85 (74–93)	47 (23–72)	100 (93–100)
LAM-ELISA	8/8 (10–82)	53/62 (80–96)	8/17 (7–70)	53/53 (84–98)
LFA unprepared CU=1	43 (35–97)	90 (56–80)	33 (9–45)	93 (85–99)
LFA supernatant CU=1	3/7 (47–100)	56/62 (60–83)	3/9 (18–67)	56/60 (88–100)
LFA unprepared CU=2	75 (9–49)	69 (76–94)	24 (6–61)	96 (81–97)
LFA supernatant CU=2	6/8 (47–100)	43/62 (72–92)	6/25 (18–67)	43/45 (90–100)
	88 (7/8)	84 (52/62)	41 (7/17)	98 (52/53)
<b>TBM (definite + probable)</b>				
Xpert MTB/RIF	86 (57–98)	85 (74–93)	57 (34–78)	96 (87–100)
LAM-ELISA	12/14 (14–68)	53/62 (80–96)	12/21 (17–77)	53/55 (77–94)
LFA unprepared CU=1	38 (5/13)	90 (56–80)	45 (12–48)	86 (73–94)
LFA supernatant CU=1	50 (23–77)	69 (56–80)	27 (12–48)	86 (73–94)
LFA unprepared CU=2	7/14 (42–92)	43/62 (60–83)	7/26 (33–82)	43/50 (80–98)
LFA supernatant CU=2	71 (10/14)	73 (45/62)	59 (10/17)	92 (45/49)
	29 (8–58)	87 (76–94)	33 (10–65)	84 (73–92)
	4/14 (29–82)	54/62 (72–92)	4/12 (22–69)	54/64 (79–96)
	57 (8/14)	84 (52/62)	44 (8/18)	90 (52/58)

CI: confidence interval; n: number of positives; N: total number of observations; LFA: lateral flow assay; CU=1: cut-off point +1 used for lateral flow assay positivity; CU=2: cut-off point +2 used for lateral flow assay positivity;

### OAP-209-30 Rapid urine-based diagnosis of tuberculosis among HIV-infected hospital in-patients with moderate or severe anemia and poor prognosis

A D Kerkhoff,<sup>1,2</sup> G A Meintjes,<sup>3,4</sup> R Burton,<sup>5</sup> C Schutz,<sup>3,4</sup> M Nicol,<sup>6,7</sup> S D Lawn.<sup>2,3,8</sup> <sup>1</sup>School of Medicine and Health Sciences, The George Washington University, Washington, DC, USA; <sup>2</sup>The Desmond Tutu HIV Centre, Institute of Infectious Disease and Molecular Medicine, Faculty of Health Sciences, University of Cape Town, Cape Town, <sup>3</sup>Department of Medicine, Faculty of Health Sciences, University of Cape Town, Cape Town, <sup>4</sup>Clinical Infectious Diseases Research Initiative, Institute of Infectious Disease and Molecular Medicine, University of Cape Town, Cape Town, <sup>5</sup>Department of Medicine, Khayelitsha District Hospital, Cape Town, <sup>6</sup>National Health Laboratory Service, Groote Schuur Hospital, Cape Town, <sup>7</sup>Division of Medical Microbiology and Institute for Infectious Diseases and Molecular Medicine, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa; <sup>8</sup>Department of Clinical Research, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK.  
e-mail: andrewkerkhoff@gmail.com

**Background:** Anemia is common among HIV-infected hospital in-patients in developing countries and may predict underlying tuberculosis (TB). We therefore determined the relationship between the prevalence of undiagnosed TB and anemia among such patients, assessed associated morbidity and mortality and evaluated methods of rapid TB diagnosis.

**Methods:** Unselected HIV-infected patients admitted to a South African district hospital were screened for TB regardless of symptoms. Sputum, urine and blood samples were obtained from all patients within 24 hours and additional respiratory and non-respiratory samples were collected throughout admission as indicated. Samples were tested using a combination of fluorescence microscopy, liquid culture, Xpert MTB/RIF and Determine TB-LAM (urine-LAM). Confirmed TB was defined by the detection of *M. tuberculosis* in any sample using either culture or Xpert. Hemoglobin levels were measured and anemia was classified according to WHO criteria.

**Results:** Of 585 patients enrolled, 421 did not have a current TB diagnosis and had complete results available. Anemia was present in 81.0% (n=340) of patients and was mild, moderate or severe in 15.2%, 35.4% and 30.4%, respectively. TB was diagnosed in 139 patients (prevalence, 33.0%). TB prevalence was 10.9% in those without anemia and reached 51.6% in those with severe anemia (p<0.001). All 18 TB-related deaths within 3 months occurred in those who had moderate/severe anemia (16.2%; p=0.024) and such patients were also 4 times more likely than those with no/mild anemia to be readmitted to hospital within 3 months (38.7% vs.10.3%; p=0.006). While the performance of sputum-based assays did not vary by anemia classification, urine-based assays had improved diagnostic yield among patients with moderate/severe anemia compared to those with no/mild anemia: sputum microscopy (19.8% vs. 17.9%; p=0.810), sputum Xpert (26.1% vs. 28.6%;

$p=0.794$ ), urine LAM (45.0% vs. 10.7%;  $p<0.001$ ), urine Xpert (63.1% vs. 42.9%;  $p=0.052$ ) and urine LAM plus Xpert (73.0% vs. 53.6%;  $p=0.047$ ).

**Conclusions:** An extremely high prevalence of TB was found in patients with moderate/severe anemia and was associated with substantial morbidity and mortality. Among such patients, urine LAM and Xpert had improved performance and greater diagnostic yield than sputum-based assays. Hospitalized patients with moderate/severe HIV-related anemia in high incidence settings should be routinely screened for TB using rapid urine-based assays.

### OAP-210-30 Experience of use of Xpert MTB/RIF for detecting TB in people living with HIV for enhancing TB case detection in a programmatic setting of India

N Raizada,<sup>1</sup> KS Sachdeva,<sup>2</sup> A Sreenivas,<sup>3</sup> R Thakur,<sup>1</sup> S Kulsange,<sup>1</sup> C N Paramasivan.<sup>1</sup> <sup>1</sup>India, Foundation for Innovative New Diagnostics, New Delhi, <sup>2</sup>Central TB Division, Ministry of Health and Family Welfare, Government of India, New Delhi, <sup>3</sup>India, World Health Organisation, New Delhi, India. e-mail: drneerajraizada@gmail.com

**Background:** TB is the leading cause of death among people living with HIV, accounting for 25% of HIV-related deaths. The major challenge in diagnosing TB among people living with HIV is establishing a reliable diagnosis. WHO recommends the use of Xpert MTB/RIF as a primary diagnostic test for all people living with HIV who have signs and symptoms suggestive of TB. Through this report, we share our experiences in offering Xpert MTB/RIF to high-risk group as HIV positive TB suspects for diagnosis of TB and drug resistant TB, in programmatic settings at peripheral level in India.

**Method:** The study was conducted from March 2012 till December 2013 covering a population of 8.8 million across 18 different sub-district level tuberculosis units (TU), with one Xpert MTB/RIF lab established at each study TU. HIV positive presumptive TB cases accessing public health facilities in study area were prospectively enrolled in the study and tested on Xpert MTB/RIF, following a standardized diagnostic algorithm.

**Results:** A total of 2722 know HIV infected presumptive TB cases were screened under the study on both Xpert MTB/RIF and smear microscopy. A total of 866 (31.1%; 95% CI 29.4% – 32.8%) were diagnosed with pulmonary TB (PTB); 779 (27.9%; 95% CI 26.3%-29.7%) were bacteriologically confirmed of which 420 (54.5%, CI: 51.0–58.0) were Xpert MTB/RIF positive and smear negative. Further, upfront Xpert MTB/RIF testing of HIV positive presumptive TB and presumptive DR-TB cases, resulted in the detection of 73 and 16 rifampicin resistance cases, respectively; Positive predictive value (PPV) for rifampicin resistance detection was high 97.7% (CI 89.3%- 99.8%) and with no statistically significant variation with respect to past history of TB treatment.

**Conclusion:** The study highlights the underdiagnoses of TB by offering direct smear microscopy alone for TB diagnosis in HIV endemic settings. Further the study

underscores the urgent need for deployment of high sensitivity diagnostic tool like Xpert MTB/RIF. The limitations of the existing portfolio of TB diagnostics often lead to a low proportion of confirmed TB in HIV co-infection and are associated with delay in diagnosis and resultant delayed treatment initiation or worse sub-optimal therapy. Xpert MTB/RIF offers an effective solution to these diagnostic and treatment challenges.

### OAP-211-30 Point-of-care C-reactive protein-based TB screening to improve the efficiency and reduce the cost of intensified case-finding among PLHIV

C Yoon,<sup>1</sup> F Semitala,<sup>2</sup> J Katende,<sup>2</sup> P Byanyima,<sup>3</sup> A Andama,<sup>3</sup> L Huang,<sup>1</sup> M Kamya,<sup>2</sup> A Cattamanchi.<sup>1</sup>

<sup>1</sup>Department of Medicine, University of California, San Francisco, San Francisco, CA, USA; <sup>2</sup>Department of Medicine, Makerere University Joint AIDS Program, Kampala, <sup>3</sup>Department of Medicine, Makerere University-University of California, San Francisco Research Collaboration, Kampala, Uganda. e-mail: christina.yoon@ucsf.edu

**Background:** To reduce the burden of tuberculosis (TB) among PLHIV, the WHO recommends symptom-based screening at every clinic visit, followed by microbiologic TB testing for all those who screen-positive (i.e., intensified case finding [ICF]). However, the symptom screen has a high false-positive rate, such that ~80% of PLHIV would require additional microbiologic testing. We evaluated the case detection yield and efficiency of ICF when TB screening was based on point-of-care C-reactive protein (POC-CRP) levels instead of symptom assessment.

**Design/Methods:** We performed the WHO symptom screen, POC-CRP testing (iCHROMA POC-CRP Reader; normal  $\leq 10$  mg/L), and sputum-based TB testing (Xpert MTB/RIF x1 and liquid culture x2) on consecutive adults presenting to an HIV/AIDS clinic in Kampala, Uganda for antiretroviral therapy initiation. We compared the proportion of culture-positive TB cases detected (case detection yield) and the number of Xpert assays performed per case detected among patients who screened positive by either symptoms or  $\text{CRP} \geq 10$  mg/L.

**Results:** Of 271 patients (56% female, median age 34 years, median CD4 count 202 cells/ $\mu\text{L}$ ), 27 (10%) patients had culture-positive pulmonary TB. The symptom screen was positive in 227 (84%) patients, including 25/27 patients with TB (sensitivity 93%, 95% CI 76–99%) and 202/244 patients without TB (specificity 17%, 95% CI 13–23%). Xpert testing of the 227 symptomatic patients identified 11 culture-positive TB cases (yield 41%) and required 21 assays/case detected (Table 1). POC-CRP levels were elevated in 69 (25%) patients, including 22/27 patients with TB (sensitivity 82%, 95% CI 62–94%) and 47/244 patients without TB (specificity 81%, 95% CI 75–86%). Xpert testing of the 69 patients with elevated POC-CRP levels identified 10 culture-positive TB cases (yield 37%) and required 7 assays/case detected. Case detection yield was similar (difference –4%,  $p=0.78$ ) when TB screening was based on POC-CRP levels but required 3-fold fewer Xpert assays. Xpert

testing of all 271 patients (i.e., without screening) identified 11/27 culture-positive TB cases (yield 41%, 95% CI 22–61%) and required 24 assays per case detected.

**Conclusion:** TB screening with POC-CRP instead of the WHO symptom screen considerably improves the efficiency of ICF and results in similar case detection. Rapid tests with higher sensitivity than Xpert, or that improve incremental yield in combination with Xpert, are needed to further improve ICF-case detection.

**Table 1. Yield and efficiency of TB screening strategies for Xpert-based intensified case-finding (ICF) among 271 HIV-infected patients initiating antiretroviral therapy.**

	TB screening strategy		Difference (95% CI)	p-value
	WHO symptom screen	POC-CRP		
Positive TB screen, N (%, 95% CI)	227/271 (84%, 79–89%)	69/271 (25%, 20–31%)	-58% (-65 to -52%)	<0.0001
Positive Xpert, N (%, 95% CI)	11/227 (5%, 2–9%)	10/69 (15%, 7–25%)	+10% (+1 to +18%)	0.006
Yield for culture-positive TB,* N (%, 95% CI)	11 (41%, 22–61%)	10 (37%, 19–58%)	-4% (-15 to +7%)	0.32
Xpert assays per TB case detected	21	7	--	--

**Abbreviations:** WHO (World Health Organization); POC-CRP (point-of-care C-reactive protein); CI (confidence interval); TB (tuberculosis).

**Legend:** \*N=27 culture-positive TB cases.

### OAP-212-30 Higher-than-expected non-tuberculous mycobacteria disease prevalence in HIV setting in Botswana: implications for Xpert MTB/RIF diagnostic algorithms

T Agizew,<sup>1</sup> J Basotli,<sup>1</sup> H Alexander,<sup>2</sup> R Boyd,<sup>1,3</sup> A Auld,<sup>2</sup> A Date,<sup>2</sup> N Ndwapi,<sup>4</sup> A Finlay.<sup>1,3</sup> <sup>1</sup>TB/HIV Research, Centers for Disease Control and Prevention (CDC) Botswana, Gaborone, Botswana; <sup>2</sup>Division of Global HIV/AIDS, CDC, Atlanta, GA, USA; <sup>3</sup>Division of Tuberculosis Elimination, CDC, Atlanta, GA, USA; <sup>4</sup>Ministerial Strategy Office, Ministry of Health, Gaborone, Botswana. Fax: (+267) 3932904. e-mail: agizewt@bw.cdc.gov

**Background:** Non-tuberculous mycobacteria (NTM) can cause pulmonary infection and disease especially among people living with HIV (PLHIV). PLHIV with NTM infection can therefore screen positive using the World Health Organization (WHO) -recommended four-symptom *Mycobacterium tuberculosis* (MTB) screen. Xpert® MTB/RIF (Xpert) has high sensitivity and specificity for diagnosing pulmonary MTB but cannot detect or rule out NTM. We describe the prevalence of both MTB and NTM from sputum samples collected from patients enrolled in the Xpert Package Roll-out Evaluation Study. **Methods:** PLHIV attending HIV care and treatment services at 26 clinical sites in Botswana were recruited for systematic MTB symptom screening and diagnosis with Xpert. Patients who screened positive for one or more MTB symptoms (cough, fever, night sweats and weight loss) were asked to submit sputa for Xpert and culture testing. An analysis of available participant laboratory test results and clinical information was collected to describe the prevalence of NTM infection and MTB among patients.

**Results:** From 10/2012 to 02/2014, 1114 PLHIV presented with MTB symptoms and were able to submit at least one sputum specimen for Xpert and culture

testing. Among these, 242 had  $\geq 1$  positive culture result with *Mycobacterium* species identified, 107 (44%) MTB and 135 (56%) with NTM only. There were 115/242 patients with laboratory results who were started on anti-MTB treatment (ATT) by local clinicians: 102 had culture confirmed MTB and 13 had NTM only. Among patients receiving ATT, 105/115 had Xpert results available to the local clinician at the time of diagnosis. Among these, 11/105 (10%) had a negative Xpert result; culture later identified NTM only and patients did not have signs of extra pulmonary MTB, indicating that ATT may not have been required.

**Conclusions:** In this setting, the prevalence of NTM among PLHIV with symptoms and a positive sputum culture result was very high (56%). This study suggests sputum culture for MTB symptom-positive PLHIV with negative Xpert results remains important to facilitate possible NTM diagnosis. Further research is needed to evaluate trends in NTM and MTB disease incidence in PLHIV, and to establish best management strategies for symptomatic Xpert-negative clients while waiting for culture results.

### OAP-213-30 Peer educators improve HIV testing and enrollment in HIV care for TB patients in Lusaka, Zambia

J Morse,<sup>1</sup> S Besa,<sup>1</sup> J Harris,<sup>2</sup> M Mubanga,<sup>1</sup> G Samungole,<sup>3</sup> N Kanchea.<sup>1</sup> <sup>1</sup>Tuberculosis, Centre for Infectious Disease Research in Zambia, Lusaka, Zambia; <sup>2</sup>Epidemiology, University of Alabama at Birmingham, Birmingham, AL, USA; <sup>3</sup>Tuberculosis, Lusaka District Health Office, Lusaka, Zambia. e-mail: jill.morse@cidrz.org

**Background** Seventy percent of tuberculosis (TB) patients in Lusaka are co-infected with HIV. Provider initiated HIV testing and counselling (PITC) was introduced to Lusaka District TB clinics in 2006-07 but successful implementation was limited by shortage of nurses required to perform testing and counselling procedures. In response, the Lusaka District Health Office and the Centre for Infectious Disease Research in Zambia (CIDRZ) developed a TB/HIV Peer Educator model to assist with HIV testing and referral activities.

**Design/Methods** We trained Peer Educators in TB/HIV epidemiology, adherence counselling, HIV testing procedures, reporting and referral systems. Each TB clinic was assigned 1–2 peers who worked 20 hours per week and received a small monthly stipend. Duties included patient education, counselling and onsite rapid HIV testing, coordination of TB/HIV referral systems, and defaulter tracking. The aim of this evaluation was to assess the effectiveness of the peer program by comparing the number of TB patients newly identified as HIV-infected and enrolled into HIV care during the 12 month period before and after implementation. Data was collected from monthly PITC reports and the national electronic HIV care register and compared using paired t-tests. Ethical approval was received by the University of Zambia and the University of North Carolina.

**Results** We trained 29 peer educators to work in 20 district-run health facilities starting in September, 2009.



Twelve months post program implementation saw the number of HIV-infected patients identified through PITC increase from an average of 9.1 to 16.0/clinic/month (mean difference=6.9; 95% confidence interval (CI), 1.5–12.3;  $p=0.02$ ). Similarly, the average number of patients enrolling into HIV care each month increased from 7.0 to 10.0/clinic/month (mean difference=3.0; 95% CI, 1.3–4.7;  $p=0.002$ ).

**Conclusion and Recommendations** Identification of HIV-infected TB patients and early referral for HIV care is critical to improving patient outcomes. In our setting, with health care worker shortage, peer educators played a critical role in increasing the proportion of TB patients identified and referred for HIV care. Challenges include the need for supervision, re-training and the on-going cost of stipends. These findings need to be confirmed in similar settings including on-going evaluation of quality and sustainability.

#### **OAP-214-30 Acceptability of home based HIV testing during household tuberculosis contact investigation in Dar es Salaam, Tanzania**

E Fair,<sup>1</sup> C Miller,<sup>1</sup> L Samu,<sup>2</sup> M Hudson,<sup>1</sup> G Chamie,<sup>3</sup> S G Mfinanga,<sup>2</sup> P Hopewell.<sup>1</sup> <sup>1</sup>Curry International Tuberculosis Center, University of California, San Francisco, San Francisco, CA, USA; <sup>2</sup>Muhimbili Medical Research Centre, National Institute of Medical Research, Dar es Salaam, United Republic of Tanzania; <sup>3</sup>Division of HIV/AIDS, University of California, San Francisco, San Francisco, CA, USA. Fax: (+1) 415 695 1551.  
e-mail: efair@globalhealth.ucsf.edu

**Background:** The HIV pandemic continues to present a serious challenge to global tuberculosis control. The risk of developing TB is estimated to be up to 20 times greater in people living with HIV. One of the 12 WHO-recommended collaborative TB/HIV activities is to provide HIV testing and counseling to patients with presumptive and diagnosed TB. Our objective was to assess the feasibility, acceptance, and diagnostic outcomes of conducting home-based HIV testing simultaneously with household TB contact investigation.

**Design/Methods:** Prospective pilot study nested within an ongoing feasibility study of household TB contact investigation in Dar es Salaam, Tanzania. We enrolled 31 newly diagnosed cases of pulmonary smear positive TB. An HIV nurse and a TB contact investigator visited each household and conducted a TB symptom screen and HIV rapid tests (DETERMINE and UNIGOLD). A survey was administered to contacts  $\geq 14$  years to acquire information about their knowledge of and attitudes toward TB and HIV and acceptance of the home-based HIV testing.

**Results:** 31 index TB cases were enrolled and tested for HIV at the TB clinic. 19 were HIV-negative, 10 were newly diagnosed with HIV at the time of their diagnosis with TB, and 2 were known to have HIV (self report). 119 household contacts were identified, 6 (5%) of whom were not found. Of the 113 contacts found, 3 were currently being treated for TB. 74 (67%) of the remaining 110 contacts had at least one symptom of

TB, but no new TB cases were diagnosed. 2 of the 113 contacts found (2%) self-reported to be HIV-infected, 4 (3%) declined HIV testing, and 3 (3%) were not considered HIV contacts. Of the remaining 104 contacts tested for HIV, 2 (2%) new cases of HIV were diagnosed, both contacts of newly diagnosed index cases. 91 (88%) of tested contacts completed the survey, of whom 62 (68%) were knowledgeable about HIV (answered at least 70% of questions about HIV correctly), and 85 (93%) reported high acceptability to at-home HIV testing (defined as positive response to 80% of acceptability questions). Acceptability did not differ by level of HIV knowledge.

**Conclusions:** Home-based HIV testing combined with TB contact investigation proved to be feasible and highly acceptable. However, yield of newly detected cases of both HIV and TB were lower than expected, and suggest further streamlining and/or targeting of such active case-finding interventions to populations most at-risk of disease or poor health outcomes.

#### **OAP-215-30 Value of urine LAM score and second LAM test for optimising clinic-based screening for active pulmonary tuberculosis among HIV-infected adults**

P Drain,<sup>1</sup> E Losina,<sup>1</sup> S Coleman,<sup>2</sup> D Ross,<sup>3</sup> R Walensky,<sup>1</sup> K Freedberg,<sup>1</sup> J Giddy,<sup>4</sup> I Bassett.<sup>1</sup> <sup>1</sup>Medicine, Massachusetts General Hospital; Harvard Medical School, Boston, MA, <sup>2</sup>Data Coordinating Center, Boston University, Boston, MA, USA; <sup>3</sup>Medicine, St. Mary's Hospital, Durban, <sup>4</sup>Medicine, McCord Hospital, Durban, South Africa.  
e-mail: pkdrain@gmail.com

**Background:** We sought to determine the value of the urine LAM (lipoarabinomannan) test score and a second LAM test for active pulmonary tuberculosis (TB) screening among HIV+ adults in an outpatient clinical setting.

**Methods:** We enrolled newly-diagnosed HIV+ adults ( $\geq 18$  years) at 4 outpatient clinics in Durban, South Africa, excluding those on TB therapy. Participants provided sputum for AFB microscopy and mycobacterial culture. Trained nurses conducted two urine LAM (Determine TB LAM, Alere) tests on a single urine sample from each participant and interpreted results after 25 minutes. Positive LAM tests were scored from low (faint or 1+) to high (5+), according to the manufacturer's reference. Nurses scored a test as "faint" if a line was visible, but not dark enough to be considered 1+. The 'gold standard' of active pulmonary TB as positive sputum culture. We calculated LAM diagnostic test characteristics and evaluated screening strategies combined with AFB microscopy using area under receiver operating curves (AUC).

**Results:** Among 320 HIV+ adults, 51% were male, mean age was 33 years, median CD4 was 248 (IQR 107–378)/mm<sup>3</sup>, and 17% (54/320) had culture-positive pulmonary TB. 52 (16%) participants were urine LAM+ by either test; concordance between the two LAM tests and their scores was high (Kappa=0.93). Overall, urine LAM test sensitivity and specificity were 41% (95% CI 28–54%)

and 90% (95% CI 85–93%) for the first test, and 43% (95% CI 29–56%) and 89% (95% CI 85–93%) using a 2-test strategy. Among the 12 “faint” positive results, 17% had culture-positive TB; specificity improved to 92% (95% CI 88–95%) using a LAM score  $\geq 1+$  threshold. The number needed to screen with a second LAM test to detect 1 additional TB case was 32. When compared to AFB microscopy alone (AUC=0.57; 95% CI 0.52–0.62), a strategy of either 1 LAM test with score  $\geq 1+$  or a 2-test strategy both significantly increased the AUC value. The highest AUC was a sequential screening strategy of first performing 1 urine LAM test, and if the score is “faint” ( $<1+$ ) or negative performing AFB microscopy (AUC=0.70; 95% CI 0.63–0.77).

**Conclusions:** In this first clinic-based study of urine LAM screening, a “faint” line was generally a false-positive result and a second LAM test added little value to diagnostic sensitivity. In this cohort, an optimal screening strategy included 1 LAM test, using a positive threshold score  $\geq 1+$ , followed by sputum AFB microscopy for people urine LAM-negative.

### 03. M-HEALTH: EXPANDING THE FRONTIERS OF TB CONTROL

#### OAP-216-30 Implementation of e-TB manager in Ukraine: better data for better health outcomes

D Moskalyk,<sup>1</sup> J Folmsbee,<sup>1</sup> A Salakaia,<sup>2</sup> O Pavlova.<sup>3</sup>

<sup>1</sup>USAID-funded Systems for Improved Access to Pharmaceuticals and Services (SIAPS) /Ukraine, Management Sciences for Health, Kyiv, Ukraine; <sup>2</sup>SIAPS, Management Sciences for Health, Arlington, DC, USA; <sup>3</sup>TB, State Institution “Ukraine Center for Socially Dangerous Diseases Control of the Ministry of Health of Ukraine”, Kyiv, Ukraine. e-mail: dmoskalyk@msh.org

**Background:** Ukraine has the second highest burden of tuberculosis (TB) in the WHO European region and is the leading cause of death from infectious diseases in the country. The Government of Ukraine has adopted a strategy to strengthen TB control, which includes using a web-based information system that organizes and manages data for decision making and designing effective interventions.

**Intervention:** In October 2012, Ukraine’s Ministry of Health approved e-TB Manager for managing information needed by national TB control programs, including TB/MDR-TB cases, laboratory data, and medicines, as well as generating standardized and customizable reports. e-TB Manager is a web-based solution that was adapted for country-specific needs and introduced in Ukraine by the US Agency for International Development (USAID) -funded Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program in cooperation with the national TB program.

**Results:** e-TB Manager is a country-scale solution for effective TB data management. It is used in all 27 regions of the country, and data is entered on a regular basis

according to approved standard operating procedures. There are more than 1,200 users of the system at 650 TB facilities. Currently, 119,000 TB/MDR-TB cases have been entered into the system. The e-TB Manager in Ukraine is used for regular and ad-hoc reporting, monitoring and evaluation, epidemiological surveillance at regional and national levels, identifying gaps in national and regional TB programs’ implementation, monitoring medicine use, and providing data for forecasting pharmaceutical needs. With e-TB Manager, the amount of time needed for routine TB report preparation has decreased from days to one to three hours. Compliance between national quarterly TB07 reporting and the same report generated by e-TB Manager increased from 77% (third quarter 2013) to 85% (fourth quarter 2013) and then to 98% (first quarter 2014). Moreover, the use of e-TB Manager has contributed to increasing adherence to the national standard TB treatment protocols through functionalities monitoring the use of non-standard treatment regimens. **Conclusions:** e-TB Manager has significantly improved data quality and its processing and use. Ukraine’s experience of transitioning from paper-based to an electronic TB information system can be used as a model by other countries in the region.

#### OAP-217-30 Identifying symptomatics with a contact tracing app

S Batra,<sup>1</sup> S Ahuja,<sup>1</sup> A Sinha,<sup>1</sup> S Batra,<sup>1</sup> C Delmore.<sup>1</sup>

<sup>1</sup>Development, Operation ASHA, New Delhi, India. e-mail: colin.delmore@opasha.org

**Background** Open cases of TB can infect 10–15 others annually. Close contacts of patients, i.e. family members and work colleagues are likely to contract TB. An urgent need is to scale up detection of these hidden patients, thus providing them with health and increased productivity. There are 1.8 million new cases of TB in India each year, so active case finding is an urgent need.

**Intervention** The “ContactTracing App” developed by Operation ASHA is currently given to our community providers. It runs on Android-enabled mobile phones and tablets. Providers visit families of existing patients, factories where patients work and also go door-to-door in areas they serve. They use the App to educate the community on symptoms of TB, ask them to answer a basic questionnaire, and subsequently facilitate sputum testing and diagnosis of symptomatics. The App also is used to connect with patients and form a wireless link with the microscopy centres so that no patient is lost to follow-up. This App has the capability to strengthen our impact by reaching out and detecting vulnerable, at-risk persons. Rather than waiting for patients to go the public hospitals, we have successfully designed an innovative solution. There is so much social stigma that patients hide their disease and do not come forward for diagnosis even if they are very sick. This project is the solution for large scale impact. Contact tracing is a simple addition to our existing model, and by implementing it, we intensify our reach. The benefits are advantageous for whole

communities, for the App shall strengthen us in our fight to eradicate TB. In the absence of an effective vaccination for TB, active case finding and prompt treatment is our only solution to curb the rising tide of TB cases. The contact tracing App makes the provider's work simpler and increase detection. It enables them to give targeted counselling and follow up TB symptomatics.

**Results** We have found interesting results in this study. The work began in March 2013. As of April 2014, we have screened total number of 1719 contacts of existing TB patients. Out of these, 85 have been found to test positive for TB and have been subsequently enrolled in the DOTs program.

**Conclusions** The Contact Tracing App is a simple and effective tool for finding hidden TB cases in the community. Further large scale interventions are now needed to scale and replicate this technology to identify the hard-to-reach TB patients.



#### OAP-218-30 Challenges or practices in implementation of mHealth in tribal district for TB care and control in India

S Kumar,<sup>1</sup> A Trivedi,<sup>1</sup> S Prasad,<sup>2</sup> K Sagili,<sup>1</sup> D Tamang,<sup>1</sup> S Chadha.<sup>1</sup> <sup>1</sup>Tuberculosis, International Union Against Tuberculosis and Lung Disease (The Union), New Delhi, <sup>2</sup>Tuberculosis, Lilly MDR-TB Partnership, New Delhi, India. Fax: (+91) 11 4605 4429. e-mail: skumar@theunion.org

**Background:** Identification of TB symptomatics referred by Rural Health Care Providers (RHCPs) and getting tested at Designated Microscopic Centre (DMC) has been a persistent challenge. RHCPs are most often the first point of contact for curative services in many villages, especially in tribal and remote areas. There was a need to develop mobile application to ensure that all the referred symptomatics reach the DMC. Mobile applications were developed with support from Dimagi and are being used in tribal district, Khunti (Jharkhand, India).

**Methods:** Two applications have been developed, one for RHCP and the other for Lab Technician (LT). TB symptomatics are registered by RHCPs and referred to DMC using mobile application. Application includes basic patient information, name of DMC referred to and date of referral for sputum test. LTs use the application to share the result of sputum test with RHCP, NGO Supervisor and symptomatics. If symptomatic does not

reach DMC within 7 days of referral, system categorises him or her as lost to follow up case. Mobile application aid RHCPs with real-time guidance and key counselling messages. Each counselling message is reinforced by image and audio clip.

**Result:** RHCPs and LTs have been trained to use android phone and application. 476 referrals were made by 25 RHCPs of which 56 were diagnosed with TB and 54 were initiated on DOTS. However certain challenges were encountered during implementation. Lava Iris 349 mobile selected wasn't taking up Hindi translation which was replaced by Lava Iris 351. Some of the RHCPs were reluctant to use mobile application and often tried to skip few forms in the application. Regular maintenance is required because of improper handling which requires remote interventions and also involves additional cost & efforts. Android phone selected because of larger screen to show counselling messages are not sturdy for use in remote tribal areas.

**Conclusion:** Mobile platform is an effective tool to trace & track TB symptomatics in tribal districts. To overcome challenges, focus and effort must be on the training to emphasize on all features of the application including counselling forms to promote adherence and give humane touch to TB patients. These counselling messages can be used in patient-provider meetings if RHCPs are not able to counsel patients separately. Basic training on maintenance of phone or application must be incorporated to minimise the maintenance or service issues.

#### OAP-219-30 Mobile phone text messaging for promoting adherence to anti-tuberculosis treatment: a community-randomised trial in Jiangsu, China

H Peng,<sup>1</sup> WEI Lu,<sup>1</sup> WG Xu.<sup>1</sup> <sup>1</sup>Chronic Infectious Disease Control, Jiangsu Provincial Center for Disease Control & Prevention, Nanjing, China. e-mail: vickyph@163.com

**Background and challenges to implementation:** Although China has an excellent national TB programme and made remarkable progress in the last 20 years following the modern TB control strategy, the disease is still a considerable public health problem. Meanwhile, the Directly Observed Treatment Short-course (DOTS) is difficult to fully implement and patients poor adherence remains a challenge. Researchers have proposed using short message service (SMS) or text messaging to improve TB treatment adherence. China has high access to mobile phones, with reported over 1.2 billion mobile phones in service in 2013. The high prevalence of mobile phone use presents opportunities to develop innovative ways to engage patients in care.

**Intervention or response:** A community-based cluster randomized trial was conducted in 4 counties in Jiangsu province in China from June 2011 to July 2012. The intervention group in which participants receive daily SMS reminders through special SMS platform instead of conventional DOTS mode and a control group following standard DOT procedure. Patients meeting the inclusion



criteria were recruited and enrolled consecutively from June 2011 to January 2012 and followed by study staff during the 6-months treatment period. Data were collected monthly and analyzed until all participants completed their treatment. Investigations conducted to measure the satisfaction of patients and the health care providers and the costs calculated to evaluate the affordability and acceptability.

**Results and lessons learnt:** A total of 527 eligible patients were effectively enrolled into the trial. There were no significant differences in the sex distribution and smear microscopy results between the SMS group and the DOTS group. While age distribution (18–59 accounted for 68.2% in DOTS group and 79.5% in SMS group) has significant difference between the two ( $P=0.011$ ). The SMS group had a higher rate of timely clinic appointment attendance for follow-up examination compared to control (98.6% vs. 92.5%, respectively), and the difference is statistically significant ( $\chi^2=58.9$ ,  $P < 0.05$ ). Meanwhile, 93.4% (214/229) and 94.0% (220/234) of patients were successfully treated in the DOTS group and SMS group respectively ( $P > 0.05$ ). Furthermore, the average cost of participant in SMS group was 39.26 dollars each, 33.56% of the cost of participant in control group (116.97 dollars each).

**Conclusions and key recommendations:** The mobile phone text messaging can effectively improve TB patients' adherence and is more cost-effective, which can be promoted to a larger-scale application.

#### **OAP-220-30 On the spot colour-coded automated feedback generated in Smartphone® for TB supportive supervision in Nigeria**

K Agbaijoro,<sup>1,2</sup> L Ekblad,<sup>1</sup> O Adeleke,<sup>1</sup> A Dieng,<sup>1</sup> J O Obasanya,<sup>2</sup> T Oduose,<sup>3</sup> O Oladimeji.<sup>4,5</sup> <sup>1</sup>Health Finance and Governance Project, Abts Associates, Bethesda, MD, USA; <sup>2</sup>National Tuberculosis Program, Federal Ministry of Health, Nigeria, Abuja, <sup>3</sup>TB-HIV Program Management, United States Agency for International Development, Abuja, <sup>4</sup>Tuberculosis Research Unit, Zankli Medical Center, Abuja, Nigeria; <sup>5</sup>Research, Liverpool School of Tropical Medicine, Liverpool, UK. e-mail: droladfb@gmail.com

**Background:** Nigeria is tenth among high TB burden countries with weak program supervision which was paper based, bulky, it could tear, wet or get lost (no back-up), time consuming and feedback were not provided immediately to ensure plan of actions to resolve issues. We objectively carried out an assessment of how the color-coded on the spot automated-feedback smartphone with data back-up has improved in supportive supervision.

**Design/Methods:** We recently conducted key informant interviews in three zones in the country among the smartphone users at the Health facility, Local government, State and Federal levels. To have their feedback concerning the key differences between the paper based checklist and on the sport automated-feedback smartphone®. Users were trained to use smartphone®.

**Results:** The median time to receive objective feedbacks was 24 (range 12–36) hours before the intervention with the smartphone. We were informed by the users that the phones automatically calculate TB indicators at the facility-level and then analyze them against national standards. This rapid automated feedback is further utilized to deliberate on issues and look in to remedial options to solve them. This is also documented in the Action Plan booklet for follow-up.

**Conclusion:** This method has reduced the delay in the timing of feedback, the smartphone is very easy for the supervisors to use, faster to conduct supervision, the final supervisory feedback is backed-up in the cloud for data baking. This also provides platform for clinical supervisors to devise immediate based on the data-driven quality improvement plans during routine monitoring/supervision. We recommend scaling up by the National Tuberculosis Program

#### **OAP-221-30 Mobile health and tuberculosis treatment adherence: a way forward?**

T S Nguyen,<sup>1</sup> S Dao,<sup>1</sup> NT Nguyen,<sup>1</sup> B Bao,<sup>1</sup> R Byrkit.<sup>1</sup>

<sup>1</sup>TB Program, Program for Appropriate Technology in Health (PATH), Ha Noi, Viet Nam. e-mail: snguyen@path.org

**Background:** Viet Nam has achieved a high tuberculosis (TB) treatment success rate (>90%). However, poor treatment adherence in some cases has led to the retreatment of many TB cases, 19% of which are multi-drug resistant (MDR) TB, and an emergence of MDR-TB in 2.7% of new TB cases (WHO, 2013). As the National TB Program (NTP) transitions to a 6-month treatment regimen, treatment adherence is critical to maintain the treatment success rate and curb the increase of MDR-TB in Viet Nam. In collaboration with the NTP, PATH has been piloting a m-Health application in 17 communes of Vung Tau City. This software links to the national TB treatment management database and sends SMS to patients reminding them to take medicine and present at TB units for health checks.

**Design/Methods:** An assessment was conducted to evaluate the impact of the software on TB treatment adherence. Data on when TB patients presented at TB units for health checks and treatment outcomes before and after the intervention was collected. The baseline group consisted of 270 new pulmonary TB patients who enrolled in treatment in 2011. The intervention group consisted of 136 new pulmonary patients who enrolled and received SMS reminders during treatment from July 2012 to October 2013. Qualitative data from TB staff and patients on the acceptability of the software was collected after 7 months of implementation.

**Results:** The number of on-time visits to TB units for sputum tests increased in the intervention group compared to the baseline; however, only the third visit was statistically significant (Table 1). The treatment success rate increased from 91.1% to 98.1%, a difference that is statistically significant ( $P$  value=0.04). TB patients and staff highly appreciate the software. It reminded patients to take medicine and present for check-ups on time. In

addition, community health workers can easily access individual patient data via mobile phone, allowing them to update the system with home-visit data so upper level managers have real time access to patient treatment adherence information.

**Conclusion:** Preliminary findings showed the m-health application can improve treatment adherence and success rates of TB patients. However, continued and expanded implementation of this model is necessary to provide additional evidence as to its effect on treatment adherence, which is especially valuable as Viet Nam moves to the 6-month treatment regimen.

**Table 1.** Percent of on-time visits to the TB unit for sputum smear tests

Sequence of visit	Baseline group		Intervention group		P (Pearson Chi2)
	N	%	N	%	
1 <sup>st</sup> visit	225	83.3	122	89.7	0.10
2 <sup>nd</sup> visit	205	78.5	78	83.8	0.31
3 <sup>rd</sup> visit	146	72.3	47	87.0	0.03*

### OAP-222-30 Innovative use of mobile technology for community-led TB control intervention

A Trivedi,<sup>1</sup> S Kumar,<sup>1</sup> S Prasad,<sup>2</sup> D Tamang,<sup>1</sup> A Tandon,<sup>1</sup> M Izenberg,<sup>3</sup> D Sarin,<sup>3</sup> K Sagili.<sup>1</sup> <sup>1</sup>Tuberculosis, USEA The Union, New Delhi, <sup>2</sup>CSR, Lilly MDR-TB Partnership, New Delhi, <sup>3</sup>Software development, Dimagi, New Delhi, India. e-mail: atrivedi@theunion.org

**Background and Challenges to implementation:** Front Line Workers/Rural Health Care Providers (RHCPs) are most often “first point of contact” for curative services in many villages especially in tribal and remote geographic areas. A paper based referral mechanism is used to capture the data on referrals made, results of their sputum examination and the management of those diagnosed with TB. However, Front Line Workers (FLWs) including RHCPs and Lab Technicians (LTs), often lack information about referred chest symptomatic cases. Validating the referrals at designated microscopic centres is resource intensive, time consuming and difficult.

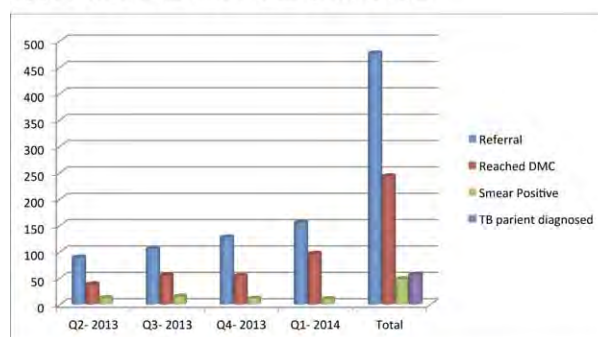
**Intervention:** Mobile application is developed with support from Dimagi and is being piloted in three blocks of Khunti, a tribal district in Jharkhand, India covering a population of 2, 55,372. This mobile platform is an easily customizable that tracks the referred cases, supports RHCPs and creates a central database on real-time basis. Two applications have been developed. One application is being used by RHCP and NGO supervisor and one by LTs. 10 FLWs are provided with Lava Android phones which have been scaled up. The application aids FLWs with guidance on key counselling points and each counselling point is reinforced by image and audio clip.

**Results and Lessons Learnt:** In ten months of implementation, 476 symptomatics have been referred by 25 RHCPs. Amongst these 56 are diagnosed TB patients and 54 have been put on DOTs. 37 RHCPs have become

DOTs provider for these diagnosed TB patients. Despite few challenges in implementation like training of RHCPs on use of android phones, reluctance of RHCPs to use complete application and maintenance of hand sets, this mobile based management system developed is assisting in follow up of referred chest symptomatics by RHCPs for diagnosis and treatment of Tuberculosis efficiently. It reduces the delay in communication of the test results and saves resources by reducing the number of visits by RHCPs to the diagnostic centres.

**Conclusion:** Mobile platform creates a real-time central database which in turn helps in retrieval of cases. This application gives the data of lost to follow up symptomatics also. This platform facilitates compilation and analysis of data. The project is exploring possibilities of sustainability and scaling up the use of mobile technology to promote TB care and control.

**Engagement of Rural Health Care Providers through Mobile Platform**



### OAP-223-30 Engagement of rural health-care providers: improves national health program performance in implementing districts

A Trivedi,<sup>1</sup> S Prasad,<sup>2</sup> S Satapathy,<sup>1</sup> S Kumar,<sup>1</sup> K Sagili.<sup>1</sup> <sup>1</sup>Tuberculosis, USEA The Union, New Delhi, <sup>2</sup>CSR, Lilly MDR TB Partnership, New Delhi, India. e-mail: atrivedi@theunion.org

**Background:** Rural Health Care Provider (RHCP) envisages a community of health worker at the village level. They are most often the first contact for healthcare services in many villages, especially in tribal and remote geographic areas with limited availability of public health services. Four districts Alirajpur (MP), Ghazipur (UP), Khunti (Jharkhand) and Pali (Rajasthan) with low symptomatic referrals and annualised case notification rates where Axshya Project is not implemented were selected for training of RHCPs in India. Objective of intervention is to engage RHCPs, enhance their capacity and establish effective linkages with the programme and pilot innovative tracking and patient support mechanisms.

**Intervention:** The intervention is being implemented through local NGO partners. Under this intervention we are piloting innovative tracking and patient support mechanisms through use of mobile technology. This mobile application provides text messaging which guides implementation of a diagnostic algorithm and advises

treatment support through the messages. The mobile application developed in collaboration with Dimagi is currently being implemented at Khunti and being scaled at Ghazipur.

**Results:** There is increase in performance in suspects' examination rate, no. of Smear positive patients' diagnosed and total case notification rate in implementing sites. Number of suspects examined per lakh population varies from 58 in 1Q12 to 241 in 2Q13 at Khunti. No. of smear positive patients diagnosed is ranging from 83 to 168 at Khunti. The rate is increased from 524 in 1Q12 to 631 in 2Q13 at Ghazipur. The total case notification in the community in all project sites have either consistently increased or maintained. During the period June to Dec 2013, the number of referrals by 588 trained RHCPs is 1079. Out of 1079 referrals, 110 (10%) have been diagnosed with TB. Out of 110 diagnosed, 80 are being provided DOTS by trained RHCPs. RHCPs are also engaged in sputum collection and transport, 37 RHCPs have done sputum collection and transport of 368 samples which has resulted in diagnosis and treatment initiation of 45 TB patients.

**Conclusion:** Trained RHCPs have become good linkages between national TB control programme and community with early gains in programme outcomes. RHCPs trained in mobile application were able to do more referrals compared to other RHCPs. 25 RHCPs have referred 314 TB symptomatics as compared to 1079 referrals by 588 RHCPs.

#### Performance on Major Indicators over the period

Project Districts	Suspects Examination Rate				No of Smear positive patients diagnosed				Total Case Notification Rate			
	1Q-12	1Q-13	2Q-12	2Q-13	1Q-12	1Q-13	2Q-12	2Q-13	1Q-12	1Q-13	2Q-12	2Q-13
Khunti	58	76	78	241	83	81	80	168	75	82	97	96
Alirajpur	79	99	107	144	74	93	105	232	63	76	83	64
Pali	93	116	98	N/A	193	308	376	N/A	107	105	N/A	98
Ghazipur	79	84	83	82	524	503	575	631	75	76	88	86

## 04. TB IN HEALTH CARE WORKERS

### OAP-224-30 Prevalence of tuberculosis among health-care workers in health service network region 9

K Janthima,<sup>1</sup> P Kamolwat,<sup>1</sup> P Monchatree.<sup>1</sup>

<sup>1</sup>Tuberculosis, Office of Disease and Prevention Control 5, Nakornratchasima, Thailand. e-mail: kul4080@yahoo.com

There is still no well determined data define that Health Care Workers who work in health facilities such as physician, dentist, nurse and pharmacist were higher risk prone to be tuberculosis than other general personnel and general population. The objective of this research was to determine the prevalence of tuberculosis among HCWs who worked in health service network region 9. The data was collected during April to June 2012. 8,135 samples were replied from HCWs of 73 public hospitals and

analyzed by descriptive and inferential statistics. Percentage and Odd ratio of the relationship and difference between the characteristics of the sample and disease was defined by Chi-square and Fisher's exact test. 97 cases were tuberculosis, accounting for 1.2 percent (or prevalence equal to 238.4 per 100,000 population), mainly pulmonary tuberculosis (73.5%) and (26.5%) of non-pulmonary tuberculosis. The percentage of abnormal finding found by chest x-ray, clinical assessment and sputum exam were sequence by abnormal shadow in chest radiation followed by clinical assessment and sputum exam (percentage of 93.8, 60.6 and 48.5). The percentage of contact TB history in case was 69.2. Most cases confined in the first 3 departments were inpatient department, outpatient department and emergency room (percentage 27.8, 18.5 and 8.0, respectively) and most cases confined in 3 professional groups, nurses, medical doctors and pharmacists, with the rate of 1,331, 842, and 854 per 100,000 population, respectively. By using dentist professional group as statistic reference in comparing found that the risk of tuberculosis (with 95 %CI) in the first 3 high risk professional groups were 1.9 (CI 0.46 to 11.36), 1.22 (CI 0.24 to 8.39) and 1.24 (CI 0.20 to 9.8), respectively, which seem to be no statistically significant. Result of this study indicated that the sickness of tuberculosis among HCWs is increasing and the sickness is likely to relate with professional group, working place and having tuberculosis sickness coworker in the same workplace. Therefore it should have personnel TB surveillance database, personnel TB screening and early intervention. The hospital administrative and HCWs must have awareness of the importance of tuberculosis precaution and follow the tuberculosis precaution guideline strictly.

### OAP-225-30 Tuberculosis screening at the St Anne Hospital in Paris: results of first and second IGRA

A Nienhaus,<sup>1</sup> PK Garipey.<sup>2</sup> <sup>1</sup>Center for Epidemiology and Health Service Research for Healthcare Professionals, University Medical Center Hamburg-Eppendorf, Hamburg, Germany; <sup>2</sup>Department of Occupational Safety and Health, Hospital St Anne, Paris, France. e-mail: albert.nienhaus@bgw-online.de

**Background:** Healthcare workers (HCW) are exposed to *Mycobacterium tuberculosis* (MTB) and therefore are screened for tuberculosis (TB).

**Results** of TB screenings with the Interferon- $\gamma$  Release Assay (IGRA) in a French hospital without a TB ward are described.

**Design/Methods:** At the Hospital St Anne, a referral centre for psychiatric patients throughout the municipal region of Paris, IGRA screening is performed during pre-employment and general health examination or after potential contact to MTB. The QuantiFERON Gold in tube (QFT) is used and data on TB history are assessed in a standardized manner.

**Results:** Between August 2008 und August 2013 in total 1.192 HCWs were tested and the QFT was positive in 265 (22.2%). Probability of a positive QFT increased



with age. A second QFT was performed in 144 HCWs with a positive QFT and 53 (36.8%) HCWs had a reversion. With a positive QFT close to the cut-off (e.g. 0.35-0.7 IU/ml) the odds ratio for a reversion was 4.6 compared to an INF- $\gamma$  concentration of  $\geq 3.0$  IU/ml. Probability of reversion was not influenced by preventive chemotherapy, which was completed by 28 (19.4%) HCWs with a positive QFT. No active TB was detected. **Conclusion:** Prevalence of positive IGRA is high in French HCWs as is the number of reversions in IGRA. Reversion rate is particularly high around the cut-off of the IGRA. A borderline zone will therefore reduce the influence of test variability.

### OAP-226-30 Establishing a serial testing algorithm using interferon- $\gamma$ -release assays (IGRA) in health care workers in low prevalence countries

W Thanassi,<sup>1,2</sup> A Noda,<sup>2</sup> B Hernandez,<sup>2</sup> D Marder,<sup>3</sup> P Terpeluk,<sup>4</sup> J Yesavage.<sup>1,2</sup> <sup>1</sup>Medicine, MIRECC and/or WRIISC, Veterans Affairs Palo Alto Health Care System, Palo Alto, CA, <sup>2</sup>Emergency Medicine or Psychiatry, Stanford University Hospital and Medical Center, Stanford, CA, <sup>3</sup>University Health Services, University of Illinois, Chicago, IL, <sup>4</sup>Occupational Health, The Cleveland Clinic, Cleveland, OH, USA. e-mail: wendy.thanassi@gmail.com

**Background:** Serial tuberculosis (TB) screening with the IGRA QuantiFERON (QFT) of health care workers (HCW) in low-risk countries has revealed unexpected variability in a small percentage of those tested, but has created considerable concern regarding the reproducibility of the results and reliability of treatment recommendations made based on those results. Reversion rates hover around 50% and are most pronounced in the weakly positive, where "positive" is  $>0.35$  IU/ml. A serial testing algorithm, based on statistical analyses, is needed to guide clinicians in the best care of these employees. We present a multicenter analysis of 31,439 US HCWs from 7 US cities and its resultant algorithm for proceeding with serial QFT testing.

**Methods:** The multivariate analysis tool, a modified receiver operating characteristic analysis, was applied to lab results from  $>31,400$  serially tested HCWs in 7 US states to identify patient or test variables that could influence reversion or predict consistently positive results.

**Results:** Reversion of a positive QFT occurred in 55% of the 1,094 initially positive adult HCWs. The only variable that predicted reversion in this expanded cohort was a TB antigen-nil  $<1.1$  IU/ml ( $p<0.001$ ), with 77.1% of those between 0.35 and 1.1 IU/ml reverting on the next test. No other variable (time between tests, TB skin test result, age, nil value, mitogen value, TB antigen value) had a statistically significant influence on weakly positive reversions. For HCWs  $>1.1$  IU/ml and for whom TST status is known ( $n=181$ ), there is only a 6% chance of reversion ( $p<0.001$ ), but for the TST negative with an initial IGRA  $>1.1$  IU/ml, there is a 59% likelihood of reversion ( $p<0.001$ ). For those who test positive 2 times in series ( $n=349$ ), reversion occurs in

20% (69) on the 3<sup>rd</sup> test. This cohort's predictor of reversion is the 2nd test  $<0.73$  IU/ml ( $p<0.001$ ). The time interval between tests, the patient's age and other test values are not significantly predictive of reversion.

**Conclusion:** North American Occupational Health clinicians who are mandated to serially test low-risk (unexposed) HCWs should 1) retest all HCWs with values  $<1.1$  IU/ml, 2) retest TST negative employees who are  $>1.1$  IU/ml, 3) retest those with a 2<sup>nd</sup> test value  $<0.73$  IU/ml, or return them to the serial testing pool, 4) perform that retesting before initiating radiologic examination or chemotherapy, and 5) the time interval between tests should be based on attaining the greatest compliance.

### OAP-227-30 Tuberculosis in health-care workers in the UK

J Davidson,<sup>1</sup> M Lalor,<sup>1</sup> L Anderson,<sup>1</sup> L Thomas.<sup>1</sup>

<sup>1</sup>Tuberculosis Section, Respiratory Diseases Department, Public Health England, London, UK.

e-mail: jennifer.davidson@phe.gov.uk

**Background:** Tuberculosis (TB) in healthcare workers is a serious public health concern; healthcare workers are at risk of infection from occupational exposure, and active pulmonary disease in healthcare workers presents a risk of nosocomial transmission. Previous studies have shown an increased risk of TB amongst healthcare workers in the UK. This study aims to describe the characteristics of healthcare workers with TB in the UK, to help inform focused preventive activities.

**Design/Methods:** TB cases aged between 16 and 64 years of age, notified to the UK TB surveillance system between 1<sup>st</sup> January 2009 and 31<sup>st</sup> December 2012, with known occupation, were included in this analysis. Cases were classified as healthcare workers or non-healthcare workers and demographic and risk factor characteristics were compared, in order to identify those associated with TB in health care workers.

**Results:** Between 2009 and 2012, occupation was recorded for 85.7% (24,155/28,180) of TB cases and of these 7.8% (1,882) were healthcare workers. The majority of healthcare workers were female (68.0%, 1,262/1,857), aged 25 and 44 years (71.3%, 1,341/1,881) and foreign born (85.0%, 1,518/1,793), of which 69.0% (893/1,294) were long-term residents (had lived in the UK for at least five years before diagnosis). The most common country of origin was India (25.5%, 449/1,759) followed by the Philippines (11.0%, 193/1,759). Almost half (43.6%, 193/443) of all TB cases from the Philippines were healthcare workers. The type of healthcare occupation differed by country of origin; the majority of healthcare workers from the Indian sub-continent were doctors, whereas cases from sub Saharan Africa and South East Asia were mostly nurses. Of those cases culture confirmed between 2010 and 2012 (643), 309 (48.1%) were in 291 MIRU-VNTR clusters with each other and/or other TB cases.

**Conclusion:** The occurrence of large numbers of cases of TB in healthcare workers in the UK highlights the need to

strengthen TB occupational health screening and vaccination programmes. Particular emphasis should be placed on ensuring that healthcare workers in the demographic groups identified in this study have appropriate occupational health assessments. MIRU-VNTR clusters containing healthcare workers should be investigated to identify whether nosocomial transmission has occurred.

### **OAP-228-30 Saving those who save lives! Integrated approach to surveillance of TB among health-care workers in a TB hospital in Mumbai**

D.P. Misquitta,<sup>1</sup> R Nanavare,<sup>2</sup> M Khetarpal,<sup>3</sup> A Bamne,<sup>3</sup> V Chavan,<sup>2</sup> L Anande,<sup>2</sup> U Aigal.<sup>2</sup> <sup>1</sup>Healthcare Management, Goa Institute of Management, Goa, <sup>2</sup>Group of TB Hospitals, Sewree, Municipal Corporation of Greater Mumbai, Mumbai, <sup>3</sup>RNTCP, Municipal Corporation of Greater Mumbai (MCGM), Mumbai, India.  
e-mail: dysonmisquitta@gmail.com

**Background:** TB among healthcare workers is a grave public health concern as evidenced by various sources. Mumbai has had reported morbidity and mortality of HCWs due to TB. Records from a TB hospital informs of 35 staff deaths attributed to TB disease over the last 5 years. In June 2011, the Hospital instituted a HCW surveillance mechanism to screen and detect HCWs with TB and put them on appropriate treatment. Based on staff demand, TB screening was integrated into a comprehensive screening with other health disorders like Diabetes, Hypertension, chronic illnesses.

**Objectives:** Increase active TB case finding among staff

**Methods:** From June 2011, quarterly (3 monthly) active screening using clinical symptoms identify TB suspects who in turn were subjected to Chest X ray (need basis), sputum microscopy and Rapid DST/LPA. Dedicated team of a Doctor and a Nurse were stationed. In 2012, staff identified other NCDs as important areas for attention in addition to TB, and general screening for blood sugar, blood pressure, BMI, etc. Once diagnosis is confirmed, staff is put on appropriate treatment for TB/DR-TB.

**Results:** The staff strength of the hospital is approximately 893, of which an average of 65% (44.79–89.70%) were screened every quarter. 24 cases of TB were detected over 2 years, of which 15 were MDR TB. Few challenges existed to have higher rates of screening, such as vacation periods; inconvenience of repeated screening; staff felt that they were not ill to seek care. Amongst other risk factors observed in staff having TB were Alcohol abuse (50%), Diabetes (29%), Hypertension (4%), and Anaemia (4%). Since the initiation of the surveillance system, 11 HCWs (2011) and 13 HCWs (2012) have been identified with TB, of these 15 have DRTB. In regard to occupation, Ward attendants (50%), Sweepers (20%) and Nurses (8%) of the total cases detected. In addition to treatment, staff are given sickness leave to take treatment accordingly. Staff contacts are also screened accordingly.

**Conclusion:** The approach developed has improved acceptability of surveillance strategy amongst staff. The integrated surveillance mechanism has identified cases amongst staff that would have gone undetected and could have resulted in undesirable consequences. Some of the asymptomatic/low symptom cases would have continued to spread infection, and has broken the chain of transmission through early detection and appropriate treatment. It is observed that TB was more among non medical staff.

### **OAP-229-30 Tuberculosis and HIV infection in health workers in the Maputo Central Hospital, the national reference hospital of Mozambique**

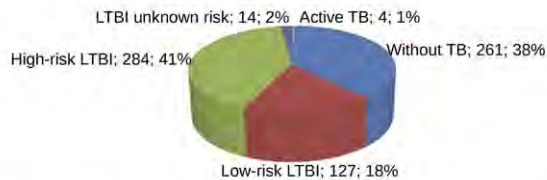
S Graves,<sup>1</sup> C David,<sup>2</sup> F Torriani,<sup>1</sup> S Viegas,<sup>3</sup> A Hassane,<sup>2</sup> S Amade,<sup>2</sup> S Peleve,<sup>2</sup> E Nunes.<sup>2</sup> <sup>1</sup>Internal Medicine, Division of Infectious Diseases, University of California, San Diego, San Diego, CA, USA, <sup>2</sup>Internal Medicine, Maputo Central Hospital, Maputo, <sup>3</sup>National Tuberculosis reference laboratory, National Institute of Health, Maputo, Mozambique. e-mail: susannah.graves@gmail.com

**Background:** In Mozambican hospitals, HIV drives transmission of tuberculosis (TB). This study employs active case finding along with latent TB infection (LTBI) and HIV screening to identify health workers (HW) at high risk for active TB.

**Methods:** 690 HW at Maputo Central Hospital (MCH) were enrolled with exclusion criteria: recent active TB, current immune-suppressive therapy or <1 year of service at MCH. Participants completed a symptom screen, chest X-ray, tuberculin skin- (TST), HIV- and Quantiferon TB-gold (QFT) testing. Sputum samples for acid-fast smear, mycobacterial culture and GeneXpert were solicited from symptomatic patients and those with suspicious X-ray findings. HW with LTBI were risk-stratified based on HIV status and quantitative TST and QFT results. A logistic multivariate analysis was used and adjusted odds ratios reported.

**Results:** Among 690 enrolled HW, 4 cases of active TB were diagnosed. 425 (62%) LTBI cases were identified of whom 284 (67%) were classified as high-risk LTBI. Of 333 workers with HIV and/or high-risk LTBI who were offered isoniazid preventive therapy, 186 are on treatment. HIV positivity did not significantly differ for those with and without TB infection including LTBI (both 12%,  $p=0.3$ ). The TST had a positive predictive value for QFT positivity of 82% in HIV+ individuals (95% CI 63–94) which did not differ significantly in HIV- individuals (79%, 95%CI 74–84). In the multivariate analysis, duration of service at MCH for >10 years had a significant positive association with TB infection (OR 1.67, 95%CI 1.21–2.30), as did service in the departments of Surgery (OR 4.25, 95%CI 2.33-7.75), Emergency and Critical Care (OR 3.36, 95%CI 1.41-7.97), Pathology (OR 2.76, 95%CI 1.42-5.38), and Obstetrics (OR 1.98, 95%CI 1.15-3.41) when compared with the Internal Medicine department. Service in other departments, including Pediatrics and Administration, was not significantly associated with higher rates of LTBI ( $p>0.05$  for all).

**Conclusions:** Active TB prevalence among HW at MCH is similar to the background prevalence of 553/100,000 (WHO 2012) in Mozambique. However, workers in several departments are at significantly higher risk of LTBI suggesting occupational risk, and indicating good targets for intervention including implementation of “FAST” (Finding TB cases Actively, Separating safely, Treating effectively). Follow-up is planned to evaluate the incidence of LTBI, active TB, and adherence to isoniazid preventive therapy.



**Figure 1.** TB infection status and classification of screened participants (total n=690, data shown as n; %). High-risk LTBI defined as: HIV+ with TST  $\geq$  5mm, OR HIV- with TST  $\geq$  15mm AND QFT  $\geq$  1.0. Low-risk LTBI defined as HIV+ with TST < 5mm, OR HIV- with TST between 10-14mm OR QFT between 0.35-1.0.

### OAP-230-30 TB screening for health-care workers in Swaziland

M Matsebula,<sup>1</sup> M Dlamini,<sup>2</sup> J Ongole,<sup>1</sup> S Haumba,<sup>1</sup> P Mamba,<sup>2</sup> N Shongwe,<sup>1</sup> A Smith-Arthur.<sup>3</sup> <sup>1</sup>TB/HIV Assist Project, University Research Swaziland, Mbabane, <sup>2</sup>TB/HIV, Wellness Centre Swaziland, Manzini, Swaziland; <sup>3</sup>Centre for Human Services, University Research Headquarters, Bethesda, WA, USA. Fax: (+268) 24047199. e-mail: makhosazanam@urc-sa.com

**Background and challenges to implementation:** Globally, healthcare workers (HCWs) are among the highest risk groups for TB and MDR-TB infection, due to their direct contact with patients in their workplace. Of the estimated 9 million annual new cases of active TB worldwide, at least 3 million are estimated to be undiagnosed or unreported due to various health system challenges these pose the highest risk to health workers and can lead to unintended nosocomial transmission. In Swaziland, a country with the world's highest TB incidence rates (1340/100,000, an MDR-TB prevalence of 7.7% among new cases and 33% among re-treatment cases and a HIV co-infection rate among TB patients of 80%, it is important to develop strategies targeted to preventing and managing TB among HCWs. The Wellness Centre is a dedicated, all-purpose health center designed to support the health workforce in Swaziland. The Centre focuses on the needs of healthcare workers and allows for the testing of novel approaches to reach health workers with TB services.

**Aim:** The Wellness Centre launched a pilot project in 2012–2013 with technical assistance from the ASSIST project, which among several objectives, aimed at developing a system for regular TB screening among HCWs in 14 healthcare sites.

**Intervention or response:** The pilot project was conducted in 14 health facilities (8 hospitals and 6 health centres) located in all the regions of Swaziland. The project had set a target of 75% of HCWs screened for TB by each facility. The outcome measures were number and proportion of HCWs screened and diagnosed with TB in each of the facilities. Data were entered into an excel sheet and analysed using Microsoft Excel 2010. HCWs comprised all staff working at the health facilities.

**Results and lessons learnt:** Out of the 3325 HCWs working in all the 14 facilities, 72% (2378) were screened for TB and of those, 33% (793/2378) had positive TB symptoms. A total of 4% (30/793) of the presumptive TB cases were diagnosed with TB. Amongst the 14 pilot facilities only 2 sites reached the targeted 75% screening per facility with 100% and 96%.

**Conclusions and key recommendations:** Healthcare workers are constantly exposed to TB, and there is a need for continuous periodic TB screening in order to facilitate early diagnosis & treatment of TB. The findings highlighted the severity of the problem and the need to integrate and scale up TB screening into routine services offered in the wellness clinics.

### OAP-231-30 Analysis of occupational tuberculosis in the Brazilian national recording system, 2007–2011

G Nunes,<sup>1</sup> T Do Prado,<sup>1</sup> F Souza,<sup>1</sup> Lia Possuelo,<sup>2</sup> C Sales,<sup>1</sup> E Leonor Noia Maciel.<sup>1</sup> <sup>1</sup> Centro De Ciências da Saúde, Universidade Federal do Espírito Santo, Vitória, ES, <sup>2</sup> Saúde, UNISC, Santa Cruz do Sul, RS, Brazil. Fax: (+55) 3335–7287. e-mail: gabrielaf.nunes@live.com

**Background:** The objective of this study was to compare the proportion and epidemiological characteristics of occupational tuberculosis (TB) between Healthcare workers (HCW) and non-HCW using the Brazilian national surveillance system.

**Methods:** Cross-sectional study utilizing the Brazilian national surveillance system (SINAN) database, comparing results from 2751 non-HCW with those from 298 HCW. The Pearson chi-square test or the likelihood-ratio chi-square tests were used to compare the proportions and a multivariate analysis to analysis of the epidemiological characteristics of occupational tuberculosis in the two groups.

**Results:** The proportion of TB cases attributable to occupational TB based on data from 2007 to 2011 in Brazil was 1.6%. We analyzed 3,049 subjects, of whom 298 (10%) were TB – HCW and 2,751 (90%) were TB – non-HCW. Males were less prevalent among HCW and an age of 43 years or greater increased the odds of having occupational tuberculosis (OR = 1.96, 95% CI 1.37 – 2.79) in this group. The odds were also greater for those with more than 8 years of schooling (OR = 27.47, 95% CI 16.64 – 45.34) and alcoholism was less prevalent among HCW (OR = 0.17, 95% CI 0.05 – 0.54). The HCW group had lower odds of developing extrapulmonary TB (OR = 1.60, 95% CI 1.12–2.28) and were less



likely to be covered under the DOTS program (OR = 0.58, 95% CI 0.43-0.77).

**Conclusions:** The prevalence of occupational TB was 1.6%, which highlights the importance of establishing a plan for occupational tuberculosis control in Brazilian health facilities and other workplace settings with a high risk of TB exposure. In Brazil, the results of our study highlight tuberculosis as an occupational disease, which is important to strengthening the discussions around labor rights.

## 05. TUBERCULOSIS EPIDEMIOLOGY: PREDICTING THE FUTURE

### OAP-232-30 Tuberculosis treatment delays and associated factors within the Zimbabwe National Tuberculosis Programme

B Nyathi,<sup>1</sup> K Takarinda,<sup>2,3</sup> M Ngwenya,<sup>2</sup> A D Harries,<sup>3,4</sup> T Apollo,<sup>2</sup> C Sandy,<sup>2</sup> M Nqobile,<sup>1</sup> N Siziba.<sup>2</sup> <sup>1</sup>TB CARE I Project, International Union Against Tuberculosis and Lung Disease, Harare, <sup>2</sup>AIDS and TB, Ministry of Health and Child Care, Harare, Zimbabwe; <sup>3</sup>Research, International Union Against Tuberculosis and Lung Disease, Paris, France; <sup>4</sup>Clinical Research, London School of Hygiene and Tropical Medicine, London, UK. e-mail: ktakarinda@theunion.org

**Background:** Delayed presentation of smear-positive tuberculosis (TB) patients for treatment from onset of symptoms is associated with individual disease progression and TB transmission. There is little information about treatment delays in Zimbabwe, therefore we set out to determine the extent of these delays and their associated factors in smear-positive TB patients consecutively registered and treated in Zimbabwe.

**Design/Methods:** A structured questionnaire was administered at 48 randomly selected health facilities in Zimbabwe by trained health workers to all patients aged  $\geq 18$  years with confirmed TB who were started on TB treatment between 01 January and 31 March 2013. Logistic regression was used to calculate multivariate-adjusted odds ratios (aOR) and their 95% confidence intervals (CI) for factors associated with patient delay  $> 30$  days or health system delay  $> 15$  days.

**Results:** Of the 383 recruited patients, 217 (57%) were male with an overall median age of 34 years (IQR, 28–43). Most patients (66%) were from rural areas, unemployment was high (59%) and 216 (57%) had attained secondary school education or higher. Patient delays were noted in 188 (49%) of study participants whilst only 22 (6%) patients encountered health system delays. There was a median of 28 days for patient delays (IQR, 21–63) and 2 days for health system delays (IQR, 1–5). Factors associated with patient delays were: starting TB treatment at rural primary healthcare facilities compared to district/mission hospitals [aOR=2.06, 95% CI 1.04–4.08] and taking self-medication when experiencing cough symptoms [aOR=2.19, 95% CI 1.13–3.58]. Health system delays were only noted among those patients who had four or more visits

to health facilities prior to TB diagnosis [aOR=3.34, 95% CI 1.11–10.03].

**Conclusion:** Patient delays were high particularly in rural settings, suggesting the need for health education of the population to seek timely and appropriate medical consultation when experiencing symptoms suggestive of TB. Health system delays were uncommon, suggesting an efficient national TB programme. However, there is a need to strengthen TB case diagnosis and management trainings to reduce unnecessary visits to health facilities which may also resultantly minimise losses of TB cases prior to their initiation on TB treatment.

### OAP-233-30 Non-adherence in tuberculosis treatment: predictors in Brazil

M Silva,<sup>1</sup> J Da Cruz Pereira,<sup>2</sup> RR Da Costa,<sup>3</sup> ICG Leite.<sup>2</sup>

<sup>1</sup>Embrapa Dairy Cattle, Brazilian Agricultural Research Corporation, Juiz de Fora, MG, <sup>2</sup>Health Sciences Postgraduate Programme, Federal University of Juiz de Fora, Juiz de Fora, MG, <sup>3</sup>Regional João Penido Hospital, Hospital Foundation of Minas Gerais State - FHEMIG, Juiz de Fora, MG, Brazil. e-mail: marcio-roberto.silva@embrapa.br

**Background:** Poor adherence to antituberculosis treatment is the most important obstacle to tuberculosis (TB) control. The aim was to evaluate risk factors for nonadherence in TB treatment, by means of a cohort study.

**Design/Methods:** This was a cohort study of all patients notified with TB in outpatient clinics of three centers, in Juiz de Fora, Minas Gerais, Brazil, from 2008 to 2009. Nonadherence was defined as treatment default or discontinuation (TD) for at least 1 month. Multivariate logistic models with three hierarchical levels of explanatory variables (distal, middle and proximal) were constructed. The variables with significance  $p < 0.20$  in the univariate analysis were included in the multivariate model and were adjusted to a higher level of hierarchy. In the final multivariate model, the variables that did not present significant were removed one by one (method backward) until all were significant ( $p < 0.05$ ).

**Results:** Of the total number ( $n=220$ ), 172 (78.2 %) and 48 (21.8 %) had cure and TD as outcomes, respectively; 148 (67.27 %) and 72 (32.72 %) were male and female, respectively; 124 (67.27 %), 77 (35.00 %) and 19 (8.63 %) were treated in the outpatient clinics of the Specialized Clinics Unit (UCE), the Regional John Penido Hospital (HRJP) and the Specialized Service Care (SAE), respectively. In the multivariate model, there was a direct association between the intensity of the drug use and the incidence of TD. The risks of TD were increasing in the direction of ex-users (OR = 4.12, 95%CI 1.11 - 15.20), cocaine users alone or in combination with marijuana (OR = 5.67, 95%CI 1.34 - 24.03) and crack users alone or combined with other drugs (OR=12.25, 95%CI 3.04 - 49.26). The model also showed that alcoholics had more risk to abandon the treatment than individuals who did not drink or drink in a moderate way in the last year (OR = 2.94, 95% CI 1.08 - 7.99). Finally, the patients treated at the HRJP had more risk (OR = 8.22, 95%CI 2.79 -

24.21 %) of TD compared with those treated at the UCE (Table).

**Conclusion:** TB should be seen not only in the physical point of view, but taking into account its complex relationships with the various social factors outside the health unit such as alcoholism, drug addiction and health care type. These factors need to be taken into account both in the prevention and treatment of disease. These data provide support to directly observed therapy in TB.

**Table.** Multivariate logistic regression analysis in hierarchical levels for the nonadherence in tuberculosis treatment

Hierarchical Level	Variable	OR (IC 95%)	p-value
Middle	Treatment site UCE <sup>a</sup> SAE <sup>b</sup> HRJP <sup>c</sup>	1.00 1.79 (0.24 – 13.37) 8.22 (2.79 – 24.21)	0.56 <0.001
Proximal	Intensity of drug use	1.00 4.12 (1.11 – 15.20)	<0.05
	Never or not in the last year Ex-users Cocaine alone or combined with marijuana Crack alone or combined with other	5.67 (1.34 – 24.03) 12.25 (3.04 – 49.26)	<0.001
0Proximal	Alcohol Consumption in the last year No or moderate (CAGE <sup>d</sup> < 3) Alcoholism (CAGE 3–4)	1.00 2.94 (1.08 – 7.99)	<0.05

Model Summary (–2 Log likelihood=112.732; Cox & Snell R Square=0.267; Nagelkerke R Square=0.441) Hosmer and Lemeshow Test  $\chi^2$  (1.597, p=0.902)

<sup>a</sup> Specialized Clinics Unit

<sup>b</sup> Specialized Service Care

<sup>c</sup> Regional João Penido Hospital

<sup>d</sup> CAGE questionnaire

### OAP-234-30 Undiagnosed tuberculosis cases among previously tuberculosis-affected families: results of a prevalence survey in Peru

M Tovar,<sup>1,2</sup> T Wingfield,<sup>2</sup> R Montoya,<sup>2</sup> E Ramos,<sup>1</sup> T Valencia,<sup>1</sup> M Rivero,<sup>2</sup> S Carrera,<sup>1</sup> C Evans.<sup>1,3</sup> <sup>1</sup>IFHAD: Innovation For Health And Development, LID 218 Universidad Peruana Cayetano Heredia, Lima, <sup>2</sup>IPSYD: Innovacion Por la Salud Y el Desarrollo, Asociacion Benefica PRISMA, Lima, Peru; <sup>3</sup>IFHAD, Infectious Diseases & Immunity, Wellcome Trust Imperial College Centre for Global Health Research, London, UK. e-mail: marco.tovar@upch.pe

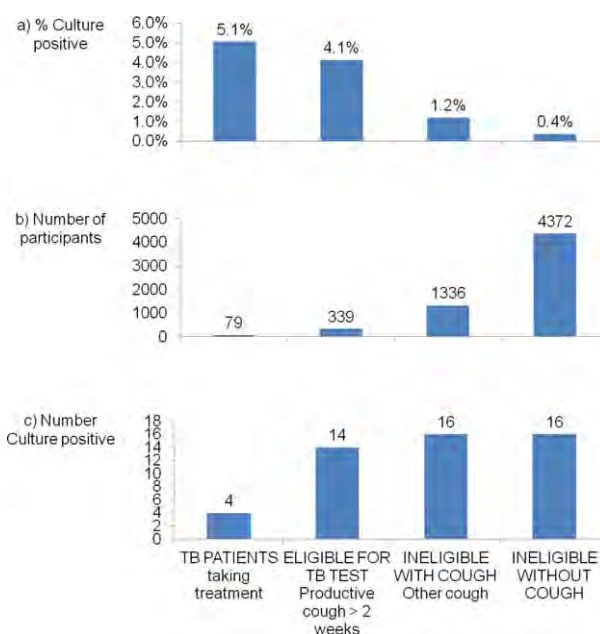
**Background:** Prevalence surveys are an important epidemiological tool with which to obtain a direct measurement of the absolute burden of tuberculosis (TB) disease. We performed a prevalence survey in impoverished Peruvian households that had previously been affected by TB.

**Design/Methods:** From December 2007 through June 2012, consecutive TB patients (index case) diagnosed by the regional national tuberculosis program (RNTP) were enrolled in Ventanilla, 16 contiguous peri-urban shantytowns. Written, informed consent was obtained from all patients. Socioeconomic and health data was collected from the TB patients and their household contacts. We revisited all index cases' households at least 2 years after the index case began anti-TB therapy with directly

observed treatment short-course (DOTS). At this visit, we obtained a sputum sample from all participants over 7 years old. All sputum samples were processed using "single step" technique and cultured on thin layer agar.

**Results:** 2054 patients and 12287 of their household contacts were enrolled. Of these, 1192 patients (58%) and 7373 household contacts (60%) were over 7 years old and available at follow-up. Sputum samples were collected from 1158 patients (97%) and 5022 household contacts (68%). 50/6180 (0.8%) had a culture-positive sample and bacteriologically confirmed pulmonary TB (809 cases per 100,000 population). Only 14/50 (28%) of these people reported productive cough for more than 2 weeks at the follow-up visit (Figure). The number needed to screen (NNS) to detect one sputum positive TB case was 24 among those with productive cough for more than 2 weeks and 269 among those without symptoms (Figure).

**Conclusion:** The prevalence survey identified a significant number of undetected TB cases. The number need to screen suggests that the use of thin layer agar to screen TB among people with a productive cough for more than 2 weeks was cost effective in this setting. Most of the people with bacteriologically confirmed pulmonary TB were asymptomatic. Novel strategies are required to identify a cost effective method of identifying people at high-risk of TB but without respiratory symptoms who would benefit from sputum testing.



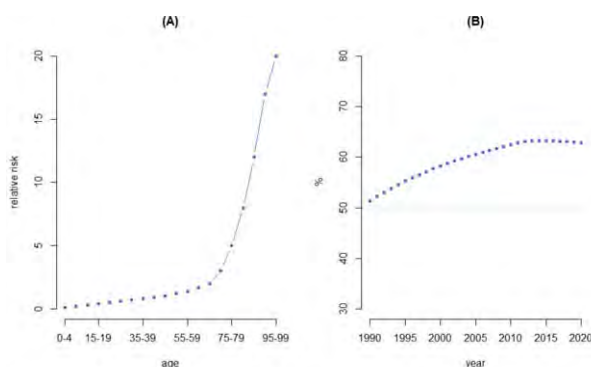
### OAP-235-30 Modeling the tuberculosis epidemic in Taiwan: the importance of age-dependent reactivation rates

H Fu,<sup>1</sup> H-H Lin.<sup>1</sup> <sup>1</sup>National Taiwan University, Graduate Institute of Epidemiology and Preventive Medicine, Taipei City, Taiwan. e-mail: b97801047@ntu.edu.tw

**Background:** Among the 13,000 notified cases of tuberculosis (TB) in Taiwan in 2011, more than half of them were older than 65 years old. The high proportion of elderly among TB cases suggested that reactivation from remote TB infection accounted for the majority of incident TB cases. However, evidence from limited molecular epidemiological studies and geospatial analysis revealed that recent transmission of TB still occurred frequently in the Taiwanese population. The relative contribution of recent infection and remote reactivation to the current TB epidemiology remains unclear and has important implication for the design of TB control policy.

**Methods:** We built an age-structured compartmental model of TB transmission to capture the transmission dynamic of TB in Taiwan over the past decades. The model structure and parameter values followed the convention of previous TB transmission models. We calibrated the model to reflect the declining trend of TB prevalence observed in the eight national prevalence surveys (1957–1993) and the age-specific notification rate (2005–2011) reported by Taiwan CDC. Using the calibrated model, we estimated the relative contribution of recent and remote transmission.

**Results:** In order to fit the age-specific incidence rate of TB in Taiwan, the calibrated reactivation rate in the TB model followed a strong age-dependent pattern, with the oldest group having a 20-fold greater risk of reactivation compared to the middle-aged group (Figure 1A). Using the calibrated model, we estimated that in the past decades the proportion of incident cases due to remote reactivation increased gradually to 63% in 2014. (Figure 1B) With the continuous rise of the elderly population in Taiwan, the model projected that the decline of TB incidence will be slow under the current control measures.



**Figure 1.** (A) Age-specific pattern reactivation rate after model fitting. (B) Estimated proportion of remote reactivation among incident TB cases.

**Conclusion:** The model-based analysis revealed a strong age-dependent pattern in risk of reactivation, although this finding needs to be validated in further epidemiological studies. The high reactivation rate in the elderly will be a challenge to TB control in settings with a high proportion of aged cases. In a middle burden country like Taiwan, recent transmission still accounts for a substantial proportion of incident cases. In order to accelerate the decline of TB incidence, intensified case finding including contact tracing and screening for high risk population should be considered.

### OAP-236-30 Prevalence of *Mycobacterium africanum* (Maf) did not change during eight years of follow-up in Bamako, Mali

B Diarra,<sup>1</sup> A Togo,<sup>1</sup> B Baya,<sup>1</sup> M Sanogo,<sup>1</sup> S Diallo,<sup>1</sup> MH Kaba,<sup>1</sup> O Koita,<sup>1</sup> R Murphy.<sup>2</sup> <sup>1</sup>SEREFO (HIV/TB Research and training center), University of STT of Bamako, Bamako, Mali; <sup>2</sup>Biomedical Engineering and Medicine, Northwestern University of Chicago, Chicago, IL, USA. e-mail: bdiarra@icermali.org

**Introduction:** Since its discovery in 1968 in Senegal by Castets et al. (1969), *Mycobacterium africanum* (Maf) is recognized as a major cause of human tuberculosis (TB) in West Africa. In this region, its prevalence can reach up to 40% of tuberculosis cases. In addition our previous data (Traore et al., 2012) and other several studies (de Jong BC et al., 2007, and 2010) have shown that Maf is more susceptible to TB first line drugs than *M. tuberculosis* (MTB). Thus, the goal of this study was to estimate the prevalence of this susceptible strain during eight years of follow up.

**Methods:** We conducted a cross-sectional study between January 2006 and December 2013. Suspected tuberculosis patients were enrolled on IRB approved protocols at the Point G University Teaching Hospital in Bamako. Confirmed *M. tuberculosis* complex (MTBc) isolates underwent drug susceptibility testing (DST) and spoligotyping to characterize the infecting mycobacteria at the SEREFO laboratory.

**Results:** Two hundred and fifty four MTBc strains were typed during this period, of which 50 (19.7%) were Maf. The highest prevalences of Maf were seen in 2006 (38.9%) and 2008 (30.3%) while no Maf was found in 2010 and 2011. There were less total MTBc strains typed in 2010 and 2009 respectively 10 and 15. However, 52 and 53 strains were typed in 2013 and 2007 respectively. Out of the 254 strains typed, 216 were tested for DST. Fifty-nine strains were found to be MDR, of which 4 (6.8%) are Maf and the remaining, 55 (93.2%) are MTB. The 4 Maf MDR strains were seen one each in 2007, 2008, 2009 and 2012 respectively.

**Conclusion:** Maf is circulating in Mali over eight year's follow up and it seems less associated with MDR. With this low association with MDR, there may be other risk factors, which are maintaining stable this susceptible mycobacterium within the community. A large cohort study is needed to understand better the distribution of Maf in Mali and West Africa.



### OAP-237-30 High initial loss to follow-up after tuberculosis diagnosis in South African gold miners

B Lange,<sup>1,2</sup> K Fielding,<sup>1</sup> V Chihota,<sup>3</sup> A Grant,<sup>4</sup> G Churchyard,<sup>1,3</sup> J Lewis.<sup>1</sup> <sup>1</sup>Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, UK; <sup>2</sup>Medicine, Division of Infectious Diseases/Center for Chronic Immunodeficiency, Freiburg University Medical Center, Freiburg, Germany; <sup>3</sup>Epidemiology, The Aurum Institute, Johannesburg, South Africa; <sup>4</sup>Clinical Research, London School of Hygiene and Tropical Medicine, London, UK.  
e-mail: berit.lange@lshtm.ac.uk

**Background:** Prompt therapy following tuberculosis (TB) diagnosis is essential for patients and TB control. Data concerning risk factors for initial loss to follow-up (ILF) is scarce. This cohort study assessed time to treatment and ILF in miners in South Africa who were tested for TB.

**Methods:** We linked demographic, socioeconomic and health service information on miners with suspected TB in gold mines participating in the Thibela TB study between Oct 2008 – Feb 2010 with data on patients starting TB treatment until December 2010 in the same setting. One spot sputum specimen was collected for those with suspected TB. Time from specimen collection to treatment initiation was evaluated in those miners who were subsequently treated for TB. ILF was assessed at 1 and 6 months after sputum collection in miners with microbiologically confirmed TB (positive smear or culture). Random-effects Cox Regression, stratified by smear status, was used to assess risk-factors for low TB treatment rates (TBTR) i.e. treatment start over follow-up-time in miners who had microbiologically confirmed TB.

**Results:** 698/2983 (23.4%) of miners with suspected TB had microbiologically confirmed TB at enrolment. 952/2983 (31.2%) of miners with suspected TB and 91/698 (13%) of miners with microbiologically confirmed TB discontinued work in the mines during six months follow-up. 52.2% (95%CI 44.4–59.8) and 25.5% (95%CI 19.4–32.8) of the miners with microbiologically confirmed TB and known treatment status had not started TB treatment at 1 month and 6 months after sputum sample collection. ILF at 6 months was 21.7% in SMP TB cases and 30.7% in SMN TB cases (Table 1). Among 754 miners treated for TB, median time to treatment was 25 days (IQR 6–43): 7 days for smear-positive (SMP) and 48 days for smear-negative (SMN) patients. In SMP cases, older age (Hazard Ratio [HR] 0.41 for 55–70 vs 18–34 years, 95%CI 0.22–0.78) and females (HR 0.22, 95%CI 0.07–0.71) had lower TBTR. In SMN cases, there was a higher TBTR among those living in hostels compared to living with family/alone (HR 1.57 95%CI 1.12–2.21) and lower TBTR among those presenting via radiological screening compared to self-presentation (HR 0.55 CI95 0.37–0.83).

**Conclusion:** In this cohort study of mine workers in South Africa, median time to treatment and initial loss to follow up were high in both SMP and SMN TB cases.

More evidence is needed regarding interventions to ensure prompt treatment in both SMP and SMN TB patients.

Table 1 Initial loss to follow up at 1 and 6 months in microbiologically confirmed TB cases

	All miners At start of follow up N	1 month after sputum sample collection		6 month after sputum sample collection	
		Known treatment status (i.e. still in workforce) N (% of all miners)	Not on treatment N (% and 95%CI* of miners with known treatment status)	Known treatment status (i.e. still in workforce) N (% of all miners)	Not on treatment N (% and 95%CI* of miners with known treatment status)
All miners with smear positive TB	397	381 (95.0%)	147 36.5% (29.7%–48.3%)	351 (88.4%)	76 21.7% (15.7%–29.1%)
All miners with smear negative, culture positive TB	301	294 (94.4%)	200 70.4% (62.5%–77.2%)	257 (85.4%)	79 30.7% (21.2%–42.3%)
All miners with microbiologically confirmed TB	698	665 (95.3%)	347 52.2% (44.4%–59.8%)	608 (87.1%)	155 25.5% (19.4%–32.8%)

\* 95% Confidence Intervals with robust standard errors

### OAP-238-30 *Mycobacterium tuberculosis* genotype distribution in tuberculosis patients from Papua and Java, Indonesia

L Chaidir,<sup>1</sup> S Sengstake,<sup>2</sup> E Burhan,<sup>3</sup> A Oktavian,<sup>4</sup> J De Beer,<sup>5</sup> D Van Soolingen,<sup>5</sup> B. Alisjahbana,<sup>1</sup> R Van Crevel.<sup>6</sup> <sup>1</sup>Faculty of medicine, Universitas Padjadjaran, Bandung, Indonesia; <sup>2</sup>Biomedical Research, Royal Tropical Institute (KIT), Amsterdam, Netherlands; <sup>3</sup>Pulmonology, Persahabatan Hospital, Jakarta, <sup>4</sup>Biomedical research, National Institute of Health Research, Jayapura, Indonesia; <sup>5</sup>National Tuberculosis Reference Laboratory, National Institute for Public Health and the Environment, Bilthoven, <sup>6</sup>Medicine, Radboud University Medical Center, Nijmegen, Netherlands. e-mail: lilya.chaidir@gmail.com

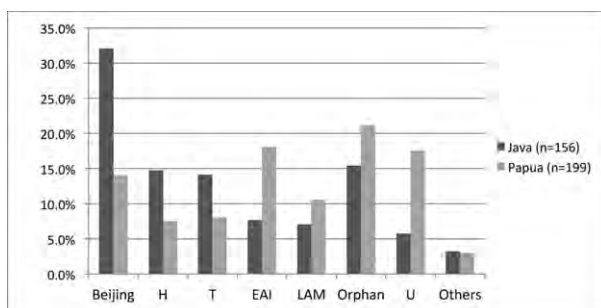
**Background:** Similarly to human mankind, *Mycobacterium tuberculosis* shows marked genetic variation between different geographic areas. This may be due to its evolutionary adaptation to the human immune system, with certain human populations being more susceptible to particular *M. tuberculosis* genotype families. The degree of evolutionary adaptation might also affect the clinical phenotype of active tuberculosis. We examined these hypotheses in the unique setting of human and pathogen diversity in the Indonesian archipelago

**Design/Methods:** Between 2011–2013, 674 patients from two cohorts of pulmonary TB patients were established in West Java (n=330) and Papua (n=344). Clinical and socio-demographic data were collected and *M. tuberculosis* isolates (156 from West Java and 199 from Papua) were genotyped using spoligotyping. Papuan isolates were further genotyped using SNPs-typing and MIRU-VNTR. Genotype distribution was compared between patients in Java and Papua according to age, BCG vaccination, and history of TB treatment.

**Results:** Patients in Java were older compared to Papua (median 35 vs 28 yrs). Using spoligotyping, a high degree of genetic diversity was observed among isolates in both regions (Figure). Beijing strains were predominant in Java (32% vs 14% in Papua), while EAI strains were highly prevalent in Papua (18% vs 8% in Java). SNPs typing was performed to Papuan isolates which was able to assign orphan and unknown-spoligotypes into certain genetic lineages. By combining MIRU-VNTR and spoligotyping, we showed low clustering level of Papuan

isolates (32.7%). Drug resistance mutations were present in 11% among primary and 27.5% among retreatment cases. MDR-TB was found in 4.0% of patients. Among patients from Papua, Beijing strains were more often found in patients who had a BCG-scar as well as a history of previous TB treatment on clinical examination.

**Conclusion:** Our result showed a considerable degree of heterogeneity among *M. tuberculosis* isolates and a significant difference in *M. tuberculosis* population structures at the different geographical study sites. A study of possible associations between host and mycobacterial genetics may help to establish if differences in *M. tuberculosis* population structures are caused by evolutionary adaptation of particular mycobacterial lineages to certain human populations.



#### OAP-239-30 Tuberculosis in pregnancy: an estimate of the global burden of disease

J Sugarman,<sup>1</sup> C Colvin,<sup>2</sup> R Menzies,<sup>1</sup> A Moran,<sup>2</sup> O Oxlade.<sup>1</sup> <sup>1</sup>Respiratory Epidemiology and Clinical Research Unit, McGill University, Montreal, QC, Canada; <sup>2</sup>Bureau of Global Health, Office of Health, Infectious Disease and Nutrition, United States Agency for International Development, Washington, DC, USA. Fax: (+1) 514 843 2091. e-mail: olivia.oxlade@mcgill.ca

**Background:** The major causes of maternal death have shifted in recent years from direct obstetric causes, to non obstetric causes, including infectious diseases like tuberculosis (TB). TB remains a substantial global public health concern. It is responsible for up to 15% of all maternal mortality, and other unfavorable outcomes are common. The burden of TB disease in pregnant women is not known. Sound estimates are needed to guide programmatic efforts to improve the diagnosis and treatment of TB. The objective of our study was to estimate the global burden of TB disease among pregnant women, and to estimate how many TB cases could potentially be detected through maternal care services using different approaches to diagnosis.

**Methods:** We derived an estimate of the number of pregnant women with active TB in 217 countries using publicly accessible country level demographic and epidemiologic data. We estimated the proportion of TB cases with access to antenatal and labor and or delivery care in each country by multiplying the country-level estimate of TB cases by two different country-level indicators of access: 1) at least one antenatal care visit

and 2) birth attended by skilled health professional. Finally, we estimated the proportion of cases that could be detected using different diagnostic tests for initial case detection by multiplying each country-level estimate (after adjustment for access to maternal health services) by the reported sensitivity of three different TB diagnostic tests for TB: smear microscopy, chest radiography and Xpert®RIF/MTB.

**Results:** We estimated that 585,596 (95% UR 514,855–669,568) TB cases existed in pregnant women globally in 2011. The greatest burden was in the WHO African and South East Asian regions with 220,013 and 206,975 cases in pregnant women, respectively. Chest X-ray and Xpert®RIF/MTB, delivered through maternal care services, were estimated to detect as many as 312,043 cases and 328,799, respectively.

**Conclusion:** Maternal care services may provide an important platform for TB detection, treatment initiation and subsequent follow up, especially in settings where case detection in the general population is low. The substantial burden of disease estimated in pregnant women indicates there remains an urgent need to improve access to TB screening and diagnosis, especially in high TB and high HIV burden settings. More research is imperative to improve delivery and uptake of care in this vulnerable population.

#### 06. DEVELOPING NEW REGIMEN FOR MDR-TB TREATMENT

##### OAP-240-30 Cost effectiveness of bedaquiline for the treatment of multidrug-resistant tuberculosis

L Wolfson,<sup>1</sup> R Hettle,<sup>2</sup> A Walker,<sup>2</sup> X Lu,<sup>3</sup> C Kambili,<sup>4</sup> A Murungi,<sup>5</sup> G Knerer.<sup>5</sup> <sup>1</sup>Global Public Health, Janssen Pharmaceutica NV, Beerse, Belgium; <sup>2</sup>HERON Commercialization, PAREXEL International, London, UK; <sup>3</sup>Market Access, Janssen Pharmaceutica NV, Beerse, Belgium; <sup>4</sup>Global Public Health, Janssen Global Services LLC, Raritan, NJ, USA; <sup>5</sup>Janssen, Janssen-Cilag, High Wycombe, UK. e-mail: lwolfson@its.jnj.com

**Background:** The objective of this study was to evaluate the cost-effectiveness of adding bedaquiline to the intensive phase of the background regimens (BR) of drugs for multidrug-resistant tuberculosis (MDR-TB) in the UK (UK).

**Design/Methods:** A cohort-based Markov model was developed to estimate the incremental cost-effectiveness ratio of bedaquiline plus BR (B+BR) versus BR alone (BR) in the treatment of MDR-TB in the UK, over a 10-year time horizon. A National Health Service (NHS) and personal social services perspective was considered. The effectiveness of treatment was evaluated in terms of Quality Adjusted Life Years (QALYs) and Disability Adjusted Life Years (DALYs). Data were sourced from a phase II, placebo controlled trial of bedaquiline, NHS reference costs, and the literature; the US list price of bedaquiline was used and converted to pounds (£

18,800). Costs and effectiveness were discounted at a rate of 3.5% per annum. Probabilistic and deterministic sensitivity analysis was conducted.

**Results:** The total discounted cost per patient on B+BR was £107,123, compared with £116,616 for BR. The total discounted QALYs per patient were 4.85 for B+BR and 3.81 for BR. The addition of bedaquiline to a BR resulted in a cost-saving of £9,493 and an additional 1.04 QALYs pp over a 10-year period, and is therefore considered to be the dominant (less costly and more effective) strategy over BR. B+BR remained dominant versus BR in the majority of sensitivity analyses, with a 74% probability of being dominant versus BR in the probabilistic analysis.

**Conclusion:** In the UK, bedaquiline is likely to be cost-effective and cost-saving, compared to the current standard of care for MDR-TB under a range of cost scenarios. Cost-savings over a 10 year period were realized from reductions in lengths of hospital stay, which offset the bedaquiline drug costs. Bedaquiline remained cost-saving in several sensitivity analyses, thus highlighting the certainty surrounding the results of the model. These results also indicate that the B+BR regimen can provide significant social economic benefits versus the BR only regimen

#### OAP-241-30 High rate of successful outcome of a nine-month standardised treatment of multidrug: resistant tuberculosis in Niger

B Souleymane,<sup>1</sup> S Hassane Harouna,<sup>1</sup> A Piubello,<sup>1</sup> S Morou,<sup>1</sup> I Boukary,<sup>1</sup> T Sanda,<sup>2</sup> D Fundi,<sup>3</sup> A Van Deun.<sup>4,5</sup>

<sup>1</sup>Tuberculosis, Damien Foundation, Niamey, <sup>2</sup>Central Unity, National Tuberculosis Program, Niamey, <sup>3</sup>Tuberculosis, International Federation of Red Cross and Red Crescent Societies, Niamey, Niger; <sup>4</sup>Tuberculosis, International Union Against Tuberculosis and Lung Disease, Paris, France; <sup>5</sup>Mycobacteriology, Institute of Tropical Medicine, Antwerp, Belgium. e-mail: bachirsoul@gmail.com

**Background:** MDR-TB program in Niger declared a high rate (89.2%) of successful and relapse-free outcome with a 12-month treatment from 2008 to 2010 in 65 patients. The aim of this observational study is to evaluate the effectiveness of a 9-month standardized treatment for patients with proven MDR-TB previously untreated with second-line drugs.

**Methods:** Between January 2011 and December 2012, 48 consenting suspect patients were enrolled on a 9-month standardized regimen with high-dose gatifloxacin, clofazimine, ethambutol and pyrazinamide throughout, supplemented by kanamycin, prothionamide and high-dose isoniazid during the intensive phase for a minimum of 4 months. Smear, culture, identification and susceptibility testing were performed at start of treatment and patients were monitored bacteriologically monthly. Follow up after cure will be continued for 24 months.

**Results:** A total of 48 patients started the treatment; 14 with non-proven MDR-TB were excluded from analysis (12 culture negative and 2 with other mycobacteria). Thirty-four cases with proven MDR-TB (24 failures of

retreatment and 10 relapses after retreatment) were analyzed for treatment outcome. Twenty-eight (82.4%) were males; median age was 28 years (range 17–49). All the patients accepted to undergo an HIV test and 4 (11.8%) were positive; sixteen (47.1%) were severely or very severely underweight and 7 (20.6%) were underweight. All the subjects had bilateral radiological disease, 18 (52.9%) with cavities, while 27 (79.4%) had 2+ or 3+ acid-fast bacilli sputum smears. We found 2 strains with resistance to ofloxacin and none to kanamycin. Cure was obtained for 30 patients (88.2%; 95% CI: 77.4–99), 3 died during the early intensive phase (8.8%) and 1 defaulted (2.9%). The major adverse event was vomiting (N=17; 50%) during the first days of treatment, hearing impairment (N=4; 11.8%) and hyperglycaemia (N=2; 5.9%). Kanamycin was replaced by capreomycin in one patient because of hearing loss. Twenty (66.7%) patients completing 6 months follow up after cure remained negative on smear and culture, 7 (23.3%) are waiting for culture result, 2 (6.7%) moved to other jurisdiction and 1 (3.3%) with low initial resistance (2mg/L) to ofloxacin and resistance to pyrazinamide, relapsed.

**Conclusion:** A 9-month standardized treatment for MDR-TB appears to be as promising as a 12-month treatment in a resource-constrained setting with low HIV prevalence and little exposure to second-line drugs.

#### OAP-242-30 Effect of acquired resistance to second line anti-TB drugs on treatment outcomes among multidrug-resistant (MDR-TB) patients from eastern Europe

J Ershova,<sup>1</sup> E Kurbatova,<sup>1</sup> T Dalton,<sup>1</sup> G Volchenkov,<sup>2</sup> V Leimane,<sup>3</sup> K Kliiman,<sup>4</sup> B. Kazenny,<sup>5</sup> P Cegielski.<sup>1</sup>

<sup>1</sup>Tuberculosis Elimination, U.S. Centers for Disease Control and Prevention, Atlanta, GA, USA; <sup>2</sup>Tuberculosis, Vladimir Oblast Tuberculosis Dispensary, Vladimir, Russian Federation; <sup>3</sup>Tuberculosis, Riga East University Hospital Centre of Tuberculosis and Lung Diseases, Riga, Latvia; <sup>4</sup>Tuberculosis, Tartu University Hospital, Tartu, Estonia; <sup>5</sup>Tuberculosis, Orel Oblast Tuberculosis Dispensary, Orel, Russian Federation. Fax: (+1) 404 639 1566. e-mail: jhe3@cdc.gov

**Background:** The Preserving Effective Tuberculosis Treatment Study (PETTS) is a prospective, observational cohort study of MDR-TB patients enrolled during 2005–2008 in 9 countries designed to determine the rate of, risk factors for, and consequences of acquired resistance (AR) to second-line drugs (SLD) during treatment. In this study we described impact of AR to SLD on treatment outcomes among MDR-TB patients from Eastern Europe.

**Design/Methods:** Adults with pulmonary MDR-TB at the start of SLD treatment were enrolled in Estonia, Latvia and Russia. Drug susceptibility tests (DST) were performed at CDC. AR was defined as drug resistance at the last DST after susceptibility to the same drug at the baseline DST, confirmed by genotyping as the same strain. AR to SLD was analyzed in relation to treatment outcome using standard WHO definitions and modified univariate Poisson regression with robust error variance.



**Results:** Among 346 patients, 285 had both baseline and follow-up isolates. Of these, 172 had initial and final DST results at CDC. Of 172 patients, 30 (17%) had resistance to any fluoroquinolone (FQ) at the start of treatment, 70 (41%) to any injectable SLD (SLI) and 15(9%) had XDR-TB. Among those without baseline resistance, 11/142 (8%) acquired resistance to FQ, 14/102 (14%) to SLI and 12/157 (7.6%) acquired XDR-TB. Patients with AR had consistently worse outcomes compared to patients who started with resistance to the same drug(s) at baseline and those without any resistance to the drug(s). Patients with AR to FQ had poor outcome (failure or death) in 67% cases versus 46% among patients with baseline resistance to FQ and 16% among those without any resistance to FQ ( $p<0.0001$ ). Acquisition of XDR led to failure or death in 70% cases compared to 50% among patients with baseline XDR and 19% among those without any XDR ( $p<0.0001$ ). Patients with AR to SLI, similar to patients with resistance to SLI at the start of treatment, had poor outcome in 33% of cases compared to 18% of cases among patients without any SLI resistance ( $p=0.06$ ).

**Conclusion:** Acquisition of resistance to SLD was associated with significantly worse treatment outcomes among MDR-TB patients in Eastern Europe countries. Repeat DSTs to SLD during treatment of MDR-TB cases are essential to maintain an adequate regimen and improve treatment outcomes.

#### **OAP-243-30 Efficacy and safety of MDR-TB clofazimine containing regimen: the Brazilian cohort experience**

M P Dalcolmo,<sup>1</sup> R Gayoso,<sup>1</sup> J Braga Ueleres,<sup>1</sup> J Rocha,<sup>1</sup> L Borgia,<sup>1</sup> J Keravec.<sup>2</sup> <sup>1</sup>ENSP, Oswaldo Cruz Foundation (FIOCRUZ), Rio de Janeiro, RJ, Brazil; <sup>2</sup>GDF-WHO, MSH/GDF-WHO, Geneva, Switzerland.  
e-mail: regina.gayoso@yahoo.com.br

**Background:** Patients with multidrug-resistant tuberculosis (MDRTB) have been treated with standardized regimens for 20 years in Brazil. In early 2000s, the regimen was based on an injectable agent (amikacin), one fluoroquinolone (ofloxacin and then levofloxacin), ethambutol, terizidol, and clofazimine. In 2005, following WHO recommendation clofazimine (CFZ) was discontinued and replaced by pyrazinamide (PZA). Although it is justified, many researchers have pointed out that this change may have contributed to increase toxicity without extending the effectiveness of the treatment. In order to add knowledge about the safety and effectiveness of MDRTB treatment, we studied 2723 patients (1697 using CFZ and 1026 using PZA) treated as outpatients in the reference facility, in Rio de Janeiro, from 2000 to 2010.

**Methods:** Patients' clinical outcomes (cure and adverse effects) from these two groups were compared using a non-concurrent quasi-experimental design. Data analysis compared cure rates and adverse effects controlled for individual (age, sex, education, alcohol consumption and illicit drugs use), clinical (comorbidities, HIV infection)

and care (directly observed therapy - DOTS). Independent effect measured by odds ratio, considering a significance level of 5%, was obtained by multiple logistic regression model.

**Results:** Patients were on average 39 years old, predominantly male (66%), most had less than 7 years of education (56%), and 45% received DOTS. Ten percent were alcoholics, 4% drugs abusers, and 7% were diabetic. There was no difference in cure rates in the treatment groups, but patients with DOTS had a higher cure rate than those without supervised treatment. Although studied factors were also associated with favorable outcome in this study, such as patients' age and HIV infection, the treatment group with the CFZ-containing regimen had a lower risk of severe adverse events (grades 3 or 4) with an adjusted OR=0.26, 95%CI (0.09 to 0.79) controlled for alcohol consumption, use of illicit drugs and supervised treatment.

**Conclusions:** These findings indicate that the therapeutic regimen based on CFZ is safer than PZA based one. In addition, there is no evidence that the CFZ regimen is less effective than treatment with PZA. As our experience indicates an increasing number of MDRTB patients with comorbidities and HIV infection, it is possible that the use of clofazimine may represent a safer therapeutic alternative in the management of such cases.

#### **OAP-244-30 Preliminary results with a 9-month regimen for multidrug-resistant tuberculosis (MDR-TB) in francophone Africa**

V Schwoebel,<sup>1</sup> C Kuaban,<sup>2</sup> Z Kashongwe Munogolo,<sup>3</sup> V Fikouma,<sup>4</sup> T Ndikumana,<sup>5</sup> S Hassane Harouna,<sup>6</sup> A Bakayoko,<sup>7</sup> A Trébucq.<sup>1</sup> <sup>1</sup>TB & HIV, The Union, Paris, France; <sup>2</sup>Medicine, University, Bamenda, Cameroon; <sup>3</sup>Medicine, University, Kinshasa, Democratic Republic of Congo; <sup>4</sup>Medicine, University, Bangui, Central African Republic; <sup>5</sup>Programme National Intégré Lèpre Tuberculose, Ministry of Health, Bujumbura, Burundi; <sup>6</sup>TB multirésistante, Action Damien, Niamey, Niger; <sup>7</sup>Pneumo-Phtisiology, CHU Treichville, Abidjan, Côte D'Ivoire.  
e-mail: vschwoebel@theunion.org

**Background:** A 9-month regimen (4KmMfxPtoHCfzEZ / 5MfxCfzEZ) for multidrug-resistant tuberculosis (MDR-TB) has proven successful in Bangladesh. We report preliminary results from an observational cohort study coordinated by The Union which aims to evaluate the effectiveness and tolerance of this regimen in 9 countries of francophone Africa.

**Methods:** The study started in 2013 in Benin, Burundi, Cameroon, Côte d'Ivoire, Niger, Central African Republic and Democratic Republic of Congo. Patients receive treatment under strict daily observation after giving informed consent and undergoing standard clinical and laboratory examinations. Follow-up is monthly until treatment completion and 6-monthly thereafter for two years. Number of MDR patients detected and enrolled, and drug stocks are monitored quarterly. Adverse drug events and response to treatment are monitored through individual anonymous databases maintained in each country and controlled for quality by The Union. These

data were used to describe patient characteristics, sputum conversion, and adverse drug events among patients enrolled in 2013.

**Results:** As of 1<sup>st</sup> April 2014, 361 patients had been enrolled. Among the 208 patients enrolled in 2013, 25% were HIV-positive, the median body mass index was 18.1 (range 11.7 – 26.6). Rifampicin resistance was detected by molecular test in 92%. The majority of patients (59%) had prior treatment failure, 31% had relapsed, and 10% were new cases. All had pulmonary TB. At month 4 (M4), the median weight gain was 5 kg; microscopically 74% had negative smears, 13% rare bacilli, 9.5% 1+, and 3.5% 2+ positive smears. By culture, 96% were negative at M4. Twelve patients (5.7%) died, 75% of whom within 2 months of treatment start and 6 of them were HIV-positive. Mild gastric discomfort or vomiting was reported by 43% at M1, with a substantial decrease after M2. Hearing loss  $\leq 70$  decibels (dB) was detected in 16/92 patients, and  $>70$  dB in 9/92 at M4. An abnormal audiogram at baseline was associated with a higher probability of hearing loss at M4.

**Conclusions:** These preliminary results are consistent with a high regimen effectiveness. It shows that follow-up can be managed successfully within the national tuberculosis programme. Among the reported adverse events, hearing loss was the most prominent. Measures were taken for early detection to allow kanamycin dosage reduction where indicated.

### OAP-245-30 Discrepancies between Xpert MTB/RIF rifampicin resistant results and confirmatory tests

E Ardizzoni,<sup>1,2</sup> C Hewison,<sup>2</sup> R Dela Tour,<sup>3</sup> E Sanchez,<sup>4</sup> A Van Deun,<sup>1</sup> F Varaine,<sup>2</sup> B De Jong.<sup>1</sup> <sup>1</sup>Mycobacteriology, Institute of Tropical Medicine, Antwerp, Belgium; <sup>2</sup>Médecins sans Frontières, Paris, France; <sup>3</sup>Medical Department, Médecins sans Frontières, Geneva, Switzerland; <sup>4</sup>TB Department, Epicentre, Paris, France. Fax: (+32) 3 247 63 33. e-mail: eardizzoni@itg.be

**Background:** WHO previously recommended confirming Xpert®MTB/RIF (Xpert) rifampicin (RMP) resistance with another rapid test in low-prevalence populations. The recommendation was recently modified as false resistant results would mostly be due to misidentifications, not technical errors. Unexpected resistant results should now be confirmed by a second Xpert on another specimen. Xpert RMP-susceptible patients should still not be tested by conventional DST. We aim to verify whether the new WHO algorithm for use of Xpert is justified.

**Methods:** All discordant results from one year of Xpert use with MGIT confirmation in three Médecins sans Frontières projects were resolved by LPA and extended sequencing of the *rpoB* gene. From Kenya and Cambodia, only Xpert resistant results were confirmed by MGIT. In Swaziland Xpert was routinely run in parallel with MGIT.

**Results:** In Kenya and Cambodia 41 of 48 Xpert RMP resistant samples were also tested by MGIT. MGIT declared 9 (22%) susceptible. All 7 RMP-resistant by

Xpert from Swaziland were confirmed by MGIT, and of 68 Xpert susceptible, 3 (4.4%) were MGIT resistant. Overall 2 (4.2%) discrepant results due to labeling error were excluded from further testing. Of 46 re-checked Xpert RMP resistant results, 8 (17%) were considered susceptible by MGIT. DNA sequencing confirmed the presence of known RMP-resistance conferring mutations in all the 8 strains with discrepant results between Xpert and MGIT, while LPA detected mutations in 6 (Table 1). All 8 patients were started on MDR treatment based on Xpert RMP results, and 2 were stopped later based on the MGIT result. All 3 Xpert RMP-susceptible/MGIT resistant showed mutations on sequencing, but none on LPA. **Conclusion:** In this experience from the field from 3 countries, Xpert proved 100% technically specific for RMP resistance applying a phenotypic gold standard complemented by DNA sequencing. Confirmation by MGIT could have led to inadequate treatment of 17% of these cases. Two discrepancies were due to mislabeling. Together with the failure of LPA to detect a few resistant patients, our findings support the changed WHO recommendation to confirm by repeating Xpert. However, both Xpert and LPA missed a high proportion of cases detected by systematic MGIT testing in one setting. Phenotypic testing after a susceptible genotypic result in suspected cases can thus be justified. RMP-resistance detected by any technique should lead to initiation of MDR treatment.

Tab. 1 Xpert MTB/RIF results versus confirmatory tests

Project	Xpert RMP result	MGIT RMP	LPA	<i>rpoB</i> sequencing
Cambodia	R	S	delWT8	Leu 531 (TTG)
Cambodia	R	S	delWT2	Pro 511 (CCG)
Cambodia	R	S	delWT7	Cys 526(TGC)
Cambodia	R	S	delWT7	Asp 526(GAC)
Cambodia	R	S	delWT7	Arg 526(CGC)
Kenya	R	S	WT	Pro533(CCG)
Kenya	R	S	WT	Arg511(CGG)
Kenya	R	S	delWT8&7	Val532(GTG), Asn526(AAC)
Swaziland	S	R	WT	Phe572(TTC)
Swaziland	S	R	WT	Phe572(TTC)
Swaziland	S	R	WT	Phe572(TTC)

### OAP-246-30 Unacceptable treatment outcomes among India's initial cohorts of MDR-TB programme

M Parmar,<sup>1</sup> KS Sachdeva,<sup>2</sup> R S Gupta,<sup>2</sup> K Rade,<sup>1,2</sup> R Pant,<sup>3</sup> A Sreenivas,<sup>1</sup> P Dewan.<sup>4</sup> <sup>1</sup>Communicable Diseases, World Health Organization Country Office for India, New Delhi, <sup>2</sup>Central TB Division, Ministry of Health and Family Welfare, Government of India, New Delhi, <sup>3</sup>Biostatistics, Public Health Foundation of India, Hyderabad, <sup>4</sup>Communicable Diseases, Bill & Melinda Gates Foundation, India Country Office, New Delhi, India. e-mail: parmarm@searo.who.int

**Background:** Globally, India has world's highest burden of multidrug-resistant tuberculosis (MDR-TB). Programmatic Management of MDR-TB (PMDT) in India began in 2007 and nationwide coverage achieved in early 2013. While rapid scale-up continues, poor initial microbio-

logical outcomes in initial cohort prompted detailed analysis.

**Objective:** To evaluate initial sputum culture conversion, culture reversion and final treatment outcomes among MDR TB patient registered nationwide from 2007–2010. Patients were offered MDR-TB diagnosis if they failed treatment with first-line anti-TB drugs, and were treated with a standard 24-month regimen by daily-observed treatment.

**Methods:** Retrospective cohort study. Clinical and microbiological data were abstracted from PMDT records. Initial sputum culture conversion, culture reversion and treatment outcomes were defined by standard WHO definitions. Proportional hazards' modelling was used to evaluate factors associated with non-conversion of sputum culture, controlling for demographic and clinical characteristics.

**Results:** Among 3713 MDR TB patients registered, 2714 (74%) had initial sputum culture conversion at 100 median days (IQR 92–125), of which 511 (19%) had culture reversion at 279 median days (IQR 202–381). Each prior round of TB treatment was associated with 1.4 times increased hazard for non-conversion (95% CI 1.2–1.6). Among, 2208 cases with treatment outcomes available, 785 (36%) had treatment success, 645 (29%) died, 647 (29%) defaulted, 101 (4%) failed and 23 (1%) changed to XDR TB treatment. Among a sub-set of 107 consecutive MDR-TB patients from 2007 with baseline SLDST results from a reference laboratory, fluoroquinolone (FQ) resistance was detected amongst 63 (66% tested isolates); resistance to FQ and kanamycin (XDR TB) was uncommon (6 patients, 6%).

**Discussion:** In this patient cohort with extensive prior TB treatment experience, a quarter of patients never culture-converted, and a fifth of those who culture-converted subsequently reverted to culture positive. Poor culture conversion was associated with increasing prior TB treatment experience. Treatment outcomes were discouragingly poor, with most patients dying or defaulting. India's MDR TB programme urgently needs revision and strengthening, including early detection through rapid molecular tests, second-line DST at baseline to all MDR TB patients, appropriate DST-guided treatment regimens, and intensified adherence and social support.

### OAP-247-30 Treatment of drug-resistant pulmonary tuberculosis: the clinical effectiveness and tolerability of fluoroquinolones including gemifloxacin

V Petrenko,<sup>1</sup> G Radysh,<sup>1</sup> V Krasiuk,<sup>1</sup> N Rybak,<sup>2</sup> T Flanigan.<sup>3</sup> <sup>1</sup>Tuberculosis and Lung Diseases Department, Bogomolets National Medical University, Kyiv, Ukraine; <sup>2</sup>Dept of Infectious Diseases, Alpert Medical School of Brown University/Rhode Island Hospital, Providence, RI, <sup>3</sup>Dept of Infectious Disease and Immunology, Alpert Medical School of Brown University/ Miriam Hospital, Providence, RI, USA. Fax: (+1) 401 444-5650. e-mail: tasharybak@gmail.com

**Background:** As multi-drug resistant tuberculosis (MDR-TB) has been increasing in recent years additional active therapies against tuberculosis including fluoroquino-

lones have been used. Fluoroquinolones such as ofloxacin and levofloxacin are used more commonly for tuberculosis therapy but less is known about other fluoroquinolones including gemifloxacin. This study aimed to evaluate gemifloxacin effectiveness and tolerability in comparison to ofloxacin, levofloxacin and gatifloxacin during the intensive phase of the anti-tuberculosis therapy of drug resistant tuberculosis.

**Design/Methods:** We evaluated 156 drug resistant TB patients who were followed prospectively after being divided into 2 groups with similar drug resistance profile. The 1<sup>st</sup> group received an anti-TB drug regimen containing gemifloxacin, while the second group received a similar anti-TB drug regimen with another fluoroquinolone; ofloxacin, levofloxacin, or gatifloxacin. The assessment of treatment effectiveness was made using the rate of smear conversion, healing of pathologic X-ray findings and resolution of clinical signs of active tuberculosis. The tolerability including side effects was also recorded for all regimens.

**Table 1. Comparative results of treatment effectiveness after the initial phase and treatment outcomes at the end of the continuation phase**  
(absolute and relative frequency, 95% confidential intervals)

Treatment results	Group and number of cases									
	I (n=78)					II (n=78)				
	Gmx		Gfx (n=26)		Lfx (n=26)		Ofx (n=26)		All (n=78)	
	abs	%	abs	%	abs	%	abs	%	abs	%
<b>Treatment effectiveness</b>										
Improvement in clinical signs and symptoms of TB	65	83#	24	92 <sup>off</sup>	23	88#	17	65	64	82
	(73,3; 92,7)		(77,1; 100,0)		(70,9; 100,0)		(41,8; 88,2)		(72,1; 91,9)	
Smear conversion	62	79 <sup>off</sup>	22	85 <sup>off</sup>	21	81	15	58	58	74
	(68,5; 89,5)		(66,6; 100,0)		(61,2; 100,0)		(34,1; 82,0)		(62,8; 85,2)	
Healing of pathological X-ray findings	58	74 <sup>off</sup>	20	77 <sup>off</sup>	20	77 <sup>off</sup>	13	50	53	68
	(62,8; 85,2)		(56,0; 98,0)		(56,0; 98,0)		(25,8; 74,2)		(56,2; 79,8)	
No smear conversion	16	20 <sup>off</sup>	4	15 <sup>off</sup>	5	19	11	42	20	26
	(9,7; 30,3)		(0; 33,4)		(0; 38,8)		(18,1; 65,9)		(14,8; 37,2)	
<b>Treatment outcomes</b>										
Cured	62	80 <sup>off</sup>	21	81	20	77	13	50	59	69
	(68,5; 90,3)		(61,2; 100,0)		(56,0; 98,0)		(25,8; 74,2)		(57,3; 80,7)	
Failed	4	5	1	4	0	0	1	4	2	2
	(0; 11,2)		(0; 15,9)		-		(0; 15,9)		(0; 6,4)	
Defaulted	5	6	1	4	1	4	1	4	4	5
	(0; 12,6)		(0; 15,9)		(0; 15,9)		(0; 15,9)		(0; 11,2)	
Died	7	9*, <sup>off</sup>	3	12	5	19	11	42	19	24
	(1,3; 16,7)		(0; 29,1)		(0; 38,8)		(18,1; 65,9)		(13,1; 34,9)	

Gmx – gemifloxacin, Gfx – gatifloxacin, Lfx – levofloxacin, Ofx – ofloxacin

\* – significant difference in comparison to the II group (p<0,05)

<sup>off</sup> – significant difference in comparison to the II-Ofx group (p<0,05)

# – approaching significant difference in comparison to the II-Ofx group (p=0,05)

**Results:** All four fluoroquinolones were well tolerated as anti- TB therapy. Gemifloxacin efficacy in the treatment



regimen for drug resistant TB patients did not differ from the effectiveness of other fluoroquinolones of the 3<sup>rd</sup>-4<sup>th</sup> generation, as 78% of patients in the gemifloxacin group vs. 74% of patients in the other quinolone group converted to smear negative. In this study, patients treated with ofloxacin did poorer than others with lower rates of smear conversion and cure and higher rates of death.

**Conclusion:** 1) All of the fluoroquinolones were well tolerated and gemifloxacin had a similar tolerability profile as other fluoroquinolones used for tuberculosis treatment. 2) Despite small numbers gemifloxacin seemed to have similar effectiveness as the other fluoroquinolones for TB outcomes such as smear conversion and cure. Despite these small numbers this study demonstrates that further analysis of effectiveness of different fluoroquinolones in TB treatment is warranted especially in light of growing drug resistant strains.

## 07. CLEARING THE SMOKE: THE SYNERGISTIC ROLE OF THE FCTC AND MPOWER

### OAP-248-30 Smoke-free legislations in sub-Saharan African countries: progress update

M Oluwasanu,<sup>1</sup> O Adetokunboh.<sup>2</sup> <sup>1</sup>Health Promotion and Education, University of Ibadan, Ibadan, Nigeria;

<sup>2</sup>Interdisciplinary Health Sciences, Stellenbosch University, Cape Town, South Africa. e-mail: ope3m@yahoo.com

**Background** Exposure to second hand smoke is a major contributor to deaths, diseases and disabilities associated with the tobacco epidemic. There is strong scientific evidence that Smoke-free indoor workplaces and public places can reduce the burden associated with tobacco use and this has been recognized as a best buy intervention. Many African countries are signatories to the WHO Framework Convention on Tobacco Control (FCTC) which came into force in 2005 and stipulates that countries pass measures that provide universal protection from tobacco smoke in all indoor public places, indoor workplaces, and public transport within five years of entry into force of the treaty for that country. The objective of this study is to assess the extent of development and ratification of smoke free legislations in forty three (43) sub-Saharan African countries (SSA), nine years after the FCTC came into force.

**Design/Methods:** The data for this study was obtained from the 2013 World Health Organisation (WHO) Global Health Observatory Data Repository. The data on selected indicators for smoke free legislations (2007–2012) in 43 SSA countries was extracted and analyzed using descriptive statistics. The trend in the formulation of policies on the selected indicators was assessed.

**Results:** The percentage of SSA countries with national smoke free legislation from 2007 to 2012 was (27.9% to 41.9%) for health care facilities; education facilities

except universities (18.6% to 37.2%); universities (2.3% to 25.6%), government facilities (14% to 30.2%), indoor offices (9.3% to 18.6%), restaurants (2.3% to 14%), bars and pubs (0% to 14%) and public transport (9.3% to 30.2%). Twenty three countries (53.5%) had no national smoke free legislation for any of the indicated public places.

**Conclusion:** African countries have recorded some progress in enacting laws on second hand smoke however; many of the population are yet to be protected because there are no legislations declaring all public places in these countries smoke free. There remains a lot to be done in enlisting meaningful political priority for ensuring comprehensive smoke free legislations in these countries. Key stakeholders must intensify efforts in ensuring the legislation of comprehensive smoke-free legislation and there is need for research to assess the extent of enforcement. SSA countries must be accountable to the principles, guidelines and timelines set out in the WHO Framework Convention on Tobacco Control (FCTC).

### OAP-249-30 Cigarettes pricing in India: impact of tax raise in 2009–2014

A Pandey,<sup>1</sup> P Lal,<sup>2</sup> R Kumar.<sup>2</sup> <sup>1</sup>Operations, International Union Against Tuberculosis and Lung Diseases, New Delhi,

<sup>2</sup>Tobacco Control, International Union Against Tuberculosis and Lung Diseases, New Delhi, India.

e-mail: apandey@theunion.org

**Background** India is home to 118 million smokers of which 45.6 million are cigarette smokers. Global evidence points that tax increases is the single most effective intervention to reduce demand for tobacco products. In India, above the central excise tax (levied at the factory gate), states administer a value added tax (VAT) which varies from 65% (in Rajasthan) to 12.5% (in Arunachal Pradesh). While the tax incidence on cigarettes in all states falls below the 66–80% target recommended by the World Bank, tax rates on cigarette in the region are even more inappropriate with respect to consumers' affordability. In the past five years, several states have increased VAT intermittently, and this has the potential to impact local consumption in the long term.

**Intervention** Tax structure on cigarette, its pricing and volume (in million stick) were reviewed through government and industry level data available in public domain. Lessons learnt By measuring the affordability of cigarettes in 11 states of India, the implication for taxation of tobacco products is assessed. The following are the broad findings: 1: High VAT rates do not necessarily translate in same proportion to raising retail prices for cigarettes across states. 2: Cigarette industry monitor prices carefully and raise prices at the time consumers are anticipating (usually twice a year) and therefore in real terms per pack and per stick price of cigarette seldom changes.

**Conclusions** The effect on overall tobacco consumption is likely to be only modest if any. Evidences show that there is a need for substantial continuous increases in taxes on tobacco products to show public health benefits.

The Government of India and states together can establish a benchmark to achieve 'tax consistency' for cigarettes for every segment. Affordability must also be measured by assigning appropriate weights (i.e. the absolute level of excise relative to income as opposed to percentage measures of tax incidence).

### **OAP-250-30 The supply chain of smokeless tobacco in south Asia: Is it feasible to analyse it?**

A Khan,<sup>1</sup> R Huque,<sup>2</sup> K Scammell,<sup>3</sup> K Siddiqi.<sup>4</sup> <sup>1</sup>Public Health, The Initiative, Islamabad, Pakistan; <sup>2</sup>Economics, University Of Dhaka, Dhaka, Bangladesh; <sup>3</sup>Public Health, University of York, York, <sup>4</sup>Department of Health Sciences/Hull York Medical School, University of York, York, UK.  
e-mail: aminakhan67@gmail.com

**Background:** Over 250 million people use smokeless tobacco (SLT) products in South Asia (SA). Despite their popularity little information is available on the supply chain of SLT products, making it difficult for policy makers to develop effective control measures and implement Framework Convention for Tobacco Control (FCTC). We assessed the feasibility of conducting a large multi-country study investigating the supply chain of SLT in SA and test the appropriate data collection tools and methods to be used in future.

**Design/Methods:** We interviewed 130 actors from point of sale retailers, wholesalers, manufacturers, raw tobacco dealers and farmers involved in the supply chain of SLT in Bangladesh, Nepal and Pakistan. The first group was the SLT retailers, who were recruited using purposive sampling. Other actors were identified and interviewed using mainly snowball sampling technique. The questions were tailored for each type of actor, asking specifically about their customers; products; marketing practices; suppliers; profit margins, awareness and adherence to legislation.

**Results:** All categories of actors involved in the supply chain were identified. The supply chain was not found to be linear, as most of the actors have multidirectional involvement. For example, retailers tend to buy from the wholesalers as well as the manufacturers directly. On the other hand, farmers sell their products directly to wholesalers, manufacturers, retailers and raw tobacco dealers. Our findings indicate, illicit trade making a substantial impact on the prices and availability of various SLT products. The common reasons identified by the retailers and wholesalers for the sales of SLT were its cheap price, good profit margins and high demand. According to the retailers, raw tobacco dealers and farmers, customer volumes have increased considerably in the last five years along with increase in the sale of SLT. It was found that competition among different types of suppliers in the market is increasing day by day due to the expansion in SLT trade.

**Conclusion:** SLT products manufacturing, marketing and sale is on the increase and the supply chain is complex due to the involvement of a number of actors. It is possible to identify and interview these actors and use the information to regulate SLT supply chain. Valuable

information was obtained to inform recruitment strategies and refinements in data collection tools in order to design a larger multi-country study in SA in future.

### **OAP-251-30 Documentation of tobacco advertising, promotion and sponsorship in Bangladesh**

M E H Bhuiyan,<sup>1</sup> A Sikder.<sup>2</sup> <sup>1</sup>Tobacco Control, Environment Council Bangladesh, Dhaka, <sup>2</sup>Management, Environment Council Bangladesh, Dhaka, Bangladesh.  
e-mail: emdadhaque2021@gmail.com

**Background:** Although direct advertisements of tobacco products are restricted in Bangladesh, high level of indirect marketing including advertisement at point of sale (POS) are going on. Aim: To investigate the different ways of TAPS activities in Bangladesh.

**Methods:** A cross sectional survey was conducted in selected nine districts in Bangladesh during the months of February to June 2013. Both quantitative and qualitative methods were used to identify and collect information on the ongoing TAPS. KII and FGD were also done among the shop owner or salesperson or tobacco companies staff/representatives, tobacco promoters, anti tobacco activists' and tobacco users regarding the tobacco advertisement ways in the locality.

**Results:** Interviews were conducted among 1686 respondents from 9 districts (Urban: 1159, Rural: 527). About 38% of the cigarette box or the showcases at point of sale were supplied by the tobacco companies. Almost all shops (99.4%) having POS for tobacco were visited by the sales representatives from various tobacco companies in the last one month for promoting their brands. A very high proportion of sales person at POS (68.8%) had proposition of gift from tobacco companies. Tobacco industries mostly offered free cigarettes as gift (72.5%) and 33% of POS also had cash money offer. While for smokeless tobacco there were very few gift offerings to sales person. 27.9% retailers received shop decoration material for promoting tobacco sale and 60% of the surveyed shops had visible flyer decorating the area, 48.5% had poster displayed, 77.2% had visible decorative items made of cigarette packets, 32.3% had large dummy cigarette packets. 7.4% of the retailers reported that tobacco companies had provided scholarship to the poor students. Activities in the name of corporate social responsibilities (CSR) were done in the area especially high tobacco cultivation areas.

**Conclusion:** This investigative survey has documented that tobacco companies are actively involved in promotion of their products and advertisement at POS has become the mainstay along with CSR activities. Bangladesh needs to strengthen enforcing mechanism of recently amended tobacco control act for addressing ban on indirect advertisements.

### OAP-252-30 A study on compliance to smokefree rules in Mizoram: analysis of 3 compliance studies (2009–2013)

J Ralte,<sup>1</sup> R J Singh,<sup>2</sup> L Lalnuntluangi,<sup>3</sup> Zo Chhakchhuak,<sup>4</sup> H Renthlei.<sup>5</sup> <sup>1</sup>Health & Family Welfare, Mizoram State Tobacco Control Society, Aizawl, <sup>2</sup>The Union, The Union South-East Asia, New Delhi, India, <sup>3</sup>Health & Family Welfare, NPCDCS, Aizawl, <sup>4</sup>Health & Family Welfare, Mizoram State AIDS Control Society, Aizawl, <sup>5</sup>Management, Mizoram University, Aizawl, India. e-mail: tluangtlei@gmail.com

**Background:** Mizoram, a tiny predominantly tribal populated state in Northeast India has adult tobacco use prevalence of 67% (GATS 2009-10); highest in India. Morbidity and mortality related to tobacco use is a major public health concern. It is widely held that tobacco consumption, smoked and smokeless, has cultural origins and is equally accepted. Mizoram State Tobacco Control Society (MSTCS) is the nodal agency implementing smoke-free rules (SFRs) as laid out in Section 4 of the Cigarettes and other Tobacco Products Act (COTPA). The main objective of the study is to find out whether there has been any improvement in compliance to putting up of signage prohibiting smoking and incidence of smoking in public places by analyzing compliance studies conducted in 2009, 2011 and 2013.

**Design/Methods:** Observational surveys were conducted in 2009, 2011 and 2013 by the MSTCS covering 193, 803 and 860 public places respectively in the 8 district headquarters in Mizoram over one month. Multi-level stratified sampling method was used; 95% confidence interval. Public places were categorized into offices, schools/educational institutions, hospitals, hotels/restaurants, halls/markets and others.

**Results:** In 2009, 48% of the public places visited had some form of no-smoking signage put up with none compliant to the specifications of COTPA. In 2011, some form of no-smoking signage was found in 67% of the public places and 84% were compliant. In 2013, 88% of the public places surveyed had some form of signage prohibiting smoking put up and 97% were compliant. Active smoking observed is the single most important variable determining compliance to SFRs. In 2009, active smoking was observed in 61.7% of all venues visited. This figure was down to 18.2% in 2011 and 7.9% in 2013. Presence of cigarette/bidi/zoial (local cigarette) butts is a relevant indicator of smoking in a public place even when active smoking is not witnessed. This variable was introduced in 2011 when cigarette butts were observed in 24.8% of the public places visited. This figure was down to 11% in 2013. In 2011, ashtrays were seen in 8.3% of the public places visited. In 2013, this figure was down to 4.6%.

**Conclusions:** In Mizoram, there has been steady improvement in the number of public places where no-smoking signage is put up. It can be concluded that smoking in public places has also decreased as evidenced by the number of people seen smoking and the number of cigarette butts and ashtrays observed.

### OAP-253-30 Smokefree environments, second-hand smoke, and air quality monitoring: a study across six low- and middle- income countries

F Aslam,<sup>1</sup> K Bleymann.<sup>1</sup> <sup>1</sup>Tobacco Control, The International Union against Tuberculosis and Lung Disease, Edinburgh, UK. e-mail: kbleymann@theunion.org

**Background and Aims:** MPOWER is a policy package intended to assist in the country-level implementation of effective interventions to reduce the demand for tobacco, as ratified by the World Health Organization (WHO) Framework Convention on Tobacco Control. One of the six evidence-based components of MPOWER is 'Protect people from tobacco smoke'. Air quality monitoring is a key tool for measuring second-hand smoke (SHS) levels and hence compliance to smoke-free (SF) laws and regulations. Using a validated, innovative, and low-cost method, we aimed to: (1) visit a selection of hospitality venues covered by existing SF laws in cities across six LMICs and to determine the air quality within these venues, how this compares to air quality outdoors, and to consider what this tells us about compliance with the legislation within that country; (2) use the results in discussions with policy makers at the national and sub-national level about the success of existing SF legislation or the need to strengthen enforcement; and (3) to build capacity in measuring SHS levels and SF law compliance using the Dylos low-cost methodology

**Methods:** Sampling was conducted in 600 hospitality venues covered by existing SF laws in cities across 6 LMICS (Mexico, Chad, Bangladesh, India, Indonesia and Pakistan) to measure SHS levels. Outcomes included air PM<sub>2.5</sub> measurements, recorded using validated Dylos equipment, and observational assessment sheets completed by trained in-country data collectors. Dylos and assessment sheet data were analysed and reported back to in-country teams for use for local policy advocacy.

**Results:** Data were collected for 600 venues. SF law/regulation compliance levels varied between the six countries more than between individual venues. Preliminary findings suggest SF compliance is strong in some of the countries, but not in others. The findings are being used to shape discussions by The Union and in-country partners on existing legislation and for programmatic guidance.

**Conclusions:** The study supports the use of Dylos equipment as an effective, low-cost, and easy-to-use method of measuring air quality levels and, in turn, the effectiveness or otherwise of existing SF laws and regulations. Baseline data also may be used in future to evaluate the impact of advocacy interventions on improving compliance and air quality.



### OAP-254-30 Influence of second-hand smoke exposure at home on acute respiratory conditions of under five children

KK Paul,<sup>1,2</sup> MS Flora.<sup>1</sup> <sup>1</sup>Epidemiology, National Institute of Preventive and Social Medicine (NIPSOM), Dhaka, <sup>2</sup>Centre for Communicable Diseases, International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), Dhaka, Bangladesh. e-mail: kishor\_kp\_61@yahoo.com

**Background:** Acute respiratory infection is a major cause of child mortality and significant amount of morbidity around the globe especially in developing world including Bangladesh. Asthma in children is also a leading cause of emergency department visits and hospitalizations all over the world, which is, occasionally life threatening. The study was done to find out the influence of second hand smoke on acute respiratory illness. **Methodology:** A case-control study was carried out from January to December 2013 on 70 acute respiratory infection and asthma cases, and 70 age- and sex-matched controls at Paediatrics department of three tertiary care hospitals in Dhaka. Data were collected by face to face interview of mothers of the cases and controls using a semi-structured questionnaire and measuring weight and height/length of cases and controls using standard procedure.

**Table 1: Secondhand smoke exposure of cases and controls (in last 7 days)**

Variables	Controls (n = 70) Number (%)	Cases (n = 70) Number (%)	p	OR (95% CI of OR)	AOR (95% CI of AOR)
Secondhand smoke exposure at home					
No <sup>‡</sup>	51 (72.9)	20 (28.6)	<0.001		
Yes	19 (27.1)	50 (71.4)		6.71 (3.20- 14.05)	14.15 (1.57 - 127.33)
Smoking in front of child					
No <sup>‡</sup>	59 (84.3)	41 (58.6)	0.001		
Yes	11 (15.7)	29 (41.4)		3.79 (1.70- 8.45)	0.20 (0.03 - 1.15)
Father's smoking status at home					
No <sup>‡</sup>	53 (75.7)	33 (47.1)	<0.001		
Yes	17 (24.3)	37 (52.9)		4.41 (2.14- 9.09)	0.22 (0.03 - 1.63)
Number of cigarettes smoked at home					
G. Mean	6.49	20.20	<0.001		
± SD	± 12.54	± 18.74			

**Result:** About forty percent enrolled cases, controls were infants (41.1%), and aged above two years (39.3%). About three-fourth of cases (71.4%) of acute respiratory illness were exposed to second hand smoke in last seven days at their home compared to only about one-fourth of controls (27.1%). Cases were about seven times (OR 6.71; 95% CI 3.20-14.05) more likely to be exposed to second hand smoke and four times (OR 3.79; 95% CI 1.70-8.45) more likely to experience smoking of cigarettes in front of them in comparison to controls. On average, three times more cigarettes were smoked in last seven days at the home of cases (20.20±18.74)

compared to the controls (6.49±12.54). After adjusting for other variables the influence of second hand smoke exposure at home on acute respiratory conditions in under five children persisted but dose response relationship disappeared.

**Conclusion:** The main finding in this study is that under five children with acute respiratory conditions including acute respiratory infection and bronchial asthma are more likely to have exposure to secondhand smoke at home compared to those who did not have the condition. Strategies to encourage smoking restrictions at home are likely to protect the health of children from harmful exposure to secondhand smoke.

<sup>‡</sup>Reference group; OR = Odds Ratio; CI = Confidence Interval; AOR = Adjusted OR

### OAP-255-30 Predictors of cessation in smokers suspected of tuberculosis and enrolled in a cluster randomised controlled trial in Pakistan

O Dogar,<sup>1</sup> H Elsey,<sup>2</sup> K Siddiqi.<sup>1</sup> <sup>1</sup>Health Sciences, University of York, York, <sup>2</sup>Faculty of Medicine and Health, Leeds Institute of Health Sciences, Leeds, UK. e-mail: ofd500@york.ac.uk

**Background:** This is the first study to identify predictors of smoking cessation in patients with suspected tuberculosis (TB) treated with behavioural support alone or in combination with bupropion in a cluster randomised controlled trial conducted in Pakistan between 2009 and 2011.

**Design/Methods:** In this trial, health centres in two districts of Pakistan were randomly allocated to receive behavioural support (BSS) therapy (in two sessions over a week), BSS plus a seven-week course of bupropion (BSS+) or usual care (self-help leaflet) in this trial. Multilevel Poisson regression, adjusting for clustering was used to examine baseline variables as predictors of six-month continuous smoking abstinence verified by carbon monoxide. Having known the effect of both interventions on continuous smoking abstinence, these were included in the regression models. This approach allowed us to assess the effect of baseline variables on smoking cessation over and above the effects of both intervention conditions. Relative risks (RR) and 95% confidence intervals (95% CI) were imputed.

**Results:** Participants receiving behavioural support alone or in combination with bupropion were significantly more likely to achieve continuous smoking abstinence at 6 months compared with usual care (RR for BSS+, 8.2 [95% CI, 3.7 to 18.2; p= <0.001]; RR for BSS, 7.4 [CI, 3.4 to 16.4; p= <0.001]). However, old age (RR 0.99 [95% CI, 0.985 to 0.998; p= 0.02]), longer duration of smoking (RR 0.99 [95% CI, 0.983 to 0.997; p= 0.005]) and larger quantities of cigarettes/hookah smoked (RR 0.98 [95% CI, 0.97 to 0.998; p= <0.001]) are associated with reduced likelihood of quitting smoking at 6 months. Age of starting smoking, gender, monthly household income and presence of other smoker(s) at home and/or in workplace, were not significantly associated with continuous smoking abstinence at 6 months.

**Conclusion:** If offered smoking cessation interventions, patients suspected of TB are less likely to quit smoking after six months, if they tend to be older, have been smoking tobacco for many years and in large quantities.

Table: Association of baseline variables with six month continuous smoking abstinence among TB suspects, Pakistan (2009–2011)

Predictor variables	RR (95% CI)	p-value
Intervention: Behavioural support	7.4 (3.4 - 16.4)	<0.001
Intervention: Behavioural support plus bupropion	8.2 (3.7 - 18.2)	<0.001
Older age of the smoker	0.99 (0.985 - 0.998)	0.02
Longer duration of smoking	0.99 (0.983 - 0.997)	0.005
Larger quantity smoked	0.98 (0.97 - 0.998)	<0.001
Early age of starting smoking	1.00 (0.99 - 1.02)	0.3528
Gender	0.87 (0.59 - 1.28)	0.4872
Other smokers at home	1.13 (0.95 - 1.34)	0.1601
Other smokers at workplace	1.23 (0.97 - 1.55)	0.08
Monthly household income	1.00 (0.99 - 1.00)	0.6657

## 08. EVALUATION OF DIAGNOSTICS, DRUGS AND VACCINES

### OAP-256-30 Induction of autophagy by phenylbutyrate in human macrophages is mediated by LL-37 with subsequent killing of *Mycobacterium tuberculosis*

R Rekha,<sup>1,2</sup> SSV Muvva,<sup>3</sup> M Wan,<sup>4</sup> P Bergman,<sup>1</sup> R Raqib,<sup>2</sup> S Brighenti,<sup>3</sup> GH Guðmundsson,<sup>5</sup> B Agerberth.<sup>1</sup>

<sup>1</sup>Laboratory Medicine, Karolinska University Hospital, Huddinge, Stockholm, Sweden; <sup>2</sup>Nutritional Biochemistry Laboratory, International Centre for Diarrheal Disease Research, Bangladesh (icddr), Dhaka, Bangladesh; <sup>3</sup>Center for Infectious Medicine, Karolinska University Hospital, Huddinge, Stockholm; <sup>4</sup>Medical Biochemistry and Biophysics, Karolinska Institutet, Stockholm, Sweden; <sup>5</sup>Biomedical center, University of Iceland, Reykjavik, Iceland. e-mail: birgitta.agerberth@ki.se

**Setting:** Autophagy is a normal lysosome mediated catalytic process that has a significant impact on killing of intracellular pathogens. The human cathelicidin LL-37 is the main mediator of vitamin D3-induced autophagy in human macrophages. In a healthy volunteers trial we have demonstrated that 4-phenylbutyrate (PBA) induces LL-37 expression in synergy with 1,25-dihydroxyvitamin D3 {1,25-(OH) 2D3} in macrophages, which is correlated with enhanced killing of *Mycobacterium tuberculosis* (Mtb). In this study, we aim to explore the mechanism(s) behind PBA-induced autophagy and Mtb-killing.

**Methods:** Human monocyte derived macrophages (MDM) and the monocytic cell line THP-1 were infected with a virulent strain of Mtb (H37Rv) and stimulated with PBA and 1,25-(OH) 2D3 separately or in combination. MDM-mediated killing of Mtb was performed by conventional culture methods. LL-37 knockdown THP-1 cells were generated by using LL-37 specific shRNA plasmid.

**Results:** Mtb down-regulated the expression of LL-37 peptide and transcript in MDM and THP-1 cells and blocked autophagy activation. PBA induced LL-37 expression in MDM, which activated the autophagy-related genes Beclin-1, Atg5 and LC3B-II expression. In LL-37 knockdown THP-1 cells PBA treatment failed to induce autophagy. However, when LL-37 knockdown cells were treated with exogenous LL-37 autophagy was induced. An additive effect of enhanced autophagy was observed when cells are treated with a combination of PBA and 1,25-(OH) 2D3. Intracellular killing of Mtb was significantly increased in PBA and 1,25-(OH) 2D3 treated macrophages.

**Conclusion:** These results suggest that LL-37 exhibits a direct antimicrobial effect on Mtb and is a potent functional molecule of PBA induced autophagy.

### OAP-257-30 Clinical trial of oral phenylbutyrate and vitamin D adjunctive therapy in pulmonary tuberculosis in Bangladesh

R Raqib,<sup>1</sup> A Mily,<sup>1</sup> S M M Kamal,<sup>2</sup> S Brighenti,<sup>3</sup> M Rahim,<sup>1</sup> R Rekha,<sup>1,4</sup> B Agerberth,<sup>4</sup> GH Guðmundsson.<sup>5</sup> <sup>1</sup>Center for Vaccine Sciences, icddr, Dhaka, <sup>2</sup>National Tuberculosis Reference Laboratory, National Institute of the Diseases of the Chest and Hospital, Dhaka, Bangladesh; <sup>3</sup>Center for Infectious Medicine, Karolinska University Hospital Huddinge, Stockholm, <sup>4</sup>Department of Medical Biochemistry and Biophysics, Karolinska Institutet, Stockholm, Sweden; <sup>5</sup>Institute of Biology, University of Iceland, Reykjavik, Iceland. e-mail: rubhana@icddr.org

**Background:** Tuberculosis (TB) caused by *Mycobacterium tuberculosis* (Mtb) is a leading cause of death due to a single infectious agent globally. Multidrug-resistant TB is widespread especially in sub-Saharan Africa and Asia, and is a threat for global health. Thus, novel alternative treatment strategies are urgently needed to combat TB. We have earlier shown that oral 4-phenylbutyrate (PBA) and vitamin D3 (Cholecalciferol, vitD3) supplementation in healthy adults synergistically induce LL-37 expression in macrophages and enhance intracellular killing of Mtb ex vivo.

**Design/Methods:** In a 4-cell, randomized, double-blind placebo-controlled trial in adult Bangladeshi patients with freshly diagnosed smear-positive pulmonary TB, we evaluated the effect of two months oral adjunctive therapy with i) 5000 IU of vitD3 once daily, ii) vitD3 plus twice daily PBA 500mg, iii) PBA 500mg and iv) placebo in improving response to standard short course TB therapy towards a rapid clinical recovery (using scores: cough, chest x-ray, fever, weight, haemoptysis, anorexia, chest pain). Another objective was to evaluate functional measures of alternative treatment outcome in terms of ex vivo killing capacity of macrophages from TB patients, infected in vitro with Mtb. The trial was registered at ClinicalTrials.gov NCT001580007.

**Results:** About 97.5% patients (281 of 288) completed 12 week (wk) follow-up visit, while 12% patients dropped out at 24 wk (n=34). At baseline, ~90% patients had insufficient plasma 25-hydroxy-vitamin D3 [25(OH) vitD3] status (<50 nmol/L). 25(OH) vitD3

concentration increased in patients receiving vitD3 [vitD3, PBA+vitD3] compared to those who did not [PBA, placebo] at wk 4, 8 and 12 ( $P<0.0001$ ). Sputum culture conversion (available from 277 patients) was achieved in 65% patients by 2 wk, 90% patients by 4 wk and 99% patients by 8 wk. There were no differences in culture conversion between the groups. Intriguingly, clinical scores declined earliest in PBA group at week 4 ( $P=0.053$ ) compared to the placebo group, while scores of three groups PB, PBA+vitD3 and vitD3 remained significantly lower than the placebo group ( $P<0.02$ ) at week 10 & 12 (excepting vitD group at wk 12). PB group sustained significantly lower scores at week 24 compared to the other 3 groups. Only vitamin D group showed significantly higher killing capacity of macrophages at week 8 compared to the three groups.

**Conclusion:** The findings indicate that PB alone or in combination with vitD3 given as adjunctive therapy to standard short course TB therapy has the potential to accelerate clinical recovery in newly diagnosed active TB.

#### OAP-258-30 Factors associated with Quantiferon-TB Gold in Tube negative status in South African adults

A Luabeya,<sup>1</sup> Sara Suliman,<sup>1</sup> P Bang,<sup>2</sup> S Hoff,<sup>2</sup> S Zhongkai,<sup>3</sup> P Andersen,<sup>2</sup> M Hatherill,<sup>1</sup> T Scriba.<sup>1</sup>

<sup>1</sup>SATVI, University of Cape Town, Cape Town, South Africa;

<sup>2</sup>Vaccine Development and Infectious immunology, Statens Serum Institut, Copenhagen, Denmark; <sup>3</sup>AERAS, AERAS, Rockville, WA, USA. Fax: (+027) 233465406.

e-mail: aluabeya@gmail.com

**Background:** Several new TB vaccines are being developed to prevent *Mycobacterium tuberculosis* infection and ultimately TB disease. Despite a high level of *Mycobacterium tuberculosis* transmission in South African communities, some adults remain uninfected, as defined by a Quantiferon –TB Gold in Tube (QFT-GIT) negative test.

**Objectives** To identify the factors associated with Quantiferon –TB Gold in Tube negative status in healthy, HIV uninfected adults in a high TB burden region in South Africa.

**Methods:** Participants were screened at baseline for eligibility for a Phase 2a clinical trial of a new TB vaccine (H56:IC / AERAS-456) (Statens Serum Institut, Denmark). Medical history, clinical examination, QFT-GIT tests and laboratory safety parameters were evaluated. Socio-economic, demographic and smoking data were recorded. Univariate and multivariate logistic regression models were used for analysis.

**Results:** We analysed 253 adults, of which 109 were male (43.1%); median age was 26 (IQR: 21–34) years; median body mass index was 24.3 (IQR: 20.5–30.4); 108 were smokers (42.9%) and 109 were working (42.9%). High school education was the highest level of education in most participants ( $n=232$ , 91.7%). 45% ( $n=115$ ) of participants were living in low income housing. Public transport was used by 17.3 % ( $n=44$ ) of participants. Only 69 participants had QFT-GIT negative results (27.6%) at screening. In the univariate analysis, older

participants had lower odds of a negative QFT-GIT result [OR 0.93 (95CI: 0.89 –0.96) ]; while non-smokers [OR 2.54 (95CI: 1.39- 4.63) ] had significantly higher odds of a negative QFT-GIT result. In the multivariate logistic model, age [AOR 0.94 (95% CI 0.90-0.98) ] ( $p=0.01$ ) and non-smoking status [AOR 2.3 (1.2–4.57) ] ( $p=0.01$ ) remained the most significant determinants of a QFT-GIT negative result

**Conclusion:** In high TB burden countries, younger age, consistent with reduced duration of exposure, and non-smoking status, is associated with lower risk of *Mycobacterium tuberculosis* infection as defined by QFT-GIT conversion.

#### OAP-259-30 Pre-clinical evaluation of a replication-deficient intranasal influenza vector vaccine expressing two *Mycobacterium* antigens

A-P Shurygina,<sup>1</sup> B Khairullin,<sup>2</sup> T Vinogradova,<sup>3</sup>

N Zabolotnyh,<sup>3</sup> M Kassenov,<sup>2</sup> J Buzitskaya,<sup>1</sup>

A Nurpeysova,<sup>2</sup> M Stukova.<sup>1</sup> <sup>1</sup>Molecular Virology and Genetic Engineering, Research Institute of Influenza, St. Petersburg, Russian Federation; <sup>2</sup>Vaccine Production, Research Institute for Biological Safety Problems, Gvardeyskiy, Kazakhstan; <sup>3</sup>Experimental Tuberculosis and New Medical Technologies, Saint-Petersburg Research Institute of Phthisiopulmonology, St. Petersburg, Russian Federation. e-mail: shurygina@influenza.spb.ru

**Background:** Tuberculosis is a major global threat to human health. The demand for the development of new tuberculosis vaccines is determined by the non-satisfactory efficacy of the widely used *Mycobacterium bovis* BCG vaccine. As tuberculosis is an airborne disease the ability to induce mucosal immunity is one of the potential advantages of an influenza vector based vaccine against tuberculosis. We developed a novel intranasal influenza vector based vaccine TB/FLU-04L expressing two mycobacterium antigens: Ag85A and ESAT-6.

**Methods:** We generated genetically stable replication-deficient recombinant influenza A strain expressing the ESAT-6 and Ag85A antigens of *M. tuberculosis* from the NS1 reading frame of influenza virus. The vaccine virus was produced in Vero cells cultured under serum free conditions followed by multistep purification. Preclinical studies of safety, immunogenicity and protective efficacy of TB/FLU-04L were performed in different animal models: mice, guinea pigs and cynomolgus monkeys. A vaccine toxicology studies to assess the acute and chronic toxicity were performed in mice, ferrets and rats in preparation for phase I clinical trial.

**Results:** We were able to demonstrate good safety profile of the TB/FLU04L vaccine candidate: it was very well tolerated and did not reveal any toxicologically finding throughout the 50 days observation period. No viral shedding from the respiratory tract in any vaccinated animals was observed. Vaccine had the potency to induce a tuberculosis-specific Th1 immune response in mice and cynomolgus monkeys after one and double intranasal immunizations in three weeks interval. Protective studies have demonstrated a level of protection exceeded to that



induced by BCG vaccine 5 and 20 weeks after virulent *M. tuberculosis* challenge in both murine and guinea pig models of experimental pulmonary tuberculosis. Moreover it was shown that TB/FLU04L vaccine candidate conferred greater protection against tuberculosis in mice than BCG alone when used in a prime-boost regimen.

**Conclusions:** Our findings show that intranasal immunization with new influenza vector vaccine expressing two mycobacterium antigens is safe and induce a protective immune response against virulent *M. tuberculosis*. This approach might be attractive as both alternative to BCG vaccine or an effective way to boost immune protection induced by BCG vaccination.

### OAP-260-30 Designing and conducting a TB trial with an adaptive design: lessons learnt from PanACEA MAMS-TB 01

P Phillips,<sup>1</sup> N Heinrich,<sup>2</sup> S Rehal,<sup>1</sup> G Plemper Van Balen,<sup>3</sup> R Aarnoutse,<sup>3</sup> S Gillespie,<sup>4</sup> M Boeree,<sup>3</sup> M Hoelscher.<sup>2</sup>

<sup>1</sup>Tuberculosis, MRC Clinical Trials Unit at UCL, London, UK;

<sup>2</sup>Infectious Diseases and Tropical Medicine, Medical Centre of the University of Munich (LMU), Munich, Germany;

<sup>3</sup>Tuberculosis, Radboud University Nijmegen Medical Centre/UCCZ Dekkerswald, Nijmegen, Netherlands; <sup>4</sup>Infection, University of St. Andrews School of Medicine, St Andrews, UK. Fax: (+44) 2 076 704 829.

e-mail: patrick.phillips@ucl.ac.uk

**Introduction:** On behalf of the PanACEA consortium. Adaptive designs hold promise for accelerating development of new regimens. In particular, the Multi-Arm Multi-Stage (MAMS) design allows for the evaluation of multiple regimens in one study, saving resources by using a common control arm and by early stopping of arms which do not meet pre-specified thresholds for sufficient efficacy likely to permit treatment shortening.

**Methods:** We designed and implemented PanACEA MAMS-TB-01 as the first TB trial with a MAMS design. The design allowed for the three drug development programmes of SQ109, moxifloxacin and high dose rifampicin to be integrated into one 5-arm phase IIB trial evaluating 4 new combination regimens. Time to stable culture conversion to negative in liquid culture was chosen as the primary endpoint most likely to reflect the ability of a regimen to permit treatment shortening. Interim analyses were to be triggered by a preset number of events on the control arm. Patients were recruited in 7 sites in South Africa and Tanzania. Challenges in study design included modifying the methodology for our context, determining the target hazard ratio for sample size calculations and thresholds for interim analyses, and building adequate data management systems to handle the multiple data sources and facilitate the adaptive design.

**Results:** The interim analysis was successfully performed in February 2014, with the trial steering committee agreeing to terminate further recruitment to two study arms and continue to the remaining two experimental arms and the control. Recruitment was completed ahead of schedule, obviating the need for the second interim analysis. Tablet computers for data entry to a central

database added both speed and complexity to data management. Experience within the team from other MAMS trials assisted with seamless changes to the randomisation lists. A key challenge was timing the interim analysis and coordinating the necessary review and decision meetings. As a result, the overall reduction in sample size was modest. Overcoming the delays inherent in TB culture, data reporting and data cleaning would enhance the efficiency of the MAMS design. A molecular assay in place of a culture-based endpoint and direct data transfer from TB labs to the study database would be tools to overcome such delays.

**Conclusions:** Adaptive designs such as MAMS are feasible for multi-centre TB clinical trials and should be used to speed regimen development.

### OAP-261-30 Diagnostic accuracy of rapid urine LAM test for diagnosing active tuberculosis among in HIV infected adults in Ghana

S Bjerrum,<sup>1,2</sup> E Kenu,<sup>3</sup> M Lartey,<sup>3</sup> M Newman,<sup>4</sup> K.K. Addo,<sup>5</sup> A Bengaard Andersen,<sup>1</sup> IS Johansen.<sup>1</sup>

<sup>1</sup>Department of Infectious Diseases, Odense University Hospital, Odense, <sup>2</sup>Infectious Diseases, University of Southern Denmark, Institute of Clinical Research, Odense, Denmark;

<sup>3</sup>Fevers Unit, Korle-Bu Teaching Hospital, Accra, <sup>4</sup>Department of microbiology, University of Ghana Medical School, Accra,

<sup>5</sup>Department of Bacteriology, Noguchi Memorial Institute of Medical Research, University of Ghana, Accra, Ghana.

e-mail: steph@medicinsk.dk

**Background** Diagnosing HIV-associated tuberculosis (TB) is challenging leaving many cases undetected and delaying antituberculous treatment. The Determine TB LAM test is a lateral flow immunochromatographic test applied directly on urine to detect the mycobacterial lipoarabinomannan (LAM) antigen. We assessed diagnostic accuracy of the Determine TB LAM assay for TB diagnosis at the point-of-care.

**Design/Methods** We prospectively enrolled HIV-infected adults (>18 years) with CD4 cell count  $\leq 350/\text{mm}^3$  from the out and in patient departments (OPD/IPD) at Fevers Unit, Korle-Bu Teaching Hospital, Accra, Ghana. Determine TB-LAM testing was performed on fresh urine with a defined positivity threshold of grade  $\geq 2$  band. Sputum smear microscopy and culture were done for all participants with additional Xpert MTB/RIF assay for in-patients. Our gold standard was a positive culture for *M. tuberculosis* and/or a positive Xpert MTB/RIF. Diagnostic accuracy was calculated for the LAM test alone and in combination with sputum microscopy, and stratified by CD4 cell count and recruitment site.

**Results:** We screened 559 patients of whom 378 were eligible and able to produce 1 - 2 sputum and urine samples. Among participants 317 (85%) were from the OPD and 237 (63%) were female. Median age was 38 and median CD4 count was 102 cells/mm<sup>3</sup>. A total of 47 patients had microbiological confirmed TB (prevalence 12.4%, 95% CI; 9.5–16.2) and Nontuberculous Mycobacteria (NTM) were cultured in 31 cases (prevalence 8.2%, 95% CI; 5.8–11.4). LAM test sensitivity for TB was 49% and specificity 90%, compared to 57% and

98% for sputum microscopy alone. LAM sensitivity did not increase when stratified by CD4<100 or CD4<50 cells/mm<sup>3</sup> respectively, but increased to 53% among in-patients. When LAM assay was used in combination with sputum microscopy, sensitivity increased to 68% overall and 77% among patients with CD4< 50 cells/mm<sup>3</sup>, while specificity dropped to 88% and 80%, respectively. LAM test agreement was high between spot and morning urine test results ( $k=95.8\%$ ) and between two independent readers ( $k=98.9\%$ ).

**Conclusions:** Urine TB LAM test in combination with sputum microscopy is more sensitive than any of the tests used alone, especially among patients with very low CD4 cell count where 77% of TB cases were correctly identified. Misclassification of TB cases due to an imperfect gold standard and LAM test cross reactivity with NTM might explain low specificity, and needs further investigation.

**Table 1. Diagnostic accuracy of urine LAM and/or sputum smear microscopy**

	Sensitivity		Specificity		PPV	NPV
	N	% (95%CI)	N	% (95%CI)	% (95%CI)	% (95%CI)
<b>Determine TB LAM</b>						
All participants (n=378)	23/47	49 (34-64)	297/321	90 (86-93)	40 (28-54)	93 (89-95)
<200 (n=285)	18/38	47 (31-64)	220/247	89 (85-93)	40 (26-56)	92 (87-95)
<100 (n=185)	13/27	48 (29-68)	133/158	84 (76-90)	34 (20-51)	91 (85-95)
<50 (n=133)	6/13	46 (19-75)	99/120	83 (75-89)	22 (9-42)	93 (87-97)
OPD (n=317)*	14/31	45 (27-64)	260/286	91 (87-94)	35 (21-52)	94 (90-96)
IPD (n=57)*	8/15	53 (27-79)	34/42	81 (66-91)	50 (25-75)	83 (58-93)
TB suspect** (n=341)	23/46	50 (35-65)	261/295	86 (84-92)	40 (28-54)	92 (88-95)
<b>Sputum smear microscopy</b>						
All participants (n=378)	27/47	57 (42-72)	324/331	98 (96-99)	79 (62-91)	94 (91-96)
<200 (n=285)	21/38	55 (38-71)	242/247	98 (95-99)	81 (61-93)	93 (90-96)
<100 (n=185)	15/27	56 (35-75)	153/158	97 (93-99)	75 (51-91)	93 (88-96)
<50 (n=133)	8/13	62 (32-86)	115/120	96 (91-99)	62 (32-86)	96 (91-99)
OPD (n=317)*	18/31	58 (39-76)	282/286	97 (97-100)	82 (60-95)	96 (93-98)
IPD (n=57)*	9/15	60 (32-84)	40/42	95 (84-99)	82 (48-98)	87 (74-95)
TB suspect** (n=341)	27/46	59 (43-73)	288/295	98 (95-99)	79 (62-91)	94 (91-96)
<b>Determine TB LAM and/or Sputum smear microscopy</b>						
All participants (n=378)	32/47	68 (53-81)	292/331	88 (84-92)	45 (33-57)	95 (92-97)
<200 (n=285)	26/38	68 (51-83)	217/247	88 (83-92)	46 (33-60)	95 (91-97)
<100 (n=185)	19/27	70 (50-86)	130/158	82 (75-88)	40 (26-56)	94 (89-98)
<50 (n=133)	10/13	77 (46-93)	96/120	80 (72-87)	29 (15-48)	97 (91-99)
OPD (n=317)*	21/31	68 (49-83)	257/286	90 (86-93)	42 (28-57)	96 (93-98)
IPD (n=57)*	10/15	67 (38-88)	33/42	79 (63-90)	53 (29-76)	87 (72-96)
TB suspect** (n=341)	32/46	69 (54-82)	256/295	87 (82-90)	45 (33-57)	95 (92-97)

\*For 4 patients recruitment site was not recorded; \*\*TB suspect defined as a person reporting any one of the symptoms of current cough, fever, weight loss or night sweats according to WHO Guidelines for intensified tuberculosis case-finding and isoniazid preventive therapy for people living with HIV in resource-constrained settings. Geneva, World Health Organization, 2010;

PPV = Positive predictive value; NPV = Negative predictive value; OPD = Out-patient Department; IPD = In-patient Department

## OAP-262-30 A novel serum derived protein signature to distinguish children and adult with active tuberculosis from latent infection and other diseases

S Hamilton,<sup>1</sup> LJM Coin,<sup>2</sup> B Eley,<sup>3</sup> H Dockrell,<sup>4</sup> R Wilkinson,<sup>1,5</sup> RS Heyderman,<sup>6</sup> P Langford,<sup>1</sup> M Levin.<sup>1</sup>

<sup>1</sup>Department of Medicine, Imperial College London, London,

<sup>2</sup>Department of Epidemiology and Biostatistics, Imperial College London, London, UK; <sup>3</sup>Paediatric Infectious Diseases, Red Cross Children's Hospital, Cape Town, South Africa;

<sup>4</sup>Department of Infectious and Tropical Diseases, London School of Hygiene & Tropical Medicine, London, UK;

<sup>5</sup>Institute of Infectious Diseases and Molecular Medicine, University of Cape Town, Cape Town, South Africa;

<sup>6</sup>Paediatric Infectious Disease, Malawi-Liverpool-Wellcome Trust, Blantyre, Malawi. e-mail: s.hamilton@imperial.ac.uk

**Background:** Rapid diagnosis of tuberculosis (TB) is desirable to reduce mortality and more efficiently screen persons at risk. This problem is especially acute in children, as microbiological confirmation is obtained in

less than 40% of cases. In addition, HIV-1 co-infection predisposes to progression of atypical disease and may result in cases showing both tuberculin skin test (TST) and interferon gamma release assay (IGRA) non-reactive. A rapid, sensitive and affordable serological point-of-care diagnostic for TB is urgently needed.

**Methods:** For the biomarker discovery phase, serum samples (n=1020) were collected from children and adults (HIV-1 infected and uninfected) with active TB (culture confirmed), latent TB (IGRA+ and TST+) and control participants (other infections and inflammatory conditions). Participants were recruited from two regions of sub-Saharan Africa with differing patterns of HIV, TB and parasitic infection in an attempt to generalize findings. Proteomic profiles were obtained by Surface-enhanced laser desorption ionisation time-of-flight (SELDI-TOF) mass spectrometry using cationic, anionic and immobilized metal affinity ProteinChip™ arrays.

**Results:** From 10,200 serum protein profiles generated, 701 (children) and 781 (adults) proteins were identified as potentially differentially abundant between patients with active TB versus the combined latent TB and other disease group. Biomarkers of TB infection common to both children and adults were observed. A variable selection method was developed to select the smallest combination of proteins to discriminate active TB from latent TB and other diseases. A signature based on five proteins was found to distinguish TB from LTBI with 92% sensitivity and 95% specificity and OD with over 82% sensitivity and specificity in adults, irrespective of HIV status. In children, a signature based on four proteins can distinguish TB from LTBI and OD with a sensitivity and specificity of 71% and 85%, respectively. **Conclusions:** A minimal set of proteins can distinguish patients with active TB and can be used as a robust signature in the diagnosis of children and adults, irrespective of HIV status or region. We are currently confirming the identity of each protein comprising our signatures and quantifying their expression levels by ELISA. These signatures will then be tested in a larger and more heterogeneous validation cohort.

## OAP-263-30 Systematic review of the determine TB LAM Ag lateral flow urine lipoarabinomannan assay for active TB in people living with HIV: preliminary findings

M Shah,<sup>1</sup> C Hanrahan,<sup>2</sup> K Steingart,<sup>3</sup> S D Lawn,<sup>4</sup> N Dendukuri.<sup>5</sup>

<sup>1</sup>Medicine/Infectious Diseases, Johns Hopkins University, Baltimore, MD, <sup>2</sup>Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA; <sup>3</sup>Cochrane Infectious Diseases Group, Liverpool School of Tropical Medicine, Liverpool, <sup>4</sup>Clinical Research, London School of Hygiene and Tropical Medicine, London, UK;

<sup>5</sup>Epidemiology, Biostatistics, Occupational Health, McGill University, Montreal, QC, Canada.

e-mail: mshah28@jhmi.edu

**Background** Determine TB LAM Ag (LF-LAM, Alere, USA), a lateral flow assay for urine lipoarabinomannan, may have utility for TB diagnosis among HIV-infected patients missed by smear microscopy and Xpert MTB/

RIF. This systematic review assessed the accuracy of LF-LAM for active TB in HIV-infected adults, at different thresholds for test positivity (grades 1 and 2).

**Methods** We searched multiple databases for publications in any language up to 30 December 2013 and contacted Alere and TB researchers. We included RCTs and cross-sectional studies involving HIV-infected adults ( $\geq 15$  years) with and without TB symptoms. We assessed the quality of studies with QUADAS-2. We performed meta-analyses to estimate pooled sensitivity and specificity of LF-LAM against a microbiological reference standard using random-effects models (bivariate model for studies using a common threshold, HSROC for multiple thresholds) and performed subgroup analyses by role of testing (screening or diagnosis) and setting (inpatients or outpatients).

**Results** We included 9 studies involving 4834 participants. All studies were performed in low- or middle-income countries. The conduct of the reference standard may have introduced bias due to variability in the number and type of specimens tested. Moreover, some studies only included selected patients able to produce sputum. We found 1) Screening: grade 1: pooled sensitivity 25% (95% CI 20–30%), pooled specificity, 97% (95% CI 90–99%) (4 studies, 1900 participants); grade 2, sensitivity 39% and 50%, specificity 90% and 99% (2 studies, 955 participants). 2) Diagnosis: grade 1: sensitivity 38–59%, specificity 66–81% (three studies, 1750 participants); grade 2, sensitivity 23–50%, specificity 75–97% (3 studies, 1807 participants). 3) Inpatients: pooled sensitivity 46% (95% CI 41–52%), pooled specificity 94% (95% CI 81–98%) (4 studies, 1719 participants). 4) Outpatients: pooled sensitivity 28% (95% CI 21–35%), pooled specificity 96% (95% CI 89–99%) (7 studies, 3428 participants).

**Conclusions** Although sensitivity of the LF-LAM assay for TB in HIV-infected individuals was low overall, it was considerably higher in inpatients compared with outpatients. This suggests LF-LAM may be most useful in diagnosing TB in sicker patients. Future analyses will examine sensitivity stratified by CD4 counts, explore whether specificity was associated with the quality of the reference standard and define the incremental value of LF-LAM when used with other assays.

## 09. TB AND DIABETES: THE NEW DEADLY DUO

### OAP-264-30 Low isoniazid and pyrazinamide levels in patients with tuberculosis and diabetes mellitus

HK Agibothu Kupparam,<sup>1</sup> G Ramachandran,<sup>1</sup> C Vedachalam,<sup>1</sup> R Vijayalakshmi,<sup>1</sup> VN Azger,<sup>1</sup> L J,<sup>2</sup> K Periaswamy,<sup>2</sup> S Swaminathan.<sup>1</sup> <sup>1</sup>Biochemistry & Clinical Pharmacology, National Institute for Research in Tuberculosis, Chennai, <sup>2</sup>Chennai Corporation, Government of Tamil Nadu, Chennai, India. Fax: (+91) 44 28362528. e-mail: akhemanth20@gmail.com

**Background:** Type 2 diabetes mellitus (DM) is becoming more frequent and is an important co-morbid condition

linked to tuberculosis (TB). Limited information is available on the pharmacokinetics of rifampicin (RMP), isoniazid (INH) and pyrazinamide (PZA) in TB patients with DM.

**Methods:** A prospective cohort study was undertaken in adult patients diagnosed with pulmonary/extra pulmonary TB. These patients were receiving TB treatment with intermittent regimens, at Corporation TB centres in Chennai, India. During the intensive phase of TB treatment, 2-hour plasma concentrations of RMP, INH and PZA were determined after directly observed administration of drugs. Drug concentrations were measured by HPLC. Patients with known DM and those with random blood glucose  $> 200$ mg/dl on the study day were considered as diabetic. Sub-therapeutic values were taken as  $< 7\mu\text{g/ml}$  for RMP,  $< 2\mu\text{g/ml}$  for INH and  $< 20\mu\text{g/ml}$  for PZA.

**Results:** A total of 285 TB patients were recruited; 105 were females, 174 had pulmonary TB, 135 were newly diagnosed with TB and 59 had DM. The DM patients comprised of 14 newly known DM, 14 and 31 respectively with random blood glucose  $<$  and  $> 200$ mg/dl on the study day. Females had significantly higher INH plasma concentrations than males (8.9 vs  $7.4\mu\text{g/ml}$ ;  $p = 0.03$ ). Patients with DM had significantly lower plasma INH ( $7.1$  vs  $8.3\mu\text{g/ml}$ ;  $p = 0.038$ ) and PZA ( $29.8$  vs  $33.5\mu\text{g/ml}$ ;  $p = 0.033$ ). DM patients with blood glucose  $> 200$ mg/dl had lower plasma INH ( $5.8$  vs  $9.1\mu\text{g/ml}$ ) and PZA ( $28.4$  vs  $30.6\mu\text{g/ml}$ ) than those with glucose  $< 200$ mg/dl; the differences did not attain statistical significance. There was a trend towards more diabetic patients having sub-therapeutic INH than non-diabetics (24% vs 14%;  $p = 0.08$ ). Overall, 85%, 16% and 17% of all patients had sub-therapeutic RMP, INH and PZA concentrations respectively. A significant negative correlation between plasma glucose and plasma INH ( $p = 0.003$ ) and PZA ( $p = 0.025$ ) was observed. Multiple regression analysis by stepwise method showed blood glucose significantly influenced plasma INH ( $p = 0.009$ ) and PZA ( $p = 0.025$ ) concentrations.

**Conclusions:** A very high proportion of TB patients on standard thrice-weekly therapy had sub-therapeutic RMP concentrations, which is a matter of concern. Patients with TB and DM, especially those with high blood glucose had lower INH and PZA levels, which have important clinical implications. This cohort is being followed for TB treatment outcomes.

### OAP-265-30 Tuberculosis is frequently diagnosed within 12 months of a diabetes mellitus incidence

EY Heo,<sup>1</sup> N-K Choi,<sup>2</sup> B-R Yang,<sup>2</sup> B-K Koo,<sup>1</sup> SS Hwang,<sup>3</sup> CH Lee,<sup>1</sup> YA Kang.<sup>4</sup> <sup>1</sup>Internal Medicine, Seoul National University College of Medicine, Seoul, <sup>2</sup>Medical Research Collaborating Center, Seoul National University Hospital, Seoul National University College of Medicine, Seoul, <sup>3</sup>Social & Preventive Medicine, Inha University School of Medicine, Incheon, <sup>4</sup>Internal medicine, Yonsei University College of Medicine, Seoul, Republic of Korea. e-mail: mdkang@yuhs.ac

**Background:** Recently, the importance of bidirectional screening for tuberculosis (TB) and diabetes mellitus



(DM) has emerged. Screening for TB in DM patients is important for early diagnosis and improved control of TB. However, the optimum time point for screening DM patients for TB is unclear. Therefore, we conducted a study that aimed to identify not only the incidence of TB but also the trends in its diagnosis in newly diagnosed type 2 DM patients using a nationwide claims database. **Design/Methods:** This was a retrospective cohort study of the claims database of the Health Insurance Review and Assessment Service (HIRA, Seoul, South Korea), a government-affiliated agency that examines the accuracy of claims for National Health Insurance (NHI, which covers ~97% of the South Korean population) and National Medical Aid (covering ~3.5% of the South Korean population). The study population consisted of newly diagnosed type 2 DM patients between January 1, 2009 and December 31, 2009 who were 20 to 89 years of age. The study outcome was a incidence of TB between January 2009 and December 2011 among patients newly diagnosed with type 2 DM. TB incidence rate were estimated using the number of incident TB patients divided by the person-years of follow-up and, also calculated by each of the 6-month periods.

**Results:** We identified 336,078 patients with newly diagnosed type 2 DM in 2009. Among these patients, 4,477 who had ICD-10 codes for TB or anti-TB drug prescriptions before the diagnosis of DM were excluded. Finally, a cohort of 331,601 patients newly diagnosed with type 2 DM in 2009 was identified, and they contributed 831,486 person-years of follow-up until the conclusion of the study in December 2011. TB was newly diagnosed in 1,533 of the 331,601 newly diagnosed type 2 DM patients during the follow-up period. The incidence of TB was  $33/10^4$  patient-years (95% CI 30.0–35.6) in the first 6-months and decreased to  $19/10^4$  patient-years (95% CI 16.5–20.6) in the next 6-month periods. After this periods, the incidence of TB was about  $15/10^4$  patient-years.

**Conclusion:** Patients with newly diagnosed type 2 DM were more likely to have active TB at the time of DM incidence. This result indicates the need for TB screening in newly diagnosed type 2 DM patients, especially within 12 months of the DM incidence.

### OAP-266-30 Screening of tuberculosis patients for diabetes mellitus in Kerala, India: How well are we doing?

K Dsa,<sup>1</sup> S Balakrishnan,<sup>1</sup> A Sreenivas,<sup>1</sup> N K.v.,<sup>2</sup> S Mrithunjayan,<sup>3</sup> J Subramoniyapillai,<sup>3</sup> C R Mohandas,<sup>1</sup> A Kumar.<sup>4</sup> <sup>1</sup>Tuberculosis, WHO Country Office for India, New Delhi, <sup>2</sup>General Hospital, Manjeri, Directorate of Health Services, Kerala, Malappuram, <sup>3</sup>State TB Cell, Directorate of Health Services, Thiruvananthapuram, <sup>4</sup>Research, International Union Against Tuberculosis and Lung Disease (The Union), South- East Asia Regional Office, New Delhi, India. e-mail: drdkarthik@yahoo.com

**Background:** A 2011 study in Kerala using glycosylated haemoglobin (HbA1c) showed that the prevalence of diabetes mellitus (DM) among tuberculosis (TB) patients was 44%. Following this and other studies, a national

policy decision to routinely screen all TB patients for DM was taken. In this study, we share the initial implementation experience in Kerala State and report on the number (%) of TB patients screened for DM and number (%) diagnosed as DM in the years 2012 and 2013.

**Design/Methods:** TB patients were screened if they already were diagnosed or treated for DM. Those not having DM were counselled and referred for DM testing from peripheral health institutions (PHI) to sub-district level government health facilities. Fasting blood glucose (FBG) of  $>126$  mg/dl and/or post-prandial blood glucose (PPBG) of  $>200$  mg/dl was considered DM as per national guidelines. All TB-DM patients were offered care within the general health system. In this cross-sectional study, we reviewed the programme records (treatment cards and TB register) to extract the required information.

**Results:** Of 25912 TB patients registered in 2012, 19576 (75%, ranging from 59–98% across 14 districts) were screened and 3761 (19%, range 11–26%) had DM. Of 24016 TB patients in 2013, 21115 (88%, range 70–100%) were screened and 3941 (19%, range 9–26%) had DM. There was an increased in the proportion screened for DM in all the 14 districts (100% in one district and 98% and 99% in other districts). We could not assess the proportion of TB-DM patients linked to DM care as there was no systematic documentation regarding the same.

**Conclusion:** A high proportion of TB patients were screened for DM indicating the feasibility of this intervention under routine settings. Efforts should be made to provide DM testing at PHI level to attain universal coverage and reduce patient inconvenience involved in travel and its costs. Future research should explore on the feasibility and cost-effectiveness of using HbA1c under programmatic settings. Programme staff should be sensitized to improve the recording of data with regards to linkage to DM care.

#### Screening of Tuberculosis patients for Diabetes Mellitus in Kerala, India: How well are we doing?

Year	Total No of TB patient Registered	Total No of TB patient screened for DM	% of TB patients screened for DM	No of TB patients diagnosed with DM	% of TB patients diagnosed with DM
*2011(Study with HbA1c)	660 (estimated number)	552	84%	243	44%
2012	25912	19576	75%	3761	19%
2013	24016	21115	88%	3941	19%

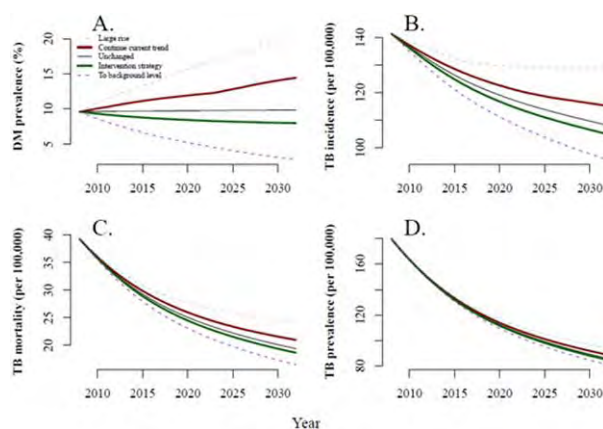
\*Balakrishnan S, Vijayan S, Nair S, Subramoniyapillai J, Mrithunjayan S (2012). High diabetes prevalence among tuberculosis cases in Kerala, India. *PLoS One*, 7(10): e46502  
<http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0046502>

### OAP-267-30 The impact of diabetes on the control of tuberculosis in high tuberculosis burden countries

S-C Pan,<sup>1,2</sup> C-C Ku,<sup>2</sup> CT Fang,<sup>1,2</sup> H-H Lin.<sup>2</sup> <sup>1</sup>Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan, <sup>2</sup>College of Public Health, National Taiwan University, Institute of Epidemiology and Preventive Medicine, Taipei, Taiwan. Fax: (+886) 223707772. e-mail: scpbpan@gmail.com

**Background:** After the implement of Tuberculosis Directed Observed Treatments globally, there are still 22 high tuberculosis burden countries (HBCs). Along with the changing of demographic figure and urbanization, other chronic diseases, as diabetes (DM) may increase people's risk for TB and dampen the current effort of TB treatment and prevention. The study aims to use mathematic modal to predict the impact of DM on the TB epidemic.

**Design/Methods:** We used a dynamic tuberculosis transmission model to simulate the effect of DM on the TB control. The compartment model contained TB susceptible, latent, infectious, and recovered compartments. 5 scenarios were created as the high bond of historical DM prevalence, elevated as current trend from 2000–2008, stationary (as the level on 2008), moderate control, and low bond. The transmission parameter was fitted to available incidence data from World Health Organization among 13 HBCs, excluding 9 countries with concurrent high HIV endemic. Preventable new incidence TB cases were compared between different scenarios projected from 2013 to 2032 after population adjustment.



**Figure** The prevalence of diabetes and projected incidence, prevalence and mortality of TB in different scenarios

**Results:** If the prevalence of DM increased as current trend, the estimated DM prevalence among the 13 countries will increase from 9.5% to 13.7% during 2008 to 2032, and decreased from 9.5% to 7.7% if under moderate control. For the 13 HBCs, if the prevalence of DM can be reduced by moderate control than changing with current trend, 3.6 million (95% CI:1.6-6.2 million) new incidence TB cases and 0.9 million (95% CI:0.5-1.4 million) mortality cases would be prevented during 2013–2032. Comparing with parameters associated with

TB (transmission parameter, case detection rate, treatment successful rate), the prevalence of DM predominant on the effect of preventable TB cases in each country.

**Conclusion:** In conjunction with current TB prevention and treatment strategies, the chronic disease as DM need to be incorporated in the health plan in HBCs, especially among the countries would have high DM prevalence. Substantial new cases of TB can be prevented with DM prevention and the effect needed to be evaluated further in countries with concurrent TB and HIV epidemic.

### OAP-268-30 Tuberculosis infection among diabetes mellitus patients in Hasan Sadikin Hospital, Bandung, Indonesia

R Koesoemadinata,<sup>1</sup> S McAllister,<sup>2</sup> R Livia,<sup>1</sup> A Verrall,<sup>2</sup> N Nathalia,<sup>3</sup> R Ruslami,<sup>4</sup> B. Alisjahbana,<sup>3</sup> R Van Crevel.<sup>5</sup>

<sup>1</sup>TB-HIV Research Centre, Faculty of Medicine, Universitas Padjadjaran, Bandung, Indonesia; <sup>2</sup>Centre for International Health, Department of Preventive and Social Medicine, University of Otago, Dunedin, New Zealand; <sup>3</sup>Department of Internal Medicine, Faculty of Medicine, Universitas Padjadjaran, Bandung, <sup>4</sup>Department of Pharmacology and Therapy, Faculty of Medicine, Universitas Padjadjaran, Bandung, Indonesia; <sup>5</sup>Department of Internal Medicine, Radboud University Nijmegen Medical Center, Nijmegen, Netherlands. e-mail: craspati@yahoo.com

**Background:** In a large cohort of tuberculosis (TB) patients in Indonesia, 15% had diabetes mellitus (DM), four times more than age-matched healthy control subjects. In the same setting, DM was a strong risk factor for treatment failure of TB. Screening of DM patients for latent TB infection may provide a possible opportunity for preventive therapy, and the WHO post-2015 strategy for TB considers screening high risk groups (such as DM patients) for TB. Unfortunately, active screening and preventive treatment for DM patients has not yet been implemented as a national policy in Indonesia. This abstract reports the characteristics of DM patients screened for TB infection.

**Methods:** As part of the TANDEM program ([www.tandem-fp7.eu](http://www.tandem-fp7.eu)) on TB and diabetes in different countries, we conducted a cross sectional study at the Endocrine Outpatient Clinic, Hasan Sadikin Hospital in Bandung, Indonesia. DM patients were screened for latent TB infection using Interferon gamma release assay (IGRA) from February to April 2014. A symptom screen and chest x-ray were performed to screen for possible active TB. Those with radiographs suggestive of TB disease and/or symptoms of coughing more than two weeks were asked to give sputum for smear and culture for *Mycobacterium tuberculosis* (M.Tb).

**Results:** A total of 101 DM patients had an IGRA test, of whom 16 had previously been diagnosed with TB. Of the remaining 85 patients, 32 (37.6%) were IGRA positive, 49 (57.6%) negative, and 4 (4.7%) inconclusive. IGRA positive patients were more often female (65.6%) compared to IGRA negative patients (53.1%), but there was no relation with age (58 cf. 59 years), BMI (27.0 cf. 25.6), Karnofsky score (89.4 cf. 88.8), HbA1c (8.2 cf. 8.0), and presence of a BCG scar (71.8% cf. 63.2%).

Duration of DM was inversely related with IGRA-positivity. A greater proportion of IGRA positive patients had a chest x-ray reading suggestive of TB (12.5%) compared to IGRA negative patients (4.1%). Only 2 IGRA positive patients and 3 IGRA negative patients reported cough with phlegm for more than two weeks. Of all patients suspected of having active TB ( $n=11$ ), 7 were sputum smear negative and four patients were unable to produce sputum.

**Conclusions:** Among DM patients included in this study almost 40% had a positive IGRA test. Active TB should be excluded before considering prophylactic treatment.

### OAP-269-30 Impact of diabetes mellitus on clinical presentation and treatment outcome of pulmonary tuberculosis in an urban area in China

ZY Wu,<sup>1</sup> JT Guo,<sup>1</sup> Y Huang,<sup>2</sup> EM Cai,<sup>2</sup> P Chen,<sup>2</sup> X Zhang,<sup>2</sup> Z An Yuan,<sup>1</sup> X Shen.<sup>1</sup> <sup>1</sup>Tuberculosis Control, Shanghai Municipal Center for Disease Control and Prevention, Shanghai, <sup>2</sup>Tuberculosis Control, Shanghai Changning Center for Disease Control and Prevention, Shanghai, China. e-mail: wzhyjerry@gmail.com

**Background:** Diabetes mellitus (DM) is a well-known risk factor for pulmonary tuberculosis (PTB) and related to poor PTB outcomes. China is a country with high burdens of both PTB and DM. However, few studies investigated the influence of DM on PTB in China. We performed a retrospective study to determine the impact of DM on clinical presentation and treatment outcomes of PTB patients in Shanghai, China.

**Methods:** We selected Changning District, Shanghai as the study setting where ageing of population was serious and resulted in rising burdens of DM and PTB. All newly diagnosed PTB patients during 1 January 2007-31 December 2009 were enrolled. A questionnaire for each patient was used to collect information on demographics, treatment records and outcomes. Relapse cases were identified using the municipal PTB surveillance system. Differences in patients with and without DM were analyzed using both univariate and multivariate analysis.

**Results:** During the study period, 217 newly diagnosed PTB patients were detected, among which 201 patients with complete information on DM status were included in the analysis. Of 201 patients, 39 (19.4%) had DM before PTB diagnosis. No patient was newly diagnosed with DM during the PTB treatment. Univariate analyses revealed that PTB patients with DM were more likely than those without DM to be old ( $\geq 50$  years, OR=6.42, 95%CI=2.77-14.86), to be male (OR=4.80, 95%CI=1.78-12.90), to have cavities on initial chest radiography (OR=2.54, 95%CI=1.16-5.09), and positive both initial and second month sputum smear (OR=5.24, 95%CI=2.08-13.17; OR=3.06, 95%CI=1.25-7.46, respectively). No significant differences were found between the two groups regarding anti-PTB drug resistance rate, treatment duration and treatment outcomes. During the 36-month follow-up period after completion of anti-PTB treatment, 2(5.6%) relapse cases in patients with DM and 2(1.3%) in

patients without DM were identified. In multivariable logistic regression model, aged  $\geq 50$  years (aOR=5.19, 95%CI=2.10-12.83), male (aOR=3.10, 95%CI=1.07-8.96) and positive initial sputum smear (aOR=3.82, 95%CI=1.42-10.25) remained significant.

**Conclusion:** Prevalence of DM was much higher in PTB patients than in general population in Changning District, China. Early bi-directional screening for the two diseases could help to reduce the transmission of *Mycobacterium tuberculosis*. Collaboration and co-management could improve the control effects of these two diseases.

### OAP-270-30 Implementation of systematic screening of people with diabetes for tuberculosis and HIV in Tanzania: a case for integrated care

J Hella,<sup>1</sup> B Doulla,<sup>2</sup> F Mhimbira,<sup>1,3,4</sup> N Boillat Blanco,<sup>1,3,4</sup> Z Ngoma,<sup>5</sup> A Swai,<sup>5</sup> K Ramaiya,<sup>5</sup> L Fenner.<sup>1,3,4</sup> <sup>1</sup>TB research, Ifakara Health Institute, Dar es Salaam, <sup>2</sup>Central Tuberculosis Reference Laboratory, National Tuberculosis and Leprosy Programme, Dar es Salaam, United Republic of Tanzania; <sup>3</sup>Medical Parasitology and Infection Biology, Swiss Tropical and Public Health Institute, Basel, <sup>4</sup>University of Basel, University of Basel, Basel, Switzerland; <sup>5</sup>Tanzania Diabetes Association, Tanzania Diabetes Association, Dar es Salaam, United Republic of Tanzania. e-mail: jhella@ihi.or.tz

**Background:** Tuberculosis (TB) and HIV are a major public health problem in sub-Saharan Africa. HIV is the most important risk factor for TB, but diabetes mellitus (DM) also increases the risk of TB. DM and TB is particularly important in countries such as Tanzania where an increase in the prevalence of DM has been observed. The well-developed system of diabetes care in Tanzania offers a unique opportunity to implement systematic screening for TB and HIV.

**Methods:** The study was conducted in eight large Diabetes Clinics in the three districts of Dar es Salaam during two months between February 17 and April 18, 2014. All DM patients attending the clinics were systematically screened for TB symptoms (coughing  $>2$  weeks, fever, unexplained weight loss  $>10\%$ , night sweats), and counselled for HIV testing according to national guidelines. All patients with any TB symptom were referred to a TB clinic for confirmation according to the guidelines.

**Results:** Data was available from a total of 1,153 DM patients, with a median age of 54 years (interquartile range 44-63); 700 (60.7%) were females, and 1,061 (92%) had type II diabetes (Table). Of 877 DM patients tested for HIV, 22 (2.5%) patients were HIV-infected; 10 (1.2%) were new HIV patients. Overall, the most frequently reported symptoms were coughing (23 patients, 2%) and weight loss (49, 4.2%), followed by night sweats (26, 2.3%) and fever (24, 2.1%). Presumptive TB was associated with female sex (72.7% females among presumptive TB vs. 60.0% among all other patients,  $p=0.04$ ), but there was no evidence for an association between presumptive TB and HIV infection. Among 66 (5.7%) presumptive TB patients with any symptom, TB



was confirmed in 2 (3%) patients. Eighty-two (7.1%) of all DM patients had a history of previous TB treatment, and this was associated with HIV infection (12.2% HIV infection among patients with compared to 1.1% without a history,  $p < 0.001$ ). Among the patients with a history of TB, 47 (58.5%) had a TB diagnosis at the time or after diagnosis of DM, with a median delay of 2.1 years after DM diagnosis.

**Conclusions:** Prevalence of HIV among DM patients was low, but the number of undetected HIV patients identified by systematic screening considerable. TB symptoms requiring further confirmation of diagnosis and a history of TB were frequently reported. DM patients benefit from systematic TB and HIV screening for early case detection, and models of integrated care for all three diseases need to be explored.

### OAP-271-30 Screening individuals with diabetes for tuberculosis (TB): preliminary data from the TANDEM programme in Peru, South Africa, Romania and Indonesia

C Ugarte-gil,<sup>1</sup> B. Alisjahbana,<sup>2</sup> A Riza,<sup>3</sup> G Walzl,<sup>4</sup> S. Kerry,<sup>5</sup> P Hill,<sup>6</sup> R Van Crevel,<sup>7</sup> J Critchley.<sup>5</sup> <sup>1</sup>Laboratorios de Investigacion y Desarrollo, Universidad Peruana Cayetano Heredia, Lima, Peru; <sup>2</sup>TB-HIV research center, Medical Faculty, Universitas Padjadjaran, Bandung, Indonesia; <sup>3</sup>Human Genomics Laboratory - UMFCV, Universitatea de Medicina si Farmacie din Craiova, Craiova, Romania; <sup>4</sup>Stellenbosch University Immunology Research Group (SUN-IRG), Stellenbosch University, Cape Town, South Africa; <sup>5</sup>Population Health Research Institute, St George's, University of London, London, UK; <sup>6</sup>Centre for International Health, University of Otago, Dunedin, New Zealand; <sup>7</sup>Nijmegen Medical Centre, Radboud University, Nijmegen, Netherlands. e-mail: cesar.ugarte@upch.pe

**Background:** Diabetes mellitus (DM) increases risk of TB about three fold and worsens TB treatment outcomes. DM prevalence has been increasing rapidly globally; particularly in urban centres in low and middle income countries. In many of these centres, TB remains endemic. The Collaborative Framework for TB-DM recommends bi-directional screening. However, there is little agreement or evidence on how to implement screening in practice, or the likely yield and cost-effectiveness of proposed screening programmes. TANDEM ([www.tandem-fp7.eu](http://www.tandem-fp7.eu)) is a multi-country TB-DM project with field sites in Indonesia, Peru, Romania and South Africa. We present preliminary data on results of screening DM patients for active TB

**Design/Methods:** DM patients attending for routine appointments were screened for TB using symptom-based enquiry and chest x-ray (CXR). The criteria for referral for TB investigations (sputum and culture in all sites, with the addition of Xpert in Stellenbosch) were productive cough plus CXR abnormalities indicative of TB, or clinical suspicion of TB. Data collection commenced December 2013-March 2014

**Results:** 693 patients had been recruited until April 2014. Mean age varied between 51 to 60 and mean BMI 25–29 across sites (table). A high proportion (20% to 64%)

were insulin dependent DM and Mean HbA1c varied from 8% to 10%. Typical TB symptoms (including cough, night sweats and weight loss) were frequently reported and unrelated CXR abnormalities were also common (32%). In Bandung, 22% of patients were referred for TB investigations based on the screening algorithm and 6 were diagnosed as clinical TB. However, 5 of these 6 patients were simultaneously being investigated for TB and diagnosed elsewhere. In Stellenbosch, 2 patients were diagnosed with TB using Xpert of 50 screened by this method; 1 TB positive among 27 screened with culture in Peru and none in Romania. We plan to recruit 1950 patients by the end of 2014

**Conclusion:** It is feasible to screen DM patients for TB in routine DM clinics using simple symptoms and CXR. However the detection rate has been low to date and the yield and likely cost-effectiveness remains uncertain

	Peru N=326	Indonesia N=263	South Africa N=52	Romania N=52
% Male	31.6	48.0	48.1	48.
Age Mean	59.8	58.3	51.6	56.7
Age Range	20–89	20–87	19–69	27–78
Insulin dependent DM %	19.9	43.7	56.7	64.1
HbA1c Mean(SD)	8.2(2.7)	8.3(2.0)	10.4(2.2)	9.7(2.1)
Mean BMI(SD)	28.3(5.5)	25.4(4.5)	29.0(5.9)	29.4(6.9)
Previous diagnosis of TB Yes(%)	6.4	13.7	25.5	9.6

## 10. ALL HANDS ON DECK: COMMUNICATION ENGAGEMENT AND TB PROGRAMMES

### OAP-272-30 Pharmacists and rural health-care providers in TB care and control, including all stakeholders

V Panibatl,<sup>1</sup> J Banavaliker,<sup>1</sup> S Prasad.<sup>2</sup> <sup>1</sup>Programs, TB Alert India, HYDERABAD, <sup>2</sup>Lilly MDR TB Partnership, Eli Lilly and Company(India), Gurgaon, India. e-mail: vikas@tbalertindia.org

**Context:** National TB Programs (NTP) efforts in tackling and eliminating TB should be supported by wide variety of stakeholders in the community. Pharmacists & Rural Health Care Providers (RHCPs) are such important community stakeholders in India. They are integral part of health system and are the first contact point for consultation for any sort of illnesses

**Intervention:** Realizing the need for engaging Pharmacists and RHCPs as important players in TB Care and Control, TB Alert India has taken up a project in four Tuberculosis Units (approx. 500,000 population each) in Andhra Pradesh State, India. Project is a United Way Worldwide grant on behalf of the Lilly MDR-TB Partnership. The capacities of Pharmacists and RHCPs are built in identifying, referring TB symptomatic persons, linking TB symptomatic to testing and treat-

ment facilities run by NTP. Around 177 Pharmacists and 298 RHCPs were trained on TB and on NTP guidelines.

#### Results:

**Results** are very encouraging especially with respect to Pharmacists. Around 60% (115/177) of the trained pharmacist are actively participating in the project and in NTP. From Feb '13 to Jan '14 Pharmacist have referred 871 TB symptomatic persons for TB testing, around 91% (792/871) referred persons have reached for testing indicating good quality of counselling. Near about 11% (90 out of 792 tested) of the persons tested are diagnosed with TB. Near about 10 Pharmacists provided DOTS to 11 people on Cat 1 treatment in the same period. Among the 10 people with TB taking treatment from Pharmacists 5 have completed full course of treatment and are cured, four people have completed intensive phase of the treatment and are declared as negative in the 1<sup>st</sup> follow up testing. Remaining two are under treatment. Pharmacists are also recognized as DOTS providers by the NTP. Referrals from the pharmacists on an average have accounted 5% in a month among the total symptomatic tested in the Tuberculosis Units. **Learning:** Pharmacists perceive referring /treating a TB case effectively could improve their business in terms of linking larger community to their shop

**Conclusion:** Pharmacists can refer TB symptomatic and can be a good DOTS providers. Their engagement will enable early TB detection and prevent TB patient from getting into unnecessary treatment shopping. Pharmacists need to be motivated constantly to focus on social initiatives.

### OAP-273-30 Effectiveness of sputum collection center and transportation model and its impact on Tuberculosis notification in Chhattisgarh, India

P Nayak,<sup>1</sup> A Kumar,<sup>2</sup> S Srinath,<sup>2</sup> P Chinnakali,<sup>3</sup> K Khaparde,<sup>1</sup> T K Agrawal,<sup>4</sup> S Chandraker,<sup>4</sup> A Sreenivas.<sup>1</sup>  
<sup>1</sup>Country Office, India, World Health Organization, New Delhi, <sup>2</sup>The Union South East Asia Office, International Union Against Tuberculosis and Lung Disease (The Union), New Delhi, <sup>3</sup>Department of Preventive and Social Medicine, Jawaharlal Institute of Postgraduate Medical Education & Research (JIPMER), Puducherry, <sup>4</sup>State Tuberculosis Cell, Directorate of Health Services, Raipur, Chhattisgarh, India.  
 e-mail: pikoo.2007@gmail.com

**Background and challenges to implementation:** Quality assured sputum smear microscopy is the backbone of tuberculosis diagnosis under the Revised National Tuberculosis Control Programme (RNTCP) in India. To improve the reach and access of TB diagnostic services to the needy populations, non-governmental organization/private sector supported sputum collection centres have been established across the country. However, there have been concerns about the quality of sputum specimens transported from the collection centres and the low yield of sputum positive cases in such specimens. This is referred to as "Sputum Collection Center and Transportation" (SCCT) model. We aimed to assess the quality of

sputum specimens and smear positivity among sputum specimens collected via SCCT model as compared to those examined among patients reaching in-person at microscopy centres.

**Intervention or response:** In this cross sectional study among all presumptive TB patients examined during July-December 2013 in five districts of Chhattisgarh, we reviewed the laboratory forms and registers at the microscopy centres to extract information on macroscopic quality of specimens (mucopurulent, salivary or blood-stained) and results of sputum microscopy (positive for acid-fast bacilli or not and grading).

**Results and lessons learnt:** Of 7100 presumptive TB patients examined (66% male; median age of 31 years), 723 (10%) were through the SCCT model (90% transported within a day). Among them, 72(10%) were positive for acid-fast bacilli and was similar to that in the other group (579/6377=9%, p value=0.3). About 50% of all positive specimens were graded 'scanty' or '1+' and there was no difference between the two groups. Overall, 66% of the specimens were mucopurulent and was similar across the two groups (67% versus 66%, p=0.25).

**Conclusions and key recommendations:** We did not find any difference in the macroscopic quality of specimens and sputum positivity of specimens collected via SCCT model as compared to those collected in-person from the patients at the microscopy centres, thus allaying the concerns. SCCT model accounted for about 11% of all smear positive patients diagnosed and we recommend that this needs to be continued and expanded across the state. Measures including patient and provider education regarding the importance of good-quality specimen need to be undertaken to further improve the yield.

### OAP-274-30 Drama sets the stage for adolescent TB vaccine trials

M Tameris,<sup>1</sup> A Abrams,<sup>2,3</sup> V Baxter.<sup>4</sup> <sup>1</sup>South African TB Vaccine Initiative (SATVI), IDM and SCAH, University of Cape Town, Cape Town, <sup>2</sup>Cochrane Centre, Medical Research Council, Cape Town, <sup>3</sup>School of Anthropology, University of Cape Town, Cape Town, <sup>4</sup>Drama School, University of Cape Town, Cape Town, South Africa.  
 e-mail: michele.tameris@uct.ac.za

**Background** Young adults and adolescents are important participants in novel vaccination strategies to prevent tuberculosis (TB). South African Tuberculosis Vaccine Initiative (SATVI) has been conducting clinical trials of novel tuberculosis vaccines in Worcester, Western Cape since 2005. We set out to demonstrate the effectiveness of the medium of drama amongst high school learners as an engagement, educational and awareness raising tool when used to introduce concepts of TB and TB vaccine clinical trials

**Methods** In collaboration with University of Cape Town Drama School a local high school developed a play discussing participation in a TB vaccine trial, and performed it at eight high schools in the area. In-depth focus groups were conducted amongst adolescents in the audience before and after production. In addition, all

scholars attending the performance completed knowledge (KAP) surveys pre and post-performance.

**Results** During the third quarter of 2013 there were thirteen performances of the play "Carina's Choice" at eight schools, reaching over 8000 adolescents. Three pre-intervention focus groups informed topics relevant to drama content e.g. stigma, transmission of TB and confusion between HIV and TB. Post-performance focus groups confirmed that we had addressed these issues, that the audience had enjoyed the songs and raps in the play thoroughly and could still recall their messages. However concern re transmission of TB during pregnancy emerged as not having been addressed. Learners involved in the production as performers reported that they were seen as a resource on TB information in their communities, and often approached with questions about TB. Subsequent to the performances, SATVI staff reported that working within the school system and recruitment of participants into an adolescent vaccine trial was facilitated by prior sensitisation through the drama production.

**Conclusion** By increasing knowledge of the TB epidemic and need for a solution in an age-appropriate, entertaining way, this drama production was an effective tool for community engagement and sensitisation for future recruitment into TB vaccine trials in an adolescent population.

#### **OAP-275-30 Assessment of NGO PP schemes implemented at CHF's in TB case finding activity**

Y Patel,<sup>1</sup> G Singh,<sup>1</sup> M Puthenchirayil,<sup>1</sup> P Varghese,<sup>1</sup> b Vadera,<sup>2</sup> P Patel,<sup>3</sup> D Kapadiya.<sup>4</sup> <sup>1</sup>Not for Profit NGO, CBCI Coalition for AIDS and Related Disease, New Delhi, <sup>2</sup>RNTCP, World Health Organization, Ahmedabad, <sup>3</sup>Health and Family Welfare, Intermediate Reference Lab, Ahmedabad, <sup>4</sup>Health and Family Welfare, State TB Cell, Ahmedabad, India. e-mail: yogshipatel@yahoo.co.in

**Background:** Engagement of health providers from all sectors is an important activity for TB control. It is more of relevance in India where more than 40% of TB patient are seeking care outside Government health facilities. To facilitate this, NGO PP schemes are established for the involvement of other than Government organization with RNTCP in India. CBCI CARD is an organization that provides technical supports to the catholic health facilities (CHF's) to work effectively with RNTCP for improve coverage of TB care services. Present study aimed to evaluate contribution of this mechanism in case finding efforts of RNTCP in Gujarat. Methodology: The study was conducted with cross sectional design in which contribution of CBCI supported CHF's in case finding efforts of RNTCP was evaluated in the state of Gujarat in India. In Gujarat, 4 microscopy centres, 8 sputum collection and/or transportation centres were functional in coordination with RNTCP. To measure improvement in access of TB care, 11 TUs selected where signed CHF's were located. Data on number of TB symptomatic examined for smear microscopy was extracted from monthly reports of CHF's during Jan to Dec 2013 while data on diagnostic services were extracted from labora-

tory registers of all DMCs of TUs where CHF's were located. Univariate analysis was conducted for proportion of contribution.

**Results:** Out of total 27788 patients attended OPD at CHF having DMCs, 197 patients were diagnosed from 1290 screened. CHF having collection and transportation scheme has facilitated 945 TB symptomatic to diagnosed 82 TB patients during 2013. Around 5% of symptomatic (64 symptomatic) underwent repeat sputum examination got yield of 14 TB patients. During follow up examination 14 were found positive from total 117 examined at CHF DMC. CBCI Signed schemes contribute 6.1% of symptomatic examined and 4.9% TB patients diagnosed at TU level. Average 10.6% TB symptomatic screened and 10.1% diagnosed TB patients were facilitated at CHF DMC while sputum collection and transportation schemes contributed 3.9% and 2% respectively at TU level.

**Conclusions:** With limited presence in the state, CHF's contributed to significant proportion in case finding efforts under DMC and sputum collection center/ Pick up and transportation scheme; more over it improved the access to care.

#### **OAP-276-30 Supporting the capacity of community level civil society organisations to increase TB case detection in high-burden districts in South Africa**

E Mhlope,<sup>1</sup> R Makombe,<sup>1</sup> A Ratshefola.<sup>1</sup> <sup>1</sup>USAID TB Program South Africa, University Research CO. LLC, Pretoria, South Africa. Fax: (+27) 124849383. e-mail: evelynm@urc-sa.com

**Background and challenges to implementation:** NGO/ Civil Society Organizations continue to play an important role in supporting the government mandate of Intensified Case Finding to increase TB case detection to 70%, adopted in March, 2011. Through the support of the USAID TB Program, 48 NGO/CSOs were funded for FY13 to complement the work already conducted by the project in the nine provinces. The main activities are related to Intensified Case Finding (ICF), DOT, ACSM, c-MDR-TB, TB/HIV Integration including integration of TB into existing workplace HIV programs.

**Intervention or response:** Post-award workshops were conducted soon after awarding the grants to all the NGO/CSOs. Capacity assessments conducted one month after granting the award showed that 38 NGO/CSOs had limited knowledge in TB related activities. Existing training materials on Basic TB information were adapted and a series of 3-day workshops conducted on Basic TB Management for all 38 NGO/CSOs. To complement this, an on-line training course on Basic TB Information was also developed and a link was created for all funded NGO/CSOs to access the course whenever needed. Other supporting materials were developed to facilitate understanding and easy reporting of the activities conducted; e.g. job aids on counseling a client on TB (in a form of flipchart) and sputum collection, data collection tools, referral forms and registers. To ensure effectiveness of



their activities, the 38 NGO/CSOs were linked to 178 health facilities and monthly monitoring conducted by the Provincial Project Coordinators.

**Results and lessons learnt:** 193 463 community members were reached with TB messages, where 105 910 was screened for TB. Of these, 17 293 were identified with presumptive TB symptoms and 4507 confirmed with TB (all forms) Further analysis of the data from a sample of 10 CSOs was consistent with the national norm for Intensified Case Finding, as follows: 18503 people were screened for TB 2451 (13%) were referred to public health facilities with presumptive TB 186 (7.6%) were confirmed with active TB 4 (1.6%) were confirmed with MDR-TB

**Conclusions and key recommendations:** Strengthening the capacity of NGO/CSOs and providing systematic monitoring and support is essential for their effectiveness in contributing to TB Program indicators.

### **OAP-277-30 Engaging the Rural Health Care Providers (RHCPs) in TB control: report from Tamilnadu, Southern India**

K K,<sup>1</sup> A Ramya,<sup>1</sup> A Das,<sup>1</sup> N Krishnan.<sup>1</sup> <sup>1</sup>Health, Resource Group for Education and Advocacy for Community Health, Chennai, India. e-mail: pm.reachaxshya@gmail.com

**Background and challenges to implementation:** TB symptomatics and TB patients in India seek care from a range of private health care providers ranging from Allopathic practitioners to traditional, non-allopathic, or paramedical providers with limited qualifications. Rural health care providers (RHCPs) are an important group of traditional healers especially to inaccessible, hard to reach communities and certain vulnerable and marginalized population groups. They are often the first point of contact for these patients. Within the government TB control program, there has been no active engagement of this group of providers

**Intervention or response:** Through Project Axshya (Global Fund Round 9 project ) a strategy was designed to engage these practitioners for TB care and control. In 14 selected districts of Tamilnadu, wherein REACH has been implementing the project, 438 rural health care providers were trained for engagement in TB control efforts from April 2013 to March 2014. The training encouraged the RHCPs to engage in the following ways-referral of chest symptomatics, as DOT providers in sputum collection and transport activities.

**Results and lessons learnt:** Of the 438 RHCPs trained, majority (78%) were AYUSH (Ayurveda, Yoga & Naturopathy, Unani, siddha and Homeopathy) practitioners, 12% were community pharmacists and 10% were traditional healers. Overall 52 % are engaged under project Axshya of whom majority are AYUSH practitioners (61%). Of the 902 referrals from the RHCPs, majority (52%) were from AYUSH. The sputum positivity among the referrals was highest in the RHCPs (9%), followed by traditional healers (6%) and community pharmacists (5%). About 112 RHCPs provide Direct Observation Treatment Short-course (DOTs) for

147 patients which includes 82 AYUSH for 102 patients, 18 pharmacists for 21 patients and 12 traditional healers for 18 patients. Overall 190 sputum samples have been transported by the RHCPs with a sputum positivity of 4.2 %

**Conclusions and key recommendations:** These findings highlight that nearly 52 % of the trained RHCPs have been successfully engaged in TB control efforts with the maximum engagement by the AYUSH practitioners. This potential group could also be engaged in other areas such as DOT provision and sputum collection and transport. In the context of universal access, RHCPs, especially the AYUSH Practitioners are an important group who needs to be engaged in a systematic manner to increase case detection.

### **OAP-278-30 Improving contact investigation and tracking of treatment interrupters through engagement of civil society organisations in Kenya: Amref Health Africa**

D Moegi,<sup>1</sup> B Ulo,<sup>1</sup> m Mungai,<sup>1</sup> A Munene,<sup>1</sup> J Kitonga,<sup>1</sup> T Kiptai,<sup>1</sup> C Mwamsidu,<sup>1</sup> S Musau.<sup>1</sup> <sup>1</sup>HIV/TB and Malaria, Amref Health Africa, Nairobi, Kenya. e-mail: duke.mobegi@amref.org

**Background:** Amref Health Africa is the principal recipient for Global Fund grants TB component in Kenya (2011 to 2015). The project is implemented through 17 Civil Society Organizations (CSOs) in collaboration with the National Tuberculosis Program (NTP). The overall goal is to accelerate quality DOTS expansion to achieve and sustain national TB control targets in line with Global TB control targets and the Millennium Development Goals (MDGs). Inadequate community involvement in contact investigation and tracking of treatment interrupters has been one of the main weaknesses in achievement of the MDGs. Retention and sustainability of CSOs had not been addressed clearly in the health delivery systems leading to low achievement of early case finding and holding indicators. The NTP has recognized the role played by communities in TB control and the need for strengthened structures to support community TB care in line with the MoH community strategy.

**Interventions:** From January 2012 to July 2013, the CSOs supported by Amref Health Africa implemented community based TB activities in Kenya through trained community Health Workers (CHWs) who received a stipend per client. Contacts of smear positive TB clients were investigated and symptomatic contacts referred to health facilities for further investigations. Treatment interrupters were traced and brought back to treatment. Health education was provided to the index client and their contacts.

**Results:** Of the 2136 contacts screened, 30 % were symptomatic and referred out of which 10.7 % (N= 641) were diagnosed with TB. Of the 2533 treatment interrupters traced, 56% were found and referred back for treatment, 10% had died, 10% had migrated and 2%

were not known in the locality. Outcomes were not indicated for 9% and 13% were not found.

**Lessons learnt:** Involving CSOs in contact investigation leads to early identification and diagnosis of new TB cases. In addition the CSOs are central in tracing treatment interrupters and returning them to treatment.

**Conclusion:** Continued engagement of CSOs in community TB care in the context of community strategy will contribute to and sustain the gains made in TB control. The MoH should continue engaging CSOs effectively in community TB control.

### **OAP-279-30 Creating TB-free environment through community-based TB activities in Merak**

D Yulianti,<sup>1</sup> N Harsini,<sup>2</sup> MR Christian,<sup>3</sup> E Varella.<sup>4</sup>

<sup>1</sup> National Tuberculosis Program, Ministry of Health Republic of Indonesia, Jakarta, <sup>2</sup>Pulo Merak TB Community Groups, Banten, <sup>3</sup>Tuberculosis, World Health Organization, Jakarta, <sup>4</sup>ACSM, KNCV Tuberculosis Foundation, Jakarta, Indonesia. e-mail: regina.loprang@gmail.com

**Background and challenges to implementation:** Indonesia has the fourth highest TB caseload in the world. The estimated TB incidence in Indonesia for 2011 is 187/100,000. Estimated mortality is 27/100,000. It is estimated that, every hour, 52 new TB patients are added. Every hour, 8 patients die. But despite all the current efforts of government there is little improvement in the ability to find all the people who have TB and need diagnosis and treatment. One third of patients are either not found or not reported. Moreover due to the difficult access, the existence of TB stigma in the community, the fear of losing jobs, patients are reluctant to start treatment and many are loss to follow up.

**Intervention or response:** In 2004, initiated by the primary health care in Merak, Pulo merak community TB group were established in order to provide support group. The member of this group are cured TB patients and TB patients on treatment. The main activities of the group are: 1) giving IEC to the patients, 2) act as treatment observer, 3) create a focus group discussion to support among each other, 4) help TB services in DOTS clinic, 5) patient testimony, 6) share experiences to other districts, 7) provide nutritional support, 8) acted as a cadre, 9) actively finding and refer TB cases among their community. Moreover, every member of the group will contribute some amount of money every week, and use the collected money to provide nutritional support for the patients, and provide transportation cost for the poor patients

**Results and lessons learnt:** There are now 16 active members of Pulo Merak community TB groups. They have trained 178 cadres, of which routinely help the TB activities in the puskesmas. They have managed to get funding from CSR budget to independently run their operational activities and also held gathering events each year during the ramadhan, and provide nutritional support to TB patients. Through series of advocacy to the local government, they succeed to have the local

government provides budget for transportation for the cadres, thus bring more people to TB treatment.

**Conclusions and key recommendations:** Cured TB patient group can be strong influence to better TB program. They can be a role model to other patients because they have experiences and motivation to create a TB Free environment. Patient group have a better access to reach the missing cases. The model of this patient based organization need to be enhanced and shared.