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**ABSTRACT BOOK**

**43rd World Conference  
on Lung Health of the  
International Union Against  
Tuberculosis and Lung Disease (The Union)**

**KUALA LUMPUR • MALAYSIA  
13-17 NOVEMBER 2012**

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# The International Journal of Tuberculosis and Lung Disease

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# 43rd World Conference on Lung Health of the International Union Against Tuberculosis and Lung Disease (The Union) Kuala Lumpur, Malaysia, 13–17 November 2012

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## SYMPOSIA: THURSDAY 15 NOVEMBER 2012

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### TB REACH: RESULTS FROM TUBERCULOSIS CASE FINDING INNOVATIONS IN THE FIRST TWO WAVES

#### Summary of latest results from TB REACH projects

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To address the stagnating TB case detection, in 2010 the Canadian International Development Agency (CIDA) provided funding for a new initiative called TB REACH to the Stop TB Partnership. TB REACH supports innovative projects that can show results quickly and then ideally be scaled up with other funding if successful. TB REACH provides one year grants through a competitive selection to institutions and organizations involved in TB control who present proposals aimed at increasing case finding. Immediately after its inception in January 2010, TB REACH launched a call for proposals, and a group of 30 projects was selected by a proposal review committee for a first wave of funding in May of the same year. The main outcome of interest for TB REACH wave 1 projects was the number of additional smear positive cases found in the evaluation population. All projects report monthly to TB REACH on the number of cases reported to the NTP in the evaluation population as well as process indicators including numbers of people screened for TB and, those with symptoms, numbers tested, etc. Additional cases are defined as the increase in TB case notification within the NTP reporting area (i.e., evaluation area) during the project period compared to the same area's figures from the previous year. From October 2010 until March 2012, 29 projects in 19 countries started and completed at least 4 quarters of case finding activities.

We present the findings of an evaluation of the first wave of TB REACH projects as well as an update on the progress of Wave 2 projects which began in October 2011.

### Monitoring and evaluation, additionality and yield from TB REACH interventions

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The TB REACH funding mechanism supports innovations in early and increased case finding of tuberculosis with a focus on poor and underserved populations. Putting in place a robust monitoring and evaluation framework is essential to evaluate the impact of the funding and to maximize learning from these interventions.

The M&E framework, developed by HLSP and KIT in collaboration with the TB REACH secretariat includes three main elements. First it captures project outcome by measuring cases diagnosed through the project. Second, the effectiveness against effort for chosen intervention strategies within projects is reviewed through detailed data on each step in the diagnostic pathway. Third, the intervention's impact was measured through changes in official NTP case notification at BMU level. For this purpose projects were encouraged to define an evaluation population and control population.

On-going monitoring of direct yield and analysis of detailed data on the steps in the diagnostic pathway assisted in identifying the most effective and least effective interventions in each project and formed the basis for advice on mid-term strategy changes. Comparison of direct yield of intervention strategies with changes in notification at BMU level provided a good basis to estimate the impact of strategies within a given context.

The results of twenty nine projects in the first funding wave of TB-Reach will be presented. The effectiveness of the adopted intervention strategies within the different contexts and their likely contribution to increasing case notification will be discussed.

### Using community resources and new tools for active tuberculosis case detection in South Africa

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**Setting:** Sisonke is a rural district in KwaZulu-Natal, South Africa.

**Objective:** To increase diagnosis and treatment of drug susceptible and drug resistant TB (DRTB).

**Design:** TB-HIV Care Association received a TB REACH grant to increase TB case finding and treatment through TB symptom screening and sputum collection by mobile HIV counseling and testing (HCT) teams and community health workers (CHWs) with sputum examination by Xpert MTB-RIF (GeneXpert). All people with presumptive TB in Sisonke have sputum examined by GeneXpert. Community Health Facilitators (CHFs) at each laboratory check results daily and inform CHFs in clinics of any positive results. CHFs in clinics use cell phones to contact patients directly or CHWs to trace patients to ensure that they are started on TB treatment. If patients have difficulty in coming to the clinic, they can be initiated on treatment in their homes. Patients with rifampicin resistance were initiated on DRTB treatment at a decentralized unit.

**Results:** From October 2011 to June 2012, there were 10854 people with presumptive TB tested by GeneXpert and 915 (8.4%) TB cases diagnosed of whom 901 (98.4%) were started on TB treatment. Of the remaining 14 patients, 9 died, 2 were transferred out, 1 refused treatment and 2 were not found. There were 99 (10.8%) cases who were resistant to rifampicin of whom 93 (94%) started treatment for multidrug resistant TB. Of the remaining 6, 5 died and 1 transferred out.

**Conclusions:** Community based TB screening by mobile HCT teams and CHWs, diagnosis by GeneXpert and communication of results by CHFs and CHWs using cell phones are effective methods to increase case finding and treatment of drug susceptible and drug resistant TB in a rural setting.

### Active screening of the Tibetan refugee populations in India

K Dierberg,<sup>1</sup> K Dorjee,<sup>2</sup> F Salvo,<sup>3</sup> W Cronin,<sup>1</sup> T Sadutshang,<sup>2</sup> R Chaisson.<sup>1</sup> <sup>1</sup>The Johns Hopkins University Center for TB Research, Baltimore, MD, USA; <sup>2</sup>The Tibetan Delek Hospital and the Central Tibetan Administration Department of Health, Dharamsala, Himachal Pradesh, India; <sup>3</sup>Emerging Pathogens Unit, San Raffaele Scientific Institute, Milan, Italy

**Background:** The prevalence of tuberculosis among Tibetans-in-exile is among the highest in the world.

In 2010, the prevalence was 420/100 000 among Tibetans living in India. Over half the TB cases occur among students, monks and nuns, who live in congregate settings, which contributes to high rates of TB and MDR-TB transmission. The main objective of this TB REACH project is to increase TB and MDR-TB case detection rates in Tibetan congregate living centers in India.

**Methods:** We conducted active case-finding for TB (ACF) in Tibetan schools, monasteries, and the Reception Center for new arrivals, where participants were screened for TB symptoms (cough, fever, night sweats or weight loss of any duration). Participants reporting any TB symptom were considered TB suspects, underwent a chest X-ray, and submitted sputum for smear microscopy or GeneXpert MTB/RIF (GXP) rapid assay.

**Results:** Between September 2011 and August 2012, 20565 people were screened and 2598 TB suspects underwent further testing at 13 Tibetan schools, 19 monasteries and the Reception Center. The overall rate of TB was 302/100 000 among those screened (62 cases). The overall rate of TB was 440/100 000 in Tibetan schools and 173/100 000 in monasteries, but the rate was 400/100 000 in the monasteries in one Tibetan settlement. Among those cases identified by ACF, 29% (18 of 62) were sputum smear positive and 35% (22 of 62) were sputum smear negative and GXP positive. Four cases (6%) were rifampicin-resistant by GXP.

**Conclusions:** Implementation of ACF with the GXP test enabled early and rapid detection of undiagnosed TB cases in Tibetan congregate living settings and enabled diagnosis of additional cases of pulmonary TB not identified by routine sputum smear microscopy. However, the burden on laboratory personnel during ACF activities was substantial and will need to be addressed during ongoing ACF and GXP scale-up.

### Providing tuberculosis care to clients of private laboratories and practitioners in Pakistan and Bangladesh

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**Background:** In South Asia, most tuberculosis (TB) patients seek treatment in the private sector. Patients frequently end up paying for off-indication and poor quality tests, treatment regimens are often inaccurate, and processes to ensure treatment completion are absent at private facilities.

**Activities:** Two TB REACH initiatives set up enhanced case-finding (ECF) interventions across Karachi and Dhaka with 78 general practitioner (GP) clinics, 11 private labs and 3 hospital outpatient departments (OPD). Individuals presenting at participating sites were verbally screened for symptoms of

TB by screeners using mobile phones. Screeners at GP clinics and 2 of the hospital OPDs worked on performance-based incentives. All TB suspects who were able to provide sputum were offered free smear tests and a chest X-ray (CXR) and a subset also received a GeneXpert test (GXP).

**Findings:** Over 1285347 individuals were screened (93% Karachi, 7% Dhaka) between 1-Jan-11 and 15-Aug-12, resulting in the identification of 32597 (3%) TB suspects, 23281 (71%) smear tests being performed and the detection of 3798 TB cases. Over 3500 GXP tests have been performed for smear-negative, CXR suggestive suspects, yielding an additional 612 (17%) confirmed cases. The median monthly incentive reward was \$49/mo for screeners. No mechanisms exist to sustain these interventions without further external funding.

**Interpretation:** ECF activities in the private sector significantly increased case notifications in the evaluation populations, tested diagnostic algorithms that include GXP and demonstrated the low costs of performance-based rewards for mass screening at scale. Our experiences have been adapted to propose sustainable private sector TB care using social enterprise models under the new UNITAID TBXpert project in Pakistan, Bangladesh and Indonesia. Starting in 2013, the social enterprises will conduct ECF activities to achieve partial subsidization for GXP testing by the end of 2015.

## PHARMACISTS CAN HELP PROTECT TUBERCULOSIS DRUGS AND DO MORE TO SUSTAIN TUBERCULOSIS CONTROL: HOW CAN TUBERCULOSIS PROGRAMMES ENGAGE THEM?

### Tuberculosis drugs are hard to find in private pharmacies in Ghana: what makes this possible?

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Uncontrolled, irrational, and harmful use of anti-TB medicines, may contribute to poor treatment results, drug-resistance development and amplification, adverse drug reactions, and high costs to patients. However, in a democratic state getting legislation that restrict or imposes ban on anti-TB medicines importation could be challenging, especially in the era of free market based economy and promotion of the private sector as engine of growth. In 1988 anti-TB medicines had been categorized as Programme Drug at the establishment of the Essential Medicines List (EML), as such, limiting the possibilities of a private service provider to apply for an import license to bring anti-TB medicines into the country without the

approval of the NTP and MOH. However, anti-TB medicines could still be found in the private sector in the free market based economy. Not surprising, there was rampant irrational prescribing of these medicines by private TB service providers who were not adhering to any form of STG or even trained to diagnose or manage TB. It was within such context that in 1999, the NTP facilitated and adopted a self-imposed restriction of anti-TB medicines outside the National TB Control programme, through collaboration with healthcare professional bodies and private practitioners, using existing legal framework which identifies anti-TB medicines as programme drugs and without an official legal ban through an Act of Parliament.

The following approach was adopted.

- NTP recognize the problem of irrational use of TB drugs
- Map out all the stakeholders
- Map out strategies
- Make TB drugs unprofitable
- Engage pharmacies, regulatory authorities and professional associations in TB control
- Create sustain public education
- Train health staff and engage health training institutions.

**Conclusion:** It is possible to restrict anti-TB medicines without formal ban, even though one may not have controls on medicines which enter the country through smuggling.

### Engaging retail pharmacists as partners in tuberculosis programme: the Indian experience

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**Background:** Indian Pharmaceutical Association (IPA) took initiatives to pilot a public-private partnership project of engaging pharmacists, in Revised National Tuberculosis Control Program (RNTCP) in Mumbai, funded by Eli Lilly & Co. (India) Pvt Ltd.

**Objective:** Objective of IPA's initiative was to develop retail pharmacists as new pool of pharmaceutical human resources for TB care and control and scale up the work nationally to strengthen the national TB programme.

**Design:** Pharmacists were trained for case detection, DOTS provision and rational use of antibiotics. Post training, work is undertaken by 300 plus trained pharmacists in 8 different city corporation areas in state of Maharashtra and these pharmacists are now partners with local TB program. The project sites evidenced increased trend in case detection and patient centric DOTS delivery. These findings of initial projects were

communicated to the Policy Makers in a workshop and was followed up consistently.

**Result:** Encouraged by these pilot project findings, RNTCP signed a Memorandum of Understanding with IPA to carry forward pharmacists' engagement to pan India. As per the MoU, RNTCP has formed a National Core Committee to review participation of pharmacies in RNTCP. The model is now being scaled up to 3 states followed by other states in phased manner.

**Conclusion:** Capacity building and skill enhancement, helped in developing skillful human health resource for TB control. Focused persistent advocacy efforts influenced the national policy change. IPA's work served as 'Agent of CHANGE' benefiting TB patients and enhancing image of pharmacists as partners of the government TB programme.

### How can Stop TB Partners assist countries in restricting misuse of tuberculosis drugs and technologies? The Cambodia experience

T E Mao,<sup>1</sup> B K Team,<sup>1</sup> J Tonsing.<sup>2</sup> <sup>1</sup>National Center for Tuberculosis and Leprosy Control, Phnom Penh, Cambodia; <sup>2</sup>TB CARE I/FHI 360/USAID

**Background:** An assessment of Private Providers for Tuberculosis in Cambodia in 2004 pointed out that 63% of TB suspects in Cambodia use private providers as their first choice for advice and care. This is a great concern as it results in inappropriate treatments and diagnostic delays leading to further spread of TB in the communities and to drug resistance TB. Moreover, the MoH issued a ban on import of TB drugs and their substances; and pharmacies are not authorized to sell these drugs. Cambodia NTP and its partners designed Public-Private Mix referral strategy which requires all private providers to refer TB suspects to public DOTS services for diagnosis and treatment.

**Objective:** Increase TB case detection, contribute to stop pharmacy selling anti-TB drugs and prevent the risk of multidrug-resistant tuberculosis.

**Method:** The PPM-DOTS strategy focuses on the referral of TB suspects to the public DOTS. This strategy has been implemented since 2005 in 10/24 provinces and 37/77 operational districts. All private providers in the PPM network in these provinces are obliged to refer TB suspects from their facilities to the public DOTS facilities for TB diagnosis and treatment.

**Results:** From January to December 2011, 5024 TB suspects were referred by private providers to public DOTS facilities. Among those, 2920 were reported at public facilities. 691 were diagnosed TB. All cases were treated under DOTS.

**Conclusion:** Results of the PPM shows that large numbers of TB suspects have been referred from the private providers and are reaching the public facilities

for diagnosis and treatment. Increasing involvement of private providers in TB control is a strategy to increase case detection and contribute to stop pharmacy selling anti-TB drugs, also prevent the emergence of MDR-TB.

### PROGRESS AND PROSPECTS: SUSTAINABILITY OF TUBERCULOSIS VACCINE DEVELOPMENT

#### Potential public health impact of new tuberculosis vaccines

C Lienhardt. World Health Organization, Geneva, Switzerland

Much progress has been made in the research and development of new TB vaccines over the last decade. There are currently twelve vaccine candidates in clinical trials, with two candidates currently in Phase IIb clinical trials in sub-Saharan Africa and four in Phase IIa trials. Research on new TB vaccines is now at a crucial juncture. While the past decade focused on the discovery of novel approaches and moving new vaccine candidates from the laboratory to early clinical trials, the focus of the next decade will be to build on the tremendous progress that has been made. This will entail learning from the efficacy of vaccine candidates in clinical development, identifying much needed markers and correlates of immune protection that will greatly assist in the selection of the next generation of vaccine candidates, but also laying the groundwork for the licensure and introduction of new TB vaccines in countries. As shown by modeling studies, the introduction of new, effective TB vaccines and vaccination strategies is crucial to meet the TB elimination target, and should be done in close synergy with the introduction of novel diagnostic and treatment strategies. The potential epidemiological and public health impact of new vaccines will depend on the demonstrated vaccine efficacy, vaccine coverage and epidemic background, as well as on the populations the new vaccine will target—i.e., unexposed or infected populations. Although the prevention of infection is of the highest importance in areas of intense transmission, the protection of people who have already been infected will be vital during the elimination phase of TB control. More work is needed to develop models to inform on how to optimize public health impact of TB vaccinations while maintaining feasibility.

### **Leveraging capacity, partnerships and innovation for large-scale tuberculosis vaccine trials**

H Mahomed, M Tameris, M Hatherill. South African TB Vaccine Initiative, University of Cape Town, Cape Town, South Africa

Twelve TB vaccines are actively being tested in clinical trials with two in phase IIb trials. Given the absence of an immune correlate of protection and the need to use clinical endpoints in TB vaccine efficacy trials, phase IIb and III trials will of necessity have to recruit large numbers and have lengthy follow up periods making such trials costly. TB is a major contributor to global morbidity and mortality and new TB vaccines are a key component of international strategies to combat TB. No single institution will be able to shoulder the burden of these necessary trials so partnerships between major funders such as the Gates Foundation, European Developing Countries Trials Partnership (EDCTP), National Institutes of Health (NIH), Wellcome Trust, private sector and major TB vaccine organizations such as Aeras and the Tuberculosis Vaccine Initiative (TBVI) will be crucial to ensuring the viability of TB vaccine development. These trials would need to be conducted in diverse high burden settings. The TB Vaccines Sites Network (TBVACSIN) enables clinical trial sites to share experiences and to increase capacity for TB vaccine trials. TBVACSIN currently includes sites primarily in Africa, but may include potential trial sites in Asia. The NIH National Institute of Allergy and Infectious Diseases networks are starting to participate in TB vaccine clinical trials. Utilising existing trial networks working in other disease areas is one way of leveraging capacity and saving site development costs since these sites are experienced in clinical trials and often have high TB burdens as well. Innovative approaches are needed given funding constraints so adaptive trial designs should be explored. The search for a human challenge model, for immune correlates of protection and ways of detecting high risk populations are domains of scientific innovation that may also facilitate progress towards a new effective TB vaccine.

### **The role of China and India in tuberculosis vaccine development**

J Lou. China National Biotech Group, Beijing, China

China bears one of the highest burdens of tuberculosis (TB) in the world, and a recent study indicated that nearly 1 in 10 cases of TB in China is multidrug-resistant. Given its burden of disease, its resources as an emerging economy, China has the potential to play a significant role in the development of new TB vaccines. The government of China has become increasingly committed to the prevention and treatment of TB. With support and involvement from government

agencies such as the Ministry of Science and Technology (MOST) and China CDC, private and government owned enterprises alike have been increasing their input in the research, development, and manufacturing of new and effective TB vaccines. As a major EPI vaccine manufacturer in China, China National Biotech Group (CNBG) has been making great efforts in the project.

### **CHALLENGES IN THE DESIGN AND CONDUCT OF CLINICAL TRIALS FOR IMPROVING THE TREATMENT OF TUBERCULOSIS**

#### **Challenges in the design of clinical trials**

A J Nunn. Medical Research Council Clinical Trials Unit, London, UK

Although the need for new regimens for tuberculosis (TB) is undisputed and there are now several promising drug candidates emerging, the research pathway is far from straightforward. Regimens for drug sensitive disease usually consist of four drugs and the number of combinations allowing for possible differences in dosages present challenges of choice in early phase studies. There is an urgent need for well validated surrogates to assist in selection of the regimens with the best chance of success in longer term efficacy studies. Because of the highly successful results usually attained with standard regimens in phase III trials the superiority design is no longer appropriate in most settings. Non-inferiority trials have their limitations and often require large sample sizes. Trials in MDR-TB while avoiding some of the issues in drug sensitive disease present their own particular challenges, not least because of the heterogeneity of the patient population group. Current approaches to address some of the challenges in both early and late phase trials will be discussed.

#### **Challenges of conducting multicentre trials for new MDR-TB treatments: a sponsor's perspective**

I D Rusen. International Union Against Tuberculosis and Lung Disease, Paris, France

**Background:** Arrangements for the implementation of clinical trials can vary in terms of relationships and roles between donor, sponsor and implementing agency. The challenges of trial implementation from the sponsor's perspective are dependent on these working relationships. STREAM (standardised treatment regimen of anti-tuberculosis drugs for patients with multiple drug-resistant tuberculosis) is a multicentre clinical trial evaluating a shortened treatment regimen for MDR-TB which is primarily funded

through a Cooperative Agreement between the United States Agency for International Development (USAID) and the International Union Against Tuberculosis and Lung Disease (The Union).

**Objectives:** To describe the framework for trial implementation within STREAM and the resulting challenges from the sponsor's perspective

**Findings:** STREAM has utilized a hybrid model of delegation of responsibility for trial implementation to the Medical Research Council-UK, while maintaining ownership of specific trial tasks, as well as close involvement in day to day trial activities. Against this backdrop, the main challenges have been coordination of procurement activities, provision of insurance coverage and reconciling various donor requirements with trial implementation needs.

**Conclusion:** The STREAM trial has effectively utilized a hybrid model of direct sponsor involvement and delegation to a specialized research institution. The challenges experienced relate to both coordination between multiple partners and to specific components of trial implementation.

### Challenges of conducting multicentre trials for new MDR-TB treatments: an investigator's perspective

D Kokebu. St. Peter's Hospital, Addis Ababa, and Global Health Committee, Addis Ababa, Ethiopia

**Background:** Ethiopia is one of the high burden MDR-TB countries with an estimated prevalence of 1.6% among new patients and 11.8% among re-treatment cases. MDR-TB treatment was initiated in the country in February 2009 by the Federal Ministry of Health in collaboration with a non-governmental organization, the Global Health Committee and other partners. Ethiopia is one of the STREAM clinical trial sites. The presence of an active MDR-TB program and support by health authorities, local institutions and other stakeholders increase the likelihood of being selected as a trial site for new MDR-TB treatment. Availability of TB laboratory is one of the necessary conditions to conduct TB clinical trial. Integrating the trial protocol patient management plan with the existing MDR-TB program model of care needs careful planning. Approval processes by ethical review committees usually take a long time and it is important to be familiar with application processes and country-specific requirements. Site agreements also need to be finalized as early as possible in the course of the trial. Human resource issues can pose several challenges. It is advisable to involve in the trial as many staffs working in the routine program as possible to create a sense of ownership and acceptance. Allocation of adequate budget, building the capacity of the laboratory, establishing sample and other materials transport mechanism, clear plan to avoid delays in the importation process of medica-

tions and equipments are other areas that need special attention.

**Conclusion:** MDR-TB treatment clinical trials can be conducted successfully with careful planning and an insight into potential challenges at the local level. The challenges can arise from limited experience of local sites in conducting clinical trials and limited international experience in conducting MDR-TB treatment clinical trials.

### The impact of exogenous reinfection on the conduct and interpretation of clinical trials

A Bateson, T McHugh. Centre for Clinical Microbiology, Department of Infection, University College London, London, UK

Patients may fail tuberculosis treatment as a result of the failure of antibiotics to eradicate the primary infection by the end of treatment, or as a result of recurrent infection after the completion of therapy. This recurrent infection may be due to endogenous reactivation of the primary infectious strain or due to an exogenous infection with a new strain. These are termed relapse and reinfection respectively. It is critical for the evaluation of efficacy in a clinical trial to distinguish between these two categories of recurrent infection. Current practice for the identification of strains of *M. tuberculosis* is to use MIRU typing and/or IS6110 RFLP analysis, however, the advent of whole genome sequencing has introduced a new level of discrimination. In the clinical trial setting, the sensitivity of the molecular typing technology will impact on the assignment of relapse or reinfection. This may lead to an under or over estimation of patients with an unfavourable outcome during the follow up period, as reinfection with a new strain is generally not considered unfavourable. The relative merits of the typing methodologies will be discussed in the light of our experience from ongoing trials.

### Adaptive and other novel trial designs for late-phase clinical trials

P P J Phillips. Medical Research Council Clinical Trials Unit, London, UK

A growing number of novel combination regimens are being studied in phase II and phase III clinical trials that include new chemical entities, new doses of established drugs or approved drugs without a TB indication. Relapse-free cure is the established endpoint for clinical trials and therefore phase III trials following patients for a minimum of 18 months are necessary to confirm the efficacy of a new combination regimen. Development of new regimens to shorten and improve the treatment of drug sensitive or drug resistance TB is a long process with multiple phase I safety and phase II efficacy trials even before a combination enters phase III. In a traditional fixed sample

size clinical trial, the analysis of the trial data is only conducted at the end of the trial when the required number of patients have completed follow-up. In an adaptive clinical trial, interim analyses are conducted during the trial using accruing trial data and the results used to make changes to aspects of the trial such as sample size or the experimental regimens being studied. Any changes and thresholds triggering these changes must be pre-specified in the protocol. Adaptive and other novel trial designs for phase II and phase III trials are drug development tools that can be used to speed combination development. Novel trial designs that are being implemented by different research groups in current and planned phase II and phase III clinical trials to improve the treatment of TB will be discussed, including presentation of how these designs are more efficient than the traditional fixed sample size designs.

## CAPITALISING CORPORATE SECTOR STRENGTHS TO ADDRESS TUBERCULOSIS AND HIV CHALLENGES

### Global perspectives: the role of the corporate sector in tuberculosis care and control

M Uplekar, H Dias. Stop TB Department, World Health Organization, Geneva, Switzerland

There are currently 3 billion people in the world of work. Of these, nearly 1.3 billion do not earn enough to lift themselves out of poverty, making them vulnerable to diseases such as tuberculosis (TB). Businesses across the board—small and big—can contribute in diverse ways to TB care and control. While big companies may be able to provide a wider range of TB and TB-HIV services to their workers, small businesses are likely to offer limited TB care services (Figure). As a first step all companies should define and develop a TB or TB-HIV workplace policy in collaboration with all stakeholders as a sign of commitment. This can then be followed by the implementation of activities based on the need, the capacity and

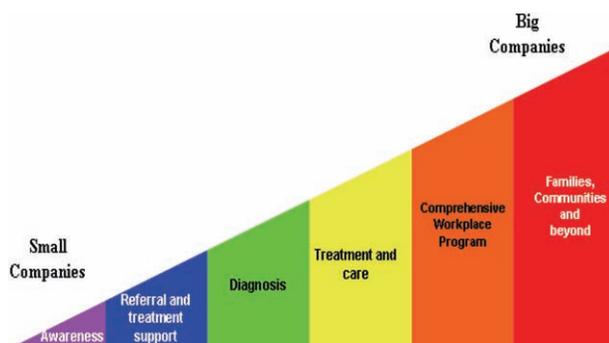


Figure Menu of options.

available resources. This presentation outlines some of the successful initiatives and country examples of engaging the corporate sector in TB care and control. The Stop TB Department of the World Health Organization, jointly the International Labour Organization, UNAIDS and other partners, has developed global guidance on partnering with the business sector for TB care and control. Highlights of this guidance document will be presented and discussed.

### Contribution of the mining industry to tuberculosis care: successes and challenges

G Churchyard,<sup>1,2</sup> K L Fielding,<sup>2</sup> E Vynnycky,<sup>2,3</sup> R G White,<sup>2</sup> A D Grant.<sup>2</sup> <sup>1</sup>Aurum Institute, Johannesburg, Gauteng, South Africa; <sup>2</sup>London School of Hygiene & Tropical Medicine, London; <sup>3</sup>Health Protection Agency, London, UK

Tuberculosis (TB) has been an important health problem in the South African gold mining industry for more than a century. TB case notification rates among gold miners are high (~3%/year) due to a high prevalence of HIV (~30% in 2000) and silicosis. Comprehensive TB control programmes, which include active case finding, active promotion of voluntary HIV testing and ready access to isoniazid preventive therapy (IPT) and free antiretroviral therapy (ART) has failed to control TB in gold mines. In order to find a solution to an extreme epidemic the mining industry participated in the 'Thibela TB' study that evaluated the impact of community-wide IPT for all workers regardless of HIV status, added to standard TB control. Community-wide IPT in addition to standard TB control did not reduce TB incidence or prevalence at a population level even though TB incidence was reduced by 63% at the individual level while taking IPT. Possible explanations for the lack of population-level impact include variable IPT coverage, high TB transmission rates, and increased TB susceptibility due to HIV and silicosis. Mathematical modelling suggests that combination strategies that include reducing treatment delays, use of more sensitive diagnostics for screening, maximizing ART coverage and continuous IPT targeted to HIV-infected persons would improve TB control in this setting. The lessons learnt from the mining industry provide a model for combination prevention to improve TB control in other high HIV settings.

### Working with the tea estates in Kenya for provision of tuberculosis and HIV services

J Sitienei,<sup>1</sup> J Ong'ang'o,<sup>2</sup> K Hillary,<sup>1,3</sup> M Maurice.<sup>4</sup> <sup>1</sup>Ministry of Public Health and Sanitation, Nairobi; <sup>2</sup>Kenya Medical Research Institute, Nairobi; <sup>3</sup>World Health Organization, Nairobi; <sup>4</sup>USAID, Kenya, Nairobi, Kenya

**Background:** Control of tuberculosis is beyond the ministries of health and all players are needed to actively participate. Tea estates in Kenya provide

employment opportunities especially for low skilled laborers as tea picking is still manual. However, TB remains a big challenge in this community because of overcrowding, HIV infection amongst other reasons.

**Objective:** To evaluate awareness about TB and HIV/AIDS among employers and employees in tea estates of Kenya and quantify the contribution to reduction of TB-HIV stigma and discrimination by the tea estates towards improving access to TB-HIV services.

**Methodology:** The Tea estates that contribute towards TB and HIV control through provision of health services were visited and evaluated through qualitative methods.

**Results:** Tea estates in Kenya have an organized health care delivery system that is linked to the public sector. TB is still a strange problem to most people and therefore stigma and discrimination remain a major problem contributing to increased transmission of TB in the work place. In addition, the type of housing in the tea estates provides TB transmission environment. Several players including the community, insurance and individuals play a role in control of disease.

**Conclusion:** Tea estates in Kenya contribute substantial role in TB control.

**Recommendations:** There is an urgent need to develop workplace policies and guidelines on implementation of TB control activities in the corporate sector. Advocacy at all levels should be increased to tap into resources available through corporate social responsibility. Additionally, there should be aggressive promotion to include a TB component in companies with HIV workplace programs.

## ENSURING THE QUALITY OF TUBERCULOSIS LABORATORY SERVICES

### The GLI stepwise implementation guide for building and sustaining quality tuberculosis laboratories

S M van Beers, T A M Datema, L Oskam, P R Klatser.  
KIT Biomedical Research, Royal Tropical Institute, Amsterdam, The Netherlands

To implement a quality management system (QMS) a laboratory can use standards, guidelines and checklists. Standards sum up requirements with which a QMS must comply without providing any guidance; guidelines provide deeper understanding of laboratory processes but do not describe how a QMS should be implemented step-by-step; checklists are useful for assessing progress but generally do not provide guidance either. The GLI Stepwise Process Towards TB Laboratory Accreditation provides a step-by-step pathway that provides guidance for implementing an ISO 15189 QMS in a tuberculosis laboratory that

aims for accreditation. The tool has the form of a website and can be found at [www.GLIquality.org](http://www.GLIquality.org). In the GLI tool the process of implementing a QMS is divided into four phases, with each phase having a specific focus. In each phase the tool provides a framework with a suggested order of steps for day to day implementation of the QMS but the tool also shows which activities need to be performed for each of the CLSI defined twelve Quality System Essentials. Every laboratory should not have to reinvent the wheel when implementing a QMS. Besides funding and commitment, the laboratory needs during this process provision of tools, templates of QMS documents for TB laboratories such as Standard Operation Procedures, and background information for deeper insight in specific quality management principles. With each step in the GLI tool links are provided to such materials. The tool was launched at the Union World Conference in Lille in 2011 and is currently being piloted. As the GLI tool has the form of a website it can continuously be adapted: output of the pilot is directly used for improvement of the tool.

### Documenting and recognising quality laboratory management and testing using SLIPTA

J B Ndiokubwayo, J Nkengasong. WHO-Regional Office for Africa, Brazzaville, Congo

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 WHO/AFRO, the US Centers for Disease Control and Prevention and other partners for clinical laboratories in the African region. One to five stars are accredited to laboratories based on the level of compliance with a checklist. The content of the checklist covers all aspects of total quality management; it strongly prioritizes resource management activities. WHO-AFRO recognizes the gap between the current state of laboratories in Africa and the requirements of ISO 15189, noting that many laboratories would require an interim accreditation as the ISO 15189 accreditation is out of reach. The SLIPTA is meant to fill this gap and is not aimed at replacing the ISO 15189 accreditation standard. The SLIPTA follows a stepwise approach rather than a binary pass/fail system as is used for most international standards. Accreditation is given in five tiers, awarded in the form of stars. The aim is to achieve full five-star accreditation, and, where deficient, prioritize efforts to improve the accreditation rating in a timely manner. The requirements of the SLIPTA accreditation are formulated in the form of questions in its checklist.

The number of stars being awarded to a laboratory depends on the level of compliance with the checklist. The checklist consists of 110 questions (totalling 250 points) subdivided over 12 sections. The launch of the SLIPTA accreditation scheme in itself has already sensitized policy makers to the importance of quality laboratory services and shows laboratory managers the existence and importance of quality management. This may facilitate more efficient and faster uptake and implementation of QM in the (clinical) laboratory.

### Improving the quality of HIV and tuberculosis laboratories: the Rwanda experience

A Umubyeyi Nyaruhirira. Management Sciences for Health, Laboratories, Kigali, Rwanda

**Background:** Rwanda has started the journey of accreditation preparedness at central level with 5 laboratories in January 2010 using the Stepwise Laboratory (Quality) Improvement Process Towards Accreditation (SLIPTA) established by WHO-AFRO to strengthen laboratory systems of his member states. In August 2011 the preparedness process has been decentralized at regional level.

**Methods:** Data from baseline assessments using the SLIPTA checklist were compared to those collected 16 months after three successive SLMTA workshops and mentored improvement projects to describe achieved levels of quality improvement. Total score and percentage improvement were analyzed by facility level, component, and management area. In May 2012, a readiness assessment was carried out for 5 central laboratories to prepare them on the formal application to an international accreditation body.

**Results:** For the 5 central laboratories at baseline one lab achieved a compliance level to the checklist above 65% (2 stars). The remaining labs were under 50% (0 stars). At the post-SLMTA assessment in May 2011, 4 labs improved more than 30%, reaching 3 stars for 2 labs (>75%), 2 stars for 2 labs (>65%) and one star for one lab (>55%). Changes have been observed regarding documentation, biosafety, and stock management. Lesson learnt from the accreditation preparedness at central level were able to design sustainable interventions and achieved measurable progress as soon as laboratories staff are committed. It has been confirmed when shifting the process from central labs to the 5 regional laboratories. In May 2012, 4 lab at central level reached 4 stars and one 3 stars.

**Conclusion:** Committed staff and tailored action plans are able to introduce quality culture even before SLMTA training and mentoring process starting. The national mentor team built after SLMTA process at central level is able to assist a decentralized level to strengthen the Rwandan laboratory network.

### Sustaining improvements in laboratory services through quality assurance: the Thailand experience

S Rienthong. National TB Reference Laboratory, Bureau of TB, Department of Disease Control, Ministry of Public Health, Bangkok, Thailand

The laboratory services play an importance role in TB diagnosis and care. However, the impact of laboratory services on patient care depends critically on the reliability of the results obtain with quality assurance. In Thailand, the EQA of smear microscopy has established since 1995 by LQAS system, blinded re-checking method. The first controllers are an importance person for blinded rechecking slides. In the first implementation of this program, the technicians of RRL and NTRL have been acting as the first and second controller, respectively. Unfortunately, after the expansion through the country, the highly workload under the limited of man power is reflect to the quality of the program. Then, the addition controllers need to be increased. So, we have set up the controller course and selected the lab technician staffs that interest and good willingness to join the program from provincial hospitals. The well trained and certified persons from the course will be act as the first controller according to the NTP guideline for the community hospitals in that province. NTRL and RRL are the second controller and also be responsibility for the monitoring and supervision for sustainable and ensuring the quality of TB laboratory services in Thailand.

### Impact of improved quality management of AFB-microscopy laboratory networks

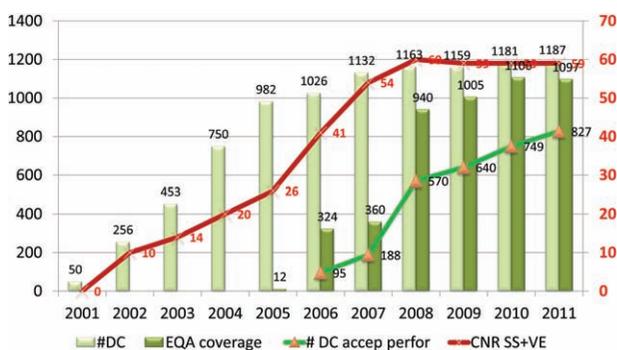
S Tahseen,<sup>1,2</sup> E Qadeer,<sup>2</sup> M Hussain,<sup>1</sup> A Ansari,<sup>3</sup> Z Tahir,<sup>4</sup> F Nasir.<sup>5</sup> <sup>1</sup>National TB Reference Laboratory, NTP, Islamabad, <sup>2</sup>National Tuberculosis Control Programme, Islamabad, <sup>3</sup>Provincial TB Control Programme–Sindh, Karachi, <sup>4</sup>Provincial TB Reference Laboratory–Punjab, Lahore, <sup>5</sup>Provincial TB Reference Laboratory–KP, Peshawar, Pakistan

**Background:** Pakistan adopted the DOTs strategy in 2000 and implementation started in 2001 which then expanded rapidly to cover all public sector health facilities by 2005. Number of AFB microscopy laboratories increased from less than 50 to more then 1000 but little was done for quality assurance (QA) of diagnostic services. With improved coverage case notification rate (CNR) increased from –0% in 2001 to –26/100K in 2005. QA programme for microscopy network was piloted in one district in 2005 and was then gradually expanded to cover >90% of AFB laboratories by 2010. Huge inputs were put in place for implementing quality assurance scheme for AFB microscopy network (MNW) at peripheral, intermediate and central level.

**Objective:** To study impact of improved quality management of AFB-microscopy laboratory networks on case finding and treatment monitoring.

**Method:** Routine laboratory performance and national data on case notification and proportion of smear positive cases were analyzed to study impact of introduction of quality management system into AFB-MNW.

**Result:** Parallel with implementation of QA scheme for AFB-MNW a rapid increase in case notification was observed from baseline of 26/100K in 2005 to 56/100k in 2009 (Figure). A much gradual improvement was seen in proportion of smear positive pulmonary TB cases from 42% in 2005 to 49% in 2010. Impact variation was observed between district. In general maximum increase in case notification was seen in largest province with significant rise in suspect positivity rate from <10% (2005) to >14% (2008) in most of the districts. In other province improvement in sensitivity of microscopy was clearly evident from increase in average proportion of positive follow up smears from 3.3% in 2005 to 5.6% in 2008.



**Figure** Impact of improved microscopy and EQA coverage on SS+ve case notification.

**Conclusion:** QA scheme of AFB microscopy is instrumental in improving TB control efforts but sustained strenuous efforts are required to maintain quality of services.

## WHO HAS THE RIGHT TO HEALTH CARE, AND WHO IS RESPONSIBLE FOR ENSURING IT?

### MDR-TB: are drugs available to all those who need them?

A Trébuq. International Union Against Tuberculosis and Lung Disease, Paris, France

Although multidrug-resistant tuberculosis (MDR-TB) is high on the international health agenda, access to the specific drugs that are required to cure the patients is still very challenging. Several ethical questions will be raised during this presentation:

- 1 If drugs are not available, is it ethical to diagnose MDR-TB without procuring treatment? Is it useful for the individual? Is it useful for the community?

- 2 What regimen should we use to treat MDR-TB patients? International guidelines propose a regimen that is known to result in treatment success rates of around 55%. The GRADE system used by the WHO to document the strength and the quality of these recommendations gives, for most of them: conditional recommendation/very low quality evidence. How, in these circumstances, ethical is it to use/test other regimens? What are the challenges we have to face in the day to day world?
- 3 How can we balance the priorities between 'normal' TB and MDR-TB within a National Tuberculosis Programme? Who should pay for the MDR-TB drugs?

### How can they breathe? Do all patients with asthma have access to recommended drugs?

K Bissell. International Union Against Tuberculosis and Lung Disease, Paris, France; The University of Auckland, Auckland, New Zealand

**Aim:** To describe why not all patients have access to recommended medicines for asthma and explore the solutions and responsibilities at national and global levels.

**Results:** Health equity aims to accelerate health progress among poor and socially excluded groups. The poor and marginalised seem far more likely to suffer more from the widespread problems of access to asthma medicines and care. Common countrywide barriers to access to essential asthma medicines include countries not having correct medicines or dosages on their essential medicines lists; poor availability and affordability of medicines and care; lack of standardised, effective national guidelines, procurement, distribution and prescription of medicines; lack of health care worker training and systems for long-term care of asthma; lack of patient education and community advocates. In addition, poor and marginalised asthmatics may be: disproportionately disadvantaged when they cannot attend school or work due to asthma; less able to control their environment (e.g., home, workplace) to reduce factors that trigger their asthma; less able to seek the necessary long-term care; less empowered to understand how to use the medicines correctly and how to self-manage their asthma. Countries need to address the countrywide barriers as well as have pro-poor strategies in place to these additional barriers. Activity at international level such as research, guideline-writing, policy-making, governance, advocacy, pharmaceutical company marketing, mechanisms involved in international aid, trade and development, can have a significant impact on national health policy, and availability of and access to medicines and care. There is a global responsibility to act more transparently and ethically to improve equity of access to essential medicines and care for asthma.

### **'Why should I not use tobacco products?' Is anti-tobacco education accessible to everyone?**

P Lal. International Union Against Tuberculosis and Lung Disease, New Delhi, India

For most of the 20th century, no conceptual umbrella existed to counter the harms of tobacco use or its growing addiction. In the 1950s, studies from many countries and growing debates in media led to independent and government-supported commissions to examine the evidence. Tobacco control efforts began in the west in the 1960s and tobacco companies began investing energy in creating markets in developing countries. As the epidemic in these countries grew silently, it became challenging to design tobacco control interventions in culturally-diverse countries with complex tobacco use and types. The spread of modern media may explain convergence, or perhaps the global development of modern consumer capitalism and its effects. What therefore are the 'governing ideas' about tobacco control and are anti-tobacco education enough?

**Results:** Today the revitalized tobacco control paradigm extends well beyond the Western world and has gone global as a 'scientific' enterprise itself. Global Adult Tobacco Surveys (2009–2011) present a complex scenario of those aware of tobacco harms and but finds that few current users effectively quit tobacco use, with or without support. Current efforts to inform may have limited effect. Weak science currently does little inform policymaking in developing countries. Nascent tobacco control programmes remains vulnerable to corporate counterattack. This prevents effective tobacco control messages to go upstream to policymakers and disseminate downstream to every individual. Tobacco control messaging needs to be contextualised, using media strategies which effectively inform communities and appeal to the individual.

## **THE ROLE OF COMMUNICATIONS IN CHANGING SOCIAL NORMS AND PROMOTING PUBLIC HEALTH POLICY IN LOW- AND MIDDLE-INCOME COUNTRIES**

### **The role of communications in a comprehensive public health strategy to reduce tobacco use**

T Turk,<sup>1</sup> S Mullin,<sup>2</sup> N Murukutla.<sup>2</sup> <sup>1</sup>World Lung Foundation, Sydney, NSW, Australia; <sup>2</sup>World Lung Foundation, New York, NY, USA

Population level communication programs are an essential component in any comprehensive public health strategy to reduce tobacco use. Bloomberg funded

World Lung Foundation communication programs conducted in 22 high tobacco burden, low- and middle-income countries (LMICs) focus on the 'W' component of the Tobacco Framework Convention MPOWER measures—Warn of the dangers of tobacco. However, communication campaigns are also successful in supporting other measures including the 'P'—Protect people from tobacco smoke and 'O'—Offer help to quit tobacco use. Less acknowledged is the critical role that communication plays in Enforcing tobacco bans ('E'), influencing policy to Raise taxes ('R') and Monitoring and prevention policies ('M'). Compelling evidence is presented of the efficacy of tobacco control communication campaigns to support MPOWER measures by rapidly setting the program agenda to increase awareness of the dangers of tobacco, change public attitudes to tobacco use, and influence policy direction. Additionally, evidence is provided on the successes of public communication campaigns to promote cessation attempts and reduce the harms of second hand smoke exposure with the efficacy of these approaches also emerging in LMICs. Lessons learned include the need for message synergy and a strategic roll-out of communication campaigns with community and interpersonal communication approaches in order to optimize behavioral outcomes.

### **The ripple effect: using subnational campaigns to model success for a national effort in China**

Y Chang. World Lung Foundation, New York, NY, USA

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. 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. Since ratifying the FCTC in 2005, the tobacco control movement in China has grown, slowly but surely. Due to its highly-decentralized political structure, momentum at the subnational level has led much of the way, particularly in the area of public education. By the end of 2011, strong public education campaigns had been mounted in over 20 key cities and provinces across the country. Still, a strong national effort was needed as less than 25% of adults were aware of the health harms associated with tobacco use and secondhand smoke exposure. In 2012, the World Lung Foundation worked with the health promotion arm of China Ministry of Health, the Chinese Center for Health Education, to design and execute China's inaugural national tobacco control mass media campaign. This presentation will look at some of the subnational

campaigns that helped pave the way, and will also introduce some of the key findings from the national campaign, and explore future strategies.

### Mass media as a social mobiliser: India's effort to reduce smokeless tobacco

N Murukutla. World Lung Foundation, New Delhi, India

Smokeless tobacco consumption in India is a significant source of morbidity and mortality. Almost 26% of adults (15 years and older) consume one or other forms of smokeless tobacco while only 14% smoke. The scale of the smokeless tobacco problem in India is growing with sales of smokeless tobacco, which were worth 210.3 billion rupees (US\$4.6 billion) in 2004, reported to double by 2014. A number of studies show that the prevalence and growth of smokeless tobacco use in India and the resultant burden of disease are linked to gender, age, educational and income disparities, regional differences and other social inequalities. Addressing the smokeless tobacco epidemic has therefore emerged as a critical public health priority. Multisectoral and multilevel efforts are currently underway to reduce smokeless tobacco usage, including attempts to ban guthka—one of the most prevalent forms of smokeless tobacco. At the population level, mass media campaigns have been critical to educate the public about the harms of smokeless tobacco, to denormalise tobacco usage, encourage quitting, and mobilize support for tobacco control policies. In this session, we discuss the mass media campaigns on the harms of smokeless tobacco usage, aired by the government of India, with technical support from the World Lung Foundation. We describe the genesis and development of the campaigns; evidence of their efficacy; synergies attempted and achieved between mass media campaigns and other social mobilization and advocacy efforts; and, the role mass media campaigns may have played in creating a fertile ground for important policy interventions. We conclude with implications in the future for comprehensive tobacco control programming in India and other LMICs.

### Supporting legislation: using mass media to support compliance and enforcement of smoke-free legislation

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In Viet Nam, around half of adult males currently smoke, while two-thirds of non-smokers report exposure to secondhand smoke (SHS) in the home and around a half report SHS exposure in the workplace. Mass media tobacco control campaigns can contribute to increasing knowledge about tobacco-related harms, influencing attitudes, reducing the social ac-

ceptability of smoking, and motivating behavior change. Importantly, mass media campaigns can also play a significant role in building support for tobacco control policies. Viet Nam ratified the FCTC in 2004 and in June 2012, the National Assembly of Viet Nam passed the country's first comprehensive tobacco control legislation, framed in line with the FCTC. The lead-up to this landmark public health achievement in Viet Nam involved a large-scale, coordinated approach by government and by local and international NGOs. As part of these efforts, World Lung Foundation worked with the Viet Nam Steering Committee on Smoking and Health (VINACOSH) to develop and implement three phases of national mass media campaigns to educate about the harms associated with tobacco smoking and SHS exposure, and to build support for passage of the comprehensive tobacco control law. The first two campaign phases in December 2010–January 2011 and November–December 2011 were primarily television campaigns, while the third phase directly leading up to the National Assembly vote on the tobacco control legislation incorporated 'new media' channels (SMS, website, Facebook) to generate a strong focus for passage of the law, with the strong support of the Viet Nam Youth Union. The campaign phases achieved high population reach (70% and 56% prompted recall), increased knowledge, and raised concerns about harms from smoking and the risks from SHS exposure, particularly for children. This presentation examines the critical role that mass media tobacco control campaigns can play in supporting passage and implementation of smoke-free legislation.

### WHO GUIDELINES ON SCREENING FOR ACTIVE TUBERCULOSIS

#### A systematic literature review of the benefits to communities and individuals of active screening for tuberculosis

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**Background:** Active tuberculosis (TB) case-finding aims to reduce barriers to early TB case detection. The ultimate goal is to improve outcome for people with TB and to reduce *Mycobacterium tuberculosis* transmission in the community through improved case detection, reduction in diagnostic delays and early treatment. Before screening programmes are recommended evidence is needed of individual and/or community-level benefit.

**Methods:** We reviewed the literature for evidence that active TB case-finding 1) initially increases the number of TB cases initiated on TB treatment,

2) identifies cases earlier in the course of disease, 3) reduces mortality and morbidity and 4) impacts on TB epidemiology.

**Results:** A total of 846 publications were identified by the search strategy, 712 publications were excluded on the initial screen and 73 subsequently leaving 61 publications which addressed at least one of the study questions. Screening increases the number of cases found in the short term. In many settings more than half the prevalent TB cases in the community are undiagnosed. Community based case-finding can add a high proportion of cases, but targeting contacts contributes fewer than 10% of cases. Active case-finding tends to find cases earlier and with less severe disease, but this may be attributed to case-finding studies using more sensitive diagnostic methods than routine programmes. Treatment outcomes among people identified through screening are similar to treatment outcomes among those identified through passive case-finding. Current studies provide insufficient evidence to show that active case-finding impacts on TB epidemiology.

**Conclusion:** Individual and community-level benefits from active TB case-finding remain uncertain. So far the benefits of earlier diagnosis on patient outcomes and transmission have not been established.

### **Sensitivity and specificity of different tuberculosis screening tools and approaches: a systematic review**

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**Background:** Screening for active pulmonary tuberculosis is increasingly recommended as a strategy for early detection of infectious cases. The accuracy of the screening tool determines, in combination with the confirmatory test, the yield of a screening program and the burden on individuals and the health service. Symptom questioning and chest radiography (CXR) are the most widely available screening tools.

**Objectives:** To conduct a systematic review to assess the sensitivity and specificity of questioning for presence of one or more selected symptoms and/or symptom combinations, chest radiography, and combinations of those as screening tools for detecting bacteriologically confirmed active pulmonary tuberculosis. Sources of heterogeneity will also be investigated.

**Methods:** The search includes the data bases

MEDLINE, EMBASE, LILIACS and HTA (Health Technology Assessment) from 1992–2012, supplemented by reference lists of relevant reviews and studies, websites of the World Health Organization (WHO) Stop TB Department, and experts consultation for relevant studies and still unpublished reports. Studies are selected for inclusion if the publication is original research and titles, abstracts, or key words suggest that symptom or CXR screening, or active case finding for TB took place. Full text articles of these studies are obtained and assessed for study eligibility using predefined inclusion and exclusion criteria.

**Data collection and analysis:** 3513 references were identified through the database search. Results of the selection, data collection and analysis will be presented during the symposium.

### **ROLLING OUT XPERT® MTB/RIF: BRINGING DONORS, LABORATORIES AND PROGRAMMES TOGETHER FOR SUSTAINABILITY**

#### **Introduction and status of the global roll-out of Xpert MTB/RIF for the diagnosis of tuberculosis**

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**Background:** Following World Health Organization (WHO) endorsement in 30 June 2012 of the Xpert® MTB/RIF assay, a total of 749 GeneXpert instruments (3602 modules) and more than 1.1 million Xpert MTB/RIF cartridges have been procured in 67 countries under concessional pricing, as of March 2012. Monitoring of procurements, coordination of partners, post-marketing surveillance, and collection of evidence on use of the diagnostic were identified as essential actions required from WHO for the global roll-out.

**Methods:** The WHO Stop TB Department has launched initiatives to systematically collect information on country and partner procurements and plans, on operational problems encountered, and on laboratory workload and results of testing using WHO-recommended algorithms (see [www.who.int/tb/laboratory/mtbrifrollout](http://www.who.int/tb/laboratory/mtbrifrollout)).

**Results:** As of July 2012, TB control programmes and/or partners in 52 countries have provided information on sites of machines and plans for procurements. A growing number of facilities have registered to provide information on operational problems, laboratory workload and Xpert MTB/RIF results; collaboration established with partners includes TBCARE, MSF, TB REACH and the South Africa NHLS.

**Conclusions:** Global monitoring of procurement and implementation plans has facilitated coordination

between country implementers, partners and donors. Post-marketing surveillance allows for the identification of any major recurring problem and aids in ensuring appropriate follow-up by the manufacturer. Collection of evidence on use will allow for the refining of guidance for implementers, enabling a more effective, wider global scale-up. A UNITAID-funded project led by WHO and the Stop TB Partnership will be further rolling-out the technology in 20 recipient countries starting in January 2013.

### Implementing Xpert® MTB/RIF in Africa through National TB Control and HIV/AIDS Control Programme collaboration and laboratory systems strengthening

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**Background:** The Cepheid Xpert® MTB/RIF (Xpert) assay provides an unprecedented opportunity for improving tuberculosis (TB) case detection among persons living with HIV (PLHIV). However, laboratories, National TB Programs (NTP), National AIDS Control Programs (NACP), donors, and partners must closely coordinate efforts and use a systems approach toward strengthening the entire TB-HIV diagnostic process to maximize programmatic and clinical impacts.

**Methods:** The Centers for Disease Control and Prevention (CDC), the Office of the Global AIDS Coordinator (OGAC), and the US Agency for International Development (USAID) developed a technical framework to guide introduction of quality-assured Xpert testing in US Government (USG)-funded projects. This approach is based on:

- 1 Coordination of technical assistance and support by the Ministry of Health (MoH).
- 2 Implementation in accord with the NTP, NACP, and National Laboratory Strategic Plans.
- 3 Phased introduction and evaluation of quality-assured testing according to WHO policy, USG guidance, and global best practices.
- 4 Roll-out coordinated with diagnostic service and treatment capacity scale-up.

**Results:** USG expects to support >200 GeneXpert machines and 300 000 cartridges in 30 countries by the end of 2012. Projects are supporting MoHs through technical assistance on the coordination of partners; development and revision of protocols and policies; training; quality assurance; operational research; and impact measurement.

**Conclusions:** Xpert introduction can be leveraged to

strengthen collaborative TB-HIV activities, laboratory networks, and the laboratory-clinic interface. Initial projects have highlighted the importance of MoH-led coordinating bodies; plans for linking specimen collection and transport, diagnostic testing, prompt result transmission, and TB-HIV care and treatment; and monitoring and evaluation systems to support impact measurement and quality improvement.

### Programmatic experience with Xpert® MTB/RIF implementation in Indonesia

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Indonesia is one of the early implementers of Xpert® MTB/RIF for improved diagnosis of tuberculosis (TB) and multidrug-resistant tuberculosis (MDR-TB). As a first step a broad stakeholders group within the National Tuberculosis Programme (NTP) was established, C-GAT. With technical assistance from TB-CARE1 a detailed plan for rapid implementation including diagnostic algorithms was developed with the priority given to MDR-TB suspects and human immunodeficiency virus (HIV) patients. After arrival of 17 GeneXpert machines and 1700 Xpert MTB/RIF cartridges, training of trainers followed by site preparation was conducted in October 2011. After a memorandum of understanding (MOU) was signed between NTP and the health services, 6 machines started operating since March 2012. Further roll-out of Xpert implementation has purposely been decelerated in order to adequately address challenges and limitations in capacity of programmatic management of drug-resistant TB (PMDT) services to adequately deal with the expected increase in MDR-TB cases. Detailed assessments of laboratories and clinics are being conducted to assure site readiness. Implementation includes an OR component to monitor implementation and collect evidence for further scale-up of Xpert MTB/RIF in collaboration with local research group (TORG). As per July 2012, a total of 969 suspects were examined using GeneXpert. Of these, 598 were diagnosed with *M. tuberculosis*, of whom 235 were confirmed as rifampicin-resistant. Immediate enrollment on treatment remains a challenge: Only 102 patients started treatment directly after GeneXpert diagnosis. Reasons given for delayed enrollment include: 1) Some clinicians want confirmation of resistance through drug sensitivity testing (DST), 2) long pre-enrollment process, 3) limited ward capacity. One patient died awaiting examination results. Current usage is 200 cartridges/month.

**Conclusion:** Implementation of Xpert has resulted to a considerable increase in notification in MDR-TB and TB in HIV patients. Main challenges relate to limitations in capacity to treat the increased number of MDR TB patients and relative shortage of SL Drugs and sustainability of roll out of Xpert MTB/RIF.

### Impact and operational challenges of use of Xpert® MTB/RIF on tuberculosis case finding in PLHIV in Botswana

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**Background:** Although the Xpert® MTB/RIF assay (Xpert) has the potential to improve tuberculosis (TB) case finding among people living with HIV (PLHIV), operational research to evaluate Xpert performance in program settings and impact on outcomes is important. Xpert roll-out evaluation study (XPRES) was developed to introduce Xpert into HIV treatment services in Botswana and to evaluate its diagnostic performance and impact on antiretroviral therapy (ART) outcomes.

**Methods:** XPRES plan and activities are guided by national steering committee chaired by Ministry of Health (MoH). Using a 'Step-Wedge' design over 9 months, 13 Xpert machines (9 placed in district laboratories and four in 'point-of-care' sites) will be deployed to support 22 high volume HIV clinics. MoH recommended microscopy-based TB diagnostic algorithm will be implemented pre-Xpert and MoH Xpert-based algorithm post-Xpert roll-out. TB diagnostic sensitivity of smear- versus Xpert-based algorithms will be compared among TB suspects identified in  $\pm 3300$  pre-Xpert and  $\pm 6300$  post-Xpert study participants. All-cause ART mortality will also be compared pre- and post-Xpert.

**Results:** Site assessment checklists helped facilities prepare for study initiation and Xpert roll-out. XPRES began on July 31st. Primary outcomes to be measured are increase in TB case detection and reduction in mortality among PLHIV. Secondary outcomes include lab and point-of-care performance of Xpert including turn-around-time for TB diagnosis and treatment and impact on drug resistant-TB services. A strong collaborative framework including MoH chaired Steering Committee with close TB-HIV program integration has enhanced the roll-out in a sustainable fashion and aided troubleshooting.

**Conclusions:** XPRES is an integrated program roll-out and evaluation. Readiness checklists helped project preparations. Integrated MoH TB-HIV leadership was essential for XPRES initiation and may ensure sustainability of Xpert roll-out.

### Experience with implementation of Xpert® MTB/RIF in India

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Currently two projects are being implemented in India on CBNAAT under India's Revised National Tuberculosis Control Programme (RNTCP).

1 The RNTCP/FIND/WHO project (September 2011 to November 2013) is being implemented at 18 sites. Project aims at assessing feasibility of decentralized implementation and cost-effectiveness of Xpert® MTB/RIF in the detection of tuberculosis (TB) and (DR) TB in TB suspects. The project also looks into the impact of upfront Xpert MTB/RIF testing on programme outcomes and potential impact on TB transmission. Project would provide inputs to RNTCP on policy decisions on XPERT MTB/RIF, like level of decentralization, target population, operational needs, etc. The 18 project sites are widely dispersed across India, at decentralized locations, having a mix of hilly, tribal, urban slums and other challenging areas. Starting March, 2012 CBNAAT labs have been established by FIND across these 18 sites in a phased manner. Approximately 4000 suspects coming to various public health facilities catered by these sites are being tested every month. Over 9000 suspects (July, 12) have been tested with a 22% MTB Positivity and 2.5% DR-TB rate.

2 EXPANDxTB CBNAAT project is the second ongoing project, with 12 XPERT MTB/RIF based DST labs are being established across the country by FIND. This project supplements the DST capacity of RNTCP laboratory network. Starting June, 2012 five CBNAAT DST labs are functional and remaining labs are expected to come up before end of September, 2012. This 1.5 year project targets offering rapid DST to more than 30000 DR-TB suspects and diagnosing more than 10000 DR-TB patients.

### Implementing Xpert® MTB/RIF for diagnosis of tuberculosis in Nigeria: a joint effort with partners

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**Background:** TB diagnosis and management has largely been dependent on AFB microscopy. Diagnosis of TB among People Living with HIV/AIDS (PLHIV) poses a challenge. Access to DR-TB diagnostics services remained low. With the support of partners, the NTBLCP commenced implementation of GeneXpert MTB/RIF technology in 2011.

**Objective:** To describe the coordination process of the implementation of GeneXpert by the NTBLCP and share challenges and lessons learned.

**Methodology:** A Country GeneXpert Coordinating Team (CGAT) was established. An implementation plan was also developed.

**Results:** Thirty-eight sites were selected through a process guided by geopolitical dispensation and availability of MDR-TB diagnostic capacity across all levels of the laboratory network. The sites were evaluated to determine appropriate placement of the Xpert machines and collect baseline data. Thirty-five laboratory personnel were trained; GeneXpert machines

and inverters for power back-up were installed. Recording forms were developed and disseminated. Joint quarterly supervision and monitoring visits were conducted to the sites to provide technical and logistic support. The CGAT meetings were organized quarterly to discuss progress in implementation as well as expansion plans from partners. From Q4 2011 to Q2 2012, a total of 1246 Xpert tests were performed in 9 sites, 483 (39%) were positive for MTB, of which 164 (34%) were RIF resistant. An error rate of 3.9% was recorded.

**Lessons learned and challenges:** Strong leadership and coordinating mechanism, critical mass of trainers, computer literacy and proficiency, support by recipient-health facilities and regular supervisory support are key for successful roll out GeneXpert technology.

**Conclusion:** GeneXpert MTB/RIF has contributed to scale up of DR-TB control in Nigeria. The next steps will entail integrating the Xpert platform into the current TB diagnosis and treatment strategy.

## TRANSLATING TUBERCULOSIS PROJECTS INTO SUSTAINABLE TUBERCULOSIS PROGRAMMES: LESSONS FROM THE WHO-CIDA INITIATIVE

### Increasing tuberculosis case detection through active case finding among people living with HIV in Swaziland

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**Setting:** Swaziland, a sub-Saharan low-middle income country faced with a severe TB-HIV co-epidemic and significantly threatened by the emergence of drug resistant tuberculosis. The country has an estimated TB incidence of 1287 per 100 000 population, 26% of its adult population (15–49 years) infected with the HIV virus, and 80% of incident TB cases are co-infected with the HIV virus. While up to 86% of enrolled TB patients have known HIV status, and 93% on CPT, and 50% provided with ART, implementation of the three I's had been slow. Intensified TB case detection among people living with HIV was critical to reduce TB-related mortality.

**Methods:** From 2009, the implementation of intensified TB case finding among PLHIV as one of the key high risk populations through WHO/CIDA supported projected. Systematic symptom-based screening following a nationally agreed algorithm was introduced in ART sites. Dedicated TB screening officers were placed at each site, standard protocols developed and screening conducted with appropriate registration and quarterly reporting forms.

**Results:** Decentralization of systematic TB screening among PLHIV in 36 sites. Cumulatively, 3040 new TB cases were detected exclusively through the ICF project from 36 implementing sites, which represents a contribution of between 7% and 10% of all TB notifications in the country from 2009 to 2012. The yield of TB cases among screened individuals ranged from 2% to 12% among implementing sites with 'cough of any duration' being the most predominant symptom albeit the increased diagnostic screening tests to be conducted and the attendant laboratory implications.

**Conclusion:** Implementation of systematic TB screening among people living with HIV resulted in an increased and detection of TB among HIV people living with HIV. About 90% of detected cases were timely initiated on the appropriate TB treatment. The project was catalytic to the strengthening the TB infection control and national IPT roll-out planning.

### Harnessing contact investigation approaches to detect tuberculosis cases in DRC

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**Rationale:** Tuberculosis: one of the leading causes of morbidity and mortality in Democratic Republic of Congo.

- An estimated 220 000 people developed active tuberculosis (TB) in 2010 and half were not detected.
- High TB mortality rate (54 per 100 000).
- Kinshasa's contribution to case notification: 20% but higher TB incidence (?).
- 132/2146 health facilities (6%) are reporting on TB.
- Approach began in 2010 to reach additional cases in coming 3 years.

#### Methods:

- Development of protocols and tools.
- Sensitization and training for staff and community members in 30 selected centers.
- Contact investigation and referral of TB households suspects.
- Regular supportive monitoring and supervision.

#### Results:

Type of TB index case	Index case identified	Index case investigated	Contact listed	Contact investigated	TB suspected	TB case detected
TPM+	8 193	5 981	44 762	31 729	15 155	434 (2.9%)
TPM°	2 361	1 821	13 023	9 734	4 269	54 (1.9%)
Children aged <5 years	534	374	2 819	1 941	979	26 (2.7%)
Total	11 088	8 176 (74%)	60 604	43 404 (72%)	2 040 (47%)	514 (2.5%)

**Analysis:**

- Additional cases: 514 since Quarter 4, 2010–Quarter 1, 2012 and 57% are SS+.
- TB incidence: twice higher around SS+ and children than SS–.

**Sustainability and scalability:**

- This initiative focuses on building and strengthening sustainable within the health system for TB care.
- Contact investigation is being integrated into NTP policy.
- Further studies needed to look at results using new diagnosis tools.

**Conclusion:** Contact investigation can be used as one of new approaches to increase TB detection case.

### Using innovative approaches to increase tuberculosis case detection in Ghana

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**Background:** National Tuberculosis Control programmes are struggling to meet case detection targets. Existing known approaches to improve TB case finding, though not strictly ‘innovative’, have not been widely and systematically used within the health system context, to increase case detection as part of routine health care delivery for sustainable benefit. The WHO-CIDA initiative project in Accra, Ghana planned a phase in implementation of various enhanced or active case finding strategies to find missed TB cases under programmatic conditions within the health system.

**Objective:** To horizontally strengthen the health system to

- identify missed TB cases in crowded outpatient departments in large hospitals in Accra
- identify missed TB cases among persons living with HIV
- identify missed TB cases among household contacts of known TB patients
- engage pharmacies and chemical sellers in identification and referral of people with symptoms of TB
- screen people with diabetes systematically

**Method:** An intervention and comparator sites were identified. In the intervention sites five large hospitals were identified and the various interventions implemented as much as possible without disrupting routine services.

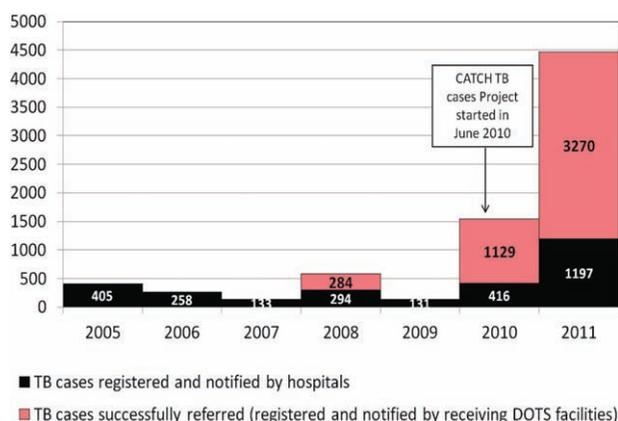
**Results:** The intervention sites kept records and routinely reports on cases detected under various interventions. More cases are identified from intervention sites than comparator sites. Other health facilities on their own volition have started implementing interventions.

**Lessons:** Initial emerging challenges of implementation and encouraging results formed the basis for developing the successful TB R10 global fund proposal which potentially will go to scale to improve TB case finding in all major hospitals and districts in Ghana.

### Sustaining and replicating successes from the WHO-CIDA project

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Despite documented progress in global TB control, every third case of TB still goes undetected in high TB-burden settings. In order to try out country-specific innovative approaches to intensify TB case detection, assess the outcomes of such approaches and share the lessons learnt for development of case detection strategies, the Stop TB Department of the World Health Organization initiated a project in diverse country settings in March 2009. The Canadian International Development Agency (CIDA) provided a grant for this project. The initiative is being implemented in five countries: Democratic Republic of the Congo, Ghana, The Philippines, Swaziland and Viet Nam. The interventions include a setting-specific mix of the following approaches: 1) intensified hospital engagement in large cities, 2) implementation of systematic TB contact investigation, 3) screening for TB among high-risk individuals such as people living with HIV (PLHIV) and people with diabetes; and high-risk populations such as prison inmates and people living in poor urban areas. This presentation summarises the evolution and interim outcomes of the WHO/CIDA initiative for intensifying TB case detection. Expectedly, the outcomes vary greatly from country to country. As the accompanying Figure from the project in the Philippines illustrates, engaging large public hospitals yielded significant un-notified TB cases in most settings. A distinct objective of the project was to achieve a seamless scale up and integration of working approaches into respective national TB



**Figure** Trend of 14 hospitals' contribution to NTP, 2005–2011. CATCH TB cases Project, Philippines.

control strategies. The presentation discusses the extent to which this objective could be achieved and reasons thereof.

## TUBERCULOSIS SCREENING PROGRAMMES FOR HEALTHY MIGRATION AND STRENGTHENING TUBERCULOSIS CONTROL PROGRAMMES

### Public-private partnership for immigration screening in the Dominican Republic

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Consultorios de Visa (CDV) is the only Panel Site performing immigration medical screening for the United States Consular Section in Dominican Republic. The Panel Site also performs screening for Canada, Australia and New Zealand, performing approximately 45 000 to 55 000 examinations per year. In order to facilitate the implementation of the Centers for Disease Control, Division of Global Migration and Quarantine (CDC-DGMQ) Tuberculosis Technical Instructions (TB TIs) using Cultures and Directly Observed Therapy (DOT) for Panel Physicians, CDV formalized a collaborative agreement with the Programa Nacional de Control de Tuberculosis (PNCT), the Dominican Republic's National TB Program (NTP). Initially, the PNCT agreed to provide DOT treatment for all applicants diagnosed with TB by CDV, while CDV would provide all the diagnostics aspects (sputum collection, smears, cultures, DST, laboratory testing, TST, etc.). The PNCT identified this agreement as an opportunity to become an example for public-private partnership in the fight against TB and to obtain TB data in a 'healthy population' actively screened for TB. As the alliance developed, the collaborative agreement expanded: CDV now sponsors two TB clinics, providing logistics, administrative assistance, and training and contributing resources for the proper operation of the clinics, as well as working with community leaders involved in the fight against TB; CDV provides workshops in radiographic interpretation for PNCT physicians and TB nurses; CDV provides training for PNCT TB nurses in TST application and interpretation, and sputum collection; and CDV, through its partner laboratory (RLC), provide training assistance for PNCT TB lab personnel. The aim of this presentation is to provide an example of the symbiotic opportunities

provided by public-private partnership in the fight against TB in a developing nation and how immigration screening can benefit tuberculosis control efforts in countries of origin.

### Laboratory development for immigrant and refugee screening programmes

W Jones. International Organization for Migration, Nairobi, Kenya

Immigrant and refugee health assessment screening programs require chest X-ray examination prior to departure; and if suspicion of tuberculosis is found, sputa smear and culture examination is required. Immigrants generally have health assessments in city centers where access to TB culture laboratories is available. In such settings, the external/internal quality control measures, mycobacteria identification techniques, validated drug susceptibility testing and molecular testing, are required. These services may or may not be available. Networks of laboratories are required to be established with primary culture and identification, and only laboratories validated and performing sufficient volume chosen to perform the drug susceptibility testing on *M. tuberculosis* isolates; for example India, and China. In some cities routine clinical tuberculosis testing menus are not available and need establishment, infrastructure upgrading and/or assistance with quality control systems. Refugee populations often live in remote settings that require the establishment of Mycobacteriology laboratories with the same services available. Examples are Wat Tham Krabok, Mae Sot, Thailand and Dadaab Kenya. In all settings, external/internal quality control measures and validation of DST testing is mandatory. Continued monitoring of the performance of the laboratories is required using the TB laboratory indicators (WHO). Drug Susceptibility validation with WHO panel isolates, re-reading of smears, comparison of DST with molecular tests; Gen Xpert, Hain's Line Probe Assay. Since 2007, this work has been ongoing in regions of East/West Africa. Indian subcontinent, China, and South East Asia and Mexico, for example.

### Health screenings for conflict-affected communities: an opportunity for tuberculosis control

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**Background:** Tunisia is a country with a medium burden of tuberculosis (TB): the annual incidence of TB all forms was 25/100 000 and pulmonary TB incidence rate was 11/100 000 in 2010. Mortality rate was 1.8%, case detection rate was 91% and treatment success rate was 85% in 2009. Several thousands of foreign workers streamed across the Tunisian border

in 2011. The aim of this study is to describe TB profile about refugees in order to improve TB control.

**Methods:** The surveillance based on mandatory declaration allowed NTP to follow cases in Mednine hospital. Because of flow of refugees from Lybia, TB passive screening was implemented in March to September 2011 for all sites of refugees in Choucha. Sputum samples were tested by Mednine hospital Laboratory for direct microscopy examination. Data have been collected by the focal point.

**Results:** NTP registered from March to September 75 suspect TB cases among 700000 refugees (10.7/100000), 36 of them were TB confirmed corresponding to TB rate of 5.14/100000. 11 cases were sputum smear negative, 11 extra-pulmonary TB. The rate of confirmed cases among suspected one was about 50%. All nationalities were diagnosed and treated free of charge. These results suggest that population of refugees is at high risk for TB and active screening was implemented to detect and treat cases early and to prevent the spread of TB to Tunisian population.

**Conclusion:** During this crisis, NTP managed TB cases in refugees thanks to the experience to fight TB since 5 decades: political commitment, lab, standards. In the form refugee movement that is more commonplace than at any time increasing TB transmission, active screening and effective interventions related to NTP activities should be undertaken to decrease the potential contact of local population with refugees.

### Capacity building beyond traditional typical health settings

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**Setting:** Tuberculosis (TB) program of Association of Medical Doctors of Asia (AMDA)–Nepal Primary Health Care Project (PHCP) for Bhutanese Refugees in the clustered huts in camps beyond the traditional typical health setting in Nepal.

**Objective:** To decrease morbidity and mortality by early diagnosis, complete treatment and preventing transmission in the community.

**Design:** The program services are Directly Observed Treatment Short Course (DOTS), laboratory, X-ray, Multi Drug Resistance (MDR) management, early referral, TB-HIV collaboration, cases follow up and defaulter tracing, nutritional supplementary feeding with multi vitamin and health education using Information Education and Communication (IEC) materials. The management of TB drugs is on monthly basis and buffer stock is always maintained with the support and coordination with International Organization for Migration (IOM) and District Public Health Office (DPHO).

**Result:** Six MDR cases were reported in 2011 and are under treatment in coordination with IOM. We

achieved the national target of cured rate (90%) and completed rate (87.6%; national target 85%). TB case finding rate in 2010 was 87.7% and has increased to 109% in 2011.

**Conclusion:** Increasing TB awareness, sensitization, staff training and community participation leading to effective case management. Systematic data recording and reporting has helped in smooth supply of TB drugs. The effective TB screening program has not merely decreased the cases in camps but has also contributed towards the third country resettlement program by effective tuberculosis control.

### The UK screening programme

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The UK has seen a resurgence of tuberculosis (TB) over the last two decades. The increase in TB has been largely driven by disease occurring in risk groups. Individuals born in high TB burden countries now constitute about 74% of newly diagnosed cases. The proportion of cases among the UK born has fallen steadily despite the increase in TB. The prompt identification of TB through active and passive case finding among immigrants has therefore been a central element of UK TB control policy. National policy includes three main elements; screening prior to arrival in the UK, detection at the port of entry and identification post entry. A decision to expand pre-entry screening was taken following a favourable evaluation of a pilot in 15 countries. The pre-entry programme will include the screening of all migrants coming to the UK for longer than six months who are subject to immigration control from countries with a high incidence of TB. Screening will consist of a radiological, and in children clinical, examination followed by bacteriological confirmation and treatment of cases prior to issuance of a visa. The port of entry screening programme will be gradually discontinued as the pre-entry screening programme is rolled out. After arrival in the UK, migrant screening is governed by guidance issued by the UK National Institute of Health and Clinical Excellence (NICE) which requires information about new entrants eligible for screening to be shared with local health authorities. In addition to screening for active TB, local TB services are required to identify latent TB infection (LTBI) using either a two step tuberculin skin test with a confirmatory interferon gamma release assay (IGRA) or a single IGRA, although the extent of the implementation of LTBI screening is variable. All migrants detected with TB in the UK benefit from free treatment.

## CHALLENGES AND SOLUTIONS FOR SUSTAINABLE TUBERCULOSIS AND TB-HIV CARE AMONG MIGRANTS AND MARGINALISED POPULATIONS

### Bridging the gap between penitentiary and community population for sustained TB-HIV care

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**Setting:** Prison facilities located in Georgia.

**Objective:** To achieve health system strengthening, through performing health need assessment for penitentiary sector.

**Design:** 18 detention facilities were identified. Out of them 16 institutions had a mixed regime (general, strict and prison) and two of them were detention health facilities. During this process of health need assessment: capacity building and human resources mobilisation was performed; human resource committed to take over TB control activities in prisons was identified and need of multi sectoral approach was established.

**Results:** The following results have been achieved: new Ministry of Correction and Legal Assistance (MCLA) was created and prison system moved from Ministry of Justice (MOJ) to MCLA; MCLA Medical Department with two units was created; MCLA approved Pilot PHC project in July 2009; Medical Department of MCLA developed first plan of Penitentiary Healthcare System Development in June 2009 and TB program serves as a tool for health system monitoring based on case detection, incidence rate, prevalence rate, treatment outcomes.

**Conclusions:** Through evaluation and needs assessment process following recommendations have been elaborated that need to be urgently addressed for adequate TB control in penitentiary sector: political commitment of MCLA to TB control should increase; staff motivation should increase and training in concepts of TB management should be performed, and systematic strengthening of infectious control, patient follow-up and health education should take place.

### Enhancing collaborative partnerships for care of TB-HIV and alcohol comorbidities

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Tuberculosis (TB) and human immunodeficiency virus (HIV) are syndemic diseases. Alcohol use disorders (AUD) are associated with poor treatment outcomes of these diseases. This may be related to challenges in care and management of TB and HIV diseases in marginalized populations including those with alcohol and substance use disorders. Effective

and sustainable care of these comorbidities require close and sustainable collaboration between patients and their health care providers. However, a critical step in this effective partnership is provision of patient centered care. This collaborative partnership can be achieved by working closely with local community based organizations and non-governmental organizations that work effectively with patients with TB-HIV and alcohol use disorders. This presentation will discuss both patient and health care providers' barriers to effective care of patients with TB-HIV and alcohol use disorders. It will also focus on existing AUD treatment modalities that can be integrated in TB and HIV programs. The presentation will also explore peer support and community based models of care of these three comorbidities.

### Ensuring quality and sustainable tuberculosis care in coal miners in Lesotho

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**Background:** With a population of 1.8 million, Lesotho has the fourth highest incidence of tuberculosis (TB) in the world (637 per 100 000 people per year) and the third highest human immunodeficiency virus (HIV) incidence, with over 23.2% of the population HIV positive. Up to 90% of TB patients are co-infected with HIV. Lesotho is completely surrounded by South Africa. Over 35 000 Basotho men are registered mineworkers in South Africa. This migrant labor system immensely contributes to the high TB incidence, poor treatment compliance and multidrug-resistant (MDR) TB cases.

**Objective:** To discuss challenges and programs that seek to ensure quality and sustainable TB care for mine workers in Lesotho.

**Design:** A descriptive account of initiatives at regional (SADC) level and by two organizations in partnership with the Lesotho government are discussed.

**Results:** Over 150 mineworkers with TB have been treated and followed up by the TEBA projects since 2005. Over 200 mineworkers with MDR-TB have been treated and followed up by PIH-Lesotho in partnership with the Ministry of Health. About 400 community health workers are involved.

**Conclusion:** Successful TB care programs for mineworkers require political will and cooperation at various levels, namely intergovernmental, Mines as well as the miner workers themselves. Community health workers play a pivotal role in providing quality and sustainable TB care for mineworkers.

### Active case finding of tuberculosis among cross-border migrants in Cambodia

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**Background:** The Cambodian border with Thailand in Banteay Meanchey Province is a major return channel for Cambodian irregular migrants, with about 98 000 individuals deported annually by the Thai immigration authorities. The time spent in overcrowded detention centres without access to sufficient nutrition and healthcare increases the likelihood of spread of TB infection as well as poor detection and treatment options.

**Objective:** Early TB detection and increased case notifications among daily flows of Cambodian irregular migrants through systematic TB screening and rapid molecular diagnostics.

**Methods/design:** Between 1 February and 30 June 2012, IOM and government health workers under the National TB Program screened migrants referred daily from the Cambodian border immigration centre to the border hospital due to more than one month detention history or TB symptoms. At the border hospital, all referred migrants received detailed TB symptom and chest X-ray screening. Post-screening, those migrants who had active TB symptoms and/or X-ray findings with abnormalities indicative of active TB (TB suspects) provided one sputum sample for the Xpert<sup>®</sup> MTB/RIF assay, which provided results within two hours. Migrants with bacteriologically positive TB results were then referred to routine treatment within or outside Banteay Meanchey Province target province under the National TB Program.

**Results:** Among the 1776 migrants screened at the hospital, 18% (328) were TB suspects, of which 302 were tested using Xpert MTB/RIF assay. In all, 17.5% (53) TB suspects were confirmed bacteriologically positive for TB and referred for TB treatment.

	Group A (detention >1 month)	Expected Group A (baseline)	Group B (detention <1 month)	Expected Group B (baseline)	All	Expected
% of TB suspects among screened	22% (162/747)	10%-17%	16.5% (166/1,018)	1%-2%	18.5% (328/1,766)	6-11%
% of TB suspects confirmed with new SS+/Bact+	12% (18/154)	25.2% to 42% of people with verbal and/or CXR abnormality	23.6% (35/148)	39-78%	17.5% (53/302)	12-24%

**Conclusion:** For the highly mobile Cambodians of Banteay Meanchey Province, active systematic TB screening and rapid molecular diagnostics at the border immigration centres offer a unique opportunity to increase TB detection and treatment referrals.

### Tuberculosis control strategies among internal migrants in China

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**Aim:** To identify the current status of TB control in floating population in China.

**Methods:** The strategies and policies for TB control in floating population were understood by literature review, and the relative data of TB patients in floating population were collected from the internet-based TB information system to analyze the registration and treatment status in 2010 and 2011.

**Results:** The floating population takes the same policies of free diagnosis and treatment in TB control with the local population in China, and the treatment management for patients of floating population are conducted by the local health workers, with the complementarities of the cross-area management's procedure. Incentive mechanisms were conducted to increase case-finding and improve patient management in some areas. There were 73 963 and 73 635 TB patients registered in floating population respectively in 2010 and 2011, which account for 7.9% and 8.1% of the patients registered in the country; 76% of cases in floating population were detected in the eastern provinces. Among the patients registered in 2010, 68 836 (93.1%) patients were managed in the local areas and 5127 (6.9%) patients were transferred to their hometown for continued treatment management. The successful treatment rate of TB cases in 2010 was 89.2%.

**Conclusion:** TB control in floating population would be well implemented with the current strategies.

## BUILDING NATIONAL AND INTERNATIONAL PARTNERSHIPS TO ENSURE A SUSTAINABLE RESPONSE TO TUBERCULOSIS CHALLENGES

### Stop TB Afghanistan: successfully developing a local fundraising strategy

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**Background:** The National Stop TB Partnership Afghanistan is a registered organization constituted in 2008 that 1) aims to promote equal and active participation of public and private health sectors, civil society, multilateral and bilateral development agencies in Stop TB activities and 2) through a charter, is mandated to expand TB care among marginalized populations through innovative resource mobilization and care delivery through its partners. The partnership has expanded to regional partnerships in key provinces (Kandhar, Mazar, Herat).

**Activities:** The partnership is working in the following areas:

- Inclusiveness and ownership: all sectors involved in TB care are part of the national partnership
- Setting strategic priorities and guiding distribution of resources: national partnership motivates donors to support TB care in areas where the NTP needs help
- Promotion of patient activism: creation of patient groups at national and subnational levels
- Addressing vulnerable populations (women): more women than men are affected by TB
- Fundraising and social support through innovative means: Ramadan zakat donation campaigns
- Creation of subnational partnerships that address local needs in Kandhar, Hirat, Bamyan, Mazar

**Fund-raising:** The partnership has developed a three pronged strategy for resource mobilization:

- 1 Sustaining support of traditional donors. Afghanistan's economy and government are almost 100% reliant on external funding. The Partnership has developed relationships with bilateral donors USAID, CIDA, Italian Cooperation, with support in the range of US\$3–6 million (2007–12). Global Fund and other donors have also been supporting TB activities.
- 2 Actively pursuing and strengthening local resources. Despite the scarcity of domestic resources, the Partnership has been using innovative means of raising funds for TB. During Ramadan, an annual donation campaign is carried out by the Partnership and the NTP. Ramadan donations have been collected in the form of money, food and other material; individual donors have contributed both nationally and regionally through cash and kind.
- 3 Finding new donors. The Afghan Chamber of Commerce and Industry are engaged, pharmaceutical companies have responded (a new genital TB ward is being developed with the help of a local company), and the World Food Programme has been providing food and nutritional support for TB patients for the past few years.

**Way forward:** With the changing security and political environment in Afghanistan, the Partnership is working to ensure continuity of TB control and care services:

- Working with traditional donors to maintain political commitment to TB through innovative advocacy products and events (e.g., CIDA acknowledged through a book and short video).
- Securing technical assistance from partners on development of sound proposals and conducting advocacy for NTP from donors (Global Fund, TB REACH).
- Promoting strategic thinking and effective resource utilization (e.g., TB Task Force, a technical body meets every week with representation of all techni-

cal and implementing partners to avoid duplication and promote optimal use of available resources).

- Promoting synergies with other health programs (e.g., Children's Hospital & Training Center Herat, a large medical care facility developed by the Italian Cooperation for Child Health, is effectively engaged for TB screening, treatment and training of health workers).

### **Stop TB Italia: hosting fundraising events to help high-burden countries in their fight against tuberculosis**

G Besozzi. Stop TB Italy, Milan, Italy

Stop TB Italy was founded in 2004, one of the first national partnerships to establish a collaboration with the global Stop TB Partnership. Its mission is to raise public awareness on the TB problem, to provide training of health professionals and financial support to TB programs in high burden countries. In Italy the current incidence of TB is 7/100 000 inhabitants; TB is not considered as a public health priority and the awareness of general population and of institutions is virtually absent. Stop TB Italy informs the population as TB is a persisting global problem, and needs research and funding capable of supporting national programs in high burden countries, which are well structured but constrained by lack of facilities, personnel and resources. The partnership with private foundations has helped to provide support to the control programs in south Africa, in India and in Senegal. We are creating other partnerships with NGOs like MSF and CUAMM to provide training for health staff working in developing countries. At a time of international financial crisis, it is necessary to do more with less: it is difficult but not impossible. Much can be done creating a network among partners that share interest and commitment, involving civil society and volunteers, creating and repeating attractive media events to give our communication continuity over time. In order to create fundraising opportunities, Stop TB Italia has chosen the arts and music. Since 2010 we have launched the campaign: 'We beat TB' in partnership with Lilly Italia: several concerts attended by people in public Italian squares, to catch their attention and to inform about our activities in Italy and worldwide. For next years, Stop TB Italy, with Stop TB Partnership, Italian foundations, Bocconi University and other Institutions, is trying to create a 'TB and art exhibition', which can stimulate the attention of general population and give the message that the story of TB is not over.

### **Viet Nam Stop TB Partnership: building a sustainable response to the tuberculosis epidemic**

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**Background:** Viet Nam is among the highest burden countries for tuberculosis (TB) and the VN National Tuberculosis Program (VNTP) has led the country's efforts to eliminate TB since 1957. TB control has been challenging despite the VNTP's strong national network, with case detection identified as a persistent challenge. To address this, the VNTP sought to maximize engagement among both international and Viet Nameese organizations with the initial goal to improve case detection for TB elimination.

**Response:** After two years of preliminary discussions among the VNTP's leadership followed by meetings with VN government agencies to gain their support, the Viet Nam STOP TB Partnership (VSTP) was formed in 2010 to support the VNTP's mission to eliminate TB. The VSTP's inaugural quarterly meeting was held June 2010.

**Results:** The VSTP is comprised of 39 partners, including both international and Viet Nameese organizations. Viet Nameese mass organizations such as the Women's Union and the Youth Union are comprised of delegates from nearly every household in VN and are also represented in Viet Nam's Politburo, providing unique potential for education and advocacy. Since June 2010, the VSTP has met quarterly and has formed two technical advisory groups (public-private mix and advocacy/social mobilization). After the VNTP declared March 2012 to be 'TB Month', VSTP partners organized events which resulted in over 20 newspaper articles on the TB epidemic and culminated in a statement by the Deputy Prime Minister to prioritize the VN health sector for TB elimination by 2030.

**Conclusions:** TB education and advocacy among VSTP partners and their constituents are the primary accomplishments of the VSTP to date. To build upon its success, the VSTP must measure its impact by defining indicators and implementing a monitoring and evaluation plan, with a longer-term goal of developing a strategy for sustainable financial, technical, and programmatic support to eliminate TB.

### **A REALISTIC ASSESSMENT OF PROGRAMMATIC MANAGEMENT OF DRUG-RESISTANT TUBERCULOSIS (PMDT) SCALE-UP ACHIEVEMENTS, CHALLENGES AND OPPORTUNITIES**

#### **Sustaining and scaling up PMDT: how Viet Nam prepares for a future with less international funding**

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Programmatic management of drug-resistant TB (PMDT) is one of most priority components of countries with high burden of MDR TB. Viet Nam has successfully started a pilot cohort of MDR TB treatment from 2009 in Ho Chi Minh City. Afterwards, PMDT has been expanded gradually to reach 9 MDR TB treatment centers and 21 adjacent provinces acting as satellite sites by the end of 2012. With this target, fund for PMDT objective from phase II round 9 GFATM is increased from 39% to 44% of the whole proposal (US\$32 mil.). Currently, PMDT is expensive and mainly supported by GFATM but is not filled all the gap of its scale up plan. In general, international funding will be less gradually. Therefore, the NTP need to prepare very well for the future with sustainability by mobilize internal funding such as investment of the Government, local authority at provinces, health assurance and so-called socialization of PMDT. At the same time, the NTP need to strengthen networks to find out the most cost-effective PMDT model, including novel regimens and maximizing involvement of communities to make sure good quality PMDT in Viet Nam. In addition, the NTP need to advocate for Viet Nam Stop TB partnership, so that Viet Nam can receive all resource opportunities for scale up PMDT. More detail about mechanisms of collaboration within partnership, policy advocacy, health assurance involvement and socialization of PMDT will be discussed.

#### **Can the GDF supply PMDT scale-up? An overview of challenges and anticipated GDF response**

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The Global Drug Facility (GDF), a procurement initiative of the Stop TB Partnership, ensures access to competitively priced, quality assured anti-TB drugs for countries in need. GDF has met an increased demand for anti-TB medicines, supplying 101 countries in 2011 for all product lines. Since its inception to date, GDF has been responsible for providing First

Line Drugs (FLD) to treat 19886158 adult patients and 784075 paediatric patients, as well as Second Line Drugs (SLD) for 55800 patients. 20726033 patients have been treated in 10 years.

The GDF:

- GDF is primarily a donor-supported organization
- Has catalyzed rapid DOTS expansion
- Has been successful in developing the market for FLD
- Substantially increased the number of quality-assured SLDs available for procurement from 11 in 2008, to 32 in end 2011
- Conducts international bidding to achieve pricing, which is competitive, transparent, and sustainable for SLDs
- Has aligned quality assurance policy with the Global Fund
- Provides technical assistance in drug management during periodic in-country monitoring visits
- Is an agency for placing planned orders

Market problems for MDR TB: Demand is not yet reflecting the earlier estimations to promote scale-up by suppliers

- Promised level of expansion from the TB world has not occurred
- Supplier not interested in spending money to upgrade production to international quality assurance standards until demand increases
- Supplier prequalification requires in average 18 months or longer on many occasions
- Price of drugs for one patient treatment provided by GDF range between US\$2070 and \$7891

Through its actions and support of donors, GDF can ensure that the future demand for anti MDR TB drugs is met and a sustainable market is created, as was evidenced with the DOTS expansion FLDs (reached 41% of FLD public market).

However, scale-up is dependent on:

- Accurate quantities and timelines from TB programs and partners
- Sufficient funding for medicines

## MONITORING THE GLOBAL TOBACCO EPIDEMIC: STRATEGIC AND SUSTAINABLE SYSTEMS

### Fundamentals of the Global Adult Tobacco Survey (GATS) and intersection with 'WHO MPOWER'

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Tobacco is the world's leading agent of death, accounting for nearly six million deaths annually, a

number that is expected to grow. More than 80% of those deaths will occur in the world's developing nations. If current trends continue tobacco use will cause up to 1 billion deaths in the 21st century. Global tobacco control has been called the 'best buy' and a 'winnable battle' in public health. This is because solutions are available and proven to be effective. What is required is an accelerated implementation of the World Health Organization's WHO FCTC and MPOWER policies at national and international levels. The dictum 'what gets measured, gets done' is fundamental to managing any issue, let alone global tobacco control. The Global Tobacco Surveillance System (GTSS) is a set of globally standardized surveys generating data to systematically monitor youth and adult tobacco use, and key policy measures. Data from these surveys allows unprecedented cross-country comparisons and critical information to implement policies, and to evaluate their effectiveness.

### Sustaining monitoring of tobacco use through the implementation of TQS

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One of the essential components of a comprehensive global tobacco control effort is an efficient and systematic surveillance mechanism to monitor the epidemic. This is emphasized by Articles 20 (Research, surveillance and exchange of information) and 21 (Reporting and exchange of information) of the World Health Organization Framework Convention on Tobacco Control (WHO FCTC). In order to maintain consistency and comparability in monitoring tobacco use, a standard set of tobacco use survey questions should be implemented across various surveillance activities. The Global Adult Tobacco Survey (GATS) was developed to meet this need by generating comparable data within and across countries. To further promote global comparability in monitoring tobacco use, GATS partners developed Tobacco Questions for Surveys (TQS) which is a subset of 20 key survey questions from GATS. TQS provides a standard set of survey questions and associated indicators on tobacco use and key tobacco control measures that can be included in any health, social or other survey to obtain a comprehensive picture of tobacco control in any population of interest. The questions cover prevalence of tobacco use (both smoking and smokeless), types and quantities of tobacco consumed, exposure to secondhand smoke, smoking cessation, anti-cigarette information, cigarette advertising, and cigarette economics. Surveys can select specific indicators and corresponding questions to include based on their particular focus or priority, or incorporate the complete set if appropriate. The goal is for TQS survey questions to become the worldwide standard, greatly enhancing the capacity of all

stakeholders for monitoring and comparing trends in tobacco use and tobacco control interventions. With the expanded use of these standardized questions, the pool of reliable data will increase, leading to quality estimates at country, regional and global levels.

### Malaysia: the Global Adult Tobacco Survey (GATS) findings and partnership model

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**Setting:** West and East Malaysia.

**Objectives:** To produce internationally comparable data on tobacco use and indicators of tobacco control.

**Design:** A multi-stage stratified sampling was used to select 5112 nationally representative households. One individual aged  $\geq 15$  years was randomly chosen from each selected household and interviewed using handheld device. Multi-partners were involved in executing GATS Malaysia.

**Results:** The overall prevalence of current smoking in 2011 was 23.1% (95%CI 21.2–25.2) and 20.9% (95%CI 19.0–22.9) of Malaysians smoked daily. Daily cigarette smokers smoked an average of 14 (95%CI 13.1–14.7) cigarettes per day. The mean age at initiation was 17.2 (95%CI 16.6–17.8) years. Nearly half of the smokers had made an attempt to quit smoking in the past 12 months. Exposure to secondhand smoke was 39.8% (95%CI 35.9–44.0), 38.4% (95%CI 35.9–41.1) and 71.0% (95%CI 67.7–74.0) among those who worked indoors, at home and inside restaurants respectively. A current cigarette smoker spent an average of RM178.80 (US\$56.25; 95%CI 140.0–217.1) per month on manufactured cigarettes. Almost three quarter Malaysians favored increasing taxes on tobacco products. A third of adults noticed any tobacco marketing. Less than half of current smokers thought about quitting because of a warning label. GATS Malaysia was implemented by the Institute for Public Health in collaboration with multi-partners at national and international levels. Each partner organization played a unique role and contributed towards the successful implementation of all aspects of GATS Malaysia in the stipulated timeline.

**Conclusions:** The overall prevalence of current smoking remains stable since 1986 and one in two males are smokers. The partnership demonstrated how the strengths of different organizations effectively link resources and expertise to achieve a common goal in tobacco control.

### Tobacco control success in Thailand and Turkey: results to replicate (Turkey)

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The Global Adult Tobacco Survey (GATS) is the global standard for systematically monitoring adult tobacco use (smoking and smokeless) and tracking key tobacco control indicators. GATS is a nationally representative survey, using a consistent and standard protocol across countries including Turkey. GATS enhance countries' capacity to design, implement and evaluate tobacco control programs as well as generate comparable data within and across countries. The GATS survey was implemented in Turkey in November 2008 in collaboration with CDC, CDC-F, WHO, TurkStat and MoH. A sample of 11200 households was made for the GATS. The overall household response rate was 93.7%; 94.8% urban and 92.7% rural. The individual response rates were 97.0% overall, 97.7% urban, and 96.3% rural. In total, 9030 persons completed the survey. In Turkey 47.9% of men, 15.2% of women, and 31.2% overall (16 million adults) currently smoke tobacco. 43.8% of men and 11.6% of women smoke daily. Almost all (31.1% of 31.2%) current smokers smoke manufactured cigarettes (45.8% of men and 14.9% of women). 5.3 in 10 are thinking about quitting, and 1 in 10 current smokers plan to quit in the next month. 6 million adults (38.5% of adults) are exposed to tobacco smoke at the workplace. 30.5 million (59.7%) live in homes where smoking is allowed, including 19.5 million non-smokers. 57.7% of men and 52.3% of women are exposed to tobacco smoke at restaurants, and 13.0% of men and 7.8% of women exposed at public buildings. 7.1% of adults have noticed cigarette marketing in stores where cigarettes are sold, on media or cinema. Among the current manufactured cigarette smokers, 95.1% of noticed health warnings on cigarette packages during the last 30 days.

### Tobacco control success in Thailand and Turkey: results to replicate (Thailand)

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**Setting:** Whole Kingdom of Thailand, 76 provinces in 4 regions and Bangkok Metropolis.

**Objective:** To evaluate any change in the prevalence of tobacco use and indicators for tobacco control the 2009 GATS and 2011 GATS.

**Design:** A multi-stage, geographically clustered sample design was used to produce nationally representative data. One individual was randomly selected from each participating household. Data was collected electronically by using handheld devices.

**Results:** Overall tobacco use remained unchanged from 27.2% in 2009 to 26.9% in 2011. Quit attempt declined; however, the advice by the health care providers to quit increased. The proportion of current smokers who thought of quitting because of a pictorial health warning (PHW) on the packages decreased from 67.0% in 2009 to 62.6% in 2011 (8 in 10 PHWs have been used more than 5 years). Proportion of adults who noticed any tobacco marketing increased from 17.8% in 2009 to 25.7% in 2011. Among current smokers of manufactured cigarettes, 10.0% purchased the cheap brands that were introduced by the Thailand Tobacco Monopoly (TTM) following the 2009 tobacco tax increase.

**Conclusions:** Thailand needs to continue to close legal loopholes and ensure strong enforcement of the current laws to ensure tobacco use goes down. Increasing the effectiveness of PHWs by continuously update and refresh the PHWs and consider adopting plain packaging. Decreasing exposure to tobacco marketing by amending the current laws according to the international guideline of the WHO FCTC 13 and developing systematic monitoring on interference by the tobacco industry.

### Using data to drive policy change in tobacco control

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Systematic monitoring of the tobacco epidemic through GATS provides a wealth of data across countries and, increasingly, over time. Harnessing this data strategically necessarily involves partnerships across stakeholders: governments, survey implementing agencies, researchers and advocates. The advantage of a standardized survey like GATS is that dissemination strategies can also be replicated as a package across countries. To make best and timely use of data, several steps are important, including identifying key indicators, developing partnerships and key messages, identifying target audiences, a well-planned release and strategies to mainstream data use. Improved and standardized data and systematic monitoring and tracking, while necessary for more thoughtful research and action, are not sufficient to ensure policy change. Policy wins arise through persistent advocacy, executive order, legislative process, or, more often, a combination of efforts timed to seize political opportunities. In recent years, stakeholders in several countries have successfully strengthened tobacco control interventions, including pushing through higher

excise taxes. Their examples highlight the need to thoroughly understand the policy context, and to leverage data in clear and simple ways to answer knowledge gaps, quantify policy impact including premature mortality averted, and to dispel misgivings and myths.

### TUBERCULOSIS IN PRISONS: BREAKING THE CYCLE THROUGH INTEGRATION WITH COMMUNITY HEALTH SERVICES

#### Harm reduction and HIV services in Malaysian prisons: tuberculosis screening and treatment opportunities

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Prisons represent one of the major institutional amplifiers for tuberculosis (TB) due to poor ventilation and the concentration of TB risk factors among the incarcerated population (HIV infection, substance misuse and low socioeconomic background). Additionally, inadequate health services to this particular population is widely prevalent in the low- to middle-income countries. In Malaysia, all newly incarcerated inmates are screened for HIV infection upon entry and if confirmed, HIV infected prisoners are housed in a separate unit but with limited access to HIV health care thereafter. Recently, a methadone maintenance program was established in some major prisons. A structured and coordinated TB screening program is however not in place. We recently conducted a study to look at the prevalence of TB infection amongst HIV infected inmates using a structured questionnaire and tuberculin skin test (TST). The majority of the 138 subjects with complete data were men (90%), Malaysian (96%), below 40 years of age (Median  $37 \pm 7.21$  years), were injection drug users (91%) and were incarcerated before (only 4% were serving their first sentence). The median CD4 lymphocyte count was  $384 \pm 248$  cells/ml. Only eight (6%) were receiving antiretroviral therapy (out of 46% eligible; CD4 count  $\leq 350$ ) and no one had previously received isoniazid course. Tuberculin reaction was positive (induration of 5 mm or more) in 84% of subjects. On multivariate analysis, subjects with CD4 count  $>350$  were more likely to be TST positive (adjusted OR 5.40, 95% CI 1.72–16.91). An integrated, evidence-based TB-HIV program needs to be urgently established in correctional settings and substance abuse treatment centers in low- to middle-income countries.

### Research to policy and practice: tuberculosis control in Malawian prisons

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Operational research is defined by The Union as research into strategies, interventions and tools to improve programme performance and health service delivery. We describe how in Malawi a simple operational research survey of the prevalence of TB in the largest prison in the country in 1995 led to a series of steps that changed policy and practice. This research led to a programme of TB control in Malawi prisons, which was jointly run by the Malawi National TB Control Programme and the Malawi Prison medical services, resulting in 6-monthly reports and a series of other operational research studies that have led to better case detection and treatment success rates for prisoners. Prison TB control services run as part of the Malawi National TB programme activities continue to this day.

### Commencing integrated HIV-TB services in prisons in Myanmar

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**Introduction:** Since October 2010, MSF has collaborated with the State Prison Department to provide integrated HIV and TB care at Insein Prison, Yangon, the largest prison in Myanmar. It houses up to 8000 prisoners many of whom have high risk behaviours (sex workers, drug users and men who have sex with men).

**Interventions:** MSF carried out the following interventions in its HIV-TB clinic: screening of HIV and of TB among HIV+ inmates; treatment for opportunistic infections (including TB), provision of ART, adherence counselling, nutritional, and psychological support and referral after release.

**Method:** Retrospective analysis of MSF's HIV database.

**Results:** Between Oct 2010 and June 2012, of 735 patients confirmed with HIV, 174 (24%) were co-infected with TB. Half of new HIV cases presented with WHO stages 3 or 4 with CD4<350.

**Outcomes of HIV survival analysis:** 45% survived, 4% died, 51% unknown. Out of 134 HIV-TB cases with available results, 53% success rate, 11.2% died, 1.5% failure and 32.8% transferred out. Of the 28 HIV+ patients that died, 15 (54%) were co-infected with TB.

**Conclusion:** Establishing HIV/TB services in prisons in Myanmar is feasible but presents several challenges: late presentation and high mortality; treatment adherence; inadequate infection control; continuity of

treatment after release; uncertainty of sustainability if MSF departs. Future perspectives include Isoniazid Preventive Therapy; MDRTB diagnosis and treatment; improving collaboration with National HIV and TB programmes to tackle the above challenges.

### Ethical dilemmas in tuberculosis and MDR-TB control in prisons: examples from Kyrgyzstan

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**Setting:** A successful partnership has been established since 2006 between Kyrgyz authorities and Médecins Sans Frontières (MSF) to implement a comprehensive TB control program in the civilian penitentiary system of the Kyrgyz Republic.

**Objective:** To illustrate common ethical dilemmas faced by health care professionals working in dedicated tuberculosis management facilities of a Former Soviet Union (FSU) country.

**Results:** Ethical issues in prisons have classically been described from the perspective of doctors' duties, their competing loyalties, and inmates' rights. In our setting, several ethical dilemmas were created by specific conditions, such as: (i) the lack of privacy of medical consultations due to security rules, (ii) social inequities imposed by the traditional cast system of detention inherited from the FSU, (iii) the need to create additional barriers for infection control purposes, (iv) a lack of access to more comprehensive medical services inside of the penal system (including treatment of co-morbidities), (v) recurrent shortages of second-line TB drugs. Furthermore (vi), medical and moral obligations to ensure the continuation of TB treatment after release are often compromised in the civil sector by the double stigma of being both a former prisoner and a TB patient.

**Conclusions:** Some of these ethical dilemmas could be addressed by technical and managerial measures aimed at improving the quality of the TB control program. Fairness and trust also entail a duty to protect ancillary staff through a well designed occupational health program, including respiratory protection and hepatitis B immunization. Ultimately, it is the responsibility of the penal sector to improve the quality of life of all inmates, regardless of their conviction status. In addition to TB management programs, adequate resources should be provided for a more comprehensive approach to health in detention, including easy access to primary and secondary health care services.

## SYMPOSIA: FRIDAY 16 NOVEMBER 2012

### STATE OF THE ART ON CHILDHOOD TUBERCULOSIS TREATMENT AND DIAGNOSTICS

#### Tuberculosis treatment considerations for neonates and infants

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**Background:** Isoniazid (INH) is the recommended prophylaxis for tuberculosis (TB)-exposed infants, although limited evidence for TB dosing exists in neonates. No pharmacokinetics (PK) data is available for low birth weight (LBW)-infants who undergoes developmental and physiological changes.

**Objectives:** To determine the PK parameters of isoniazid (INH) given at the world health organization (WHO)-recommended 10 mg/kg/daily dose in LBW-infants. To define the PK of INH in relation to the N-acetyltransferase-2 (NAT2)-genotype.

**Design:** A prospective, longitudinal intensive PK sampling study, measuring INH serum concentrations at 2,3,4 and 5 hours following dosing.

**Setting:** Tygerberg Hospital is a tertiary referral centre in the Western Cape, South Africa.

**Results:** Twenty LBW-infants (14 male; 16 HIV-exposed) were included in the study; median gestational age of 35 weeks (IQR 34–38) and median weight of 1874 grams (IQR 1366–2105). The NAT2-genotype was determined in all and 5 were homozygous slow (SS); 11 heterozygous fast (FS) and 4 homozygous fast (Table). The median elimination constant rate ( $K_e$ ), (maximum drug concentration in serum ( $C_{max}$ ), time to  $C_{max}$  ( $t_{max}$ ), area under the concentration-time curve ( $AUC_{2-5}$ ) and half-life ( $t_{1/2}$ ) were 0.13 (h<sup>-1</sup>), 5.64 µg/ml, 2.02 hours,

**Table** The median first order elimination rate constant ( $K_e$ ), the maximum drug concentration ( $C_{max}$ ), the time to  $C_{max}$ , the area under the concentration time curve ( $AUC_{2-5}$ ) and the half-life ( $t_{1/2}$ ) of isoniazid (INH) according to NAT2-genotyping

Genotype <i>n</i>	$K_e$ h <sup>-1</sup>	$C_{max}$ µg/ml	$T_{max}$ µg/ml	$AUC_{2-5}$ µg.h/ml	$t_{1/2}$ h
FF (4)	0.39*	3.9	2.02	7.01	1.8*
FS (11)	0.13	6.41	2.02	13.21	5.3
SS (5)	0.08	6.54	2.02	16.9	8.7

\*  $k_e$ -value and  $t_{1/2}$  could not be determined for 1 patient.

FF = homozygous fast acetylators; FS = heterozygous fast acetylators; SS = homozygous slow acetylators.

13.62 (µg.h/ml) and 5.55 (hours), respectively. All 20 achieved adult INH target values, which range between 3 and 5 µg/ml, 2 hours following a dose. Collected alanine aminotransferase (ALT) values were normal, apart from one 3x-elevated value, which normalized at 6 months.

**Conclusions:** All LBW-infants receiving INH at the current WHO guidelines achieved adequate INH target serum concentrations. The NAT2 expression on the clearance of INH was slower than determined by genotyping, supporting immature enzyme maturation; cautioning the administration of higher dosing. The limited safety data was reassuring. More work is needed on unique TB dosing requirements for infants.

#### Efficacy and safety of MDR therapy in children: experience with multidrug-resistant tuberculosis (MDR-TB) therapy in a cohort of South African children

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MDR-TB (i.e., resistance to at least isoniazid and rifampicin) in children is difficult to confirm and complicated to manage. Second-line anti-TB drugs are used, which are more toxic than first-line anti-TB drugs. In a study of 149 children we found adverse events to be common but mostly of low grade. Most common adverse effects were gastrointestinal disturbances (nausea, 19; vomiting, 24; diarrhoea 12), hypothyroidism (ethionamide and/or PAS, 32/142) and neuropsychiatric effects (headache, 17; sleep/mood changes, 13). Hearing loss (injectable drugs, 25/142), mainly at high frequencies, was common and usually is irreversible. Arthralgia was rare (fluoroquinolones and/or pyrazinamide). In only one child all treatment was stopped because of severe systemic reaction. Injectable drugs were stopped early in some children or replaced with PAS if clinical condition permitted. Treatment can be empirical (based on drug susceptibility test (DST) results of the source case or on regional DST results) or individualised (based on DST results from the child's isolate). In a recent meta-analysis of outcome of MDR-TB in children of 315 cases, many of which had culture-confirmed disease, successful outcome (cure or treatment completed) was >80% with median treatment duration 18 months. In our recent study of 149 children with confirmed (59; 40%) or presumed (90; 60%) MDR-TB, cure or probable cure was achieved in 137 (92%) of cases, with only 3 (2%) deaths. These improved outcomes, even in those given shorter treatment regimens may be due to earlier identification of MDR-TB cases through contact tracing.

### A framework for the evaluation of new tuberculosis drugs in children

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A novel approach for speeding access to new TB drugs and regimens in infants and young children will be presented. It involves a paradigm shift, whereby all pediatric age groups are studied simultaneously instead of the classical sequential age-de-escalation approach (oldest first, then next oldest, then . . .). An evidence base for safety in infants and young children is built not from safety in older children, but from safety demonstrated in single-dose PK studies conducted simultaneously in each age group (initial dose selection based on adult PK and modeling). Following single-dose PK studies, multiple-dose PK studies (with dose selection based on single-dose PK and safety results in each age group) are conducted simultaneously in all age groups. The multiple-dose PK and safety results then inform dose selection for investigational studies of longer-term dosing in each age group to establish an adequate safety database to inform more widespread use. The regulatory implications and risk-benefit trade-offs of this approach will be discussed. Our proposed framework stands to substantially impact the timely evaluation of novel TB drugs and regimens in children, a critically important but neglected research area.

## TUBERCULOSIS AND DIABETES COLLABORATIVE ACTIVITIES: POLICY AND PRACTICE

### Bi-directional screening for tuberculosis and diabetes in India

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**Overall objective:** To test the feasibility of bi-directional screening for tuberculosis (TB) and diabetes mellitus (DM) as outlined in the global WHO–The Union guidelines.

**Methods:** A pilot project is being implemented in partnership between The Union, Central TB Division (Ministry of Health and Family Welfare, Government of India), World Health Organization, World Diabetes Foundation (Denmark) and the 13 participating sites. The duration of the project is for 1 year starting from October 2011 to October 2012. The pilot project was initiated after a discussion in a National

Stakeholder meeting (in October 2011). Workshops to develop operational guidelines were conducted (in December 2011 and January 2012). Bi-directional screening is being implemented in 13 sites (March–September 2012) and operational challenges are being documented. This will be followed by a workshop in October 2012 to analyze the data of the pilot project. Finally in a National Stakeholder meeting (in November 2012) the results of the pilot project will be disseminated for informing policy and practice.

**Results:** The full results of the pilot project will be available after October 2012. The current available data for the period March to June 2012 shows that 93% of the TB patients diagnosed at 7 participating tertiary care health facilities and 87% of the TB patients diagnosed at 5 peripheral health facilities could be screened for diabetes. At the 6 participating diabetes clinics, 67% of the diabetes patients (in whom a suspicion of TB was made) could undergo full evaluation for TB.

**Conclusion:** In India, screening bi-directional screening appears to be operationally feasible albeit a few challenges.

### Tuberculosis/diabetes research and collaborative activities in Western Kenya

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**Background:** Disease patterns in sub-Saharan Africa (SSA) have changed rapidly over the past 25 years. Diabetes mellitus (DM) is one of the most common chronic diseases in the world and its prevalence is expected to increase in SSA and Kenya in particular. A growing body of evidence supports a strong association between DM and TB.

**Objective:** This presentation aims to show the TB/DM collaborative care and research activities in Western Kenya.

**Design/methods:** A retrospective review of the clinical database in three DM clinics in Western Kenya was performed. Subsequently, a prospective cross-sectional study was done within two of the DM clinics from September 2010 to January 2012. Patients attending the clinic were screened for TB using a previously validated cough monitor questionnaire.

**Results:** In the retrospective review, 1375 patient records were extracted. 68 (4.95%) patients had a history of TB at enrollment into DM care. In the prospective implementation of intensified case finding activities, 585 patients with DM were screened for TB including 354 (60.5%) females and 231 (39.5%) males. Mean age was 61.1 (55.5–66.8) years. A positive

symptom screen was found in 74 (12.6%) patients screened, of whom 45 (61%) had a history of productive cough and had sputum smear microscopy done. 4 (9%) of the 45 patients had positive smear microscopy; 2 patients had 2+ smear result and 2 had 3+ smear result on both spot and morning sputum.

**Conclusion:** TB is common among patients with DM and productive cough in Western Kenya. Targeted screening of diabetics for TB may be an important part of a TB case finding strategy. Further research is needed to further elucidate the association between TB and DM.

### Bi-directional screening for tuberculosis and diabetes in China

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**Objective:** To assess the feasibility and results of screening TB patients for DM, and screening DM patients for TB within routine healthcare settings.

**Methods:** Prospective observational implementation was carried out in 5 DM clinics and 6 TB clinics. Standard screening forms with reporting forms were developed. Training was conducted and participants developed implementation plans based on the agreed approach. The implementation period was from 1st September 2011 to 31st March 2012. Individual patient data were received and cross-checked, then double entered to an EXCEL file. Comparisons between groups were made using chi-squared test, with the level of significance set at 5%.

**Results:** There were 8886 TB patients registered in the 6 TB clinics. Of these 863 (9.7%) had a known diagnosis of DM. 7947 (99.1%) were screened for DM. Of these, 227 (2.9%) were newly diagnosed with DM. All newly diagnosed DM were referred to DM care. In the 5 DM clinics, 15 342 were diagnosed with DM and 11 330 (74%) were screened for TB. Of those screened, 7 already knew the TB diagnosis; 92 were found with positive TB symptoms, 88 were referred to the TB clinic for investigation and 48 were newly diagnosed with TB. All patients except one started anti-TB treatment.

**Conclusion:** Prevalence of DM in TB patients is higher than in the general population. TB case notification rate in screened DM patients is several times higher than the general population. Bi-directional screening is feasible in routine healthcare settings.

### Tuberculosis/diabetes in the Texas/Mexico border region

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The re-emerging importance of diabetes as a risk factor for TB is a concern for TB control. Diabetes prevalence among newly-diagnosed TB patients in the Texas-Mexico border is 36% which is among the highest in the world. In this community about one-fourth of the TB cases are attributed to diabetes, in contrast to less than 6% to HIV. We present data from several ongoing studies in this community. Among TB patients we evaluated the urine dipstick which is the lowest-cost alternative for diabetes screening and found that it identified 65% of diabetics with chronic hyperglycemia (PPV 91%; NPV 84%). Given the low level of awareness of diabetes in developing countries where TB is most prevalent, we propose that in resource-limited TB clinics the urine dipstick can be used for universal screening of diabetes, followed by additional blood glucose or HbA1c testing in a subset of patients for confirmation of higher-sensitivity assessment. We will also present preliminary data on ongoing studies regarding mycobacterial burden in sputum from TB patients with diabetes versus other risk factors for TB, and in TB-naïve individuals we discuss findings on in-vitro alterations of innate immunity to *M. tuberculosis*.

### Tuberculosis/diabetes in the Pacific: implementation of standards for management and research into tuberculosis and diabetes mellitus

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Very high rates of diabetes contribute to very high rates of tuberculosis among many Pacific Island countries. In several countries, more than 50% of adults with TB have coexisting diabetes mellitus (DM). It is necessary to properly recognize the strength of this association, understand the impacts of DM on TB treatment, and move towards improved care for these cases. How can small TB Control programs with limited resources address the TB-DM syndemic? Using recent literature and a 'best-practices' approach, the Pacific Region has adopted the first set of clinical standards (Figure) for improving the management of TB-DM cases. This presentation focuses on several Pacific Island nations who have already demonstrated remarkable success for diagnosing and treating TB-DM cases after implementing the 8 regional standards.

Screening for DM in persons with active TB	
<b>Standard 1</b>	<b>Every person with tuberculosis (TB) over the age of 18 should be screened for diabetes mellitus (DM)</b>
Guideline 1.1	The diagnosis of DM may be made using one of the following criteria: A fasting plasma glucose $\geq$ 126 mg/dl A random plasma glucose $\geq$ 200 mg/dl A hemoglobin A <sub>1c</sub> $\geq$ 6.5 %
Guideline 1.2	Abnormal glucose values should be verified with a repeat test in patients who have no symptoms of DM.
Guideline 1.3	Rifampin can elevate blood glucose in TB patients. Glucose testing should be repeated after 2-4 weeks of TB treatment, or if symptoms of hyperglycemia develop while on TB treatment.
Screening for TB in persons with DM	
<b>Standard 2</b>	<b>Persons from the USAPI with DM who are at increased risk of TB should be screened for active TB disease and latent TB infection (LTBI)</b>
Guideline 2.1	A tuberculin skin test (TST) or interferon gamma releasing assay (IGRA) for TB should be done at the time of DM diagnosis.
Guideline 2.2	Screening should be repeated as often as the local TB epidemiology may warrant.
<b>Standard 3</b>	<b>Patients identified with suspected or confirmed active TB should be referred to the local TB Program for TB management</b>
<b>Standard 4</b>	<b>Persons with DM who are identified with LTBI should be encouraged to take isoniazid (INH) preventive therapy for 9 months*</b>
Guideline 4.1	Because persons with DM are at increased risk of peripheral neuropathy, they should receive B6 to help prevent INH induced neuropathy (10 – 25 mg/day).
Guideline 4.2	Patients with TB should be educated for the potential side effects of INH therapy. Monthly monitoring for adherence and side effects is recommended.* * Targeted tuberculin testing and treatment of latent tuberculosis infection, MMWR 2000;49.
Treating TB in persons with DM	
<b>Standard 5</b>	<b>Ensure that TB treatment is appropriately adjusted in persons with DM</b>
Guideline 5.1	Ensure that TB medications are properly dosed. Check creatinine for diabetic nephropathy, and if present, adjust the frequency of pyrazinamide (PZA) and ethambutol (EMB) according to ATS-CDC guidelines.* Administer B6 to prevent INH-induced neuropathy (10 – 25 mg/day).
Guideline 5.2	Observe closely for TB treatment failure in persons with DM Be aware of poor absorption of some TB meds in DM. Manage the many interactions between TB and DM meds.
Guideline 5.3	“Assure the Cure” Consider extending treatment to 9 months for persons with DM, especially those patients with cavitary disease or delayed sputum clearance.* Patients with DM have relative immune suppression and often a higher burden of TB disease. Upon completion of therapy, obtain sputum for AFB smear and culture. Evaluate patients at 6 months and one year after treatment for evidence of relapse. *Treatment of Tuberculosis, American Thoracic Society, CDC, and Infectious Diseases Society, MMWR 2003;52
Managing DM in persons with active TB	
<b>Standard 6</b>	<b>Glucose testing should be repeated in TB Clinic during TB therapy</b>
Guideline 6.1	TB patients with DM should have their glucose checked at least weekly for the first 4 weeks, and less frequently thereafter if the diabetes is well controlled. Monthly glucose testing during treatment is recommended.
<b>Standard 7</b>	<b>Use the frequent DOT contact in clinic with TB patients to help manage DM</b>
Guideline 7.1	There should be a glucometer in every TB clinic for monitoring blood glucose.
Guideline 7.2	All clinic staff should reinforce lifestyle changes at TB clinic visits.
Guideline 7.3	If available, refer persons with DM to the Diabetes Clinic for long-term diabetes care. Ensure the DM clinician is aware of TB diagnosis and TB medications.
<b>Standard 8</b>	<b>Use the frequent DOT contact with TB patients to help manage DM</b>
Guideline 8.1	DOT workers should encourage lifestyle changes at every patient encounter. DOT workers should use structured culturally-appropriate diabetes educational materials.* Dietary changes and physical activity are the most important in this effort.
Guideline 8.2	Consider delivering DM meds with TB meds via DOT for persons with poorly-controlled DM who have suspected non-adherence to diabetic medications. * National Diabetes Education Program, US Dept of Health and Human Services: <a href="http://www.yourdiabetesinfo.org/">http://www.yourdiabetesinfo.org/</a> * Pacific Diabetes Education Program, a program of CDC and Papa Ola Lokahi: <a href="http://www.pdep.org/">http://www.pdep.org/</a>

**Figure** Pacific regional standards for the management of tuberculosis and diabetes.

Using this ‘best practices’ approach as a model, other NTPs can benefit from the success of these modest but sustainable program improvements.

## Tuberculosis/diabetes in the Pacific: implementation of standards for management and research into tuberculosis and diabetes mellitus

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**Setting:** The Republic of Kiribati, a Pacific Island nation with a population of about 102 000.

**Primary objective:** To determine the association between tuberculosis (TB) and adult onset diabetes mellitus (DM) in Kiribati.

**Secondary objectives:** 1) To characterize the prevalence of DM and latent TB infection (LTBI) among community residents; 2) To characterize the clinical presentation and treatment outcome in diabetic vs. non-diabetic TB patients.

**Design:** [Primary objective] Case control design with cases obtained from a single TB treatment centre on Tarawa, the capital island of Kiribati, and controls randomly selected from the population of Tarawa. Cases were defined as all adult ( $\geq$ 18 years of age) TB patients who were residents of Tarawa and who registered for treatment at the TB Centre during the enrollment period. Controls were a randomly selected sample of adults, representative of the population of the capital island of Tarawa. [Secondary objectives] 1) Prevalence survey DM and LTBI and 2) prospective cohort design with clinical data collected from both diabetic and non-diabetic TB patients who are treated at the TB treatment center in Tarawa.

**Results:** A total of 499 controls and 272 cases were enrolled. Analysis of control data has revealed that 45% have evidence of LTBI and 19% have evidence of DM. Analysis of the cases will be completed by November.

**Conclusions:** LTBI and diabetes are highly prevalent in the Republic of Kiribati. The association between the two diseases requires further analysis to inform local and regional public health policy.

## SAVING LIVES IN AREAS OF CONFLICT OR DISASTER: PARTNERING FOR RESULTS

### People to people: supporting tuberculosis care in Democratic Republic of Congo through ex-patient networks

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**Background:** Democratic Republic of Congo ranks 10th among the 22 high-burden countries for TB. Case notification is persistently low in some provinces and innovative approaches are needed to improve case detection and treatment outcomes.

**Design:** 'Club des Amis Damien' (CAD) a local NGO composed of old cured TB patients initiated. CAD started the experience with the pilot of the use of former TB patients to improve case detection and treatment outcomes in Kinshasa in 1999. Following an evaluation, the activity was expanded to five Tuberculosis Provincials Coordinating (CPLT) in 2009. The purpose of the research activity is to retrospectively assess the contribution of former patients to case finding in 2011.

**Methods:** CAD trained 419 ex-TB patients to screen and refer TB suspects for TB diagnosis and follow TB patients on treatment. We assessed their contribution to case finding by comparing their suspect registers with TB NTP laboratory registers where TB patients are diagnosed at facility level.

**Results:** In 2011, a total of 2519 TB suspects were referred to 43 health centers in 5 CPLTs. All received TB diagnosis services and 812 (32.2%) suspects were confirmed smear positive TB patients, representing 30% of the total number of smear positive cases reported by NTP. Also 83 (3.3%) suspects were diagnosed smear negative and extra pulmonary TB. Results varied among provinces, which was largely due to the timing of the intervention in each site. Further training and appropriate information tools are essential to ensure high quality monitoring and evaluation.

**Conclusion:** Ex-TB patients can contribute greatly to support TB care. And this contribution needed sustainability in the time.

### Integrating tuberculosis into primary health care in South Sudan: challenges and lesson learnt

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**Background and challenges to implementation:** Low DOTS coverage is one of the key challenges facing TB control in South Sudan. Only 6% (65/1147) of health facilities are providing TB services. In order to

increase DOTS coverage, the government of South Sudan has included TB as a basic health package and is advocating for integration of TB into general health services. An assessment was conducted to determine which health facilities have minimum criteria to integrate TB diagnosis and treatment into general health care services.

**Intervention or response:** As integration framework including a rapid assessment tool and criteria for integration of TB services was developed by the National TB Program (NTP) and partners. The minimum criteria includes a functional health facility, presence of at least 3 medical personnel, a general laboratory, the catchment population and its burden of TB and/or HIV/AIDS.

**Results and learnt:** The assessment tool was piloted in 13 health facilities in April 2011. Of the 13 health facilities, 4 (31%) were already providing TB services, 6 (46%) met the minimum criteria but did not provide TB services and 3 (23%) did not meet the minimum criteria. The visibility of this assessment is based on the simplicity of the tool and the criteria to be measured.

**Conclusion and recommendation:** Integration can rapidly expand TB DOTS services as many health facilities meet minimum criteria. Assessment should be carried-up throughout the country to involve more health facilities.

### Community contribution in tuberculosis control in Afghanistan

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**Background:** Afghanistan is one of 22 high burden tuberculosis (TB) countries with estimated incidence and prevalence of 189 and 352 in 100 000 populations. NTP Afghanistan with assistance from TB CAP/CARE I/USAID engaged community health workers (CHWs) into TB services delivery in 13 provinces.

**Method:** During 2009–2012, collectively, 9000 CHWs trained on TB suspected cases identification, referrals for diagnosis, provision of direct observed therapy (DOT) to TB patients, follow up of TB patients for scheduled examination. In April 2012, technical team from TB CARE I/MSH and NTP reviewed the performances of CHWs, and took sample size of 4053 (CI = 95%, power = 95%, RR and OR of 1.1 and 1.7, proportion of unexposed/exposed of 3.6) to identify contribution of CHWs in case findings and treatment outcome.

**Result:** During 2009–2012, CHWs referred 51 793 individuals suspected having TB for diagnosis that makes 22% of all suspects (234 803) identified in 13 provinces. Of them, 2486 (5%) were diagnosed as

sputum smear positive TB cases, it makes 13% of all TB cases (19 126) and 4198 TB patients received DOT from CHWs. Totally, in intervention group 853 (587 females, 266 males) new TB SS+-patients took DOT from CHWs and in control groups 3205 TB patients received DOT from ten basic health centers and 12 797 new SS+ TB cases from health workers country wide. Treatment outcome analysis for intervention group shows 97.65% (833,  $P < 0.00001$ , RR = 1.1) treatment-success and 822 (96%) cure rate. Contrarily, values for control group shows 90.7% (11 624) treatment success and 87% (11 175) cure rate, interestingly, treatment outcome was equally distributed for both gender.

**Table 1** Comparison of treatment outcome among new TB SS+ cases in intervention and control groups

Variable	Result of DOT from CHWs (2010) (intervention group) ( $n = 853$ ) $n$ (%)	Result of outcome at four provinces (2010) ( $n = 3205$ ) $n$ (%)	Treatment outcome national level (2010) (control group) ( $n = 12797$ ) $n$ (%)
Treatment success rate	833 (97.7)	2909 (90.8)	11 624 (90.8)
Cure rate	822 (96.4)	2855 (89.1)	11 175 (87.3)
Completion rate	12 (1.4)	54 (1.7)	449 (3.5)
Deaths rate	10 (1.2)	57 (1.8)	257 (2)
Default rate	3 (0.4)	54 (1.7)	244 (1.9)
Failure to treatment rate	3 (0.4)	25 (0.8)	122 (1)
Transfer out rate	4 (0.4)	160 (5)	550 (4.3)

**Table 2** Role of community health workers in TB case findings, 2009–2012

Year	Total SS+ $n$	SS+ ref. by CHWs $n$	Percentage
2008	1741	0	0
2009	1469	359	24
2010	2100	710	34
2011	7050	1188	17
2012 (three months)	1415	229	14
Total	12034	2486	22

**Conclusion:** From the assessment it was evident that community health workers contributed on early TB case detection and improved treatment outcome, significantly. Thus, it is strongly recommended to scale up this experience in Afghanistan and can be applied as a successful approach in similar setting elsewhere.

## THINKING OUT OF THE BOX: CATALYSING INNOVATIONS AND EXPANSION OF mHEALTH IN TUBERCULOSIS CARE

### Mobile health (mHealth) innovation in tuberculosis care and control under different conditions

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**Setting:** Diagnostic and treatment services for tuberculosis (TB) are often not provided in the same location in the private sector, while in the public sector, routine diagnostic services are often located at treatment sites, but visits to multiple facilities may be needed for advanced diagnostics. Delays in diagnosis and treatment initiation result from inadequate data sharing between laboratories, providers, patients, and community health workers. Mobile phone-based tools provide solutions to many of these challenges. Overview of mHealth for TB: mHealth technologies can be used to improve treatment outcomes for TB patients by streamlining the routine activities of TB programs. This includes enhancing mass screening, electronic reporting of test results, electronic monitoring of treatment adherence, phone based cash transfers as incentives for staff, geographical mapping of patient homes, and drug inventory management. Several TB programs have begun incorporating mHealth tools and work in this field is burgeoning. Programmatic benefits of mHealth for TB: mHealth systems allow data collected in the field to be stored in a central database as it is collected (in real-time). This gives program staff immediate access to reports using both mobile phones and web-based reporting systems, allowing, among other benefits, a reduction in primary defaults and improved patient follow-up. mHealth systems are economical to set up and are adaptable to infrastructure exigencies. Results from projects using mobile phones show improved rates of case detection, case holding, and positive responses to SMS reminders for improved treatment compliance.

**Recommendations:** Funding agencies are encouraged to support the integration of mHealth initiatives into TB programs. While early results are encouraging, the evaluation of mHealth interventions needs to be formalized. Guidelines and best practices should be widely disseminated to pave the way for future successes in TB management and control.

### Use of cell phones in HIV patients in Kenya

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**Issue:** The widespread uptake of mobile phones in resource-limited settings provides a broad range of benefits in enhancing quality of patient care and strengthening health systems. Evidence has demonstrated the capability of mobile technology, specifically text messaging, in improving treatment outcomes such as adherence to antiretroviral medications and rates of viral suppression. Lessons learned from these evidence based interventions can guide development, implementation and scale up of mHealth initiatives to support patient engagement in HIV care and treatment.

**Description:** The WelTel team in collaboration with Universities of Nairobi and Manitoba previously conducted a randomized controlled trial (WelTel Kenya1) at three HIV clinics in Kenya to assess the effects of text messaging on adherence to antiretroviral therapy (ART) in Kenya. The study findings demonstrated that patients who received WelTel two-way weekly SMS support had significantly improved ART adherence and rates of viral suppression compared with the control patients who did not receive the SMS support.

**Lessons learned:** Some of the lessons learned from this study include: the mHealth initiative should be guided by health systems needs, engage end users such as patients and healthcare providers in its development; the intervention needs to be simple, low cost, should respect privacy and confidentiality, and should be scalable with minimum burden on health workers. **Next step:** Implementation and scale up of the WelTel health model countrywide, evaluation of the health model for cost effectiveness, factors that account for successful scale up, health outcomes measurement and recommendation of a sustainable implementation/business model.

### Reaching the unreachable with high-tech and low-tech innovations in Uganda and Lesotho

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**Background:** In remote districts of Lesotho rapid diagnosis of TB suspects and treatment adherence are major challenges. In Uganda poor reporting of epidemiological data and frequent stock-outs of commodities were resulting in poor disease management.

**Method:** TheRapidSMSTM platform, an open-source framework developed by UNICEF and The Earth Institute, was adapted for use in Lesotho and Uganda. Health-workers use their personal mobile phones to send simple coded text messages to register

TB suspects (Lesotho) and report weekly disease surveillance data and stock levels (Uganda). Health centres in Lesotho receive results via SMS and suspects and patients may receive SMS alerts SMS when their results are ready and for monthly visits and follow up testing. At hospital and programmatic level access to the system is via a web-interface. No personal incentives were provided for using the system.

**Results:** In Lesotho the system is implemented in 48 health facilities. Results for 13 764 TB suspects (9% were smear positive) and 4862 follow-up patients have been reported via SMS. TAT for results from receipt of samples at microscopy centre was reduced from 7 to 10 days to 1 day. 15% of patients in the treatment register receive reminders for monthly visits and follow up testing. In Uganda health-workers in 22 districts use the system on a weekly basis to report disease surveillance data and commodity stock levels.

**Conclusion:** The system requires moderate start-up and low running costs. It has benefits for both patient and programmatic management and is limited by network coverage and the ability of health workers to send SMS.

### Expanded online training in tuberculosis and MDR/XDR-TB to increase accessibility and outreach

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The World Medical Association WMA has developed a tuberculosis TB refresher course and a multidrug-resistant tuberculosis MDR-TB course in order to build capacity of physicians and other health professionals. The two training courses were supplemented by virtual patient case trainings. Now, new models of training utilizing mHealth are being developed to increase the accessibility of the courses. The MDR-TB course is aimed at physicians involved in the detection, management and treatment of MDR-TB patients, under the guiding principles of the WHO Stop TB Strategy. The self-study course focuses on diagnosis and clinical management of MDR-TB in a variety of geographical, economic and social settings. The MDR-TB course presupposes essential knowledge of TB and therefore a TB refresher course was developed. This course emphasizes general principles and standards and is intended for use in multiple countries. The TB refresher course and MDR-TB course exist as free self-directed online learning tools in English accessible from the WMA webpage. To increase access to TB training globally, PDF version of the courses have been translated into various languages. The global scale-up to address the challenge of MDR-TB will require health care workers in low-resource countries to detect and care larger numbers of MDR-TB patients. Furthermore in many areas of the world, internet access not consistently available and together

with the greater distribution of tablet computers, new ways of increasing the outreach of the MDR-TB course are both required and possible. In cooperation with the Stop TB Department of WHO, the New Jersey Global Tuberculosis Institute, WMA is developing an online application for the MDR-TB course for tablet computers in a HTML5 format. The app will be accessible from the WMA and WHO webpage and once downloaded, will be self-contained and able to run offline. The interface will be available in English, with possibilities to expand easily into other languages.

Both TB course are intended for physicians that may be involved in the management and care of patients with TB. Though physicians are the primary audience for this course, nurses and other members of the health care team may also find the information useful. The course is based on the International Standards for Tuberculosis Care (ISTC), and the World Health Organization (WHO) Guidelines and recommendations for TB control.

- Accredited with SAMA
- Developed by the World Medical Association and the New Jersey Medical School Global TB Institute
- Supported by the Lilly MDR-TB Partnership
- 14 million prevalent cases of TB worldwide in 2010
- 8.8 million new cases in 2010
- There were an estimated 650,000 prevalent multi-drug resistant TB (MDR-TB) cases globally in 2010

Available free at [www.wma.net](http://www.wma.net)

Logos for WMA, the Lilly MDR-TB Partnership, and the Stop TB Global Tuberculosis Institute.

### An electronic system for the management of laboratory data on tuberculosis diagnosis and treatment

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**Introduction:** The proper management of laboratory results and the linking of these data to patients placed on treatment for drug-resistant tuberculosis (DR-TB) provide a means to monitor access to TB diagnostic and follow-up testing, and to adequate treatment regimens. We discuss the development of an electronic module to enhance this aspect of data management.

**Methods:** Management Sciences for Health (MSH) has developed an electronic application to handle the registration of laboratory test results performed for diagnostic and treatment monitoring purposes. This module functions as an integral part of eTB Manager, a web-based platform developed by MSH which integrates data on TB and DR-TB case management, medicines supplies and TB surveillance ([www.etbmanager.org](http://www.etbmanager.org)). eTB Manager has been in use in Brazil since 2005 and is also being introduced in low-resource settings in Africa, South-East Asia and East-Europe.

**Results:** Laboratory workers register information on patient samples on the system. These include identifiers of the patient, demographic details, testing indication, method of laboratory analysis and results. The system also features automated reports summarizing basic indicators of importance to assess laboratory performance as well as surveillance, including detection of resistance to anti-TB drugs among TB patients at risk. Indicators conform to WHO recommendations for periodic reporting. A standard operating procedure for the module is being prepared.

**Conclusion:** The laboratory module is being piloted in Uzbekistan and will be released as a standard component for all TB control programmes using eTB Manager as an electronic management information system.

### Innovative methods and novel technologies to improve tuberculosis case finding

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Tuberculosis control can be simply defined as to find it, to treat it and to prevent it. WHO annual report shows that current case detection is not enough to drive TB epidemic, especially MDR TB, TB-HIV and TB in children. Viet Nam NTP as known to be a strong NTP, but the TB case detection rate for all form is still less than 60%, that means there are a significant number of TB patients still in community and continuing transmission. This phenomenon tells us about challenges of TB case finding and the urgent needs of innovative methods and novel technologies to improve the current situation. In concrete, we need techniques with high sensitivity, high specificity and simple in performance to be easily applied. We also need new approaches to bring the novel techniques to people who need most. So far, point of diagnosis normally at district level. In Hanoi under TB REACH we do more decentralization of TB case finding applying cellScope (digital microscope with fluorescent staining) at commune health posts. At districts, we place GeneXpert and chest X-ray will be used as screening tool before collecting sputum for Xpert testing. This intervention of novel technologies and approach including communication campaign was designed with hypothesis of increased 2-fold case detection. Active case finding for TB among household contacts is also a pilot method applied in Viet Nam to answer the question of improve TB case finding. Improve TB case finding is also known as getting more case diagnosed in general hospitals and in private sector reported to the NTP. This innovation method is so called PPM in TB control. Strengthening primary health care by standardizing clinical

practice on asthma, COPD, respiratory infection and TB known as practical approach to lung health (PAL) to increase TB case finding is innovative method. PAL-PPM integrated model will be also discussed focus on how they can amplify their effects to improve TB case finding.

## FORMER TUBERCULOSIS PATIENTS: EFFECTIVE COMMUNITY ENGAGEMENT AND LESSONS LEARNT

### ACSM from a patient's perspective: tools for outreach

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**Background:** This presentation will be focusing on the TB community which includes the following; TB patients, former TB patients, HIV positive former TB patients, TB patient advocates and how the acronym ACSM is a tool for identifying, supporting and empowering this community for TB care and prevention (Control). A for Advocacy, C for Communication, SM for Social Mobilisation. Stop TB Partnership defines Advocacy Communication and Social Mobilization (ACSM), as a diverse set of related but distinct activities aimed at supporting all components of the Stop TB Strategy. ACSM promotes a comprehensive approach to TB care and control based on partnerships between NTP, NGOs, CSOs and other institutions, rather than a purely clinical approach implemented by a vertical disease program. During ACSM sub group meeting in Lille, Community TB Patient Advocates and Stakeholders recognised ACSM as a tool for achieving TB care and control.

**Objective:** Identify key challenges and issues in fully engaging patients in TB programme.

**Issues:** Treatment of TB patients with the drug regimen of six to eight months is an issue for TB patients. Poor diagnosis and drug stock out remains an issue beyond the control of TB patients.

**Challenges:** Stigma and discrimination of TB patients by the community and health facility workers. Difficulty in organizing TB patients as a group either as support group or corporate entity for the purpose of advancing TB patient charter. Planning TB program without involving former TB patients and TB patients. Slow capacity development of former TB patients.

**The way forward:** CSO actors, donors, program managers and all TB implementers should prioritise as top most the capacity development of former TB patients and TB patients. TB patients should be bold to demand for the implementation of TB patient charter. Enablers should be provided for TB patients to encourage treatment completion.

### Building, supporting and sustaining patient groups

M Sibbuku. Coalition of Zambian Women Living with HIV, TB Department, Lusaka, Zambia

**Background:** Supplementing government's efforts building strong, sustainable TB-HIV patient groups by empowering former TB-HIV patients, especially women with TB, HIV knowledge and skills.

**Objective:** To build TB patient groups, integrate TB into already existing HIV community based groups as well as through the Coalition of Zambian Women Living with HIV (COZWHA) by increasing their knowledge on TB and HIV and other supporting programs. This is to enable them support the health care centres and also carry out sensitization in the communities.

**Methods:** Development of 15 TB-HIV support groups, integrating TB into 10 HIV community groups. Form TB groups within 15 zones of (COZWHA) in Lusaka. Train them in psychosocial counselling, DOTS, defaulter tracing, treatment adherence support to enable them support health care centres in their catchment area. Offer support for income generating activities so that they can be self-sustainable.

**Results:** The former patients are equipped with skills to support in the task shifting within the overwhelmed health centres by following up defaulting TB patients, offering psychosocial and emotional counseling, ensuring completion to TB treatment through DOTS support. Communities informed through sensitization are able to demand for TB services. This empowerment has lessened stigma and encouraged other TB patients, upon completion of treatment to join the patient groups and work towards increasing case detection.

**Conclusions:** More former patients should have their capacity built, especially in the rural and peri urban areas. This work helps in building their confidence as well as fighting stigma by not only being mere recipients of care but also being productive citizen who can take part in TB control.

### Patient-led community-based organisations: community, national and international advocacy

W Mbewe. Coalition of Zambian Women Living with HIV/AIDS (COZWHA), TB Capacity Building Section, Lusaka, Zambia

**Background:** Before the roll out of free treatment for TB and HIV, many people from very poor backgrounds, infected and affected by HIV and TB had very little hope of survival once they received their positive results. Immediately after the free roll out, affected communities formed support groups that offered mostly emotional and adherence support to one another. Now many of those support groups have evolved into community based organisations (CBO)

or non-governmental organisations (NGO) contributing to the response to HIV and TB control.

**Method:** Stages that support groups TB-HIV affected communities passed through to come up with governance structures, registration of organizations to become legal entities and membership drive. Stages in organizational strengthening, capacity building of members, in resource mobilization to enable them engage in programs at national and international levels. How some have evolved into regional bodies.

**Results:** Patient-led structures are now strong NGO's, many have partnered with NGO's from the global north to carry out joint advocacy activities at national, regional and global levels. Former patients are now holding board seats on various global health initiatives and also become incubators for developing more empowered former patients to supplement government efforts as treatment supporters and community volunteers at health centres.

**Conclusion:** Patient-led organization are an important component in TB control and many national health strategies. They have become a vital resource for overwhelmed public sector institutions and need to be supported and recognized as such if we are to succeed in the fight against both diseases.

## ADVANCING MOLECULAR DIAGNOSIS WITH A SUSTAINABLE APPROACH TO IMPACT PATIENT CARE

### Use of automatic platform for diagnosis of tuberculosis and other respiratory diseases in Hong Kong

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Coupled with the demand for faster and more accurate laboratory diagnosis of TB and respiratory diseases, a number of automatic platforms have been developed that can be considered for use in program conditions. These include automatic slide staining machines, liquid culture systems, and rapid molecular diagnostic tests. Recent availability of molecular platforms that can detect pathogen and antibiotic resistance(s) at same time have sparked interest in their wider use in the field. Obvious advantages of using automatic platforms are: rendering high throughput possible, relative ease for standardization, good quality controls already in place, plus reduction in labour costs and staff training. Limitations are uncertain sustainability of systems in long term provision of equipment maintenance, upgrading and servicing. There is also dependence on a few commercial companies, and questions on long term efficiency. High running costs exist for countries that do not have

special cost negotiations with manufacturers. Automatic platforms are usually most cost effective where the test volume is high. In Hong Kong where there is highly centralized TB laboratory services for mycobacterial identification and drug susceptibility tests, these platforms can be very efficiently utilized. TB programs should be cautiously aware of own country conditions before adopting these platforms.

### High-throughput RT-PCR for tuberculosis and other respiratory pathogens

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The need for confirmation of TB and other infections is critical as clinical assessment alone is insufficient for diagnosis especially in high HIV burden settings and is this is also true for drug resistant tuberculosis. The introduction of molecular tests to large programs have enhanced the quality of diagnostics but due to the high burden of disease, the ability to provide good turnaround times has highlighted the need for high throughput solutions. Several commercial systems have come to market to address these needs. The AMTD2 test has been available for several years and is the only FDA approved test for both smear positive and negative TB but is limited to TB detection only. The Mycobacterium Detection test from Roche can detect TB and also 2 additional species *M. avium* and *M. kansasii* with an overall sensitivity of 75% for TB diagnosis and is priced at \$6. The MTBDRplus assay in its latest version has been simplified with improved performance and is equivalent to the Xpert MTB/RIF assay 86% sensitive for TB detection with the added advantage of isoniazid testing. The Xpert/MTB/RIF initially focused as a point of care test has released a high throughput system—'Infiniti' with 80 tests per run and is very simple to perform without the need for separate areas. A new development under evaluation is a 'collection to detection' system that provides a safe DNA/RNA stable medium for downstream molecular screening and next generation sequencing and opens the avenue for detection of multiple pathogens from a single collection tube. A similar broad range test system is the Plex ID (Abbott) using mass spectrometry for end point detection. This platform is well developed for several other pathogens with TB recently added. There are several options, however there are limited published studies evaluating these in high burden countries and in particular head-to-head comparative studies with description of turn-around-times and cost analysis.

## Implementing molecular diagnostic platforms for poverty-related diseases

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Tuberculosis (TB), malaria and HIV/AIDS account for 15–20% of the disease burden in the poorest countries. It is also estimated that neglected tropical diseases impair the life of more than a billion of people. For this reason the development of integrated and friendly molecular platforms able to diagnose more than disease are a priority. For TB, an integrated rapid diagnostic approach should perform species identification, drug susceptibility testing (DST) and molecular typing. Malaria kills millions of people each year also because of antimalarial drug resistance. Two new rapid diagnostic tests were developed and validated with the support of the EU FP7 funded TM-REST consortium: a test for molecular diagnosis and monitoring of TB and its drug-resistant variants and one for the detection of malaria. Tests were developed on a lab-on-chip (LoC) platform for the In-Check™ technology (ST Microelectronics). The In-Check™ is based on an integrated PCR and a DNA microarray for the endpoint analysis and consists in a single disposable device (biochip) and dedicated instruments. Main advancements over existing technology are: the possibility to perform PCR and microarray hybridization in a single device targeting high number of targets, the relative flexibility of the lay out that will allow to include new targets without an extensive re-design of the chip. The TB test can reliably identify, both from clinical samples and strains, TB complex, main non-TB species, and the most frequent mutations conferring drug resistance to the main anti-TB drugs with high sensitivity and specificity. The malaria assay allows the specific identification of all human Plasmodium species and detection of drug resistant parasites carrying mutations in Pfcrt (chloroquine resistance), Pfdhfr (pyrimethamine resistance), and Pfcytb (atovaquone resistance). The In-Check™ platform is also available for the detection and typing of human strains of influenza viruses, including H5N1.

## Results from Xpert® MTB/RIF implementation in MSF field projects

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Between April and December 2011 MSF installed Xpert® MTB/RIF for routine use in 9 countries for a total of 16 sites (Table). Thirteen instruments were used at the district and sub district level, 2 at the

regional level, and 1 in prison. Fourteen sites implemented Xpert in parallel with smear microscopy, 7 using fluorescent (FM) and 7 Ziehl-Neelsen (ZN) microscopy. A total of 10 960 sputum samples were tested with G3 Xpert MTB/RIF cartridges. Out of the total specimens, overall positivity rate of Xpert MTB/RIF was 21%; compared to microscopy Xpert MTB/RIF increased laboratory detection by 48% (27% for FM and 54% for ZN). The proportion of rifampicin (RIF) resistance detected ranged from 3% to 45%. For an average rate of 7.3%, inconclusive results decreased from 10% during the initial period of implementation (April–August), to 5% during the follow-up period (September–December). During the second period, ‘error’ was the most common cause of inconclusive results, 63% (240/381), then ‘invalid’, 33.3% (127/381) and ‘no result’, 3.7% (14/381). The most frequent type of errors were 5011 (42.2%) and 2127 (15.3%). RIF indeterminate results were 1.4%. Xpert MTB/RIF in our experience significantly increased TB laboratory detection in sputum and provided rapid screening for RMP resistance, decreasing delay to adequate treatment; empiric MDR-TB regimen was started upon receipt of Xpert MTB/RIF resistance results. Despite relative ease of use of the test, major constraints were high rates of inconclusive results, which required further training and replacement of 10 modules, and logistical and financial investment that limit Xpert MTB/RIF decentralization. Xpert MTB/RIF proved to be a valuable tool for a rapid diagnosis of TB and of RIF resistance, yet microscopy, culture and full line DST remain required for patient monitoring and confirmation of RIF resistance. Performances with new G4 Xpert MTB/RIF cartridge should be monitored. Studies on patients outcomes are essential.

**Table** Summary of Xpert MTB/RIF results (April to December 2011) by epidemiological setting

	Sites <i>n</i>	Total <i>n</i>	MTB+ <i>n</i>	MTB+/ RIF– <i>n</i> (%)	MTB+/ RIF+ <i>n</i> (%)	MTB+/ RIF ind <i>n</i> (%)	Inconclu- sive/ total <i>n</i> (%)
Low MDR, low HIV	1	706	109	101 (92.7)	6 (5.5)	2 (1.8)	126 (17.8)
Low MDR, high HIV	6	4523	1049	960 (91.5)	74 (7.0)	16 (15.3)	435 (9.6)
High MDR, low HIV	2	320	99	71 (71.7)	31 (31.3)	4 (4.0)	26 (8.2)
High MDR, high HIV	7	5411	1051	919 (87.4)	124 (11.8)	8 (0.8)	216 (4.0)

## NON-COMMUNICABLE DISEASES AND CHRONIC RESPIRATORY DISEASES: GLOBAL BURDEN AND RESPONSE

### The Union's response to chronic respiratory disease: lessons learnt

C-Y Chiang. International Union Against Tuberculosis and Lung Disease, Paris, France

Chronic respiratory disease, mainly asthma and chronic obstructive pulmonary disease (COPD), are not rare in low- and middle-income countries. World Health Organization predicted that COPD will rise to be the fourth leading cause of death globally by 2030. Asthma affects 235 million people globally and prevalence is increasing in several countries. By using inhaled corticosteroids, most asthma patients can control their asthma. The Union recognized that the main barrier to asthma control has been limited access to and poor affordability of essential asthma medicines and has established Asthma Drug Facility (ADF) to increase affordability of essential asthma medicine in resource limited settings. Since early 2010, ADF has successfully delivered quality-assured inhaled corticosteroids at low prices to Benin, Burundi, Kenya, Sudan, El Salvador, and Viet Nam. However, a 2011 survey of selected essential asthma medicines revealed that inhaled corticosteroid prices remain high in many countries. A comprehensive lung health project funded by the World Bank and implemented through collaboration between The Union and partners in Benin, China and Sudan included as one of its aims to reduce the burden of lung disease through improvement of case management of patients with persistent asthma. While it was feasible to train health workers to manage asthma patients in a standardized manner, a high proportion of patients were lost to follow-up during treatment. Further, quality-assured spirometry is not available at primary health care facilities in low- and middle-income countries, indicating that diagnosis of COPD based on pulmonary function test imposes a barrier to patients' accessing effective therapy. It is likely that removal of the classification step of pulmonary function and integration of asthma and COPD guidelines into a practical approach would improve the management of patients with chronic airflow limitation in low- and middle-income countries.

### Strategy and plan to reduce NCD/CRD burden: the way ahead

D A Enarson. Department of Scientific Activities, International Union Against Tuberculosis and Lung Disease, White Rock, BC, Canada

Non-communicable diseases (NCDs) are those that are non-infectious and non-transmissible, irrespective of their characteristics or duration. They accounted for 36 out of 57 million global deaths in 2008, 7.5 million

due to high blood pressure, 5 million from tobacco use, 2.8 million from overweight and 2.6 million from high cholesterol. Chronic respiratory diseases (CRDs) are overwhelmingly related to tobacco smoking, and to a lesser extent, due to indoor air pollution and occupational exposures. These diseases are on the rise while infectious diseases are set to decline. Global response to this emerging challenge led to the Global Non-communicable Disease Network and the NCD Alliance in 2009, a call by the UN General Assembly to address the issue in the review of the Millennium Development Goals in 2010 and the NCD Summit in 2011. The ultimate strategy to mitigate the burden of NCDs is to develop national plans for the prevention, control and management of NCDs, to fight for a tobacco-free world, to move toward healthy lifestyles, to improve care by strengthening health systems, to ensure global access to affordable medications of good quality and to promote the human rights of individuals with non-communicable diseases. The Union has been a lead player through its global leadership in tobacco prevention and control, through its approach to improving quality of health services through standard case management and through its pivotal role in enhancing access to affordable good quality medications (through the Asthma Drug Facility). Members and national associations associated with The Union are encouraged to promote each of these activities in their areas.

### Global response to chronic respiratory disease: call for action

A El Sony. The Epidemiological Laboratory, Khartoum, Khartoum, Sudan

The simple act of breathing is now a challenge. CRD signify a growing burden on public health, particularly in low- and middle-income countries. It is the main cause of 7% of worldwide deaths, and represents 4% of global burden of disease by (DALYS). CRD are not high on the agenda of governments there is no political commitment and no concrete action on national and international level. CRD are neglected by development partners, national and international development agenda. Achieving MDGs must remain an absolute priority, which is now threatened by NCD/CRD and its poverty viscous cycle. A year has passed since the UN Summit and the Union Press release on NCDs, but yet no new money committed, no targets declared, nor initiatives started. CRD prevention and control is dramatically failing the need; infrastructure is deprived, health information is not supported to put concrete plans and to monitor outcomes and impacts, and human resources are not geared up to tackle CRD. Limited access to CRD's essential medicines and supplies demonstrates inequity in health care. Further delay towards CRD will widen the gap where funding within 0.7% of worldwide

GNI will not be enough. Tangible moves should start, an ear marked money should be there, meeting with GF secretariat to start on NCD/CRD grants is crucial. Advocacy for holistic cost effective approaches for CRD and social determinants is our way a head. A domestic component of a whole government response that puts exact counterpart expenditure is also an important move. We need to be proactive in putting regulatory measures, and in scaling up of evidence based comprehensive strategies. Inclusiveness of all spectra to advocate and act beyond aid is our way to alleviate poverty and have a sustainable growth.

## THE IMPORTANCE OF PUBLIC POLICY ON TOBACCO CONTROL: A GLOBAL VIEW

### Overview of public policy progress and challenges across low- and middle-income countries

A Jackson-Morris. The International Union Against Tuberculosis and Lung Disease, Edinburgh, UK

Low and middle income countries carry the highest burden of tobacco-related disease. This overview will survey across countries and regions, and consider the different policy aspects under the Framework Convention on Tobacco Control, such as: smoke-free protection; taxation; packaging and labelling; advertising, promotion and sponsorship. Key themes in public policy relating to tobacco control will be discussed. Areas of success and progress, and examples of where this has been linked to outcomes will be discussed. Areas where progress has proved slowest or most difficult will also be identified, and the challenges will be examined, particularly those relating to social, political and economic context, such as availability of national resources, infrastructure development, local tobacco industry impact, national commitments, and linkage to policy/funding priorities.

### Public policy development in the Western Pacific Region

B Bellew. Tobacco Control Department, International Union Against Tuberculosis and Lung Disease, Edinburgh, UK

This presentation addresses five main themes within the overall symposium objectives. It will:

- provide an update on the implementation of WHO-FCTC in the Western Pacific Region;
- summarise current theory on translation of evidence into policy and practice and reflect on its application to comprehensive tobacco control in the Western Pacific;
- emphasise the role of advocacy for the implementation of comprehensive tobacco control policy;

- provide some examples of blatant interference in public health policy by the tobacco industry and highlight the importance of countering such industry interference through robust implementation of FCTC Article 5.3; and
- reflect on the importance of technically sound investment planning to underpin the sustainability of effective tobacco control policy.

### In-depth focus on Latin America: case study of policy development. Case study: Brazil's alternatives to tobacco control policy making

J Romo. International Union Against Tuberculosis and Lung Disease, Mexico, Mexico

New laws as a result of the legislative debate in Congress are needed to create the framework for tobacco control interventions. Comprehensive laws that introduce a real progress in implementation of FCTC require this process. The political nature of tobacco control laws makes it difficult to obtain the objectives in short periods of time. This is the case for Brazil, one of the largest tobacco growing countries in the world, in which the tobacco industry has played a role in mobilizing several groups to oppose and undermine tobacco control legislation. In this session, we will discuss the alternatives to that legislative process by giving examples and actual achievements of legislation obtained by other legal means such as presidential decrees, regulations by the regulatory agency and municipal acts determined by local authorities. Although not unconventional, these alternatives have been quite original in Brazil and have led to enormous progress for tobacco control. Ban on additives to tobacco products, tax increases and implementation of 100 smoke-free environments have been possible in Brazil thanks to the use of these strategies. Policy development in adverse contexts is still possible when there are legal resources in favor of public health.

## NGO AND CIVIL SOCIETIES' ROLE IN SUSTAINABLE APPROACHES FOR SCALING UP DRUG-RESISTANT TUBERCULOSIS PROGRAMMES

### MDR-TB globally: the scale of the problem, what is needed for control

C Mitnick. Global Health & Social Medicine, Harvard Medical School, Boston, MA, USA

**Aim:** This presentation will summarize the global burden of drug-resistant TB, the current treatment options, and efforts underway to improve treatment, as well as call for more aggressive, rapid improvements to treatment.

**Summary:** With roughly 500 000 new cases of

MDR-TB annually among very heterogeneous populations globally, and only a tiny fraction receiving appropriate treatment with high-quality drugs, MDR-TB threatens to undermine improvements in the population burden of TB. Standard treatment is too long, and ineffective in many patient populations, as reflected by success in only 60% of patients across settings. These figures, however, reflect cases diagnosed and treated under an old diagnostic model, which was completely based on culture-based diagnosis. Implementation of molecular diagnostics promises a far larger burden of drug-resistant TB. New patients detected may represent a very different patient population from those previously diagnosed and treated. The population requiring treatment will likely include patients with rapidly progressing TB disease, patients with comorbidities such as HIV and diabetes mellitus, as well as patients with chronic TB. Efforts to develop a single regimen, using conventional approaches to TB drug development, will be inadequate to effectively treat the individually varied patients and will fail to identify a sustainable solution to the population-level problem.

**Conclusion:** New efforts to shorten and strengthen treatment will need to quickly reach the growing population being diagnosed and be effective in populations with a variety of comorbidities and risk factors.

### **Compassionate use and the trials into shortening the regimen: regulatory requirements**

C Perrin,<sup>1</sup> G Brigden,<sup>2</sup> F Varaine,<sup>3</sup> <sup>1</sup>International Union Against Tuberculosis and Lung Disease, Paris, France, <sup>2</sup>Médecins Sans Frontières (MSF), Geneva, Switzerland; <sup>3</sup>MSF, Paris, France

Compassionate use became a standard approach over time for cancer and HIV/AIDS, to dispense potentially life-saving experimental treatments to individual patients suffering from a disease for which no satisfactory authorised therapy exists and/or who cannot enter a clinical trial. WHO approved the application of this concept to DR-TB in 2008 taking into consideration new TB compounds under clinical development. Regulatory authorities in all high burden countries should be encouraged to systematically develop legal frameworks for compassionate use. In countries where compassionate use is not an option, expanded access programs allowing treating groups of patients should also be considered by pharmaceutical companies developing new TB compounds and regulatory authorities to boost early access to new drugs in DR-TB. These two mechanisms as well as controlled approaches assessing benefits of shorter treatment regimen for DR-TB (e.g., clinical trials, observational studies) are all ways that NGOs, civil society, governments and research organisations can promote to increase access to new drugs and regimens in development.

### **HIV/MDR-TB co-infection: working together? A case study from India**

P Isaakidis. Médecins Sans Frontières, Mumbai, India

India carries one quarter of the global burden of multidrug-resistant tuberculosis (MDR-TB) and has an estimated 2.5 million people-living-with-HIV. Despite this, provision of treatment for MDR-TB remains limited, especially for HIV-infected individuals. Médecins Sans Frontières (MSF) has been treating HIV-infected MDR-TB patients in Mumbai since May 2007 with MDR-TB treatment becoming available in the public sector in Mumbai in late 2010. With a lack of information describing treatment of MDR-TB in HIV-infected patients, especially in programmatic settings in resource-constrained countries, this session will discuss experiences from this program treating co-infected patients. It will discuss the treatment outcomes in this programme and common treatment adverse events as well as highlighting clinical, psychosocial and programmatic challenges faced by patients and their care providers and how these were addressed.

### **Decentralising DR-TB care: addressing default rates and enrolment issues with new models of care**

P Du Cros. Médecins Sans Frontières, London, UK

Success rates for multidrug-resistant tuberculosis (MDR-TB) treatment are on average 60% with high default rates. Uzbekistan is one of the 27 high MDR-TB burden countries with an estimated 14% of new TB cases having MDR-TB. Médecins Sans Frontières in collaboration with the Ministry of Health Uzbekistan commenced MDR-TB treatment in 2003 in the Karakalpakstan region. Universal culture and drug sensitivity testing (DST) with molecular and culture based methods for all suspected TB cases was introduced due to high rates of MDR-TB. Due to high default rates and large numbers of patients in need of treatment, the model of care was adapted from initial compulsory hospitalization to ambulatory treatment from day 1 either as clinic based care or with home based care. Decentralisation of care required clinical guidelines and training adapted for involvement of general practitioners (GPs) in case management with supervision from TB doctors. During 2011, 731 patients were commenced on TB treatment with more than half of the patients with confirmed MDR-TB. Success rates for drug sensitive TB improved, however interim outcomes for drug resistant TB for death and default at 6 months were similar between those started in hospital compared with those commenced on ambulatory treatment. Scale-up of universal testing for TB with molecular tests, culture and DST in a high burden DR TB context requires simplified comprehensive TB guidelines, decentralization and

involvement of GPs. There is an urgent need for shorter, more effective and better tolerated MDR-TB regimens if high burden countries are to meet the aims of universal access to effective TB care.

### Barriers to MDR-TB scale-up and the way ahead

M Balasegaram. Médecins Sans Frontières, Geneva, Switzerland

MSF started MDR-TB programmes in 1999 and has been scaling up since then with MSF now being one of the biggest NGO providers of MDR-TB care. 51% of MSF TB projects are involved with treating MDR-TB, with 1300 patients treated for MDR-TB in 21 countries in 2011. Overall the success rate of treating MDR-TB within MSF is 55% and only 13% in XDR patients and despite efforts to scale up the MDR-TB these outcomes are not improving. There are a number of barriers that are preventing the necessary scale up of MDR-TB treatment programmes and this session will highlight the key ones and suggest some strategies that civil societies and NGO's can use to overcome them.

## ADVANCES IN THE TREATMENT OF MDR-TB: CURRENT RECOMMENDATIONS, SHORT COURSE MDR-TB REGIMENS AND NEW DRUGS

### Rationale and limitations of the current recommendations of the World Health Organization for the treatment of MDR-TB

E Jaramillo, D Falzon, F Wares, K Weyer. Stop TB Department, World Health Organization, Geneva, Switzerland

**Introduction:** In 2010, WHO commissioned external reviews to summarize evidence on priority questions regarding programmatic management of MDR-TB in order to update the existing global recommendations. **Methods:** A WHO multidisciplinary expert panel used the GRADE approach, adopted by WHO for guideline development, to conduct a systematic review and meta-analysis of over 9000 MDR-TB cases treated in observational studies.

**Results:** The quality of evidence in the studies meeting the selection criteria varied from low to very low. The systematic review found little evidence on effectiveness and safety of shorter MDR-TB treatment regimens, despite the inclusion of the patient data from the observational study conducted in Bangladesh (a country with low HIV prevalence, limited availability of second-line anti-TB drugs, and excellent TB laboratory support) which reported higher treatment success when regimens substantially shorter than the current standard of care were used. The expert panel

recommended the use of regimens for 20 months in most patients. This recommendation is conditional, meaning that it need not be necessarily apply to all MDR-TB cases in any setting.

**Conclusion:** Systematic reviews have limitations to estimate the treatment effect present when only a few cases or studies are included in the analysis, preventing to generalize on the findings of those specific studies. Thus, the absence of evidence in this systematic review to support the use of short regimens for MDR-TB treatment should not be interpreted as a confirmation or not that such regimens are not effective. Controlled trials are needed to improve the quality of existent evidence on the optimal composition and duration of MDR-TB treatment regimens in varied epidemiological settings. Treatment regimens which are markedly different from the ones which represent the current recommended standard of care should only be used within the context of research.

### 9-month standardised MDR-TB regimen in Bangladesh: an update

A Van Deun,<sup>1,2</sup> A K J Maug.<sup>3</sup> <sup>1</sup>TB-HIV, International Union Against Tuberculosis and Lung Disease, Paris, France; <sup>2</sup>Mycobacteriology Unit, Institute of Tropical Medicine, Antwerp, Belgium; <sup>3</sup>Damien Foundation, Dhaka, Bangladesh

We reported earlier that an inexpensive, short and standardised regimen for MDR-TB was highly effective, yielding 87.9% relapse-free cure in a cohort of 206 patients from Bangladesh (2005–2007). By the end of 2010, 539 patients had been enrolled on this same 9-month regimen, with high-dose gatifloxacin as the core drug, accompanied by clofazimine, ethambutol and pyrazinamide throughout, and kanamycin, isoniazid and prothionamide during an intensive phase till smear-conversion. Of those, 476 had proven MDR-TB, not previously treated with second-line drugs, while 63 were excluded from analysis because they were proven resistant only to rifampicin ( $n = 33$ ) or other drugs than rifampicin ( $n = 22$ ), failed susceptibility tests ( $n = 7$ ), or previous second-line treatment ( $n = 1$ ). Of 466 patients tested, 53 (11.4%) had resistance also to ofloxacin, and 2 (0.4%) also to kanamycin (both primary XDR). Outcome of treatment by standard MDR definitions for the 476 patients: 399 (83.8%) were cured, 11 (2.3%) completed treatment, 35 (7.4%) defaulted, 26 (5.5%) died, and 5 (1.1%) failed. By this time, 272 (66%) of 410 successfully treated patients have completed 24 months of active follow-up post-cure with 6-monthly smear and culture, and 92% at least 6 months. Only 3 (0.7%) relapses were detected, bringing bacteriologically adverse outcome for the total cohort to 1.7% (5 failures and 3 relapses) and success at 85.5%. Initial resistance to ofloxacin and kanamycin were significantly associated with failure and relapse (relative risk 56.3, respectively 29.0). Of the 8 unfavourable,

only one had acquired kanamycin resistance on top of initial MDR plus ofloxacin resistance, no other amplification of resistance was found. Three of the failure/relapse cases cured on second-line retreatment, the primary XDR has converted on a salvage regimen including bedaquiline and linezolid, 1 patient refused and another failed retreatment and died, and 2 patients have yet to start retreatment.

### 12-month standardised MDR-TB regimen: experience in Cameroon

C Kuaban,<sup>1</sup> J Noeske,<sup>2</sup> J L Abena,<sup>3</sup> N Ait-Khaled,<sup>4</sup> H Rieder,<sup>4</sup> A Trébuq.<sup>4</sup> <sup>1</sup>Faculty of Medicine and Biomedical Sciences, University of Yaoundé 1/Hopital Jamot, Yaoundé, <sup>2</sup>German International Cooperation (GIZ), Yaoundé, <sup>3</sup>National Tuberculosis Control Programme, Yaoundé, Cameroon; <sup>4</sup>International Union Against Tuberculosis and Lung Disease, Paris, France

**Objective:** Assess the outcomes of patients with bacteriologically confirmed multidrug resistant tuberculosis (MDR-TB) treated with a 12 month standardized regimen in Cameroon.

**Setting:** The two specialized MDR-TB treatment centers in Cameroon: TB center of Hopital Jamot in Yaounde and the Dibamba Catholic Health Center in the neighbourhood of Douala.

**Design:** Observational study of a cohort of a consecutive adult MDR-TB patients received in the specialized centers and put on a 12 month standardized regimen from 2008 to 2010. The treatment regimen consisted of a 4 month intensive phase with KmGfx-PtoHcfzEZ followed by and 8 month continuation phase with GfxPtoCfzEZ given daily. Clinical and bacteriological progress was monitored monthly during treatment until completion. On completion of therapy patients were followed up clinically and bacteriologically every 6 months for one year.

**Results:** A total of 88 patients (45 men and 43 women) with a mean age of 33.6 (range: 17–68) years were put on treatment during the study period. Eighteen (20.5%) of the patients were HIV infected. One patient had previously received second line antituberculosis drugs. The drug resistance patterns of the 88 patients were: HR: 32 patients, HRES: 28 patients, HRS: 24 patients and HRE: 4 patients. Treatment outcomes at the end of 12 months of therapy were as follows: cured: 81 (92.0%), died: 6 (6.8%), lost to follow-up: 1 (1.1%). The most important side effect was hearing impairment observed in 10 (11.4%) patients. During a total of 636 patient-months of follow-up after treatment, no relapse was observed.

**Conclusion:** The preliminary results with this regimen appear to be very promising. They underscore the fact that a standardized short course regimen may be the best pragmatic alternative to the standardized WHO regimen or individualized treatment for MDR-TB patients in resource poor settings with little exposure to second line antituberculosis drugs.

### Use of bedaquiline (TMC-207) for treatment of MDR-TB

M Haxaire-Theeuwes & the TMC207 Team,<sup>1</sup> A H Diacon,<sup>2</sup> A Pym,<sup>3</sup> M P Grobusch,<sup>4</sup> V Lemaine,<sup>5</sup> V Erokhin,<sup>6</sup> J de los Rios,<sup>7</sup> E R Ticona.<sup>8</sup> <sup>1</sup>Jassen Infectious Diseases BVBA, Beerse, Belgium; <sup>2</sup>Stellenbosch University, Capetown, <sup>3</sup>Medical Research Council, Durban, <sup>4</sup>University of the Witwatersrand and NHLS, Sandringham, South Africa; <sup>5</sup>State Agency Infectiology Centre of Latvia, Riga District, Latvia; <sup>6</sup>Central Institute of TBC, Moscow, Russian Federation; <sup>7</sup>Maria Auxiliadora Hospital, Lima, <sup>8</sup>Hospital Nacional Dos de Mayo, Lima, Peru

**Aim:** TMC207 is in Phase II evaluation for treatment of drug resistant tuberculosis. We compared sputum culture conversion rates in study participants with MDR-TB (resistant to isoniazid and rifampicin) or pre-XDR TB (MDR plus resistance to a fluoroquinolone or a second line injectable drug).

**Methods:** Newly diagnosed patients with at least MDR-TB were randomized to receive a standardized 5-drug regimen (mainly KAN+OFX+ETH+CYC/TER+PZA) plus either placebo ( $n = 81$ ) or TMC207 ( $n = 79$ ) for the first 24 weeks (400 mg q.d. for 2 weeks followed by 200 mg tiw) and then continued with the background regimen. Triplicate spot sputa were cultured at least monthly in MGIT960 tubes. Patients were considered culture converted if they had 2 consecutive negative cultures collected at least 25 days apart. This interim analysis was performed after all patients had completed at least 72 weeks of treatment.

**Results:** 103 (64.4%) of 160 patients who had received at least one dose of study medication had completed or were still in the trial at 72 weeks. Discontinuations were evenly distributed and were mainly due to adverse events (8.1%), withdrawal of consent (8.1%), non-compliance (5.6%), and ineligibility/loss to follow-up (10%). Time to culture conversion was considerably shorter and culture conversion was seen more frequently with TMC207 ( $p = 0.029$ ). Culture conversion rates in MDR TB were 71.8% versus 62.2% for TMC207 and placebo respectively, while for pre-XDR TB the conversion rates were 66.7% versus 41.7% respectively.

**Conclusion:** TMC207 administered for 24 weeks with a standardized 5-drug MDR-TB regimen improved the treatment outcome at 72 weeks with similar responses in patients with MDR and pre-XDR TB at 72 weeks. Compared to placebo, the treatment difference was larger in pre-XDR than in MDR (25% versus 9.6%).

### Delamanid: a promising new treatment for MDR-TB

C Wells. Otsuka Novel Products, Otsuka Pharmaceutical Development & Commercialization, Inc., Rockville, MD, USA

The Global Plan to Stop TB, 2011–2015, calls for the urgent development of new drugs to address the

epidemics of multidrug-resistant (MDR-) and extensively drug resistant (XDR-) tuberculosis (TB). Delamanid (OPC-67683) is a new molecular entity that has demonstrated significant in vitro and in vivo activity against *Mycobacterium tuberculosis*. Taken from the nitro-dihydro-imidazooxazole class of compounds whose mechanism of action includes direct inhibition of mycolic acid synthesis, delamanid is active against drug susceptible and drug-resistant TB strains. From May 2008 through June 2010, 17 centers in nine countries (China, Egypt, Estonia, Japan, Korea, Latvia, Peru, the Philippines, and the United States) participated in a randomized placebo-controlled trial (RCT) to evaluate the safety and efficacy of two doses of delamanid (100 mg twice daily and 200 mg twice daily) in conjunction with an optimized background treatment regimen. Preliminary results from an 8-week treatment period of 481 patients demonstrated statistically significant higher sputum culture conversion rates for patients taking either delamanid 100 mg twice daily or 200 mg twice daily vs. placebo (45.4% vs 29.6%,  $P = 0.008$  and 41.9% vs. 29.6%,  $P = 0.04$ , respectively). Adverse events were lower in the 100 mg twice daily group vs. 200 mg twice daily group. Nearly one-half of the patients then participated in a 6-month treatment extension trial. In addition, new results from a long-term analysis of final outcomes for the original MDR-TB patients randomized in the RCT, including a subset with XDR-TB, will be presented. A multi-country phase III trial is currently enrolling patients. Delamanid holds strong promise as a novel therapeutic for the treatment of MDR-TB, including XDR-TB.

## EVALUATION OF TOBACCO CONTROL PROGRAMMES: EXPERIENCES TO IMPROVE THE EFFECTIVENESS OF RESOURCES USED AND SUSTAINABILITY

### Two case studies of learning from tobacco control evaluation: China and Latin America

Y Lin, Q Gan, N Dong, H Liu, J Ma. International Union Against Tuberculosis and Lung Disease, Beijing, China

As one of the Bloomberg Initiative (BI) partners, The Union operated 24 tobacco control (TC) projects in China since 2007. To identify effective approaches and assess utilization of the BI funding, the Union applied independent external assessment (IEA), surveys, and other monitoring before major decision making. Key findings are:

- Government commitment is critical for success
- Policy change has successfully affected key indicators of prevalence
- Capacity building—substantial reach within target institutions.

The presentation will also identify positive aspects and difficulties that can be encountered in TC evaluation and discuss how these link to sustainability.

### Can evaluation be linked to sustainability? Lessons from the field

G El Nahas. Middle East Regional Office, International Union Against Tuberculosis and Lung Disease, Cairo, Egypt

**Background:** Advancing tobacco control (TC) policies in low middle income countries (LMIC) in the Middle East is a major challenge. Lack of resources both material and non material, limited expertise, and having other public health issues competing with TC makes it difficult to be placed as a priority on the agenda of countries we work with. Over the past 5 years Union Middle East office has been working with 3 countries in the region and contributed to the enhancement of TC policies at different levels.

#### Objectives:

- 1 Share the progress in TC programs in Egypt Pakistan and Lebanon
- 2 Share challenges those countries face in placing TC as a priority health issue
- 3 Discuss the urging need to rigorous monitoring and evaluation in order to ensure sustainability of those programs

### Evaluating programmes at 'grassroots' level: are such programmes sustainable?

R J Singh. South-East Asia Regional Office, International Union Against Tuberculosis and Lung Disease, New Delhi, India

**Background:** Implementation of smokefree policies in India has gained momentum after effective rules came into force in October 2008. Many states, districts, cities and villages across India were declared smoke-free based on an evaluation framework after receiving support under Bloomberg Initiative. Broadly, this evaluation framework measured factors like politico-administrative commitment, establishment of enforcement mechanisms, effective alliances, public education and policy-focused research to assess the support and progress made in implementation of Smokefree policies. The diligent implementation of provisions of the law backed by opinion polls and compliance studies that inform policy makers, public and the media played a crucial role in initiating and maintaining smokefree efforts.

**Intervention:** Smokefree implementation status in an identified jurisdiction was assessed on the basis of an evaluation framework and criteria developed by experts in a national workshop held in 2009. Till date, this framework has been used by large number of stakeholders like state and district administrations, civil societies and public health institutes in more than 40 jurisdictions. Evaluations were administered through local partners as third party evaluators and assess the effectiveness of smokefree interventions.

**Results:** The results of evaluation of smokefree implementation have been shared with policymakers, public and the media, which has helped in strengthening and expansion of tobacco control policies and in transferring good practices and lessons learnt in neighbouring and similar jurisdictions.

**Conclusions:** Success of tobacco control interventions and their sustainability depends on capacity created, political and administrative apportioned to tobacco control, partnerships and diffusion of good practices among government and civil society at the grassroots level, and creation of administrative systems that sustain tobacco control within jurisdictions.

### Is a regional approach to evaluation better than a national approach?

#### Experience from Russia

I Berezhnova, E Zeynalova. Tobacco Control Department, International Union Against Tuberculosis and Lung Disease, Moscow, Russian Federation

**Background:** Instituting sustainable smoke-free policies at regional level requires development of regional strategies and systematic measures for implementation of tobacco control programs. In light of recent revisions of the Russian national TC draft legislation, this is an opportune moment to discuss and encourage regional governments to develop regional strategies to support the national legislation. To ensure and assess the sustainability of TC activities, effective monitoring and evaluation should be set up to correspond with policy measures.

**Current situation:** In accordance with the current federal law on smoking restrictions, the federal government is solely responsible to pass legislation directing all tobacco control measures. Despite this limitation of regional authorities, both regional and national governments are responsible to enforce TC laws. All current measures on the national level are being assessed based on health statistics and smoking prevalence data. There is a need for standardized and reliable monitoring system to allow evaluation across TC activity. Some regions have been very active in developing and running evaluation activities such as legal analyses, needs assessments and different types of surveys.

**Lessons learnt:** As experience shows, a variety of evaluation activities help give feedback on project implementation. Based on this, several regions have already developed and made significant progress on implementation and promotion of their regional TC policies and in some cases secured regional budget allocations.

**Conclusion:** Evaluation assists the regions to understand what should be included in their strategies and programs, and therefore helps ensure sustainable implementation. Considering the current situation in Russia it is necessary to use both—regional and national approaches.

### Case study of learning from tobacco control evaluation: Buenos Aires moves forward in implementing smoke-free policies

J Romo. International Union Against Tuberculosis and Lung Disease, Mexico, Mexico

As the grants program grows in Latin America, more efforts are needed to assess real progress in selected interventions. The focus of The Union in the region is on the implementation-oriented projects. We have chosen the Buenos Aires smoke-free project to describe how we evaluate completion of activities and achievement of objectives. This presentation explains how the evaluation findings led to an enhanced implementation of this policy. Many outcomes produced during the life of this project allow us to measure the progress in several phases in the development of legislation, actual figures of public support, media coverage influencing decision-makers, etc. Through quantitative and qualitative indicators we are able to determine the effectiveness of the activities undertaken. They have led to an enhanced implementation of this particular public policy. Although the political context and environmental conditions were not favorable for the project, the goals were obtained. This was possible thanks to trained and appropriate staff, a thorough program of public relations and management of the press, a close monitoring of the legislative agenda, and a communication strategy to reach the general population in support of smoke-free environments.

## IMPLEMENTATION AND EVALUATION OF TUBERCULOSIS CONTACT INVESTIGATION IN HIGH BURDEN SETTINGS

### Introduction to the development of World Health Organization contact investigation policy guidelines

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World Health Organization policy requires that guidelines be developed in a standardized transparent manner and be based on a rigorous review of the existing literature. To begin the process the questions to be addressed must be identified. To develop guidelines for contact investigation the following questions were identified: 1. In what proportion of contacts of new or recurrent cases (index cases) of tuberculosis does contact investigation lead to identification of previously undiagnosed tuberculosis?

- 1.1 Who should be considered as an index case for purposes of initiating contact investigation?
- 1.2 How can the contacts at greatest risk of tuberculosis be identified?

- 1.3 In what proportion of contacts of an index case with HIV infection does contact investigation lead to identification of previously undiagnosed tuberculosis?
- 1.4 In what proportion of contacts of an index case with M/XDR TB does contact investigation lead to identification of previously undiagnosed tuberculosis?

To address these questions a previously published systematic review (data through 2005) was updated (data through August 2011). The overall yield of active TB was 4.5% of contacts investigated; contacts of HIV infected index cases, 9.4%; contacts <5 years of age, 7%; contacts of MDR index cases, 3.4%. In general the literature is poor with heterogeneous results; however, the results of the update were little changed from the original review and were also consistent with the results of a second overall review done by Fox et al. These reviews provided the evidence base for the recommendations.

### Morbidity and mortality among household close contacts of multi-drug resistant tuberculosis in Mongolia

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**Background:** The secondary attack rate is shown how any infectious disease spread at crowded place such as family, dormitory, military barrack, prison etc. To estimate secondary attack rate, it is necessary to measure infection and evaluate control's activity. The morbidity and mortality rate are high among family members of multi-drug resistant tuberculosis patients.

**Methods:** The study was used epidemiological form of 494 patients who have treated, questionnaire and provinces and districts' tuberculosis doctor's introductions which written by doctors' consultation.

**Result:** Among 172 close contacts were transmitted focally by drug sensitive and multi-drug resistant tuberculosis in Ulaanbaatar. Totally 77 close contacts have multi-drug resistant tuberculosis and 181 close contacts have drug sensitive tuberculosis. From above families' 84 close contacts were died by tuberculosis. One family's average close contact's number is 3.7. The secondary attack rate among multi-drug resistant tuberculosis household close contact's is 16.9%.

**Conclusion:** Morbidity and mortality among household close contact of multi-drug resistant tuberculosis are high in our country.

### Lessons learnt from standardising approaches to contact investigation in Kenya

J Sitienei,<sup>1</sup> J Ong'ang'o,<sup>2</sup> K Hillary.<sup>3</sup> <sup>1</sup>Ministry of Public Health and Sanitation, Nairobi, <sup>2</sup>Kenya Medical Research Institute, Nairobi, <sup>3</sup>World Health Organization, Nairobi, Kenya

**Background:** Tuberculosis transmission in the community and health care settings continue to threaten achievement of global targets in TB control. Standardizing contact investigation methods can improve contact investigation and eventually have an impact on TB transmission within the community and health care settings.

**Objective:** To document lessons learnt from standardizing the approaches to TB contact investigation in Kenya.

**Methodology:** Review of models adopted by the Ministry of Public Health and Sanitation through review of data captured using routine tools for recording and reporting in the period January to December 2012. A total of 102 514 cases reported were analyzed. Descriptive statistics were then presented after the final analysis of aggregated data collected from the whole country. Data is transmitted through semi electronic methods from the health facilities (both hard copies at lower level and electronic from the district). Primary data is collected at service delivery points where the patients and suspects are evaluated.

**Results:** Self referral contributed to the largest proportion in 2012 at 71%, followed by referral from the HIV clinic at 15%, referral by the community health care workers was third at 4% and contact invitation at 3%. The remainder included referrals from the voluntary counseling and testing clinic, sexual transmitted infection clinics, home based care, antenatal clinics, private sector and chemists contributing to 7%.

**Conclusion:** Different models adopted by the ministry yielded different results and this depended on the sensitization and advocacy done including infrastructure and human resources available in different settings.

**Recommendations:** Increased advocacy can lead to increased uptake of specific interventions depending on several factors. It is possible to identify the best fit and promote it vigorously so as to improve eventual uptake.

### Multi-center approach to tuberculosis contact investigation in Viet Nam

G Fox. Woolcock Institute of Medical Research, Sydney, NSW, Australia

**Setting:** Viet Nam is a country with a high prevalence of tuberculosis, where the national tuberculosis program primarily relies upon passive case detection strategies. The estimated case detection rate is 54% (43%–71%).

**Objective:** To test the feasibility and effectiveness of household contact investigation as a strategy to enhance case detection in Viet Nam.

**Design:** A cluster randomized controlled trial of radiological and clinical screening in 70 districts throughout the country.

**Outcomes:** Our ongoing trial is being implemented in partnership the national tuberculosis program. To date, we have recruited over 8000 patients and 18000 household contacts in control and screening groups. Our study demonstrates the feasibility of contact investigation in a range of settings in Viet Nam, and has provided many valuable lessons about how to implement contact investigation in a high prevalence country.

## BEST PRACTICE IN THE APPLICATION OF NEW TECHNOLOGIES AND INNOVATIONS

### Best practice for using GeneXpert® to diagnose and initiate treatment for someone who may have MDR-TB

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**Background:** Traditionally drug resistance is detected by culture which takes 6–8 weeks. GeneXpert® detects rifampicin resistance within 2 hours and it is a good indicator of MDR-TB. South Africa started using GeneXpert in March 2011. Experience from Ethekewini District is described here.

**Aim:** To discuss operational and patient management issues with the use of the GeneXpert from the perspective of the patient and healthcare worker.

**Implementation:** Ethekewini was the first district in South Africa where GeneXpert was introduced as it has the highest caseload of susceptible and MDR-TB in the country. Currently, 1 site is using a GX48 and 2 are using GX12. Results are sent to the clinic by SMS within 2 days. Patients come in within 2 days by previous appointment to receive their results.

**Discussion:** The rapid turn-around-time of results has led to drug resistant patients starting MDR treatment immediately instead of first going on 2–3 months of first-line drugs. Counselling was adapted to include the diagnosis and management of MDR. Anecdotal accounts of receiving results so quickly indicate that some patients go into denial because they are not feeling that ill. Others are unprepared of having to make adjustments to their work, etc. The increase in the number of MDR-TB cases, led to changes in management of MDR-TB patients from hospital versus community based management. Only sick patients are admitted for minimum of 2 months while others are treated on an outpatient basis. This entailed the establishment of community based teams. Accessibil-

ity to testing is an issue because of geographical placement. A needs analysis should be done to place the correct size machine in relation to the catchment area for optimal utilisation of the machine. Continuous training is necessary and should include buy-in to systems changes, review of algorithms and regular feedback. There is a degree of false positivity and standardised guidelines to manage these patients need to be developed

### The value of 'patient schools' for patients with tuberculosis as well as psychiatric disorders

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**Background and challenges to implementation:** TB patients with psychiatric disorders face specific challenges such as inability to recognize health problems, adjustment disorders, inadequate social skills, frequent reliance on external assistance in everyday situations. These problems may interfere with successful TB treatment.

**Intervention or response:** A patient school was conceptualized and opened in the TB ward of the Omsk Oblast Psychiatric Hospital. It is run by the nurses and embraces both individual approach (one-on-one sessions with patients and their families) and group work (a course of 10 weekly training sessions in groups of 6–10). The content may vary to suit the needs of individual patients and/or patient groups.

**Results and lessons learnt:** Questionnaires and regular oral feedback from the attendees were used to evaluate the training outcomes. In 4.5 years the total of 163 TB patients with psychiatric disorders (89 male, 74 female) have attended the school. Before training 63.43% of the attendees were unable to recognize any TB symptoms and 51.71% of them did not understand why compliance is necessary. After training 100% of the attendees could identify at least some of TB symptoms and list at least some reasons for regular drug intake, which led to better compliance to treatment. 75.8% of the attendees on TB treatment noted an improvement in their condition, especially noticeable in the most severe cases (22 patients).

**Conclusions and key recommendations:** A patient school as an element of a TB control program run in a psychiatric hospital has proved an efficient way to help TB patients with psychiatric disorders successfully deal with the specific problems they face during TB treatment.

## NUTRITIONAL SUPPORT IN THE PREVENTION OF TUBERCULOSIS AND WHO GUIDELINES FOLLOWING TUBERCULOSIS DIAGNOSIS

### Impact of nutritional support on tuberculosis treatment outcomes and nutritional rehabilitation

P Papathakis. California Polytechnic State University, San Luis Obispo, CA, USA

Undernutrition is both an important risk factor for TB and is a common consequence of TB. Most individuals with active TB are in a catabolic state and experience weight loss and some show signs of vitamin and mineral deficiencies at diagnosis. Low body mass index (<18.5 kg/m<sup>2</sup>) and lack of adequate weight gain with TB treatment are associated with an increased risk of death and TB relapse. Studies show that subjects who receive food supplements during TB treatment tend to gain more weight compared with those not receiving food supplements, but the increase in weight gain has not been associated with improvement of TB treatment outcomes. Low circulating concentrations of micronutrients, such as vitamins A, E and D, and minerals iron, zinc and selenium have been reported from cohorts of patients beginning treatment for active TB. These usually return to normal after 2 months of TB treatment and without supplementation. Since studies have not been done on dietary intake near the time of diagnosis, it is unclear whether the low concentrations are related to low dietary intake, to metabolic processes or to the disease itself. It is unknown whether the observed return to normal concentrations is dependent on the quality of dietary intake. Studies have not yet been done to determine the impact of nutrient supplementation on quality of life, cognitive function or the ability to do work; or in MDR-TB.

### BCG vaccination: a role for vitamin D?

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**Background:** BCG vaccination is administered in infancy in most countries with the aim of providing protection against tuberculosis. There is increasing interest in the role of vitamin D in immunity to tuberculosis. The objective was to determine if there was an association between circulating 25(OH)D concentrations, BCG vaccination status and cytokine responses following BCG vaccination in infants.

**Methods:** Blood samples were collected from UK infants who were vaccinated with BCG at 3 ( $n = 47$ ) and 12 ( $n = 37$ ) months post BCG vaccination. Two blood samples were also collected from age-matched unvaccinated infants ( $n = 32$  and 28 respectively), as a control group. Plasma vitamin D concentrations (25(OH)D) were measured by radio-immunoassay. The cytokine IFN $\gamma$  was measured in supernatants from diluted whole blood stimulated with *M. tuberculosis* (MTB) PPD for 6 days.

**Results:** 58% of infants had some level of hypovitaminosis (25(OH)D, 30 ng/ml) 3 months post BCG vaccination, and this increased to 97% 9 months later. BCG vaccinated infants were almost 6 times (CI: 1.8–18.6) more likely to have sufficient vitamin D concentrations 3 months post vaccination than unvaccinated infants, and the association remained strong after controlling for season of blood collection, ethnic group and sex. Among vaccinees, there was also a strong inverse association between IFN $\gamma$  response to MTB PPD and vitamin D concentration, with infants with higher vitamin D concentrations having lower IFN $\gamma$  responses.

**Conclusions:** Vitamin D may play an immunoregulatory role following BCG vaccination. The increased vitamin D concentrations in BCG vaccinated infants could have important implications: vitamin D may play a role in immunity induced by BCG vaccination and may contribute to non-specific effects observed following BCG vaccination.

### Financial interventions and modulation of malnutrition/food security in the context of tuberculosis

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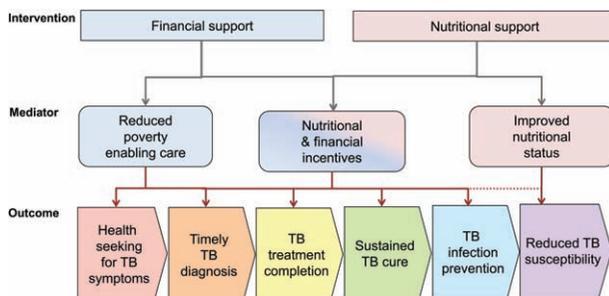
**TB and poverty:** Poverty predisposes to TB exposure through crowding and increasing contact with infectious TB patients. Poverty also increases the likelihood of TB exposure causing progression to symptomatic TB disease.

**TB and nutrition:** Under-nutrition is a mediator by which poverty may increase TB susceptibility. Low body mass index at the time of TB exposure is associated with TB susceptibility, independently of poverty. In addition to this macronutrient deficiency, low levels of micronutrients including vitamins D, A and zinc are associated with TB susceptibility and impaired TB treatment response. Furthermore, TB is known as 'consumption' because TB disease causes malnutrition. Thus under-nutrition is a mediator of the association between TB and poverty.

**TB control:** Changes in TB rates are associated with changes in socioeconomic indicators, whereas it is difficult to detect effects of biomedical TB control interventions on TB rates. Thus, despite TB diagnosis and treatment preventing millions of deaths, the principal determinants of TB rates appear to be financial and nutritional, not biomedical. This observation implies that financial and nutritional interventions may have the potential to strengthen TB control efforts.

**Financial and nutritional interventions and TB:** Economic and food support for TB patients has improved treatment adherence, accelerated microbiological response to TB treatment and increased equitable access to TB services. For TB-exposed people, micronutrient supplementation with vitamins D, A and zinc reduced the risk of TB disease only in poorer households. Financial, macronutrient and micronutrient support for TB-affected people have been the subject of remarkably little research compared with TB diagnostics and TB drugs.

**Conclusion:** Social, economic and nutritional factors are the principal determinants of TB risk and should be more extensively assessed for their capacity to strengthen TB control.



## USING GEOGRAPHIC INFORMATION SYSTEMS (GIS): NEW POSSIBILITIES FOR IMPROVING TUBERCULOSIS CONTROL PROGRAMMES

### GIS: what is it and how can we use it to improve tuberculosis control programmes?

M I Bakker, E J J Rood, S M van Beers. KIT Biomedical Research, Royal Tropical Institute, Amsterdam, The Netherlands

A common pitfall in disease control is the negligence of the heterogeneity of the disease burden. Disease control can only be effective if its implementation is well designed, planned, monitored and evaluated. Tuberculosis is a clear example of a disease affecting poor and vulnerable populations, consequently—in general—tuberculosis rates are higher among groups of vulnerable lower social-economic status. In these groups, often higher rates are found in urban communities because of crowding and greater opportu-

nity for infection. It is not uncommon for countries to have more than one third of its TB burden clustered around its main capital and big cities. How can a national TB control programme respond most effectively to the TB disease burden in its country? The first step towards effective TB control is to describe the TB pattern in country and to identify spatial patterns in disease distribution and its determinants in order to support decision-making processes for creating and targeting subsequent control interventions. The information needed for this can be provided by using the Geographic Information System (GIS). GIS is more than mapping diseases: it manages, analyses and presents data that are linked to geographical locations. Yet, GIS remains underutilized as a tool to assist public health officials and TB control programme managers. This session gives an introduction to the powerful features of GIS. It will provide examples of how GIS can be used to display and analyze tuberculosis notification rates and how the informational value of the maps can be improved. It also will give examples on how the heterogeneity of the disease burden can be analyzed and visualized, and how TB burden areas can be identified with ‘surprisingly high’ or ‘surprisingly low’ detection rates of disease and its implications for TB control management programmes.

### How to design an effective tuberculosis laboratory network: evaluating coverage and accessibility using GIS

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Adequate case-detection remains a major constraint for effective tuberculosis control. According to the WHO, 35% of the 198 reporting countries reported a case detection within their countries of less than the recommended 70% and a quarter of all countries have a case detection lower than 62%. A first requirement for adequate case-detection activities is the availability of effective and adequately covered TB diagnostic network. With the aid of GIS, the availability and accessibility to this network can be assessed, analyzed and approaches for improvement identified. This session presents a case-study from Benin by which GIS is used to describe and explain disparities in access to the health care facilities and TB diagnostic services. The number of TB diagnostic laboratory units was less than 1 per 100 000 in 2011. The work load is unequally distributed with a high proportion of units not reaching the recommended minimum target of work load for maintaining required quality provision. The availability, accessibility and unequal distribution of the health services are linked to TB notification data, and its implication

for case-detection capacity is discussed. The application of GIS spatial analysis tools provides insight and understanding on the bottlenecks and recommendations for the optimization of TB programme coverage can be made.

### **GIS: an indispensable tool for monitoring performance of tuberculosis diagnostic services?**

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The AFB smear laboratory registers in national tuberculosis programs was introduced by Dr Styblo to monitor and evaluate case-detection and treatment success in national TB control programmes. However, its utilization has been limited, and—with exceptions—has been used for calculation of work load based requirements such as laboratory supplies and more recently to monitor laboratory performance using register-based laboratory indicators. The introduction of External Quality Assessment Programs (EQA) in Uganda has provided the opportunity to collect routine information from the TB laboratory registers. Together with the collection of smears for rechecking purposes quarterly information from each laboratory was thus obtained on numbers of smears examined and its AFB results for diagnostic and follow-up purposes. By linking the AFB laboratory examination results and EQA program data to a Geographic Information System (GIS), visualization and spatial analysis techniques can be used for a more in-depth analysis taking into account the spatial distribution of the laboratories. We present in this session the results of the AFB laboratory examination and EQA program in Uganda. Spatial patterns of TB case notification are compared to the spatial distribution of the delivery and performance of TB-diagnostic services across Uganda. We show how the laboratory generated data can be used i) by the national TB program to monitor and evaluate the performance of case detection and patient selection; ii) by the laboratory supervisors to identify poor performance laboratories. Geographical visualization and spatial analysis of data from the laboratory registers and EQA program, provides essential information which facilitates a better understanding and allows effective targeting of supervision and remedial actions to improve TB control program and its supporting TB laboratory services.

### **Bringing it all together: using GIS and spatial pattern analysis for effective surveillance and response to tuberculosis**

S M Van Beers,<sup>1</sup> M Joloba,<sup>2</sup> D Affolabi,<sup>3</sup> E J J Rood,<sup>1</sup> M I Bakker.<sup>1</sup> <sup>1</sup>KIT Biomedical Research, Royal Tropical Institute, Amsterdam, The Netherlands; <sup>2</sup>National Tuberculosis Reference Laboratory, Kampala, Uganda; <sup>3</sup>National Tuberculosis Reference Laboratory, Cotonou, Benin

The notification data of the TB programmes form the basis for surveillance and effective response to TB. These data are based on administrative areas, which can hinder appropriate representation of the true burden of TB. Different visualization techniques can be applied to obtain a better understanding of the distribution and trends of the burden of TB. In-depth spatial analyses—using specific spatial weight/auto-correlation/regression techniques—allow for a more valid appraisal of TB occurrence and facilitates targeted planning and interventions. The session summarizes and illustrates GIS utilities as a tool to assist public health officials in their core functions, specifically to assess TB disease burden and its spatial distribution, to monitor trends, to analyze its risk factors or determinants, to develop policy, to advocate for greater allocation of resources, to implement and evaluate interventions, to ensure adequate coverage of interventions, and to raise questions that can be applied to further research. In addition, the session discusses requirements for setting up effective GIS services and the challenges and problems that may hinder its successful implementation.

## **OCCUPATIONAL HEALTH ENCOURAGEMENT: A PATHWAY TO ATTAINING SUSTAINABILITY**

### **Occupational lung disease in the South African mining industry: research and policy implementation**

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**Setting:** South African gold mining with an epidemic of occupational lung diseases despite decades of research and policy initiatives.

**Objective:** To identify impediments to the translation of research findings and policy initiatives into effective interventions.

**Design:** Literature review of disease burdens; research findings; policy, legislative and service initiatives; and factors influencing translation of research findings into effective interventions.

**Results:** Financial and other resources (e.g., low compensation costs); social (e.g., high rates of migrancy); and organisational (e.g., weak inspectorate)

factors probably explain much of the failure to use research evidence.

**Conclusions:** Scientific studies have motivated and informed many sound policy decisions and legislative reforms and have identified strategies for strengthening practice and health systems. But, very few studies seem to have fostered sustained remedial action. There are clear gaps between research, policy, and implementation in occupational health practice in the South African mining industry.

### Latent tuberculosis among health care workers

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Transmission of tuberculosis (TB) to health care workers is a global issue. This can be attributed to high influx of foreign workers, transmission within congregate settings, emergence of multidrug resistant tuberculosis and an increase in human immunodeficiency virus patients. Health care workers (HCWs) are a particularly important group to study relating to latent tuberculosis infection (LTBI), because their risk of acquiring LTBI is higher than average as a result of their exposure to patients with TB. In addition, should HCWs develop active TB, they are at risk of transmitting the infection to their patients. Occupational tuberculosis can lead to loss of skilled workers and impact the health care service. Studies done in Germany and Japan reported an LTBI prevalence of 9.9% among health care workers. Malaysia reported a prevalence of 10.6%. Due to the limitations posed by tuberculin skin testing, a new generation of diagnostic tests for LTBI, the interferon-gamma release assays (IGRA) have been introduced which are more specific for *Mycobacterium tuberculosis*. Treatment regimes with isoniazid and rifampicin have been recommended. Since tuberculosis is a preventable and treatable disease, the emphasis on LTBI among health care workers should be prevention and institution of control measures in the workplace to avert the transmission of the disease in high risk exposure settings. A TB infection control programme should be established to promptly detect infectious patients, ensure airborne precautions and treat patients suspected or confirmed of TB disease. The tenets of the TB control programme should encompass the three—level hierarchy of control measures: administrative measures, environmental controls and use of respiratory protection devices.

### Strategy and programmatic prospective of occupational lung health

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Occupational lung diseases, associated with manufacturing and the lack of regulations and controls to minimize exposures, have shifted toward low and middle income countries. The extent of this problem is not known. Routine surveillance is weak and scientific investigations not extensive. The number of cases is probably in the millions (estimated 3–9 million). The lung is vulnerable to exposure and the harmful effects are predominantly airflow obstruction, lung fibrosis and respiratory cancer. Estimates of attributable fraction of respiratory cancers in men vary from 2% in China to 8% in the UK. Occupational lung diseases are expected to rise steadily in low and middle income countries. Clearly prevention is the key. First, regulations and controls need to be enhanced. The initiative for this will need to come from those benefiting from the profits of industry—the managers and shareholders. A concerted effort must be developed to influence these groups of people. Second, it is crucial to replace toxic materials with those less toxic where this is possible. Progress has been made in industrialized countries where, for example, asbestos has been banned or heavily controlled in 52 countries. However, the material continues to be produced and used throughout the world. Many countries (including my own country—Canada) produce and market this material when it is in their own country. Efforts are needed here, as well, to influence policy and practice. Finally, we need to develop simple and robust methods (such as those developed by ISAAC) to estimate the size and trend of the problem throughout the world.

### Quantifying the burden and trends of occupational lung diseases

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The burden and trends of occupational lung diseases (OLD) are determined by systematic surveillance of the extent of OLD and workplace exposures to airborne hazards. The World Health Organisation Global Burden of Disease project provides comprehensive estimates of morbidity and mortality from 26 major health risks including selected occupational risks, e.g., airborne particulates and workplace carcinogens. Occupational exposures account for 9% of all cancers of the lung, trachea and bronchus, 13% of chronic obstructive pulmonary disease (COPD) and 11% of asthma cases. An estimated 152 000 deaths (969 000 DALYs) from cancers of the lung, trachea and bronchus and 43 000 deaths (564 000 DALYs) from mesothelioma are due to workplace carcinogens. All cases of pneumoconiosis are due to exposures at work. There are an estimated 9000 deaths (486 000 DALYs) due to silicosis, 7000 deaths (376 000 DALYs) due to asbestosis and 14 000 deaths (366 000 DALYs) due to coal worker pneumoconiosis. Proportion of

workers exposed to silica and asbestos are highest in mining (0.23, 0.10) and construction (0.19, 0.05) respectively. Estimated relative risks for common occupational lung carcinogens, e.g., silica, asbestos, arsenic, chromium and beryllium are 1.33, 2.0, 3.69, 2.78 and 1.49 respectively. Population Attributable Risk (PAR%) are calculated from proportion of workers exposed and relative risks. Optimistic, pessimistic and baseline projections of deaths and DALYs are made to assess trends. Cancer of the lung, trachea and bronchus and COPD are projected to continue to be among the leading causes of DALYs in 2020. Assessing burden and trends of occupational lung diseases require good surveillance systems. Better estimates of disease burden and trends in developing countries can be obtained by increasing awareness of OLD, standardising diagnostic criteria and improved reporting systems.

## ENSURING SUSTAINABLE SURVEILLANCE, DIAGNOSIS, PREVENTION AND CONTROL OF ZONOTIC TUBERCULOSIS

### The risk of *Mycobacterium bovis* infection in humans in Namwala, Zambia

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**Background:** Zambia has a high tuberculosis (TB) burden (707/100 000). The World Health Organization (WHO) ranks Zambia among the top ten countries with higher incidence of TB in the world. Zoonotic tuberculosis caused by *Mycobacterium bovis*, typically the causal agent of bovine TB, has been shown to be increasing in their public health significance throughout the world, particularly in sub-Saharan Africa, where their control is restricted by inadequate infrastructure, lack of skilled manpower and financial resource constraints. In Zambia, infections caused by *M. tuberculosis* complex (MTC) have been reported in humans, cattle and wildlife. However, the role of *M. bovis* infections as a causative agent for human tuberculosis is however, poorly understood.

**Methods/approaches:** In our study a total of 41 smear positive sputum samples from TB patients were collected from Namwala District in the Kafue Basin, where the cattle—wildlife—human interface area exists. Sputum was cultured on both Stonebrink and Middlebrook 7H9 solid media according to standard protocol. Speciation and genotyping was done using Deletion analysis and Spoligotyping respectively.

**Results:** The results from three different health facilities in the Kafue Basin region indicate that in 0.073% of samples (3/41) *M. bovis* was identified.

**Expected outcomes:** Currently, additional work is underway to understand the role of bovine TB in the epidemiology of *M. tuberculosis* complex infections in Zambia and the possibility of human to human transmission.

### Myths and practices linked to mycobacterial infection among the pastoralist communities of Uganda

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**Background:** Beliefs, myths, values, norms, taboos language, ritual and art are among the cultural aspects that influence health of a given society although the relationship between cultures, health related beliefs and health behaviour is still complex. The present study was conducted to assess community myths, perceptions, knowledge, attitudes, practices (KAP) of the pastoral farmers and explore mycobacterial infection management practices.

**Methods:** Both structured questionnaire survey and participatory rural appraisal approaches were used.

**Results:** This study revealed that mycobacterial infection especially tuberculosis as referred to in vernacular as akakonko, akasubba or akafuba because of the persistent cough and other respiratory symptoms. Knowledge attitudes and practices: congestion under extended family homes, sharing of household utensils, consumption of untreated milk and drinking untreated water as means of mycobacterial infections spread to humans. Perceptions: sharing the drinking straws and cigarette sticks. Community myths: witchcraft, family history and genetic heritability. Mycobacterial infections and human immunodeficiency virus-acquired immunodeficiency syndrome (HIV/AIDS) were closely linked and these infections issued stigmatisation among the community members.

**Mycobacterial infection management methods:** Sixty-five per cent (65%) of the respondents visited traditional healers and used local herbs while 35% visited health centres and used modern medicines. The multivariate model identified sex, marital status, and age influencing the choice of managing mycobacterial infections.

**Conclusions:** Sustainable community intervention require a thorough understanding of traditional indigenous knowledge, attitudes, practices myths, beliefs and perceptions in designing disease prevention and control strategies at the human-environment-animal interface in the pastoral ecosystems of Uganda.

### Sharing tuberculosis: humans and other mammals

A Perera,<sup>1</sup> D Barber,<sup>1,2</sup> <sup>1</sup>USDA APHIS VS, Chicago, IL, USA; <sup>2</sup>USDA APHIS IS, México, Mexico

Published accounts report human transmission of *Mycobacterium bovis* infection to cattle. Unpasteurized dairy product consumption is increasing in the United States. We explore enhancing epidemiology to include mitigate risks associated with *M. bovis* in humans who have contact with susceptible livestock species. Illinois is following the national trend in that the majority of TB cases were among individuals who were born in foreign countries where TB is common, such as Mexico, India and the Philippines. In 2009, 62 per cent of tuberculosis cases in Illinois were foreign-born. The project has 2 components, laboratory and risk management. The lab component is to ensure typing of human TB isolates to the same extent as livestock isolates. Methodology and capacity has been established at CDC and NVSL to accurately compare human isolates to veterinary isolates for potential molecular relatedness. The risk management component directs the Illinois VS Office to collaborate with One Health Partners to identify human cases of *M. bovis* who may have contact with susceptible livestock species. The project is expected to yield these outcomes:

**Standard Operating Procedure template for One Health collaboration:** VS epidemiologists have developed and implemented a real-world working draft SOP with Illinois Public Health Professionals. This draft was implemented when a newly identified case of tuberculosis in a human patient in Illinois was culture-confirmed to be *M. bovis* infection. The joint One Health laboratory and clinical epidemiological investigation is ongoing.

- Develop risk mitigation strategies
- Increase TB awareness of One Health Partners
- Provide input toward formulating VS Guidance and a Memorandum of Understanding for communication to be signed with One Health Partners regarding tuberculosis

### Creating global awareness of the risk of zoonotic tuberculosis in high risk areas

F Olea-Poppelka,<sup>1,2</sup> <sup>1</sup>Colorado State University, College of Veterinary Medicine and Biomedical Sciences, Fort Collins, CO, USA; <sup>2</sup>International Union Against Tuberculosis and Lung Disease, Paris, France

**Background:** While *Mycobacterium tuberculosis* is generally recognized as the primary causal agent of human tuberculosis (TB) cases worldwide, evidence clearly indicates that other *Mycobacterium* species, including *M. bovis*—which typically causes bovine TB—also causes disease in humans. There are fundamental differences in disease complexity in humans,

wildlife, and livestock in ecosystems where these species interact closely. However, currently, significant challenges exist for the diagnosis, prevention, and control/treatment of zoonotic TB among humans in most areas of the world.

**Objectives:** Present and discuss strategies to create awareness of the risk and importance of zoonotic TB in areas in which infection and disease caused by different *M. tuberculosis* complex species are present in livestock, wildlife and humans.

**Approach/methods:** During 2011–2012 the Zoonotic TB sub-section officers evaluated results from a previous *M. bovis* working group, participated in scientific meetings, started collaboration with the microbiology sub-section in order to improve the diagnosis of *M. bovis* infection among humans, and reached out to people working in areas with a high-risk of zoonotic TB, worldwide.

**Results:** The preliminary stages of the creation of a multidisciplinary network of professionals working on *M. bovis* and with an interest on zoonotic TB was achieved.

**Expected outcomes:** The work conducted by the zoonotic TB sub-section has outlined the foundation for the design of an integrated approach towards the diagnosis, prevention, and control/treatment of zoonotic TB in high risk areas. However, there is still much need for human, veterinary health workers, donors, civil society organizations, affected communities, policy-makers, and researchers to coordinate and implement activities relating to surveillance, diagnosis, training, prevention and control of zoonotic TB.

## SYMPOSIA: SATURDAY 17 NOVEMBER 2012

### SUSTAINABLE TUBERCULOSIS LABORATORY NETWORKS

#### A systems approach for providing sustainable, reliable tuberculosis laboratory testing

T Shinnick. US Centers for Disease Control and Prevention, Atlanta, GA, USA

In many countries, the provision of TB laboratory services depends on a network of public and private laboratories that conduct testing for diagnosis, treatment, and monitoring of therapy. A systems approach is necessary to optimize testing and information exchange in the network and to ensure that appropriate services are available in every program. Such an approach involves assessing and understanding the structure, performance, and cost of the current network of laboratory service providers and users and the use of quality-improvement principles to continually evaluate and improve the performance of the laboratory service network. The laboratory system must ensure efficient referral of specimens and isolates in the public and private sectors; prompt, effective reporting and tracking of information throughout the system; use of optimally effective testing algorithms tailored to programmatic and clinical needs; use of new technologies as appropriate; safe facilities and laboratory practices; laboratory staff with technical proficiency to perform high-quality testing; and integrated training activities involving laboratorians, clinicians, and TB controllers. Challenges to developing such a system include establishing effective lines of communication among laboratorians, clinicians, and TB controllers; decreasing the lengthy turnaround times for referring samples and reporting laboratory results; developing evidence-based recommendations for use of new laboratory technologies; maintaining staff proficiency in light of workforce shortages and loss of laboratory expertise; and upgrading laboratory information systems and connecting all partners. The National TB Laboratory should lead the development of a strategic plan for implementing and maintaining a systems approach to providing TB laboratory services. Providing reliable results in time to impact patient management and improve TB treatment and control fosters the sustainability of TB laboratory services.

#### The national tuberculosis laboratory strategic plan: cornerstone of a sustainable laboratory system

Y Zhao, H Xia, Z Liu, S Wang, B Zhao, Y Song, X Ou, Q Li. National Tuberculosis Reference Laboratory, Chinese Center for Disease Control and Prevention, Beijing, China

The National TB Control Program is reaching its goals in China, MDR-TB becomes an impediment to further disease control. The rise of drug resistance highlight the need for speeded the expansion of Programmatic Management of MDR-TB program and improved diagnostic tools. As well, improved diagnostics will be critical to support clinical trials of new drugs and vaccines. To strengthen the TB laboratory network, national development plan on TB laboratory has been developed (2008–2013), laboratory system has been integrated into NTP system, a series of documents and manuals have been drafted and abided by in place, posters and standardized operational procedure for microscopy, culture and DST have been disseminated in point laboratories, supervision checklist and standardized training material for microscopy, culture and DST has been developed. The essential requirements for laboratory at each level, bio-safety guideline is being reviewed, some new diagnostics have been evaluated and introduced in the fields. The proficient and stable staffs in some laboratories and financial input on laboratory have been increased, infrastructure of laboratories is to be improved, laboratory accreditation has been put into agenda. Collaboration with National Clinical Laboratory center to perform the proficiency test for DST in general hospitals. There has been substantial progress in laboratory network capacity building-up, through implementation of the national TB laboratory strategic plan.

#### Coordinating activities of implementing partners to build a sustainable laboratory system

N Van Hung. National TB Reference Laboratory; National Lung Hospital, Hanoi, Viet Nam

**Background:** Currently, Viet Nam's TB Lab System strongly supported by many domestic and foreign partners: WHO, CDC, USAID, LIFEGAP, MSH, KNCV, FIND, TB Expand, NIHE, TBCAP, TBCARE I. . . . The presence of many partners is a big advantage, but also difficult to run a lab system smoothly. Sometimes, it is becoming the pressure of having many partners at the same time.

**Solution:** Develop a realistic and comprehensive five year plan for TB lab system, focus on priority activities. Coordinating based implementation plan and the strengths of each partner. Capacity building for NRL plays an important role in coordination. Established technical committee includes members from the main

Labs in the system to support the NRL. Coordinate with coordinator of each project partners. Organize assess progress meetings among partners to ensure the participation of the partners do not overlap.

**Results:** The TB Lab system developed in both width and depth: Network expansion, bringing the laboratory services closer to the people; apply more intensive techniques, quality assurance. NRL, RRLs be enhanced capacity, the role of the NRL is improved, particularly in coordinating the implementation of the five-year plan. Activities of each partner brings not only as effective as the target, but also impact support for other partners.

**Conclusions:** Develop realistic and specific plan, strengthen reasonable resources for NRLs coordinating to ensure the active participation and the effect of many partners is the key to success.

### **The Uganda experience in using a systems approach to ensure sustainable access to laboratory testing**

M L Joloba,<sup>1,2</sup> D Naddunga,<sup>2</sup> M D Mubiru,<sup>2</sup> F Mugabe,<sup>3</sup> F Kangave,<sup>2</sup> H Byabajungu,<sup>2</sup> S Eyanu,<sup>2</sup> K Musisi.<sup>2</sup> <sup>1</sup>Department of Medical Microbiology, School of Biomedical Sciences, College of Health Sciences, Makerere University, Kampala, <sup>2</sup>National Tuberculosis Reference Laboratory, Kampala, <sup>3</sup>Ministry of Health, Kampala, Uganda

Uganda with a population of 34m, high HIV prevalence of 7.3% and TB notification rate of 40000 cases is ranked 16th of the 22 high TB burden countries. Before 2005 the Uganda TB laboratory network predominantly used microscopy ZN as main tool for TB diagnosis. The quality of ZN was poor. In 2005, Uganda embarked on introducing new tools and approaches to improve TB diagnosis in the network. Such approaches include microscopy external quality assurance scheme, LED fluorescent microscopes, specimen referral system, line probe assay, GeneXpert, laboratory information system, accreditation, Global Information System for mapping the network and SMS for rapid information transmission. With these tools, there has been improved quality, access and capacity to TB diagnosis. To ensure that access and quality are maintained, performance indicators are developed and monitored. For sustainability, these approaches are embedded within the existing government systems. The current status of these approaches in Uganda will be discussed.

### **In-country driven accreditation efforts and lessons learnt**

C Paramasivan. Foundation for Innovative New Diagnostics, New Delhi, India

Concerted efforts of different partners and stake holders globally have in recent years provided diverse diagnostic options for tuberculosis (TB) and multi-

drug-resistant (MDR) TB. The Revised National TB Control Programme (RNTCP) of India with support from partners has various ongoing projects for the introduction of all WHO endorsed TB diagnostics. As the laboratory scale-up plan of the RNTCP moves forward, a lot of impetus has been placed on ensuring laboratory quality. The RNTCP has put in place structured mechanism and guidelines to ensure lab quality connected with smear microscopy, solid and liquid culture/DST, and line probe assay (LPA). There are standard guidelines for establishment and proficiency testing for various TB diagnostics tools available under the programme. Based on these guidelines, any given lab in India is assessed for accreditation for service delivery. The guidelines for conventional and liquid culture and DST are based on an objective assessment of infrastructure, lab performance, available human resources, training and panel testing of randomly selected culture isolates. For LPA, the national programme has adopted mechanism originally piloted in the FIND demonstration projects in India involving panel testing of DNA extracts of sputum specimen and assessment of the lab performance on LPA on objective parameters. Similarly, panels supplied by WHO are being used for testing CBNAAT equipment at the time of installation. The efforts of the National TB Programme in accreditation of laboratories for service delivery are assisted by four National Reference Laboratories (NRLs). These NRLs are accredited for solid and liquid culture and DST by SNRL, Antwerp, Belgium. For LPA, two NRLs, namely, JALMA, Agra and NTI, Bangalore are regularly validating the sites. There are similar plans to develop EQA for CBNAAT and also to increase the number of NRLs to six to cover the large number of sites performing culture & DST activities for RNTCP.

### **CHANGING THE LANDSCAPE IN TUBERCULOSIS: HOW CIVIL SOCIETY AND COMMUNITIES CAN INCREASE THE IMPACT OF THE GLOBAL FUND IN COUNTRIES**

#### **Civil society engagement in monitoring of Global Fund grants**

I Umoru. Good Health Educators Initiative, Lagos, Nigeria

**Motivation:** Increased investment in infected and affected community in monitoring grants at the service delivery points would consolidate on the successes so far achieved by the civil society in Global Fund grants implementation.

**Approach:** At the Service delivery points, members of the infected and affected communities are identified within the cluster system where advocacy, sensitizations and Peer Support are carried out to insist

all persons who test positive to HIV are referred and followed up to the tuberculosis DOT sites in the cluster to be screened and vice versa. This group of persons should be supported to also monitor the implementation of the funds at that level and report to their constituency/networks and their CCM representatives and CCM secretariat. Findings are shared with Community Delegation members in-country where possible or from a zonal structure and forwarded to the Global Fund secretariat.

**Results:** This concept has helped in increasing Tuberculosis case detection as well as increasing access to HCT services at sites in Lagos, Nigeria. Strengthening this system for monitoring Global Fund grants would lead to Civil Society members increasing the impact of the funds and raising the red flag early should there be programmatic challenges that infringe on the new Global Fund Strategy of Investing for Impact.

**Conclusion:** Increased Civil Society engagement in monitoring Global Fund grants would make saving 10 million lives and preventing 140–180 million new infections by 2016 achievable.

### Experience of the impact of civil society in Global Fund's Country Coordinating Mechanism

C Nyirenda. Community Initiative for Tuberculosis, HIV/AIDS & Malaria (CITAM+), Lusaka, Zambia

**Background:** Country Coordinating Mechanism (CCM) brings together individuals representing a wide range of sectors in a country to look at TB, HIV and Malaria response. Requirement No. 4 of CCM Guidelines requires CCMs to include affected communities as part of CCMs. Affected communities have firsthand experience as direct beneficiaries of GF resources, who live and work among the targeted communities and bring to the table their experience and expertise which is a vital contribution to TB control. They also act as a reality check for CCMs and play an oversight role of what is really taking place on the ground.

**Method:** In collaboration with CCM secretariat and partners, transparent elections for CCM members were carried out and new representatives ushered into office. Several capacity building workshops were organized for representatives as well the larger affected constituencies. Platforms for interaction of community representatives were created including being part of the oversight committee of the CCM giving reps an opportunity to take part in site visits to principal recipients, secondary recipients and storage facilities for medical supplies.

**Results:** Better communication and feedback mechanisms were developed. It has improved participation and oversight role of CCM community representatives. TB constituencies have better understanding of GF operations and are able to hold their representa-

tive accountable. Site visits are helping hold people accountable, also enabling transparency.

**Conclusion:** TB constituency now empowered to fully participate in the process of the CCM by holding their representative accountable. The community representatives are also better equipped to represent their constituencies in CCM.

### How NTPs can work with civil society to enhance impact of Global Fund grants

F Bonsu. Ghana Health Service, National TB Control Programme, Accra, Ghana

Civil society's organizations (CSOs) are significant partners in health care service delivery. Their comparative strengths are realized in advocacy, care and support, and working in the communities. Most CSOs are in direct contact with the communities and they have the capacity to educate communities on TB issues, identify patients, provide follow up to treatment, engage the communities and mobilize volunteers, reaching more and more people at the household level.

NTPs can explore this strength by being proactive in engaging CSOs. NTPs must first orientate itself and recognize the need to work with CSOs. Secondly, explore the health sector to identify policies, or laws if they exist, so as to draw its strength from there. The existence of policies or not may inform whether the working relationships will be formal which then can allow CSOs to receive material and financial support from NTPs to compliment resources from GF. In the absence of policies a loose working relationship with mutual respect and understanding to avoid duplication of activities is essential and adequate. Impact of GF assisted activities could be enhance, if CSOs are involved from the beginning to define scope of interventions and define roles for various stakeholders. NTPs must see the role of CSOs as complimentary to achieving the overall TB control targets, therefore all efforts should be made to quantify and report on this contribution.

CSOs should be treated as equal partners. Human resource, financial management and project management capacities should be built for CSOs to ensure sustainable benefits from activities to the health sector. For CSOs that are already endowed, NTPs should further develop technical capacities and contract out targeted interventions with deliverables to achieve.

In conclusion NTPs could work with civil society organisations to achieve results as partners reinforcing each other messages and activities.

### The role of civil society principal recipients in expanding coverage, improving outcomes and impact of Global Fund grant

F Ahmed,<sup>1</sup> S Ferdous,<sup>1</sup> S Islam,<sup>1</sup> M Rifat,<sup>1</sup> B N Siddiquea,<sup>1</sup> A Husain,<sup>2</sup> J Ahmed,<sup>1</sup> A Islam.<sup>1</sup> <sup>1</sup>BRAC, Dhaka, <sup>2</sup>NTP, Dhaka, Bangladesh

**Settings:** Initiating their TB program in 1984, BRAC has been one of the pioneers of community based DOTS. While this has been proven as an effective means of controlling and curing TB, limited resources constrained proper implementation of this approach nationwide. With two decades of experience, BRAC became a PR of GF grant in Bangladesh (along with NTP PR) in 2004. Bangladesh has secured US\$267 million from GF for TB control from 2004 to 2016. Utilizing GF resources, BRAC TB program is reaching 93 million people in Bangladesh.

**Aim:** Sharing lessons learnt from civil society engagement and impact of GF financing.

**Design:** BRAC's extensive network of community health volunteers (Shasthya Shebika) is the core of TB service delivery. GF financing has enabled BRAC to improve service quality and increase access at community level; strengthen ACSM activities and diagnostic services from primary to tertiary levels. BRAC is also providing MDR-TB microscopy and ensuring uninterrupted drug and logistics supply. Moreover, GF financing has facilitated building strong partnerships with different stakeholders including private medical providers, apex institutes of manufacturing factories and prison authorities along with the MoH and Family Welfare. This partnership has been leveraged to form strong referral networks and expand access to vulnerable groups.

**Results:** GF financing has increased program coverage, strengthened health system and built capacity. Between 2003 and 2011, TB case-detection rate increased from 41% to 72% in BRAC covered areas and from 41% to 65% nationally. Treatment success rate rose from 85% to 92% during this period. From 1990 to 2010 TB mortality reduced from 58 to 43/100 000 and TB prevalence all forms reduced from 493 to 411/100 000. Smear positive TB prevalence decreased from 95 to 79/100 000 from 2001 to 2009.

**Conclusion:** One of the major impacts of GF is on combating TB. As a result, Bangladesh is currently on track to meet MDG 6.

### PALLIATIVE CARE IN DRUG-RESISTANT AND COMPLICATED TUBERCULOSIS: MODELS OF COMMUNITY-BASED CARE

#### What is palliative care, and why is it a human right?

S Connor. Worldwide Palliative Care Alliance, London, UK; Open Society Foundations, New York, NY, USA

In this session attendees will learn the definition and essential elements of palliative care with an emphasis on how palliative care is an essential component in the continuum of care for people with TB, especially MDR and XDR-TB. Both the disease and treatment of TB entail significant physical, psychological, social, and spiritual suffering. Palliative care can enhance the treatment of TB by reducing suffering offering the hope of improved compliance and survival. For those where treatments have failed there is also a moral imperative to relieve suffering, especially at the end-of-life for patients and the families that care for them. Palliative care will be shown to be a human right, not only for those at the end-of-life but for all patients with life threatening illness, including difficult to treat TB.

#### How to handle the realities: experiences with failures of M/XDR-TB treatment in South Africa

H Cox. Médecins Sans Frontières, Cape Town, and University of Cape Town, Cape Town, South Africa

Current treatment regimens for drug-resistant tuberculosis (DR-TB) are far from ideal, with treatment success levels of 60% on average. Treatment success is even lower among populations with high HIV prevalence with concomitant high rates of death during treatment. Failure of treatment is also significant and contributes to high mortality, as well as presenting particular problems for patients and clinicians. Scant attention is given to failure of treatment programmatically. A decentralised programme to diagnose and treat DR-TB has been implemented in Khayelitsha since 2007. Khayelitsha is an urban township with an estimated population of 500 000 and has high burdens of TB, DR-TB and HIV infection. The programme has been implemented based on the principles of respect for individual patient rights as well as public health protection, integration into existing primary care TB and HIV services and the need for intensified TB infection control measures at all levels. Failure of treatment raises issues of; when to modify or stop treatment, patient autonomy, false blame on poor adherence to treatment, the risk of further resistance amplification, appropriate palliative care provision and minimizing the risk of ongoing transmission, particularly among patients for whom all treatment has been stopped. This presentation will describe these challenges and attempts to overcome them in this high burden setting.

## Psychosocial distress and ethical issues in caring for patients with complicated tuberculosis

E L Krakauer. Department of Global Health and Social Medicine, Harvard Medical School, Boston, MA, and Palliative Care Unit, Massachusetts General Hospital, Boston, MA, USA

**Background:** Physical and psychological symptoms and social problems such as extreme poverty are common in patients with M/XDR-TB and TB-HIV. Social problems and adverse effects of treatment make adherence difficult and reduce cure rates. Thus, palliation of physical, psychological, and social distress is crucial to effective therapy. The best M/XDR-TB treatment programs report at least 5% mortality, at least 2% treatment failure, and at least 8% default that likely results in death. Palliative care has been shown to improve the quality of life of dying patients and their families.

**Ethical issues:** Ethical principles that guide medicine suggest that palliative care is a human right and that palliating suffering is a moral imperative. These principles include:

- **Beneficence/non-maleficence:** Physicians should work for the good of their patients and protect them from harm.
- Physicians should respect patients' values.
- **Social justice:** 1) Priority should be given to those whose suffering and vulnerability are greatest; 2) Palliative care for life-threatening conditions should always accompany efforts to prevent and treat them; 3) Where social conditions are pathogenic and patients are voiceless, physicians should participate in advocacy.
- Physicians have a duty to treat despite risk to themselves.
- Physicians have a secondary duty to protect the public health.
- **Non-abandonment:** Patients with life-threatening illnesses for whom disease-modifying interventions are no longer effective or desired should always be given palliative care.

**Conclusion:** Palliative care should be considered essential to care for M/XDR-TB patients.

## The care for patients with M/XDR-TB treatment failure in Latvia

L Kuksa. Riga East State University Hospital Tuberculosis and Lung Disease Centre, Riga, Latvia

The MDR TB treatment program in Latvia was started in 1997, with a sustained decrease in diagnosed MDR TB patients (since 2001) and improvement of case management and treatment access. Although treatment success of MDR-TB reached 71% (in 2005), groups of patients remain who failed to be cured and need special attention and medical care. A palliative care ward in Latvia was established in 1999

with infection control measures and adequate medical care. From 2000 to 2008, 312 patients who met the criteria for palliative care were hospitalized. Total amount of chronic incurable patients in Latvia decreased from 93 in 2002 to 16 in 2011 with a decreased need for specialized ward; in 2009 it was closed, leaving only rooms for patient isolation available. Retrospective analysis of failure cases for cohorts 1 January 2000–31 December 2006 showed that of all 1313 treated patients, 148 (11.3%) had outcome-treatment failure. Hospitalized in palliative ward were 88 patients (59.5%): 17 (19.3%) primary and 71 (80.7%) acquired MDR. 55 (62.5%) had resistance to  $\geq 8$  anti-tuberculosis drugs. 59 (67%) died, of whom 26 (44%) had XDR. Failure median survival is 1.5 years, ranging from 2 weeks to almost 5 years.

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Diagnosed patients		264	236	191	207	169	155	124	127	128	96	105
<b>Cohort</b>	<b>204</b>	<b>245</b>	<b>205</b>	<b>165</b>	<b>208</b>	<b>155</b>	<b>136</b>	<b>117</b>	<b>116</b>	<b>124</b>	<b>86</b>	<b>103</b>
Cured	127	164	131	113	144	108	88	75	81	78		
%	62	67	64	68	69	70	65	64	70	63		
Treatment completed	8	2	3	2	2	2	3	3	-	2		
%	4	1	1	1	1	1	2	3	-	2		
Failure	29	28	26	23	18	16	8	9	10	6		
%	14	11	13	14	9	10	6	8	8	5		
Default	26	41	28	19	32	21	22	24	16	22		
%	13	17	14	12	15	14	16	20	14	18		
Died	14	9	17	8	12	8	15	5	9	14		
%	7	4	8	5	6	5	11	4	8	11		
MDR TB prevalence	522	539	481	439	425	359	303	244	227	232	205	177
Symptomatic Tx pts			93	85	83	61	43	45	34	27	20	16

### Conclusion:

- 1 Proper isolation and palliative care for contagious incurable MDR TB patients is the solution to improve patients' quality of life and to stop the spread of extensive drug resistance.
- 2 Programmatic M/XDR-TB management with access to treatment for all existing MDR TB patients is essential to prevent and minimize the need for palliative care for curable disease.

## The inseparable work of caring and curing: a community-based model of integrated tuberculosis treatment

I Gelmanova,<sup>1</sup> A Solovyova,<sup>2</sup> S Mishustin,<sup>3</sup> D Taran,<sup>2</sup> A Golubkov,<sup>1</sup> S Keshavjee.<sup>1,4,5</sup> <sup>1</sup>Partners in Health, Boston, MA, USA; <sup>2</sup>Partners in Health, Moscow; <sup>3</sup>Tomsk Oblast Tuberculosis Services, Tomsk, Russian Federation; <sup>4</sup>Division of Global Health Equity, Department of Medicine, Brigham and Women's Hospital, 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

**Setting:** 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.

**Objective:** To assess the effectiveness of Sputnik model on treatment results in difficult to treat population of patients.

**Design:** 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 98 patients referred to the program from November 2006 to November 2010, 71 (72%) had multidrug-resistant TB; 84 (86%) suffered from chronic alcoholism, 31 (32%) were drug abusers; 39 (40%) had hepatitis, 5 (5%) were HIV-positive and 4 (4%) suffered from psychiatric diseases. Seven (7%) patients either refused any TB treatment or Sputnik personnel was not able to find them. Among those 91 patients who took at least one pill while on the program, 68 (75%) were eventually cured, 8 (9%) failed, 8 (9%) defaulted; 4 (4%) died and 3 (3%) were transferred out of the region.

**Conclusion:** Palliation of side effects and co-morbid illnesses was a critical component of the Sputnik intervention and contributed to the successful community-based treatment of previously non-adherent TB patients.

## SUSTAINABLE PRACTICES, BUILDING DESIGN, AND ENGINEERING TO REDUCE TUBERCULOSIS TRANSMISSION IN RESOURCE-LIMITED SETTINGS

### Tuberculosis infection control evaluations leading to changes in guidelines and policies in Mozambique

E Langa,<sup>1</sup> M Brouwer,<sup>2</sup> E Coelho,<sup>1</sup> Z Cuna,<sup>3</sup> D Bossemeyer,<sup>3</sup> S Stender,<sup>3</sup> L Brondi.<sup>4</sup> <sup>1</sup>Ministry of Health, National Tuberculosis Control Programme, Maputo, Mozambique; <sup>2</sup>PHTB Consult, Tilburg, The Netherlands; <sup>3</sup>Jhpiego, Maputo, Mozambique; <sup>4</sup>Freelance Consultant, Communicable Diseases Control and Prevention, Edinburgh, UK

**Setting and objectives:** Mozambique bears the double burden of a tuberculosis (TB) and HIV epidemic. Huge numbers of clients affected by TB and HIV use the country's Health Care Facilities (HCF) and therefore health care associated TB transmission is a real threat. We assessed risks and compliance with TB Infection Control (TBIC) guidelines with the aim to

develop and further implement the most effective interventions to reduce TB transmission in HCF.

**Methods:** The Ministry of Health (MOH) and partners, supported by funds of President's Emergency Plan for AIDS Relief (PEPFAR), assessed countrywide HCF for compliance with basic TBIC measures and the TBIC situation. In two different surveys, we assessed 30 and 29 HCF using standard tools with observations and interviews with health care workers. Another survey held focus group discussions with four categories of health care workers to learn about their knowledge and beliefs.

**Results:** Adherence to TBIC measures varied between facilities, though overall score was low. In 1 survey, 8 (27%) HCF had an active infection control committee. Most HCF used some administrative controls though not consistently. Ventilation in the assessed parts of the facilities ranged from adequate to none existent. In most facilities particulate respirators were available, although knowledge on its adequate use was poor. Few health care workers received training on TBIC.

**Lessons learnt:** The results of these assessments formed the basis for a new National TBIC Control Policy. MOH started a national stakeholders consultation process and the final policy and operational plan was approved. TBIC risk and situational assessments are a key step in the development of national TBIC policies and operational plans.

### Tuberculosis infection control in primary health care facilities in South Africa

M Claassens, N Beyers, R Dunbar, B Yang, E Du Toit. Desmond Tutu TB Centre, Cape Town, Western Cape, South Africa

**Background:** TB infection control measures should prevent nosocomial transmission of *Mycobacterium tuberculosis* in healthcare facilities. To measure the risk of *M. tuberculosis* transmission in facilities, a TB infection control risk assessment tool was developed to determine whether such a tool can identify high risk clinics (defined as clinics with at least one case of TB disease in healthcare workers per year) in countries with a high burden of TB.

**Methodology:** During 2009, 133 primary healthcare facilities were evaluated with a risk assessment tool for TB infection control and TB cases in health care workers were determined in five provinces in South Africa. An equal score was assigned to each area of risk of the tool. The mean score was selected as a cut-off point to define high and low risk facilities for TB transmission.

**Results:** 87 facilities were classified as high risk and 33 as low risk (missing data in 12 facilities). 26 (30%) high risk facilities and 18 (55%) low risk facilities had healthcare workers with TB ( $P = 0.007595$ ). The risk ratio was 0.5479 (95%CI 0.3501, 0.8574) for a

high risk facility to have TB cases. There was an inverse relationship between the risk score and the presence of TB cases.

**Discussion:** Further analysis will include stratification according to TB incidence at facility level. It is essential to determine whether a risk assessment tool can be used in high incidence areas to identify clinics where nosocomial transmission of TB occurs.

### Tuberculosis transmission paradigm shift in former Soviet Union countries and development of updated tuberculosis infection control regulations

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**Setting:** In the former Soviet Union (FSU) countries 'phthisiology' was considered a separate discipline with its own structure, scientific institutions, traditions and achievements. However, as a result of the isolation of the USSR, some approaches to TB were different from international standards.

**Objective:** To define the current IC TB paradigm in FSU countries and to identify priority interventions.

**Design:** The level of knowledge and competence of general practitioners (55), TB specialists (67), epidemiologists (28) and contents of regulatory documents on IC TB was monitored in the period 2009–2012.

**Results:** Before the intervention, 95.7% of doctors suggested using chlorine-containing disinfectants, open UVGI and surgical masks for doctors and as preventive measures; they considered they were safe standing 1–2 meters from a smear-positive patient. All the regulatory documents contained detailed instructions on disinfection, but did not mention separation of floats, zoning, negative pressure, shielded UVGI or respirators. The change of the IC TB paradigm in the Republic of Belarus (RB) took place in the last 4 years. Priority directions of the intervention were identified: training program, national IC TB guidelines, new health standards on TB transmission prevention, reconstruction of TB facilities, including modernisation of the ventilation systems. The change of paradigm resulted in a 28.9% decrease in the incidence of TB among medical personnel in RB in the last 3 years depending on interference intensity and character.

**Conclusions:** There was a paradigm of droplet rather than airborne TB transmission in FSU countries until recently. Factors hindering and favouring the change of IC TB paradigm in FSU countries were identified. The interconnection between interference character and intensity on IC TB implementation and change of the situation in the sphere of IC TB was determined; effectiveness indicators were identified.

### Efficacy of upper room UVGI-air mixing system in a hospital in South Africa

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**Setting:** In poor countries, facilities for patient isolation are extremely limited, and newly diagnosed TB patients often share open wards with HIV/AIDS patients. These circumstances urgently require the implementation of effective infection control measures to protect both patients and health care workers.

**Objective:** To directly measure the efficacy of upper room UVGI air disinfection with good air mixing on a real MDR-TB ward in South Africa.

**Methods:** Over a 3 month exposure period, 6 MDR or XDR patients at a time consented to occupy the experimental ward of the Airborne Infections Research (AIR) facility at the Mpumalanga Provincial MDR Referral Hospital in Witbank (eMalahleni), South Africa. Patient rooms, hallways, and a common kitchen were equipped with upper room UVGI fixtures. Slow paddle fans assured good air mixing in the rooms. All air from the ward was exhausted to two animal exposure chambers. After a baseline TST, a monthly TST determines the fraction of exposed guinea pigs in each exposure chamber that have been infected by exposure to ward air. Animals in exposure chamber A only breathed ward air on even days when upper room UVGI was on whereas animals in exposure chamber B only breathed ward air on odd days when upper room UVGI was off.

**Results:** After 4 months there were 15 guinea pigs infected breathing air on days when UV was on (Chamber A), and 48 animals infected on alternate days when UV was off (control, Chamber B). This study showed 80% efficacy of upper room germicidal ultraviolet air disinfection under real world conditions in Africa.

**Conclusion:** While UVGI is effective in reducing transmission of MDR-TB, proper design and installation, system performance monitoring and maintenance, replacement and appropriate disposal are critical factors to be considered to ensure that (i) the technology is effective and (ii) does not compromise the safety of patients or pose an occupational safety hazard to health workers.

### Cost effectiveness in a cold climate: mechanical ventilation, room air cleaners or upper room UVGI

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**Background:** Environmental controls (ECs) are essential part of TB IC interventions in cold climates, where natural ventilation is not feasible all year and administrative measures may be not effective enough to reduce TB transmission risk. Limited TB control resources and aggressive marketing of air cleaning devices make objective analysis of available ECs important. Our objective was to compare effectiveness and relative cost of available ECs in Russian Federation.

**Methods:** Equivalent Air Changes per Hour (EqACH) method was used to estimate airborne infection transmission risk reduction. Aerosolized *B. subtilis* and *S. marcescens* concentration was assessed by air sampling on nutrient agar media. Decay curves for mechanical ventilation, room air cleaners, and upper-room UVGI, and their combinations, with and without air mixing, were used to assess EqACH. Capital, supply, utility and maintenance costs of each EC was included into cost effectiveness analysis.

**Results:** The actual performance of most tested controls was lower than expected (see Table). The most effective control was upper room UVGI fixture with EqACH of 6.7. Combined use of different controls does not follow the simple sum of their efficacies. Intensive air mixing by fan improved effectiveness of all controls by 5–39%. The most cost-effective EC was upper-room UVGI and the least cost effective was room air cleaner (US\$14 and US\$267 per 1 additional EqACH per year, respectively).

	Mechanical ventilation	Upper room UVGI fixture	Room air cleaner Potok 150M-01	Room air cleaner Tree-100	Room air cleaner Aerolife-L
Effectiveness according to official manufacturer documentation	7.5	NA	4.7	3.1	2.8
Actual effectiveness according to testing results	2.5	6.7	3.6	3.6	2.2

**Conclusions:** Actual capacity of various ECs can differ significantly from manufacturer's data. Independent testing method of their efficacy is needed. Mixing fan and appropriate installation substantially improved the performance of all tested ECs. Upper-room UVGI is the most effective and least costly EC for TB facilities; however, directional air flow and containment of infectious aerosols cannot be maintained. Appropriate design, installation, commission-

ing and maintenance are critical for all environmental controls.

### BIOMARKERS IN TUBERCULOSIS: FROM DISCOVERY TO CLINICAL APPLICATION

#### A dynamic view of biomarker research

M L Gennaro, A A Lardizabal. New Jersey Medical School, Newark, NJ, USA

These speakers will introduce the symposium by reviewing the needs and the challenges associated with the discovery and evaluation of biomarkers and bio-signatures. These can be used to deliver tests that can 1) help diagnose drug-sensitive and drug-resistant tuberculosis, 2) assess the risk of progression of latent tuberculosis infection, and 3) assist in clinical trials for therapeutics and vaccines. Emphasis will be placed on the dynamic aspects of the evolution of *Mycobacterium tuberculosis* infection from its asymptomatic stages to overt disease. The clinical spectrum of *M. tuberculosis* infection correlates with immunopathological changes in the host and with changes in bacterial physiology and bacterial burden. These changes are reflected in the peripheral circulation, where biomarkers are most typically sought. Implementing a dynamic view of biomarker research requires assessing multiple, diverse analytes and designing appropriate studies for their evaluation. These will be discussed at the symposium.

#### Mycobacterial lipids as infection biomarkers

A Bendt, M Wenk. National University of Singapore, Singapore

Mycolic acids (MA) are bacteria derived, modulate host-pathogen interactions, chemically inert and contain information about bacterial species. Using mass spectrometry, targeted quantification of specific precursor-fragment resulted in high analytical sensitivity and specificity. We used mass spectrometry to quantify MA precursor fragment in a retrospective case-control study of sputum from patients with pulmonary TB with varying disease burdens from 4 countries. MAs were extracted from sputum and analyzed without the requirement for MA derivatization. Infected patients (70 including 19 HIV+) could be separated from controls (40 including 20 HIV+) with a sensitivity and specificity of 94 and 93%. Furthermore, we quantified the MA species in lung tissue of TB-infected mice and demonstrated effective clearance of MA levels following curative rifampicin treatment. Thus, our results demonstrate for the first time the feasibility and clinical relevance of direct detection of mycobacterial lipids as biomarkers of TB infection.

### Metabolic biomarkers in peripheral blood and other fluids

J Belisle. Department of Microbiology, Immunology and Pathology, Colorado State University, Fort Collins, CO, USA

The detection of *Mycobacterium tuberculosis* in the sputum or immunological response to disease and infection are the principal methods applied to tuberculosis diagnosis and assessment of treatment outcome. The slow rate of disease clearance and the slow growth rate of the infecting bacterium are two parameters that currently impact the use of current biomarkers; especially, when applied to clinical trials of new anti-tuberculosis drugs or regimens. Thus, new biomarkers for tuberculosis are needed to improve diagnostics and accelerate clinical trials. Disease states and treatments result in biochemical changes within a system and produce fluxes in metabolic profiles. Metabolomic technologies are well suited for the evaluation of large numbers of patient samples and identifying small molecule metabolites associated with disease or treatment. Thus, liquid chromatography–mass spectrometry was used for metabolic profiling of urine and serum from TB patients prior to the start of anti-tuberculosis treatment and during the course of treatment to define metabolic signatures that correlate with effective treatment. When applied to urine of tuberculosis patients, this platform allowed for identification of a biosignature comprised of metabolites that dropped in abundance over the first two months of treatment and continued this same trend to the end of treatment. Similarly, a biosignature based on small molecule metabolites of serum resulted in the ability to differentiate samples collected prior to the start of anti-tuberculosis treatment and those collected at week-8 of anti-tuberculosis therapy. The serum metabolic signature also distinguished responder patients (those that cleared bacilli based on sputum culture) and slow-responder patients (those that remain sputum culture positive at week-8 of therapy). This application of metabolic profiling is also being evaluated in the context of identifying novel biomarkers for the primary diagnosis of tuberculosis.

### Immune biomarkers in peripheral blood

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Biomarkers for different forms of MTB infection and TB disease would aid the development of new tools against TB and would increase our understanding of protection and susceptibility. We still do not fully understand what constitutes a protective immune response against the pathogen or how to eradicate the organisms through vaccination or chemotherapy. In

the absence of such biomarkers the evaluation of new chemotherapeutics and vaccines against TB will remain very challenging as clinical trials are protracted and expensive and as there are a limited number of suitable trial sites across the world to evaluate a growing number of new drugs and new vaccines. We have searched for such biomarkers in a high MTB transmission setting with a high TB disease incidence in Cape Town, South Africa, by using a combination of targeted host marker measurements and unbiased ‘omics’ approaches in peripheral blood. Host inflammatory and anti-inflammatory molecules change at different rates in active disease during chemotherapy. Increased inflammation and extent of disease at baseline predicts slow MTB culture conversion, failed treatment and relapse after initial cure. Transcriptomic analysis suggests that B cells and the complement system play important roles in treatment response. Responses to infection stage specific MTB antigens add additional complexity to the search for biomarkers and marked geographical differences in immune responses within Africa suggest that single biomarkers are unlikely to succeed but that biosignatures that are composed of several host markers look promising. In conclusion, immune biomarkers in peripheral blood hold promise as markers of different forms of MTB infection and response to treatment and may help us to better understand the complexities of host-pathogen interactions.

### HEALTH SYSTEM STRENGTHENING FOR CHILDHOOD TUBERCULOSIS: POLICY TO PRACTICE

#### Building a successful child tuberculosis programme: the link between implementation and operational research

S M Graham. Centre for International Child Health, Melbourne, VIC, Australia; International Union Against Tuberculosis and Lung Disease, Paris, France

As the Stop TB Strategy for TB control has expanded beyond DOTS to intensify case-finding among vulnerable populations (in 2006) and formulates strategies for the future (beyond 2015) to include attention to community-based care, integration and preventive care, the need for increased attention to TB in children is beginning to receive some genuine attention at global and national levels. Another compelling reason for increased attention is that TB is an important cause of maternal and child mortality. National TB control Programmes are now increasingly striving to address the challenges of caring for children with TB and children that are TB contacts. National policies and guidelines are being revised. An increasing number of NTPs are dedicating staff to coordinate child TB activities. Training and evaluation tools have

been developed for NTPs emphasising management at the primary and secondary level. But pragmatic goals, guidelines and training of the main messages may still not narrow the wide policy-practice gap that exists for implementation of effective strategies to protect children from TB. The acceptance that children can be part of a decentralised approach to TB control is recent, and could be highly cost-effective by improving access, case-finding, early treatment without requiring a major increase in resources, facilities or staff. Capabilities vary widely between and within countries. There is an opportunity for innovative approaches and operational research that could lead to improved TB control and improved child health care, that could inform better practice in a range of settings, and that could bring important benefits to vulnerable communities.

### Are we making progress? Measuring the burden of childhood tuberculosis

C Sismanidis,<sup>1</sup> A Detjen,<sup>2</sup> M Grzemska,<sup>1</sup> H Menzies,<sup>3</sup> S Graham,<sup>4</sup> P Glaziou.<sup>1</sup> <sup>1</sup>Stop TB Department, World Health Organization, Geneva, Switzerland; <sup>2</sup>The International Union Against Tuberculosis and Lung Disease, New York, NY, USA; <sup>3</sup>Centers for Disease Control and Prevention, Atlanta, GA, USA; <sup>4</sup>The International Union Against Tuberculosis and Lung Disease, Singapore

**Objective:** To present why it is difficult to estimate the burden of childhood TB (0–14 years), the methods used to produce the current estimates, and steps needed to improve them.

**Background:** Existing surveillance data do not allow for a complete assessment of the burden of TB disease among children. Key barriers to accurate monitoring of childhood TB burden include challenges in case ascertainment and diagnosis, weak surveillance systems which fail to record and report all detected childhood cases, and lack of nationwide survey data.

**Methods:** We estimated incidence using case notification data from WHO's Global TB Database and the estimated global case detection rate for all ages. We estimated mortality using WHO's age-disaggregated vital registration (VR) data and the calculated ratio of childhood to adult mortality for countries with VR systems. We predicted mortality in countries without VR data based on an ecological statistical model including a set of risk factors known to be associated with TB mortality (for example GDP per capita, HIV prevalence in the general population, percentage of TB cases with MDR-TB, treatment success rate).

**Results:** 99% of smear-positive and 84% of smear-negative and extra-pulmonary case notifications reported to WHO in 2011 were disaggregated by age. The estimated global case detection rate is 66% (95%CI, 64%–69%). In 2011, there were an estimated 500 000 (95%CI, 470 000–510 000) incident cases and 64 000 (95%CI, 58 000–71 000; HIV negative) deaths among children.

**Next steps:** To improve global and national estimates of TB in children, we are completing literature reviews to systematically collect existing data, calling for a global consultation to further develop statistical methods and prioritize ways to produce new nationwide data, advocating for more contact tracing studies and for the inclusion of TB screening activities in maternal and child health services to identify otherwise potentially undiagnosed and under-reported children.

### Linking hospital to community tuberculosis care in children

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**Background:** We have previously shown that registration and reporting of childhood tuberculosis (TB) managed in hospital settings is incomplete.

**Aim:** To estimate the total burden of childhood TB at a tertiary hospital, and to improve continuity of TB care for children between hospital and primary health TB clinics (PHCs), i.e., the community level.

**Methods:** Daily hospital and laboratory-based surveillance by dedicated personnel in the paediatric wards at Tygerberg Children's Hospital, Cape Town, South Africa. Health system strengthening interventions included: 1) counselling of caregivers of TB patients, 2) assisting routine personnel with completing appropriate referral documentation and 3) contacting TB personnel at identified PHCs to ensure continuation of TB treatment upon discharge. Outcomes were measured by comparing pre- and post-intervention registration in the provincial electronic TB register.

**Results:** During January through June 2012 we identified 200 children (median age 2.7 years, IQR 1.1–5.2; 107 (54%) male) who were routinely diagnosed or treated for TB; an additional 9 children were started presumptively on treatment but stopped once an alternative diagnosis was made. Hospital surveillance identified 90% of children. The majority (165; 86%) were treated for drug-susceptible TB. The spectrum of disease was: 116 (59%) pulmonary TB (PTB) only, 51 (26%) extrapulmonary TB (EPTB) only and 31 (16%) both PTB and EPTB; 28(14%) had disseminated disease and 5 (3%) died. Approximately 35% of children were culture-positive. Upon discharge, 133 (68%) were referred to PHCs to initiate/continue TB treatment. Intervention results will be discussed in more depth.

**Conclusion:** Tertiary hospitals carry a large burden of childhood TB with diverse spectrum of disease. Given the need for improved surveillance and reporting of

childhood TB, health systems should ensure continuation of care for children between hospital discharge and community-based TB care.

### Community-based child contact screening and management

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Young children in close contact with an infectious tuberculosis (TB) case are at high risk of infection and progression to TB disease. Child contact screening and Isoniazid Preventative Therapy (IPT) reduce the risk of disease and TB-related mortality in young children. WHO and many National TB programs have recommended contact management for many years, but implementation has been poor to non-existent in TB endemic areas. Multiple barriers and challenges have been identified, including lack of human resources, lack of an appropriate management structure and screening tools, low community awareness, and poor adherence to IPT. A decentralized, community-based approach is of great potential to close this policy-practice gap and can be done using a symptom-based screening tool such as we have prospectively evaluated in Indonesia. The involvement of primary health centres as the spearhead of contact screening can improve access, uptake and compliance, employing comprehensive interventions including the development of a simple guideline and standardized recording forms, health-care workers trainings, and education to the patient and family members. Educational material was developed based on local situations and cases to improve awareness about the risk of TB after exposure and the role of IPT in mitigating this risk. Through training and supervision, community workers can be involved by referring child contact for investigation and supervising IPT provision.

### Operational implementation of an IPT register in a high-burden setting

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**Setting:** We compared the change in management of child household contacts of pulmonary TB cases before and after implementation of an isoniazid preventive treatment (IPT) register in an urban clinic setting in Cape Town, South Africa.

**Objectives:** We determined if the presence of an IPT register was associated with an increase in the number of child contacts identified per infectious case and the proportion of identified children started on IPT.

**Design:** We reviewed routine programme data on IPT delivery to children during two time periods (May–October 2008 and May–October 2011), before and after implementation of an IPT register.

**Results:** Tuberculosis adult case demographics from the two observation periods were similar. During the post-register period, more child contacts per case were identified (0.5 vs. 0.3, 39 children in total vs. 24) and more children were started on IPT (54 vs. 4) compared to the pre-register period.

**Conclusion:** After pilot implementation of an IPT register, documented identification of child contacts and IPT initiation in TB exposed children was improved. Our findings support use of IPT registers in routine clinics in high-burden TB settings.

## TOBACCO TAXATION: A SUSTAINABILITY TOOL FOR TOBACCO CONTROL AND HEALTH PROGRAMMES

### Tobacco taxation as a tool for tobacco control

R Cherukupalli. Department of Health, Behavior and Society, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

Economists have demonstrated that tobacco excise taxes that raise the price of tobacco products relative to other goods and services are the most effective tool to reduce consumption and prevent initiation, while also bringing in revenues for governments—the proverbial ‘win-win’ situation. Tax structure matters in addition to the level of taxation. Tax structure affects to what extent producers pass higher taxes on to higher prices, the distribution of tobacco product prices, producers’ incentives to undertake strategic pricing behavior to preserve and expand markets, and, for governments, the ease of administering taxes and collecting revenues. Economists recommend simpler, higher tobacco taxes; in particular high uniform specific excise taxes to reduce consumption. Tobacco taxes, like other public policy tools, reflect the larger context of countries’ public finance systems, and can be a challenge to reform. While recognizing the diversity of countries’ particular circumstances, economists have suggested several good practices to improve the effectiveness of tobacco taxes for tobacco control. A continuing agenda for public health stakeholders is understanding the magnitude and the political economy surrounding tobacco tax revenues to find reliable ways of channeling revenues to chronically underfunded programs.

### **Tobacco tax: progress and challenges in Viet Nam**

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This two part presentation examines the issue of tobacco tax in Viet Nam; and outlines the context, developments and challenges, and uniquely, provides dual perspectives from the Viet Nam Ministry of Health and Ministry of Finance.

**Part One: Tax increase and health perspectives in Viet Nam:** Viet Nam is in the 15 countries with the highest number of smokers and cigarette prices among the world's lowest. From 1995 to 2006, the index of tobacco prices in Viet Nam remained nearly unchanged while CPI rapidly increased. In 2008, the tobacco tax of 65% of factory price (45% of cigarette retail price) was still low. Tax is thus proposed as one of the most effective strategies to reduce tobacco consumption and prevent tobacco related morbidity and mortality. Research was undertaken and demonstrated the case for this—increasing tobacco tax by 10% would save 853 tobacco-related premature deaths by 2023 and 1386 tobacco-related premature deaths by 2033 in Viet Nam. Policy advocacy efforts are promoting the case to government.

**Part Two: Tobacco tax—Ministry of Finance perspective:** Excise tax on tobacco in Viet Nam has been purposely designed to directly regulate the behaviours of consumers in an attempt to restrict and reduce tobacco consumption. The 2011 Prime Minister's Decision also outlines specific strategy for excise tax policy makers 'to study, add the excise tax subjects in order to regulate consumption in line with the social-economic developments; develop the excise tax rate roadmap imposed on cigarettes to regulate consumption and implement relevant international commitments'. The Ministry of Finance in general and the Tax Policy Department in particular is assigned to design the revised excise tax and develop a roadmap with a view to reduce tobacco consumption in Viet Nam in compliance with the signed WHO FCTC. Thus, the revised law on excise tax has been put into the National Assembly legislation agenda by 2013–2014.

### **COMMUNITY PARTICIPATION AND COMMUNITY ADVISORY BOARDS: PATHS FOR EFFECTIVE AND SUSTAINABLE TUBERCULOSIS CONTROL INTERVENTIONS**

#### **Community participation in tuberculosis and HIV research: together we are making the difference**

R Piller, V Vellozo, G Israel, B Durovni. Health Department of Rio de Janeiro City, Rio de Janeiro, RJ, Brazil

**Setting:** The TB and HIV CAB of the Health Secretariat of Rio de Janeiro, founded in 2011, as a result of the successful experience of the THRio CAB. It is an interactive channel among researchers, health care workers, patients and civil society, providing the basis for a definition of responsibilities and participation of the communities involved in the studies.

**Objective:** Disclosing the findings of the studies, its procedures, its execution and results, offering participants a source of independent information about the research results, enabling members to have full participation in research ethics forums and providing them with an effective means of expressing their rights.

**Design:** The setting up of the CAB was preceded by intense discussions among its members, all volunteers. They devised a plan establishing a set of rules and an annual schedule of their activities and meetings. They have been offered training opportunities in related issues. The group collaborates towards producing educational publications. They meet every two months to discuss the progress of the studies.

**Results:** Collaboration and commitment of the people involved; increased partnership among researchers, activists and community leaders; a permanent channel for defending the ethics on research.

**Conclusions:** CAB has promoted the integration among researchers, managers, patients and community leaders, spreading knowledge of how to strengthen actions in order to prevent TB and HIV. It is a privileged place to guarantee ethical demands toward the good practices in human being researches.

### **MODELS OF CARE AND ENGAGEMENT FOR SUSTAINING A COMPETENT WORKFORCE FOR MDR-TB-HIV CARE AND MANAGEMENT**

#### **Quality MDR-TB care in the health-care workforce crisis: utilising contract workers**

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**Background:** Namibia has a population of 2.1 million and a high TB incidence (513 new and relapse cases per 100 000 in 2011). In 2011, 192 cases of multidrug-resistant (MDR) TB and 4 cases of extensively drug-resistant (XDR) TB were reported. Namibia has a chronic shortage and maldistribution of human resources for health (HRH) between private and public health sectors.

**Intervention:** A PEPFAR and Global Fund funded drive to hire contract health workers (HWs) to provide HIV/AIDS and TB care was initiated in 2003. More than 1000 HWs (doctors, nurses, pharmacy

staff, lay counsellors, M&E officers, data clerks and TB field promoters) had been recruited by the end of 2011. These HWs have also been pivotal to the management of drug-resistant TB. Donor funded staff have assisted with addressing emerging challenges. Mentoring and support supervisory are used to build capacity of staff in regions.

**Progress and lessons learnt:** ART coverage increased to more than 107 154 (about 82%) by March 2012. 1351 patients commenced DR-TB treatment during the period 2007–2011; and there has been improved reporting and competency in case management. The government is transitioning key contract positions to government, and to date 48 medical officers have been transitioned. The staff establishment is under revision and most contract positions will be included. Decreasing donor-funding threatens HRH. Staff retention strategies are critical to the sustenance of programmatic gains. Use of contract HWs for programme implementation is associated with creation of parallel systems with unclear lines of supervision, potential to drain staff from the ministerial positions and lack of job security with consequent low staff morale.

**Conclusion:** Contract HWs can provide expertise and complementary HR for rapid programme expansion, but a long-term strategy for staff retention is crucial. Staff establishments should be continuously revised to respond to emerging health challenges.

### **Nurse-driven MDR-TB: collaboration among primary health care, NTP and hospitals for sustainability**

J Caldwell. City Health, City of Cape Town, South Africa

**Background:** Prior to the introduction of the South African new Policy Framework on Decentralised Management of drug resistant tuberculosis (DR-TB) in August 2011, all DR-TB patients were required to be admitted to inpatient facilities to access treatment. The new Decentralised Policy now requires integration of DR-TB care into drug sensitive TB (DS-TB) programmes at primary health care (PHC) level. This shift highlights the need for PHC workers to be trained in management of DR-TB; receive on-going clinical support and clear communication and support from tertiary services for complicated cases. Health services in Cape Town, have responded and addressed DR-TB training needs. The implementation of a reporting and recording system at sub-district level can assist with programme evaluation with support and communication from tertiary registration centres.

**Methods:** Nurses and medical officers working in PHC clinics are offered a three day DR-TB course. A dedicated professional nurse is allocated to each sub-district to support staff managing patients in PHC facilities and to provide a link to the specialist

tertiary services. Additional mentorship for clinicians is provided through monthly multi-disciplinary review meetings in each sub-district, supported by staff from the specialist tertiary hospital. Paper-based DR-TB registers have been implemented in each PHC clinic and a decentralised electronic recording and reporting system is being piloted in all sub-districts across Cape Town.

**Results:** More than 17 DR-TB courses have been presented in Cape Town since 2008; with more than 341 PHC clinicians have been empowered through mentorship and training to manage DR-TB patients in PHC clinics.

**Conclusions:** Decentralisation of DR-TB diagnosis, treatment and management from specialised facilities to the primary care setting can be successfully achieved with training and mentorship support for PHC clinicians, and without additional funding or human resources.

### **Nurse-initiation and management of MDR-TB-HIV: lessons learnt from operational research**

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**Background:** Treatment outcomes for multidrug-resistant tuberculosis (MDR-TB) in South Africa remain poor. Interventions that increase access to quality care and reduce delays from suspicion to treatment improve outcomes in high HIV co-infected populations. To achieve systems level changes in service delivery, interdisciplinary collaboration to begin task-sharing models of nurse-initiated MDR-TB-HIV care are essential. This practice change is outlined by South Africa's National Strategic Plan (NSP) 2012–2016 for HIV, TB and STIs, yet there is no operational research data that provides a framework on which to build this model. This abstract will detail lessons learned from the development of the country's first nurse-initiated MDR-TB-HIV program in KwaZulu-Natal.

**Methods:** The Johns Hopkins University School of Nursing, South African Medical Research Council, National Department of Health, and KwaZulu-Natal Provincial Department of Health formed an implementation science partnership to develop and programmatically implement the first nurse-initiated MDR-TB treatment model in South Africa in KwaZulu-Natal Province.

**Results:** This presentation will share lessons learned from this program. Partners will highlight successes and challenges in the following areas: 1) legislative/regulatory frameworks for nurse prescribing; 2) existing

primary healthcare clinic infrastructure; 3) training and clinical mentoring requirements for primary healthcare nurses; 4) development of MDR-TB-HIV nurse case management skills; 5) interdisciplinary communication and integrated health information systems models; and 6) leadership for translating policy to practice. Patient safety measures will also be described alongside quality improvement initiatives in MDR-TB-HIV management.

**Conclusions:** Nurse-initiated MDR-TB-HIV treatment will make significant contributions to improving access to and timeliness of integrated care, and therefore will improve treatment outcomes.

### Utilising regional training centers: collaboration and responsibility to ensure competent providers

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Financed by USAID East Africa through TBCTA (TB CAP and now TB CARE I) with KNCV being the lead agency, the Regional Center of Excellence (CoE) on Programmatic Management on Drugs Resistant Tuberculosis (PMDT) was established in Kigali, Rwanda in 2010 after a rigorous vetting process. The Training Center is located at the School of Public Health of National University of Rwanda (SPH/NUR), while the National Tuberculosis Program (NTP) and National Reference Laboratory (NRL) of the Rwanda Biomedical Center (RBC) provide trainings in relevant disciplines and host up-country field visits as the part of learning process. Those institutions constitute the three pillars which are bound by a memorandum of understanding for maximum cooperation in conducting activities of the CoE. The terms of reference for the CoE are to provide trainings on PMDT, TB IC and laboratory services for all levels of (health) staff in the region including study visits sites; assist countries to develop own CoE; p Provide TA in the Region; maintain and coordinate a 'Regional Core Group of experts on PMDT' and coordinate peer reviews; contribute to develop regional operational standards; promote operational research. The CoE has so far carried out six (6) trainings; three (3) PMDT, two (2) TB infection control (IC) and one TB laboratory trainings. Ethiopia, Uganda NTLP have visited Rwanda to learn about PMDT. The seventh training, being the 2nd laboratory training is due in late August 2012. 130 DR-TB control experts from ten countries including Botswana, Ethiopia, Kenya, Liberia, Nigeria, Malawi, Rwanda, Somalia, South Sudan, Uganda, Zambia have participated in the trainings. The trained experts are currently involved in PMDT implementation in their respective countries.

### CONTACT INVESTIGATION: OPERATIONAL RESEARCH TO INCREASE CASE DETECTION AND DRIVE SUSTAINABILITY

#### Outcomes of routine tuberculosis contact investigation implementation for fifteen years in Morocco

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Outcomes of routine TB contact investigation implementation for 18 years in Morocco from 1993 to 2010. TB contact investigation is a component of TB control in Morocco. It has been carried out for many years as a routine intervention to identify TB cases among close contacts. The requirements to implement TB contact investigation through the National TB Programme (NTP) services are described and highlighted. Furthermore, the results of TB contact investigation activities carried out, from 1993 to 2010, are reported through output and outcome indicators. For these 18 years, more than 250 000 contact investigations were undertaken and more than one million three hundred thousand household TB contacts were identified. On average, approximately 75% of the identified contacts were assessed for TB every year. The overall prevalence of TB (any type) among the household contacts evaluated for TB was nearly 3%. The proportion of TB cases identified in household contacts among registered TB cases (any type) was approximately 5.5%. This proportion was much higher in children below 10 years of age and in patients diagnosed with symptomatic primary TB complex.

**Conclusions:** Performing TB contact investigations as part of the routine activities of NTP services is shown to be feasible in low-middle income countries, like Morocco.

#### Overview of tuberculosis contact investigation experience in TB REACH projects

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TB REACH is an initiative to promote early and increased TB case detection. In the first wave of funding 30 TB REACH projects were established which improved TB case detection by an average 34% within just one year of implementation. Each TB REACH project implemented multiple case finding interventions that were best suited to address TB case detection in the targeted population. Contact investigation was one of the most commonly implemented intervention. The protocol for contact investigation varied between projects. Nineteen TB REACH Wave 1

projects implemented TB contact investigation in a variety of poor and vulnerable settings in Asia and Africa and 13 of them collected sufficient data that allowed suitable analysis. In total, over 80 000 household contacts of over 27 000 index TB cases were investigated and in them a total of 1543 new TB patients were detected and put on treatment. These TB patients may not have been detected, or detected late, if there was no contact investigation activity. The results demonstrate that contact investigation is a relatively high yield early TB case finding intervention which is feasible to implement even in difficult settings. There is now enough evidence for all NTPs in high burden countries to mainstream contact investigation and scale it up as a routine activity within DOTS programmes.

### WHO/ATS guidelines on tuberculosis contact investigation

P Hopewell. Curry International TB Center, University of California, San Francisco, CA, USA

The systematic evaluation of persons who have been exposed to potentially infectious cases of tuberculosis can be an efficient, targeted approach to intensified tuberculosis case finding that is within the purview of tuberculosis control programs. However, comprehensive global recommendations to guide programs in conducting this activity do not yet exist. The World Health Organization (WHO), The International Union Against Tuberculosis and Lung Disease (The Union) and the International Standards for Tuberculosis Care (ISTC) all recommend that children <5 years of age and persons living with HIV (PLHIV) who are exposed to infectious cases of tuberculosis be evaluated for active tuberculosis and considered for treatment of latent tuberculosis infection (LTBI) if active tuberculosis is excluded. With this need in mind, the WHO and American Thoracic Society have developed recommendations to:

- define the epidemiological and programmatic conditions under which contact investigation is indicated;
- describe tuberculosis index patients around whom contact investigation should be focused;
- identify tuberculosis contacts who should be investigated (other than children <5 years of age and PLHIV);
- recommend the procedures to be used in identifying, screening and tracking tuberculosis contacts.

The recommendations are based on recent systematic reviews of the literature on contact investigation in low and middle-income countries.

### TRANSLATING POLICIES INTO PRACTICE: BUILDING LASTING SOLUTIONS FOR TUBERCULOSIS LABORATORY NETWORKS IN COUNTRIES

#### Rapid tuberculosis diagnostics scale-up in countries: EXPAND-TB and Xpert® MTB/RIF roll-out

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The World Health Organization (WHO) Global TB Control report 2011 shows that numbers of MDR-TB patients notified by countries still fall behind targets set in the Global Plan to Stop TB 2011–2015, highlighting the need for urgent expansion of diagnostic capacity. In 2009, UNITAID approved funding for EXPAND-TB (Expanding Access to New Diagnostics for TB) Project, which is a collaboration between the WHO, the Global Laboratory Initiative, the Foundation for Innovative New Diagnostics and the GDF. The overall goal of the five-year project is to narrow the huge diagnostic gap in MDR-TB control by expanding and accelerating access to new and rapid diagnostic technologies within appropriate laboratory services at country level, accompanied by the necessary know-how for technology transfer, and ensuring these new technologies are properly integrated within TB control programmes. EXPAND-TB has full ownership by the Ministries of Health of the recipient countries and works on a model of best-practices, learning-by-doing, and optimizing resources for laboratory strengthening at country level. Experience with the countries in the project has been very positive, confirming the feasibility of rapid expansion of access to MDR-TB diagnostics through appropriate partnerships, even in resource-constrained settings. The endorsement by WHO of the Xpert® MTB/RIF assay for rapid and simultaneous detection of tuberculosis (TB) and rifampicin have contributed to the fast paced changes in the TB diagnostics landscape. These changes were accelerated by UNITAID call for proposals and subsequent approval of a large scale Xpert MTB/RIF implementation project by WHO Stop TB Department and Stop TB Partnership. Stimulated by the innovative approach outlined in the new project proposal, UNITAID together with US government agencies and the Bill & Melinda Gates Foundation took a bold step affecting global market of Xpert MTB/RIF assay and dropping the test price to unprecedented US\$9.98.

### WHO-GLI supranational laboratory network: technical assistance to countries

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The TB Supranational Reference Laboratory Network (SRLN) was created in 1994 in order to support the World Health Organization (WHO) IUATLD Global Project on TB drug resistance surveillance. The objectives of the Global Project were to estimate the magnitude of drug resistance globally, determine trends and provide data to inform WHO policy decisions. Core principles of the Global Project were to ensure accurate and representative sampling of the populations under study, allow for the differentiation of new and previously treated cases and ensure that laboratory results were quality assured.

The original terms of reference required that each of the SRLs had a permanent functional TB laboratory providing quality culture and drug susceptibility testing (DST), with a commitment to support at least two countries with DST proficiency testing (PT), to provide external quality assurance during drug resistance surveys, and to provide training on culture and DST in these countries as needed. Between 1994 and 2012, the SRLN was expanded to 29 laboratories, with four newly designated candidate SRLs, largely driven by regional initiatives and institutional interest in joining the network. The SRLN is a sub-group of the Global Laboratory Initiative and remains an important technical resource for laboratory scale-up and capacity development. Since 2010, new terms of reference for the network have been developed as well as eligibility and inclusion criteria. Formal collaboration agreements are being established between the SRLs and National TB Reference Laboratories. Improved co-ordination of the network and the establishment of a repository of technical reports on laboratory strengthening remains a key priority for the network. A time-limited taskforce of the SRLN was established in 2012 and members are working to develop a business plan to organize and fund global laboratory strengthening efforts for high TB burden settings and low- and middle-income settings.

### Large-scale introduction of new diagnostics: India's experience

C Paramasivan. Foundation for Innovative New Diagnostics (FIND/India), New Delhi, India

Introduction of newer TB diagnostics was taken up by the Revised National TB Control Programme (RNTCP) in the year 2009 with the funding support from EXPANDx TB project and Global Fund. The RNTCP identified 43 culture and DST sites for the introduction of line probe assay (LPA) and 33 sites for liquid culture (LC) for its programmatic management of drug resistant TB (PMDT). While LPA (40)

and LC (31) sites are supported by EXPANDx TB, GFATM supports an additional LPA (3) and LC (2) sites. The infrastructure support is provided by the state/NRHM/Institute; USAID and GFATM. Also, till December 2013, EXPANDx TB supports the senior technical HR at FIND/India. WHO through EXPANDx TB additionally supports the infrastructure and all national training courses in the newly established International Centre of Excellence in Laboratory Training (ICELT) facility at NTI, Bangalore. The GFATM provided additional support for HR, specimen processing equipment and consumables, on-site technical support, mentoring, rapid specimen referral, transportation and reporting. Till date, 24 LPA labs provide results for patient care under PMDT and seven LPA sites under accreditation will be providing results sooner. Before 2012, seven more LPA labs will be added. The BLS3 infrastructure is complete in 14 sites, and reporting based on LC is at various stages. The BSL3 infrastructure is planned for additional 15 sites in 2012. These massive collaborative efforts will result in examination of about 350 000 MDR TB suspects and diagnosis of an estimated 46 000 MDR TB cases by 2013.

### Role of new rapid tuberculosis diagnostic tools in strengthening TB-HIV interventions: introduction of Xpert® MTB/RIF in Swaziland

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**Setting:** In 2011 Swaziland decided to introduce Xpert® MTB/RIF at the regional level as part of its decentralization plan of diagnosis and treatment of tuberculosis. The practice was first introduced in Shiselweni region. Sputum samples from all TB suspects of the region were delivered to the regional laboratories for rapid TB diagnosis in parallel to microscopic examination.

**Objective:** To describe the experience of the introduction of Xpert MTB/RIF and its effect on detection of TB, and on the time interval between diagnosis and initiation of TB and drug-resistant TB treatment

**Design:** Between August 2011 and May 2012, 3545 sputum samples (3166 smear negative and 379 smear positive) were tested for Xpert MTB/RIF and microscopy examination. Analysis of data collected and recorded routinely in the laboratory and clinical registers.

**Results:** Among the smear negative samples (3166), 8.8% were MTB-positive on one Xpert MTB/RIF test. The median interval of time between sputum collection and producing result by the machine was 1 day. However, patients at primary health clinics received the results later than 24 hours and initiated TB

treatment even later. Comparing 2 cohorts of patients initiating drug-resistant TB treatment before and after implementation of Xpert MTB/RIF, the average number of days between sputum collection and DRTB treatment initiation was 65.9 days and 13.9 days respectively.

**Conclusions:** Xpert MTB/RIF increased the proportion of confirmed TB cases, and shortened the time gap between diagnosis and TB treatment in some patients. However, the greatest advantage was shortening the time gap between diagnosis and initiation of treatment of DRTB.

### Making new technologies work in low resource settings: experience of Swaziland and Myanmar

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**Setting:** National TB Reference Laboratories in Yangon and Mandalay, Myanmar.

**Objective:** To expand and accelerate access to diagnostics for patients at risk of multidrug-resistant TB (MDR-TB).

**Design:** To upgrade two existing laboratories with quality-assured new diagnostic technologies through EXPAND TB, a national and international partnership funded by UNITAID and supported by the Global Laboratory Initiative (GLI), World Health Organization (WHO), Foundation for Innovative New Diagnostics (FIND) and the Stop TB Partnership's Global Drug Facility (GDF).

**Results:** The agreement for the upgrading of the two laboratories was signed in February 2009. The Ministry of Health established the infrastructure to meet biosafety level three requirements. FIND provided technical assistance and WHO ensured the importation of diagnostic instruments, supplies and reagents. On 12 July 2010, the two laboratories were inaugurated.

**Conclusions:** Access to quality-assured new diagnostic technologies including liquid culture and drug susceptibility testing, rapid speciation and molecular line probe assay has been ensured. The new diagnostic technologies have been integrated into the routine work of the National TB Programme (NTP) and regular monitoring of the performance is ensured by the NTP and FIND. By July 2012, 857 MDR-TB cases have been diagnosed out of which 415 have so far initiated treatment according to WHO guidelines. The two reference laboratories will allow for the planned roll-out of Xpert<sup>®</sup> MTB/RIF, since rifampicin resistant cases detected by Xpert MTB/RIF will need to be confirmed. Planning is now undertaken to ensure that

the diagnostic capacity is coupled with access to second-line anti-tuberculosis drugs.

### Making new technologies work in low-resource settings: experience of Swaziland and Myanmar

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**Setting:** Swaziland, a small resource-constraint sub-Saharan country faced with an extreme burden of human immunodeficiency virus (HIV), tuberculosis (TB) and multidrug-resistant (MDR) TB. The 26% HIV prevalence coupled with the highest TB incidence of 1287 per 100 000 population; and an MDR-TB rate as high as 33.8% among previously treated TB cases presented a huge public health challenge. As at 2007, the largely sputum smear microscopy-dependent TB diagnosis was accessible to less than 50% of the population; and only 18% of MDR-TB patients enrolled on treatment were bacteriologically confirmed due poor access to culture and drug susceptibility testing (DST) services. Quality-assured laboratory support became the most critical need to address the huge gap in MDR-TB diagnosis and treatment.

**Methods:** A comprehensive and ambitious country-led laboratory strengthening plan based on rapid technology transfer to increase population access to quality-assured TB and MDR-TB diagnosis was embarked upon supported by a national partnership including the WHO/GLI EXPAND TB project. The plan covered infrastructural, human resources, equipment and laboratory biosafety upgrading to support the sustainable adaptation of the new technologies.

**Results:** More than 50% increase in population access to quality-assured TB microscopy, MGIT culture, rapid speciation, DST and molecular techniques including LPA and Xpert<sup>®</sup> MTB/RIF with significantly increased throughput. Cumulatively, 1201 bacteriologically confirmed MDR-TB cases detected from 2008 to 2011.

**Conclusion:** The experience of Swaziland in roll-out of new TB diagnostic tools and its impact in addressing the dynamics of the high TB-HIV and MDR-TB burden within 3 years demonstrates the feasibility of rapid technology transfer to enhance high quality DOTS and effective management drug resistant TB in a high HIV prevalence and low resource setting. It also highlights the potential challenges of inadequate human resources, inconclusive LPA validation, and inadequate national capacity for mentorship and training on new diagnostic tools.

## MANAGEMENT OF COMMON RESPIRATORY INFECTIONS IN CHILDREN

### How and why we miss acute bronchiolitis

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**Introduction:** Bronchiolitis remains the commonest cause of acute lower respiratory tract infection (ARI) in young children and still doctors are oblivious of it.

**How and why physicians miss bronchiolitis:** While, Integrated Management of Childhood Illness (IMCI)/ARI Control training programs exerted a huge impact on reducing childhood morbidity and mortality, it may have confounded the process of under-reporting or misdiagnosing bronchiolitis cases in other hand. ARI is classified as 'no pneumonia', 'pneumonia', or 'very severe disease' on the basis of gross audiovisual features like cough, fast breathing and/or chest indrawing according to IMCI/ARI. Clinical physicians and General practitioners (GPs) consider classification of ARI cases as the diagnosis. They seldom use stethoscope (80.5%) to diagnose ARI cases. And, noteworthy, a little scope exists in our country for refresher training for these physicians. Media publicity posed a perceived idea that a child with respiratory distress is most likely to suffer from 'pneumonia'. And our Management Information System (MIS) document childhood respiratory diseases following IMCI classification as usual and so bronchiolitis remains unrecorded.

**Conclusion and recommendation:** IMCI training to HCPs resulting in mis-consideration of ARI classification as the diagnosis, media campaign highlighting only pneumonia and non-documentation of bronchiolitis are responsible to miss bronchiolitis. Inclusion of bronchiolitis into IMCI module, refresher training of GPs and updating MIS/medical recording following ICD-10 may improve this prevailing scenario not to miss bronchiolitis any further.

### Addressing the misuse of antibiotics in the Asian setting

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Pneumonia remains an important cause of morbidity and mortality worldwide. Rational use of antibiotics remains one of the most effective interventions to reduce pneumonia-related mortality. Identifying the

cause of pneumonia in children is difficult in limited resources setting. Therefore, administering empirical therapy is commonly applied. When antibiotics are used irrationally, it leads to treatment failure and contributes to emerging pathogen resistance. In 5 studies in Asia, using WHO recommendations as the best practice standard, the irrational antibiotic use in treatment of pneumonia was common: up to 56.5%–62.9% of episodes. The WHO Pocketbook hospital care for children provides good evidence and guidelines for managing common illnesses in limited resources setting including pneumonia. A before-and-after study is being conducted in a teaching hospital in Yogyakarta, Indonesia, implementing the WHO antibiotic guidelines to improve rational antibiotic use. Complying with WHO guidelines leads to decreasing the episodes of irrational antibiotic use in pneumonia from 27/100 (27%) pre-intervention to 1/42 (2.4%) post-intervention (risk difference (RD)  $-0.25$ , 95%CI  $-0.34$  to  $-0.15$ ) and mortality associated with pneumonia was 8/100 (8%) to 2/42 (4.7%; RD  $-0.03$ , 95%CI  $-0.12$  to  $0.05$ ) in the general pediatric ward. In pediatric ICU, children who received irrational antibiotics reduced from 14/54 (25.9%) to 2/16 (12.5%; RD  $-0.13$ , 95%CI  $-0.33$  to  $0.07$ ), but mortality related to pneumonia in the ICU remained very high from 25/54 (46%) to 10/16 (62.5%; RD  $0.16$ , 95%CI  $-0.11$  to  $0.43$ ). A multi-modal intervention aimed at improving the rational use of antibiotics, based on guidelines, structured education and feedback can improve the treatment of pneumonia in hospitals. Because of many factors, which effect mortality from pneumonia whole-of-hospital antibiotic stewardship interventions are needed to reduce mortality, not just interventions focused in an ICU setting.

### Oxygen is an essential medicine: a call for international action

S M Graham. Centre for International Child Health, Melbourne, VIC, Australia; International Union Against Tuberculosis and Lung Disease, Paris, France

Hypoxaemia is a major risk factor for poor outcome in infants and children with pneumonia, irrespective of causative pathogen. Provision of oxygen therapy to children with hypoxaemic pneumonia in the resource-limited and high mortality setting has been shown to be effective in reducing pneumonia-related mortality by around one-third. It has also been shown to be cost-effective in that context, and the provision of oxygen therapy is also relevant for care of sick neonates, sick children with other conditions such as meningitis and sepsis, for maternal and perinatal care, and for safe surgery and anaesthesia. Effectiveness and cost-effectiveness of use of oxygen therapy are improved by improved techniques to identify hypoxaemia, oximetry. Equipment for both

detection and treatment of hypoxaemia is becoming better adapted for the resource-limited setting, more robust and cheaper. A comprehensive health system strengthening approach to the provision of care for hypoxaemia is required that includes engineers and biomedical technicians.

## COUNTERING TOBACCO INDUSTRY INTERFERENCE IN TOBACCO CONTROL: SUSTAINING OUR EFFORTS THROUGH COLLABORATION

### Tobacco industry interference in Indonesia: where have we been and what lessons have we learnt?

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**Setting:** More than 200 000 people die every year from tobacco use. Smoking prevalence is about 65% in males and 5% in females. Indonesia has not ratified FCTC yet; however, some progresses have been achieved at sub-national level on smoke-free and policy advocacy.

**Objectives:** Explain tobacco industry interferences and share lessons learnt.

**Methods:** Documentation and review of media reports.

**Results:** Tobacco industry (TI) interferences are rampant at each policy level to block tobacco control move. TI key arguments are that FCTC and tobacco control measures harm national economy, business of tobacco farmers and create unemployment and destroy image of Indonesian tobacco products of national heritage. Key results of TI interferences were that deleted of addicted clause of health law 2009, delayed adoption of implementation regulation of the health law, and dropped out tobacco control bill from a list of parliamentary discussion in 2012.

**Key TI tactics include:** 1) Direct lobby with policy makers (parliamentarian and government officials), mobilising front groups (Indonesian Tobacco Farmers' Association, Indonesian Tobacco Alliance, smokers' club, Indonesian Kretek Community), mobilizing academicians, litigations, discredit tobacco control advocates, blaming international tobacco control support, introducing weak tobacco control bill, manipulating evidences (launching of tobacco books), and use of WTO.

**Conclusions and key lessons learnt:** 1) Strong civil society proactive roles resulted reinstalled of addictive clause in the health law, 2) Partnership between MOH/sub-national governments and civil society resulted to win some TI litigations such as on smoke-free and

pictorial health warning, 3) Established Mayors' Alliance resulted to drive sub-national smoke-free and introducing a joint ministerial decree on smoke-free, 4) establishment of health professional alliance to counter TI interference and activities.

## Progress and challenges in the Philippines implementation of WHO FCTC Article 5.3

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**Setting:** Even with intensified tobacco control efforts in the country, overview of tobacco industry documents in the Philippines done by Chapman et al. in 2004, showed the Philippine tobacco industry as the strongest tobacco lobby in Asia.

**Objectives:** The goals of this study are to describe strategies tobacco industry has used and to examine how the Philippine tobacco control advocates have counteracted tobacco industry interference.

**Methods:** Analysis of information reported by tobacco control advocates and international tobacco control experts was done. To identify tobacco industry viewpoints, information from internal tobacco industry documents were extracted and media and tobacco industry supporters were monitored.

**Results:** Data was synthesized and tobacco industry strategies were identified, namely, 1) reinventing the image of the tobacco industry, 2) affordability of product, 3) political influence, 4) lobbying and legislative strategy. Three case examples were presented showing where tobacco industry have employed interference strategies and showing how the Philippine tobacco control advocates have successfully counteracted those strategies by: 1) enacting a joint memorandum circular by the DOH and Civil Service Commission, 2) conducting vigilant surveillance, 3) sustaining pressure from the civil societies and communities, 4) dedicating resources to effective enforcement of regulations.

**Conclusion:** Policy implication from this study is for tobacco control advocates in other countries with strong tobacco industry interference to develop countermeasures similar to those identified in the Philippines based on the FCTC guidelines.

## Strategies, tools and resources to counter industry interference: international perspectives I (WLF)

J Alday. World Lung Foundation, New York, NY, USA

The Philippines has among the highest prevalence of tobacco use in the world, with around half of adult

males smoking and more than half children reporting being exposed to secondhand smoke (SHS) in the home. Mass media tobacco control campaigns and earned media strategies can contribute to increasing knowledge about tobacco-related harms and counter the social acceptability created by decades of pervasive tobacco industry marketing. Such campaigns can also influence behaviour change among smokers. The Philippines passed Republic Act 9211, which aimed to promote a healthy environment and protect the citizens from the hazards of tobacco smoke and which banned all tobacco advertisements, except at point-of-sale. It also ratified the Framework Convention on Tobacco Control, an international treaty, in 2005. In support of these legal structures, Campaign for Tobacco Free Kids and World Lung Foundation have worked with government and civil society organizations to develop and implement communications strategies that counter tobacco industry interference and marketing. Earned media has played a vital role in helping to shift public opinion in favour of tobacco control policies, and several mass media campaigns have been evaluated and shown to prompt changes in knowledge, attitudes and behaviour among smokers and those exposed to secondhand smoke. This presentation will highlight successful models and lessons learned such communications strategies and will identify emerging areas, such as social media, that need to be considered as the tobacco industry adapts to successes achieved in the Philippines.

### **Strategies, tools and resources to counter industry interference: international perspectives I (Tobacco-Free Kids)**

X Yin, Y Q Wu. Campaign for Tobacco-Free Kids, Washington, DC, USA

In People's Republic of China, the tobacco industry is a state-owned monopoly. They sit on the FCTC implementation team. Countering industry interference is a huge challenge in the political and social environment in China. In March 2012, the National Office for Science & Technology Awards included the 'construction and application of Chinese-style cigarette theory' as a candidate of the 2012 National Science & Technology Progress Award and released the information on March 23 for public comment. Tobacco control advocates in China rapidly responded by voicing opposition through press briefings, media interviews, opinion editorials, blogs, microblogs, and letters to government agencies. Tobacco control groups such as ThinkTank Research Center for Health Development also reached out to new partners and convinced them to publicly express concerns for the tobacco research being considered for this prestigious award. As a result, 30 well-respected academicians from China Academy of Science sent a letter to the Ministry of Science and Technology opposing recog-

nizing tobacco research with the national prize. Additionally, editors at China's foremost science web site, ScienceNet.cn, organized a petition against giving the science prize to the tobacco company. Chen Zhu, Minister of Health and Huang Jiefu, Vice Minister of Health and President of China Association on Tobacco Control made statements supporting the position of tobacco control advocates. The collaborative efforts generated wide media coverage (over 100 original stories and 3000 reprints) and public opinion on the social media as well. Over 40 000 microblogs have been posted on China's top social media platform. Many of the microblogs were posted by influential figures and organizations, which were then reposted by tens of thousands followers. On May 4, the Ministry of Science and Technology announced the withdrawal of the research by the China National Tobacco Company from consideration for the award.

### **Strategies, tools and resources to counter industry interference: international perspectives II**

M Allen. Allen + Clarke Policy and Regulatory Specialists Ltd, Wellington, New Zealand

In 2012 the International Union Against Tuberculosis and Lung Disease developed a tool kit for World No Tobacco Day focusing on tobacco industry interference. The tool kit, comprising a set of resources for Governments, focused on practical policy and legal tools that could be used as the basis for country-specific policies and laws for curbing the influence of the tobacco industry. These tools include resources on monitoring of the tobacco industry, model government policies and protocols to actively limit and guide any engagements with the tobacco industry, model code of conduct provisions for government agency employees and agents, and conflict of interest protocols for government agencies. In support of these tools, fact sheets on Article 5.3 of the WHO Framework Convention on Tobacco Control, and the rationale why the tobacco industry needs to be treated differently to any other industry, were developed as part of the toolkit. The presenter will describe and explain the rationale for the resources that have been developed, their use to date (focusing on use in Pacific countries), plans afoot for review and perhaps expansion of these resources, and next steps for work on Article 5.3.

## ABSTRACT PRESENTATIONS THURSDAY 15 NOVEMBER 2012

### ORAL PRESENTATION SESSIONS

#### MODERN MOLECULAR TECHNOLOGIES IN TUBERCULOSIS DIAGNOSIS

##### OP-101-15 Rifampicin resistance as a proxy for multidrug-resistant tuberculosis in Botswana

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**Background:** Introduction of rapid molecular technique Xpert® MDR/RIF™ (Cepheid) for routine detection of *Mycobacterium tuberculosis* resistance to rifampicin (RMP) poses a question on to what extent resistance to RMP is an indicator for multidrug-resistant tuberculosis (MDR-TB). We assessed proportion of isoniazid susceptible (INH-S) isolates among RMP resistant (RMP-R) isolates received in Botswana for the period 2007–2010.

**Design/methods:** We conducted a retrospective patient-based analysis of drug susceptibility testing (DST) results for samples received at Botswana National Tuberculosis Reference Laboratory in 2007–2010 using 1% proportional method on Löwenstein-Jensen media.

**Results:** Proportion of INH-S isolates among RMP-R isolates in Botswana is high though decreasing with time. It was 37.3% (19/52) during drug resistance survey (DRS) 2007–2008, 28.4% (59/208) in 2009 and 14.5% (18/124) in 2010. Proportions of INH-S RMP-R isolates were not different for new and re-treatment categories of patients. They were 30.3% (10/33) and 50% (8/18) in DRS 2007–2008, 28.9% (24/83) and 28.0% (35/125) in 2009; 13.8% (5/58) and 14.9% (10/67) in 2010, for new cases and re-treatment cases, accordingly.

**Conclusions and recommendations:** High proportion of rifampicin resistant isolates in Botswana is susceptible to isoniazid. Testing for susceptibility to isoniazid should be done for patients identified by GeneXpert MTB/RIF as rifampicin resistant. Proportion of INH-S RMP-R isolates is changing with time and should be closely monitored to inform management of patients with drug resistant TB.

##### OP-102-15 Utility of diagnostic modalities for diagnosis of pulmonary and extra-pulmonary tuberculosis: how ready are we?

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**Background:** With the ever increasing prevalence, tuberculosis still remains one of the leading causes of mortality and morbidity in India. Timely diagnosis and prompt treatment of the infectious cases plays a pivotal role in combating the curable killer. Rapid diagnosis of extra pulmonary tuberculosis still remains an area for prime research as the efficiency of current diagnostic modalities are yet to be evaluated and recommended for routine use.

**Objectives:** 1) To evaluate the utility of Line Probe Assay (GenoType MTBDR plus Hain Life science, Germany) for the rapid and accurate diagnosis of Multidrug-resistant TB (MDR-TB) in both pulmonary and extra pulmonary TB, and 2) To compare with conventional smear microscopy, LJ culture and anti-biogram for 1st line drugs SHER by MIC method.

**Material and methods:** A total of 160 samples comprising of sputum (86), pus (36), BAL (22), others 16 included tissue, pleural effusion and ascitic fluid etc received during a period Jun 2010–Aug 2011 were processed for AFB smear (ZN and fluorescent stain), Conventional AFB culture (LJ-media) followed by Drug Sensitivity Testing (DST) MIC method for SHER. GenoType MTBDR plus assay for *Mycobacterium tuberculosis* identification and resistance detection towards rifampicin and isoniazid was carried out directly from clinical samples.

**Results:** Of the 160 samples 108 (68%) were smear positive for acid fast bacilli, 90 (56%) were culture positive on LJ media, 81 (.6%) were positive for *M. tuberculosis* by Genotype MTBDR plus. Of the 90 positive samples 74 (82%) were isolated from pulmonary and 16 (18%) from extra pulmonary samples. The sensitivity and specificity of MTBDR plus assay were found to be 77.8% and 74.3% respectively in detecting *M. tuberculosis* directly from both pulmonary and extra pulmonary samples. Of the 160 samples, 24 (15%) were MDR, 41 (25.6%) resistant to RMP alone and 2 (16%) to INH alone. The measure of agreement ( $\kappa$ ) between culture and MTBDR plus assay for detecting RMP and INH resistance was found to be 0.55 and 0.53 ( $P < 0.05$ ) respectively.

**Conclusion and recommendations:** With the high prevalence of extra-pulmonary TB cases in India and low sensitivity of line probe assay to detect *M. tuberculosis* from these paucibaillary specimens, and prolonged period required for culture positivity on

conventional culture methods, there is definitely a need for devising new diagnostic modalities at molecular level for diagnosing extra-pulmonary tuberculosis.

#### OP-103-15 Molecular characterisation of *Mycobacterium tuberculosis* strains from patients with tuberculous spondylitis

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Spinal tuberculosis (TB) is a most common form of extrapulmonary TB, and comprises approximately 50% of all cases of skeletal TB. The incidence of spinal TB is increasing in developed countries including Russia. The 72 *M. tuberculosis* strains from patients with tuberculous spondylitis (2008–2012) from Russia were studied by spoligotyping and 24-loci VNTR typing. Data were compared to SITVIT WEB and MIRU-VNTRplus international databases. Based on spoligotyping, majority of strains (55 of 72 [76%]) belonged to the Beijing genotype (types SIT1, SIT265 and SIT269). Other strains represented T superfamily (SIT53–5 strains, SIT52, SIT263, SIT1252 and SIT1582), Haarlem (SIT50, SIT262, SIT777 and SIT1134) and four profiles were defined as orphans. Multidrug resistance was more frequently found among Beijing strains compared to strains of other genotypes: 82% (45 of 55) and 12% (2 of 17), respectively. The 12-MIRU typing differentiated 55 Beijing strains into 8 types (HGI = 0.64) while two largest types were MIT16 (SITVIT WEB)—23 strains and MIT17 (SITVIT WEB)—24 strains. The 24-VNTR typing differentiated strains into 17 profiles (HGI = 0.83); the largest included 19 strains with code 100-32 (MIRU-VNTRplus). Population structure of the studied *M. tuberculosis* strains from tuberculous spondylitis patients was dominated by Beijing genotype 12-MIRU types MIT16 and MIT17 and 24-MIRU type 100-32, also frequently found among strains from patients with pulmonary TB in Russia. Use of 24-loci VNTR typing somewhat improves discrimination of Beijing strains but further use of additional discriminatory loci is needed.

#### OP-104-15 Molecular characterisation of the *rpoB* gene mutations of *Mycobacterium tuberculosis* isolates in China

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**Background:** Rifampicin remains the most efficient drug in the modern short-course regimen due to its excellent sterilizing activity. *rpoB* gene mutation

frequency and hotspot is critical to rapidly detect rifampicin resistance. Molecular characterization plays an important role in the development of the new molecular diagnostics.

**Methods:** A total of 3479 *M. tuberculosis* isolates from nationwide anti-tuberculosis drug resistance survey which included 402 rifampicin-resistant and 3077 rifampicin-susceptible isolates from 31 provinces, China, were analyzed by DNA sequencing of the 81-bp rifampicin resistance determining region (RRDR) of the *rpoB* gene to detect characterization of mutation in the *rpoB* gene of *Mycobacterium tuberculosis*.

**Results:** DNA sequence analysis revealed that 98.01% (394/402) of rifampicin-resistant strains showed *rpoB* gene mutation. Twenty-three nonsynonymous single mutations, two 3-bp insertions, 5 deletions, 20 double mutations and a triple mutation were identified in the *rpoB* region of rifampicin-resistant isolates. Isolates with mutations at codon rpoB531 (50.50%), rpoB526 (26.12%) and rpoB516 (7.21%) were the most common.

**Conclusion:** New mutations including six point mutations, four deletions and two insertions are first reported. Analysis of the *rpoB* gene of the 3077 rifampicin-susceptible strains revealed that 98.96% (3045/3077) of the strains had no mutation, 9 different mutations in five codons were identified with *rpoB* codons 511 (0.36%), 533 (0.29%) and 516 (0.19%) most frequently affected.

#### OP-105-15 The application of whole genome sequencing to map *Mycobacterium tuberculosis* transmission in a high-burden setting

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**Background:** *M. tuberculosis* transmission in high incidence settings remains poorly understood, as most transmission cannot be traced with standard epidemiology or DNA fingerprinting techniques. The much finer definition of whole genome sequencing may allow more detailed likely transmission chains to be constructed, which can then be linked to pathogen or host factors that may increase or reduce transmission.

**Methods:** We performed whole genome sequencing on well-described strains from Karonga District in northern Malawi. Three sets were studied: 1) Confirmed case-pairs, where the transmission link was near certain; 2) Three large RFLP-defined clusters of cases, where transmission occurred, but the actual links are unknown; and 3) A random set of strains from each lineage present in the district, where we

expect no direct transmission events to have occurred. Whole genome based strain variation was assessed for each set. Within case-pairs the association between time of episode and variation between strains was studied. This preliminary 'molecular clock' information can be extrapolated to construct likely chains of transmission within the large clusters, and ultimately to link information on likely successful transmission with drug resistance or ART status.

**Results:** Among 351 isolates there were ~10 000 SNPs compared to the H37Rv reference genome, 85% of which occurred in a coding region. The median variation between case pairs was 26 SNPs, and among unrelated cases within a lineage was 587 SNPs. Time between episodes of a case pair was strongly correlated with the variation ( $P$  value spearman correlation = 0.01). This difference should allow resolution of larger clusters into a sequence of likely transmission events.

**Conclusion:** Whole genome sequencing has the potential to elucidate transmission dynamics. The results will help answer urgent questions facing TB control, most notably how ART and drug resistance change the rate of successful *M. tuberculosis* transmission.

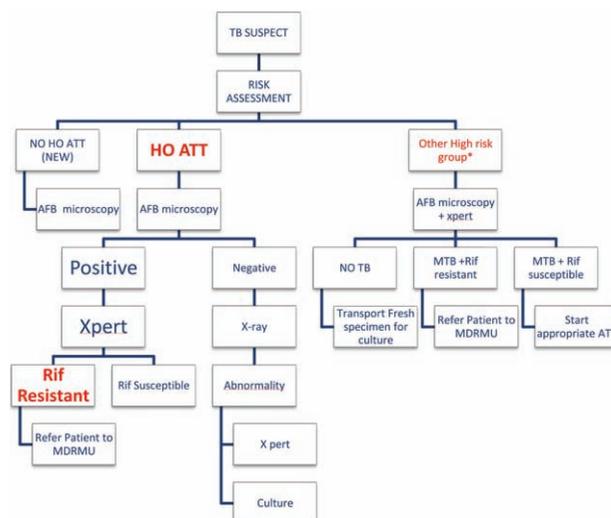
#### OP-106-15 Implementation of Xpert® for early diagnosis of rifampicin resistance: Pakistan experience

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**Background:** Xpert® MTB/RIF offers new and important possibilities for the diagnosis of sputum smear-negative tuberculosis and/or rifampicin (RMP) resistance. Pakistan is 4th among high burden countries with estimated incidence of 400 000 tuberculosis, and 3.2% MDR in new cases and 21% in retreatment cases. Keeping in view that both HIV and MDR-TB in a NEW TB case is of lesser concern, diagnostic algorithm was developed in which sputum smear microscopy remained as FIRST SCREENING test and protocol was developed for referring PTB cases/suspect both smear positive or smear negative with radiological abnormality for X-pert MTB/RIF testing.

**Objective:** To evaluate diagnostic algorithm for early diagnosis of rifampicin resistance in patient at risk of MDR.

**Method:** All patient with history of previous treatment, MDR contact and health care workers were defined as patient at risk of MDR. Twelve 4 module Xpert machines were installed at 12 sites across different parts of country. Request and report forms were developed for referral of patients. Technicians



**Figure** Diagnostic algorithm for early diagnosis of rifampicin resistance.

were trained and doctors were given briefing on protocol for referral.

**Results:** Total of 2482 patient were tested between August 2011 and March 2012, including 1299 smear positive and 1183 smear negative suspects. *Mycobacterium tuberculosis* was detected in 97% of smear positive and only 12% of smear negative samples. *M. tuberculosis* with RMP resistance was detected in 28% of smear positive cases and 25% of smear negative *M. tuberculosis*+ cases

**Conclusions:** *M. tuberculosis* was detected in 12% and RIF resistance in 3% of smear negative MDR suspect tested. High rifampicin resistance was reported both in smear +ve/*M. tuberculosis*+ (28%) and smear -ve/*M. tuberculosis* +ve case (25%).

#### OP-107-15 String test: a new tool to diagnose tuberculosis in patients unable to produce sputum

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**Background:** The use of the intra-gastric String Test (ST) has been proposed as an alternative specimen collection method for diagnosis of pulmonary tuberculosis (PTB) in patients unable to produce sputum. We compared the TB detection rate of the ST and the sputum induction (SI) in a series of adult patients presenting with PTB suspicion at the Mbarara Regional Referral Hospital in Uganda.

**Design/methods:** Two ST and SI were performed in adult PTB suspects defined by at least 2 weeks cough, chronic unexplained weight loss or fever. We used the

paediatric Entero-test® (HDC corporation, USA), that is a gelatine capsule containing a 90 cm coiled nylon string, after a 2 hours fasting and with 2 hours of intra-gastric down time. The SI was performed after the ST with 5% saline for 20 minutes. LED-fluorescence microscopy, Löwenstein-Jensen and MGIT TB cultures were performed in all specimens.

**Results:** From March 2010 to December 2011, 195 PTB suspects were enrolled. Median age was 34 years, 53% were female and 58% HIV infected. There were 3 (1.5%) ST and 25 (12.8%) SI failures. 174 patients had at least one ST and one SI result. 23 (13.2%) and 22 (12.6%) were smear positive on ST and SI, respectively ( $P = 1.0$ ). Using combined LJ and MGIT cultures, TB was detected in 39/172 (22.7%) patients using the ST compared to 41/172 (23.8%) with SI ( $P = 0.69$ ). In HIV infected patients, 10/94 (10.6%) patients were smear-positive using ST versus 10/94 (10.6%) using SI ( $P = 1.0$ ). There 17/91 (18.7%) culture positive patients with ST versus 19/91 (20.9%) with SI ( $P = 0.50$ ).

**Conclusion and recommendations:** The TB detection rate using ST was comparable to that of the SI irrespective of the HIV status. The ST is more feasible with less nosocomial risk compared to the SI and seems well adapted to low resource setting.

## HIV TESTING AND TUBERCULOSIS SCREENING: THE COMPLETE PACKAGE

### OP-108-15 Providing accessible HIV counselling and testing services: a mutual responsibility between government and civil society?

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**Background:** The South African government aims to reduce the number of new HIV and TB infections by 50% before 2016 and is advocating an annual HIV test for all, highlighting a need for HCT to be easily accessible to all South Africans. Strategically government and civil society should work together to achieve this goal. This study aimed to determine the profile of clients who access community HCT compared to clinic HCT.

**Design/methods:** A matched pairs design was used to compare 1063 participants who self referred for community or clinic HCT between February and April 2011. A self report questionnaire was used to collect data on demographic, socio-economic, access and health risk behavior indicators. Data was analyzed using descriptive statistics and Pearson's  $\chi^2$ , after which the Mantel-Haenszel test for matched samples was run on significant correlations. In addition,

interviews with 16 participants, comparing their preferences and experiences of the HCT service were completed and a thematic analysis was carried out.

**Results:** Community HCT had a significantly higher proportion of males, participants with an older age profile and a significantly lower proportion of participants engaged in formal work when compared to clinic HCT. Participants who accessed community HCT were more likely to use opportunity as a reason to test, while proximity was more likely to be used by those who accessed clinic HCT. The thematic analysis revealed that participants accessed a service, based on its accessibility, familiarity and perceived 'better service' with regard to confidentiality, staff and comprehensiveness of service.

Indicators	Community (n = 511)	Clinic (n = 552)	OR (95%CI)
Gender			2.77 (2.12–3.57)**
Males	261 (51%)	149 (27%)	
Females	250 (49%)	403 (73%)	
Age			1.3 (1.15–1.48)**
18–30 yrs	268 (53%)	352 (64%)	
31–50 yrs	201 (39%)	179 (32%)	
>50 yrs	42 (8%)	21 (4%)	
Employment status			1.39 (1.03–1.85)*
Informal/ unemployed	398 (78%)	400 (73%)	
Formal	111 (22%)	150 (27%)	
Reason for choosing provider			
Just passing	246 (48%)	6 (1%)	76.9 (31.25–200)**
Short queues	69 (14%)	13 (2%)	5.75 (3.56–9.52)**
Quick service	109 (21%)	64 (12%)	2.03 (1.47–2.8)**
Close to home/work	213 (42%)	399 (73%)	0.24 (0.18–0.31)**

\* $P < 0.05$ ; \*\* $P < 0.0001$ .

**Conclusion and recommendations:** Community and clinic HCT provide services to different profiles of clientele. Deliberate strategies around planning and monitoring and evaluation should be implemented, so that government and civil society accept mutual responsibility in providing HCT services that are easily accessible to all.

### OP-109-15 Intensified tuberculosis case detection among people living with HIV and AIDS: involvement of hospitals for rapid scale-up in Swaziland

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Swaziland faces a severe co-epidemic of TB and HIV. The country has an estimated TB incidence of 1287 per 100 000 population, 26% of its adult population (15–49 years) infected with the HIV virus, and 83% of incident TB cases HIV positive. An estimated

182 792 adults live with HIV in the country with 85 528 in need of ART (UNAIDS 2010). Currently, 86% of TB patients know their status, 93% of HIV+ TB patients receive CPT and 35% on ART (WHO 2011). About 20 out of 56 accredited health facilities provide pre-ART and ART services to 80% of PLHIV. Intensified TB case finding using a systematic symptom-based TB screening of People Living with HIV (PLHIV) receiving care at ART sites was supported via a WHO/CIDA initiative since 2009. National TB screening tools adaptation, diagnostic algorithm, patient flow and triage procedures, deployment of dedicated cough monitors, training and reporting protocols were instituted. 22 sites conducted over 200 000 TB screenings among PLHIVs from 2009 to 2011 yielding 45 269 instances (20%–27%) investigated for TB based on positive response to any of the four symptoms in the TB screening tool. TB diagnosis was confirmed in 5% (range 2% to 19% among implementing sites) resulting in additional 2365 TB cases detected representing 95% of the 2500 project period target. Nationally notified TB cases increased by an average of 7% from 2009 to 2011. The preponderance of symptoms positive on screening include cough (29%), night sweats (21%), chest pain (20%), weight loss (17%) and fever (14%). A significant proportion of PLHIV with active TB could be going undetected and therefore untreated in Swaziland annually. Engagement of large hospitals in systematic TB screening in high risk groups could increase TB detection, ensure early effective TB treatment of PLHIV to save lives. Successful TB screening requires a clearly defined algorithm, patient flow, appropriate well-adapted TB screening tools, dedicated staff and consistent reporting system.

#### OP-110-15 High prevalence of tuberculosis among Zambian HIV care enrollees: urgent need for enhanced screening approach

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**Background:** TB remains a leading cause of morbidity and mortality in sub-Saharan Africa, especially among HIV-infected patients where the TB prevalence is 1500/100 000. Despite 60% of cases being smear negative, sputum smear examination and symptom screening remain the primary diagnostic tools in Zambia. We implemented an enhanced screening program in a Lusaka HIV clinic to determine the true burden of TB among new HIV care enrollees.

**Methods:** All consenting adult enrollees without current or recent history of TB were screened for TB

regardless of symptoms. World Health Organization (WHO) recommended criteria of any cough, fever, weight loss or night sweats were recorded, as well as physical exam, digital chest radiography, and LED fluorescence microscopy on two sputum samples. Two sputum samples, one blood and one urine specimen were cultured.

**Results:** This analysis includes 301 patients with complete screening data. Mean age was 35 years; 52% were male; median body mass index was 20, median CD4 count was 202 cells/ $\mu$ l and 86% were symptomatic. The prevalence of culture-confirmed TB was 59/301 (20%); an additional 26 (9%) patients were diagnosed by clinical criteria. Only 14 (5%) patients were sputum smear positive. WHO symptom screening had high sensitivity (92%) but low specificity (15%) for detecting culture-confirmed cases. Despite thorough clinical screening, 29/59 (49%) culture-confirmed cases were initially missed. Of culture-confirmed cases, 55 (93%) had positive sputum culture; blood and urine culture identified 1 and 2 additional cases respectively.

**Conclusions:** TB prevalence in Zambian patients enrolling into HIV care is among the highest in the world. A substantial proportion of culture confirmed cases were asymptomatic. This has significant implications for resource allocation and underscores the need for more sensitive and affordable TB diagnostics. In this population revised guidelines to include universal TB screening should be considered.

#### OP-111-15 Feasibility and acceptability of in-home, rapid HIV testing among contacts of tuberculosis patients in Lima, Peru

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**Background and challenges to implementation:** As part of a large, population-based TB epidemiology study in Lima, Peru we replaced traditional lab-based HIV testing with rapid HIV testing/results delivery conducted in TB contacts' homes. The change was implemented in order to enhance care by providing patients with same-day results as well as to reduce costs associated with lab-based HIV testing, specimen transport and subsequent results delivery. Because rapid, in-home HIV testing of TB contacts in Lima had never been conducted previously on a large scale, the feasibility and acceptability of the approach were unknown.

**Intervention or response:** In August 2011, study staff was trained to conduct rapid, in-home HIV testing using the Determine<sup>®</sup> HIV 1/2 Ag/Ac Combo test of all household contacts of TB index cases. Specific

procedures were developed to guide staff in the use of the test in household settings, particularly with regards to posttest counseling, results disclosure, and confidentiality issues.

**Results and lessons learnt:** As of April 2012, 3818 in-home, rapid HIV tests were conducted among consenting TB contacts. HIV prevalence was 0.34%, (13/3818). P24 antigen was detected in 5/13 (38%) of the positive cases, indicative of recent infection. Delay for results delivery decreased from >4 weeks for the lab-based procedure to 20 minutes with the in-home, rapid test. Refusal rates for HIV testing were similar for both rapid and lab-based testing. Additionally, an estimated US\$25 000 was saved by switching procedures due to reduced test, labor and transportation costs.

**Conclusions and key recommendations:** In-home, rapid HIV testing of TB contacts in Lima, Peru is feasible, acceptable, efficient and cost-effective. Importantly, persons testing HIV-positive can begin TB-prophylaxis and HIV care in days rather than weeks, particularly in the case of early infections. This approach holds promise in both research and service applications.

#### OP-112-15 Pilot of provider-initiated HIV testing and counselling among tuberculosis suspects in the state of Karnataka, India

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**Background:** Research from India in 2010 demonstrated an HIV prevalence of 7–10% among persons referred for diagnostic sputum microscopy (TB suspects), and offered the potential to increase HIV case finding by 35–50%. The effectiveness of PITC was recognized to depend on the testing uptake. To inform national policy, we piloted the policy of HIV testing of TB suspects in the South Indian state of Karnataka (population 61 million) to assess HIV testing uptake under large-scale routine operational conditions.

**Intervention:** TB suspects attending microscopy centre for smear examination were ascertained for HIV status by the laboratory technician (LT); those with unknown HIV status were referred to the nearest HIV testing centre. Programme records were modified and HIV results captured in routine registers. LTs and HIV counsellors were trained on the new policy and use of modified records. We reviewed the monthly reports for January to March 2012 and describe the initial results.

**Results:** Of 640 microscopy centres, 638 (99%) reported for every month during the pilot period. 568/640 (88%) of microscopy centres had co-located HIV testing facilities. Of 123 273 TB suspects examined for smear microscopy, 67 783 (55%) were ascertained for HIV status and ranged from 0% to 100% across microscopy centres. Among TB suspects whose HIV status was ascertained, 7129 (11%) were HIV positive.

**Conclusion:** This is first large scale deployment of routine HIV testing of TB suspects; under routine programme conditions, all microscopy centres implemented and reported on the activity, and in the first 3 months of implementation, a majority of TB suspects had their HIV status ascertained. The policy of HIV testing of TB patients is feasible, and should be deployed nationwide as an intervention for early and improved HIV case finding in high HIV settings. Further evaluation is underway to understand the reasons for the relatively low levels for HIV testing in some microscopy centres.

#### OP-113-15 Role of physical exam as an adjunct to World Health Organization symptom screening in HIV-infected persons

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**Background:** Zambia's scale-up of HIV treatment programs has greatly increased the number of patients needing TB screening, but reliable diagnostic tools are extremely limited. As more sensitive but costly tools like the Xpert<sup>®</sup> MTB/RIF assay become available there is an urgent need for improved clinical screening criteria to identify who should undergo laboratory-based testing.

**Design/methods:** We screened HIV-care enrollees for TB using symptoms, physical exam, chest radiography (CXR), LED fluorescence microscopy, sputum, blood and urine culture. Multivariable logistic regression identified characteristics independently associated with culture-confirmed TB. Sensitivity, specificity, positive and negative predictive values (PPV, NPV) were calculated for screening characteristics. We also compared use of abnormal pulmonary findings to CXR in screening combinations.

**Results:** Fifty-five of 285 (19%) patients had previously undiagnosed culture-confirmed TB. Factors most strongly associated with TB were: abnormal pulmonary findings; pulse greater than 100 beats/minute; recent exposure to a TB patient; and current night sweats or loss of appetite. The Table presents selected screening combinations. When abnormal pulmonary

findings were replaced by CXR in these combinations, sensitivity and specificity changed by only 1–2%.

Screening criteria	Sensitivity %	Specificity %	PPV %	NPV %	Patients with criteria %
World Health Organization symptom criteria: any cough, fever, weight loss or night sweats	93	15	18	89	87
Any 2 of: abnormal pulmonary exam, pulse > 100, night sweats, loss of appetite, or recent TB exposure	87	63	36	95	46
Any 1 of: abnormal pulmonary exam, pulse > 100, or loss of appetite	95	53	33	98	56

**Conclusion and recommendations:** Pulmonary exam and pulse are simple, inexpensive procedures that could greatly increase the accuracy of TB screening. These factors should be evaluated in other populations.

#### OP-114-15 Household chart, a useful tool for improving tuberculosis and HIV case finding among other medical conditions at the community level in rural Malawi

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**Background:** Abwenzi Pa Za Umoyo (APZU), the sister organization of Partners In Health (PIH) in Malawi works intensely to get closer to the community members and address their health care needs. APZU has launched the household chart (HHC) project in order to address the health problem of the poor in rural Malawi targeting the Millennium Development Goals (MDGs) 4, 5, 6.

**Methods:** We use a simple paper-based tool, the Household Chart, with the help of Community Health Workers (CHWs) to collect data at the household level. Data are collected during the first two weeks every month by CHWs and aggregated by site supervisors and the following week the data are entered into an access database to generate a report which is sent to clinical team for follow-up and action. The CHWs refer and accompany to the health facilities the clients who need medical attention.

**Results:** In one site, 1159 households have been visited, 41 coughers identified from August 2011 through Jan 2012. About 56% (23) were accompanied to HC by CHWs. Approximately 44% were referred, not

accompanied, and received health care services. Among them 26.8% (11) submitted sputum. Among those who submitted sputum 17% (7) had smear positive TB and were put on TB treatment. About 46% (19) were tested for HIV and 31% (6) of them were HIV positive.

**Conclusion:** The HHC can significantly improve TB and HIV active case finding at the community level in a rural setting.

#### PREVENTIVE THERAPY, POPULATIONS AND PHARMACOKINETICS: SPECIAL ISSUES IN TB-HIV

##### OP-115-15 Factors associated with non-completion of isoniazid preventive therapy in HIV-infected patients in Cape Town

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**Background and challenges:** TB incidence in South Africa remains high despite high rates of successful treatment suggesting ongoing transmission and a large reservoir of latently infected persons. Isoniazid preventive therapy (IPT) is recommended as preventive therapy in HIV-infected persons. However, implementation has been slow, impeded by barriers and challenges including the fear of non-adherence. The aim was to measure IPT completion rates within a research setting and to evaluate predictors of IPT non-completion.

**Intervention:** As part of a larger study, we recruited 164 antiretroviral therapy (ART)-naïve HIV-infected adults from Khayelitsha day hospital. All underwent TB screening to exclude active disease prior to initiation of 6 months IPT with monthly follow-up visits. Adherence was encouraged initially during monthly visits only and subsequently using telephonic reminders or home visits.

**Results:** The overall completion rate was 69%. In multivariable analysis, self-reported alcohol drinkers (OR 4.05; 95%CI 1.89–9.06) had a 4-fold higher risk of non-completion, with a strong association between alcohol drinkers and smoking ( $\chi^2$  27.08;  $P < 0.001$ ). There was a 29% decrease in risk of non-completion for every year after HIV diagnosis (OR 0.81; 95%CI 0.68–0.98). Adherence improved from 42% to 75% when telephonic reminders and home visits were used.

**Conclusions and recommendations:** We identify patients with a recent HIV diagnosis and self-reported alcohol drinking and smoking as being risk factors for non-completion of IPT, suggesting these groups should be identified and targeted for adherence interventions. Our results also suggest that interventions to improve adherence should be considered when implementing IPT on a wider scale.

**OP-116-15 One patient, many systems: surveillance of persons co-infected with tuberculosis and HIV, Western Cape, South Africa, 2011**

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**Background:** South Africa has one of the highest tuberculosis (TB) burdens in the world and over half of patients diagnosed with TB are co-infected with HIV. To evaluate the integration of TB and HIV surveillance systems, we compared data completeness and concordance of TB and HIV-related variables in the Western Cape.

**Design/methods:** We reviewed the records of TB-HIV co-infected patients who had started antiretroviral therapy (ART) and received TB treatment during January–August 2011 in the Eden District of the Western Cape. Completeness was evaluated by calculating the proportion of records with a non-missing value for demographic and clinical variables from 6 sources: paper-based TB and HIV patient files, a paper-based TB register, electronic TB and HIV registers, and an integrated electronic database established by the THAT'SIT program. We then used Fleiss' kappa coefficient to evaluate data concordance across sources.

**Results:** Records were available in all 6 sources for 164 (85%) of 193 co-infected patients. Among available records, the completeness of variables differed across sources and ranged from 98%–100% for sex, to 48%–100% for TB treatment regimen, and 27%–100% for whether a patient was receiving cotrimoxazole preventive therapy. Of the TB records, 13%–66% indicated an ART start date; of HIV patient files, 87% indicated a TB treatment start date, and none of the electronic HIV register entries indicated a TB treatment start date. Overall, kappa was 0.94 for sex, 0.78 for TB treatment regimen, and –0.06 for receipt of cotrimoxazole preventive therapy.

**Conclusions and recommendations:** Variable levels of completeness and concordance of surveillance data for TB-HIV co-infected patients highlight challenges in the current TB and HIV surveillance systems. Any future integration of TB and HIV programs will need to support more accurate data collection at all levels.

**OP-117-15 HIV testing and counselling, CPT and ART uptake among TB-HIV co-infected patients under routine programme conditions: ten years experience from Malawi**

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**Background and challenges:** Malawi is one of the countries in sub-Saharan Africa severely affected by the HIV-epidemic. This has resulted in a dramatic rise in number of TB notifications, fall in treatment success rates and rise in mortality rates. In 2000, a national HIV-prevalence survey amongst TB patients showed 77% co-infection rate.

**Interventions:** In 2002, Malawi developed the first three-year TB-HIV development plan for implementation of collaborative TB-HIV activities. Key activities included routine HIV-testing and counselling (HTC) for TB patients and provision of co-trimoxazole preventive therapy (CPT) and antiretroviral therapy (ART) for HIV-infected TB patients. National guidelines were developed that included how the package was to be administered. HTC and CPT registers were developed for monitoring and evaluation. In addition, a focal point person at national level of the TB Programme was appointed; and a national TB-HIV technical working group was also established. ART services have been available in public facilities since 2004. In 2007, TB registers and treatment cards were revised to incorporate data on HTC, CPT and ART.

**Results and lessons learnt:** HTC and CPT uptake increased over the years (2004 to 2007) above 85% and 90% respectively. ART uptake increased significantly, but was still below 55% due to implementation challenges. Treatment success rates increased with concomitant decrease in mortality rates (see Table).

**Table** Treatment outcomes, HIV testing and provision of CPT and ART among TB patients in Malawi (2001–2010)

Year	No. of TB patients evaluated (all forms)	Treatment success rate	Mortality rate	% of TB patients with known HIV status	% of TB patients tested HIV+	% of TB/HIV patients on CPT	% of TB/HIV patients on ART
2001	24 707	64	31	8	77	0	0
2002	24 439	66	31	8	77	0	0
2003	25 549	72	27	14	77	87	0
2004	24 392	72	27	25	72	97	0
2005	25 036	75	23	45	69	96	8
2006	24 242	80	17	65	70	93	19
2007	24 446	83	14	86	72	89	17
2008	23 406	85	12	94	63	96	43
2009	22 989	85	12	86	64	94	45
2010	20 739	85	12	88	63	94	54

**Conclusions and key recommendations:** Collaborative TB-HIV activities have significantly contributed to TB treatment outcomes in Malawi. Efforts should

be made to strengthen these activities at all levels, especially access to ART services through screening TB patients for HIV-infection at TB sites.

### OP-118-15 Efavirenz 600 mg daily co-administered with rifampicin in HIV-infected adults with body weight $\geq 50$ kg

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**Background:** WHO recommends 600 mg efavirenz daily in HIV-infected adults receiving rifampicin for tuberculosis. However, concerns that rifampicin co-administration might lead to sub-therapeutic efavirenz plasma concentrations have been raised. Recently, U.S. Food and Drug Administration recommended an increased daily dose of 800 mg efavirenz in patients  $\geq 50$  kg. Here, we report efavirenz plasma concentrations in patients treated for tuberculosis in the CAMELIA trial (Blanc et al., NEJM 2011;365:1471–81) with a body weight (BW)  $<$  or  $\geq 50$  kg at antiretroviral treatment (ART) initiation.

**Methods:** Patients received a 6-month tuberculosis regimen including rifampicin and D4T+3TC with daily efavirenz 600 mg, irrespective of BW. Treatment was initiated 2 or 8 weeks after tuberculosis treatment onset. Efavirenz plasma concentrations were assessed 6 weeks after ART initiation in blood samples drawn  $4 \pm 2$  h after drug intake, and assayed by liquid chromatography.

**Results:** We measured efavirenz plasma concentrations in 482 Cambodian adults, including 150 individuals with a BW  $\geq 50$  kg. The median (interquartile range) efavirenz concentration in patients with a BW  $< 50$  kg or  $\geq 50$  kg was within the therapeutic range (1000–4000 ng/ml): 2859 ng/ml (1787–4749) and 2060 ng/ml (1425–3575), respectively ( $P = 0.02$ ). Twenty and 15 patients with a BW  $< 50$  kg or  $\geq 50$  kg, respectively, had efavirenz plasma concentrations  $< 1000$  ng/ml ( $P = 0.12$ ).

**Conclusion:** Adults weighing  $\geq 50$  kg receiving 600 mg efavirenz daily concomitantly with rifampicin had efavirenz plasma concentrations in the therapeutic range in 90% of cases with no significant difference in sub-therapeutic concentrations compared to  $< 50$  kg patients although they had lower efavirenz plasma concentrations.

### OP-119-15 Pharmacokinetics of rifampicin and isoniazid in TB-HIV co-infected patients on nevirapine- or efavirenz-based antiretroviral treatment (ANRS12214)

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**Background:** Despite common co-administration of tuberculosis (TB) drugs and antiretroviral therapy (ART), there are few pharmacokinetic (PK) data of rifampin (R)/isoniazid (H) in HIV-TB co-infected patients. We estimated R/H PK parameters at steady state before and four weeks after ART initiation in 39 patients enrolled in the CARINEMO-ANRS 12146 clinical trial.

**Design/methods:** 22 and 17 patients randomized to NVP (400 mg, without leading dose) or EFV (600 mg)-based ART regimen between 4 and 6 weeks after starting TB treatment, respectively were included. R and H daily doses were 10 and 5 mg/kg respectively. Blood samples were collected before and 0.5, 1, 1.5, 2, 4, 6, 8, 10, and 12 hours after R/H morning administration. R and H were analyzed in plasma with validated HPLC assay. Model independent PK parameters were calculated as follows: maximal and C2h post-dosing ( $C_{max}$  and  $C_2$ ), time to  $C_{max}$  ( $T_{max}$ ) were experimental value; AUC was calculated during a 12h or 24h interval post-dosing for H or R respectively. Data are means  $\pm$  standard deviation. Geometric mean ratios of  $C_{max}$  and AUC on over off ART and 90% confidence interval were constructed for statistical comparisons.

**Results:** Patients (59% males) were  $35 \pm 7$  years old. Characteristics at inclusion were weight  $52 \pm 8$  kg, CD4  $98 \pm 58$  cells/ $\mu$ L and HIV-RNA  $5.5 \pm 0.6$  log. PK parameters are summarized in the Table below. There were no statistically differences in exposure whether R or H were administered alone or with ART.

ART	R				H			
	None	+NVP	None	+EFV	None	+NVP	None	+EFV
$C_2$ -mg/L	6.34 $\pm 3.37$	8.71 $\pm 4.56$	5.39 $\pm 3.01$	5.12 $\pm 3.44$	3.55 $\pm 1.24$	3.49 $\pm 1.50$	4.57 $\pm 1.82$	3.13 $\pm 1.70$
$C_{max}$ -mg/L	7.27 $\pm 3.33$	9.68 $\pm 4.77$	7.23 $\pm 3.03$	6.89 $\pm 3.05$	4.88 $\pm 1.75$	6.13 $\pm 2.0$	5.71 $\pm 2.31$	5.52 $\pm 3.14$
$T_{max}$ -h	2.10 $\pm 0.98$	1.97 $\pm 1.09$	2.22 $\pm 0.93$	2.25 $\pm 1.66$	1.35 $\pm 1.00$	0.89 $\pm 0.57$	1.59 $\pm 0.75$	0.97 $\pm 0.62$
AUC-mg.h/l	34.9 $\pm 23.4$	41.2 $\pm 18.6$	30.6 $\pm 14.5$	28.0 $\pm 12.7$	20.9 $\pm 9.3$	21.6 $\pm 9.0$	24.8 $\pm 12.4$	18.8 $\pm 8.8$

**Conclusion and recommendations:** PK parameters of R and H remained unchanged when co-administered with ART, but  $C_2$  are lower than expected in this even in severely immunocompromised patients.

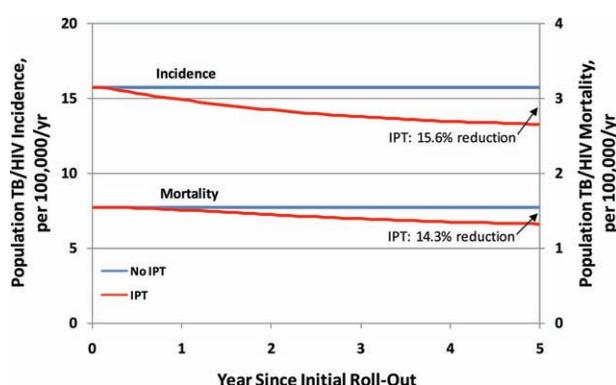
### OP-120-15 Modeling the population-level impact of isoniazid preventive therapy for HIV-infected Brazilian adults

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**Background:** Isoniazid preventive therapy (IPT) is recommended for people living with HIV/AIDS who test positive for latent tuberculosis infection (LTBI), but the potential population-level impact of reasonable IPT strategies remains unknown.

**Design/methods:** We used data from a cluster-randomized trial of IPT among HIV clinics (the TB-HIV in Rio [THRio] study) to estimate a feasible rate of population-wide IPT roll-out among HIV-infected adults in Rio de Janeiro, Brazil. We then constructed a steady-state transmission model by fitting 11 epidemiological parameters (e.g., TB-HIV incidence) to within 1% of their surveillance values. We modeled delivery of IPT under Brazilian policy (6 months of therapy in HIV-infected adults with LTBI and no prior IPT) to a constant annual proportion of the city's eligible population. We estimated the population-level reduction in TB incidence after 5 years and compared this estimate to the individual-level results from the trial.

**Results:** Empiric data from the trial fit an exponential curve well, suggesting that IPT could be delivered to 25% of the city's eligible population every year. After five years, IPT delivered at this rate had reduced TB incidence among HIV-infected adults by an estimated 15.6% (95% simulation interval, SI: 15.4%, 36.5%), with TB mortality falling by 14.3% (95% SI: 14.3%, 33.7%) (Figure). Since our conservative baseline scenario assumed the maximum allowable proportion of TB from recent infection (versus reacti-



**Figure** Five-year impact of IPT on TB incidence and mortality.

vation), a doubling of the estimated impact of IPT remained reasonable in sensitivity and uncertainty analysis. If scaled up to the entire HIV-infected population of Brazil, IPT could save between 1000 and 2000 lives within five years.

**Conclusions:** In addition to its individual-level impact as demonstrated in the THRio study, IPT—delivered at a feasible rate—has the potential to produce substantial population-level impact on the TB-HIV epidemic in moderate-burden settings.

### OP-121-15 Population-based outcomes of HIV-TB co-infections in the UK

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**Background:** Globally, HIV and tuberculosis (TB) co-infections are an important cause of morbidity and mortality. Between 2000 and 2010, 6.8% of TB patients were diagnosed as HIV co-infected in the UK. Survival is usually analysed in trials, but observed survival is important for policy development, and there is scarce evidence in the UK. The aim of the study is to analyse the survival of persons diagnosed with HIV in the UK, with particular emphasis on late HIV diagnosis and TB co-infection.

**Methodology:** We present a retrospective cohort study based on data linkage between the national HIV and TB surveillance databases. Including persons diagnosed with HIV between 2000 and 2008 in the UK and within-cohort deaths until mid-2010, we analysed survival rates by calculating hazard ratios (HR) using Cox regression modelling.

**Results:** A total of 44 175 HIV-diagnosed persons with a cohort time of 149 963 person-years were enrolled in the study. About 2909 (6.59%) had TB co-infection and 15 165 (34.33%) were diagnosed with a CD4 count of 200 or less (late HIV diagnoses). Average survival after HIV diagnosis was 2.2 years (range 0.03–10.3) for non co-infected and 1.8 (0.08–10.1) years for co-infected patients. Cox regression indicated that overall survival is significantly affected by TB-HIV co-infection (HR 2.48, 95%CI 1.66–3.71), late diagnosis (HR 2.56, 95%CI 2.24–2.91) and inappropriate anti-retroviral therapy (ART) interruption (HR 2.94, 95%CI 2.61–3.32) after adjusting for age, sex, country of birth and likely route of HIV exposure. There was no significant interaction between TB co-infection and late diagnosis.

**Conclusion:** Our study confirms that decreased survival rates amongst HIV patients were independently affected by co-infection, late HIV diagnosis and ART interruption. Important policy lessons learnt from the study include the need to raise awareness, encouraging TB case-finding in HIV patients, considering earlier TB treatment initiation and increasing adherence to ART.

## PNEUMONIA IN ADULTS AND CHILDREN: PREVENTING DEATHS

### OP-122-15 Pulmonary tuberculosis and inadequate anti-tuberculosis treatment are important risk factors of chronic obstructive pulmonary disease

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**Background:** Tuberculosis (TB) remains the leading cause of death among infectious diseases worldwide and has been suggested as an important risk factor of chronic obstructive pulmonary disease (COPD), also a major cause of morbidity and mortality. We investigated the impact of pulmonary TB as well as anti-tuberculous treatment on the risk for developing COPD.

**Design/methods:** We did a cohort study using the national health insurance database of Taiwan. From the Longitudinal Health Insurance Database 2005 in Taiwan, 4074 pulmonary TB cases and 20370 control subjects matched in age, sex, and timing of entering the database were selected. We investigated the hazard ratios of potential risk factors of COPD, especially pulmonary TB and anti-tuberculous treatment. **Results:** The mean age of pulmonary TB cases was  $52.8 \pm 19.6$ . The interval between TB start date and commencement of anti-tuberculous treatment (delay in anti-tuberculous treatment) was  $72.2 \pm 65.0$  days. Among the TB cases and control subjects, age, male, low income, and history of pulmonary TB (hazard ratio 1.924 [1.688, 2.193]) were independent risk factors for developing COPD, while diabetes mellitus was protective. The impact of TB sustained for 6 years after TB diagnosis. Among TB patients, delay in anti-tuberculous treatment and the days covered by isoniazid during intensive phase had a dose-response relationship with the risk of developing COPD.

**Conclusion and recommendations:** Some cases of COPD maybe preventable by controlling the TB epidemic, early diagnosis of TB and prompt initiation of appropriate anti-tuberculous treatment. In addition, follow-up care and early intervention for COPD may be necessary for treated TB patients.

### OP-123-15 Hypoxemia prevalence and the quality of oxygen provision in hospitalised children in an HIV-endemic African country: a multicenter study

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**Background:** To determine the prevalence of hypoxemia and the quality of oxygen treatment by local clinicians for hospitalized Malawian children.

**Design/methods:** We prospectively studied 761 pediatric admissions at 5 Malawian hospitals. Study personnel determined the quality of oxygen treatment administered by Malawian clinicians by comparing their application of World Health Organization clinical eligibility criteria for oxygen treatment (WHO-criteria) to two standards: hypoxemia defined by pulse oximetry ( $SpO_2 < 90\%$ ) and WHO-criteria as applied by experienced study staff.

**Results:** We found that 5.3% of hospitalized children had  $SpO_2 < 90\%$ . Compared to children with non-respiratory diagnoses, patients with primary respiratory diagnoses had a lower median  $SpO_2$  (96.5% vs. 99.0%,  $P < 0.001$ ) and more had  $SpO_2 < 90\%$  (17.0% vs. 2.2%,  $P < 0.001$ ). Patients with  $SpO_2 < 90\%$  were younger, and more had cough, difficulty breathing, tachypnea, chest indrawing, nasal flaring, lethargy, and malnutrition than children with  $SpO_2 \geq 90\%$ . No hospitals used oximetry routinely. Accordingly, only 9 (22.5%) patients with  $SpO_2 < 90\%$  were correctly prescribed oxygen by hospital staff. WHO-criteria, when applied by study personnel, identified almost seven-times more children (35.0%) as eligible for oxygen compared to oximetry (5.3%). Furthermore, study personnel using WHO-criteria achieved a higher sensitivity (91.4%) and lower specificity (61.0%) for oxygen eligibility than Malawian clinicians (sensitivity 25.7%, specificity 94.0%).

**Conclusion and recommendations:** Although hypoxemia is common, the absence of oximetry screening results in most hospitalized Malawian children with hypoxemia not receiving oxygen. Thus, we recommend routine oximetry screening at hospital admission and longitudinal training of local clinicians as integral to reducing hypoxemia-related child morbidity in resource-constrained settings.

### OP-124-15 A prospective study on clinical and radiological resolution of community acquired pneumonia

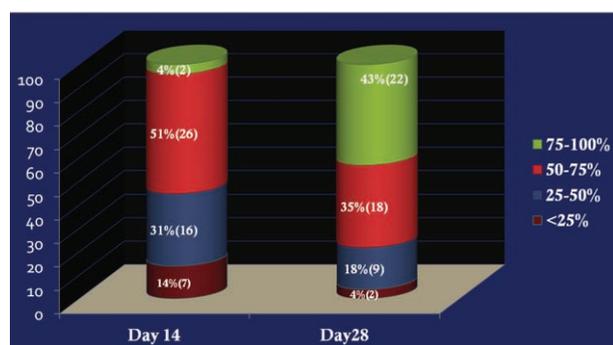
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**Background:** Despite exhaustive literature on community-acquired pneumonia (CAP), studies assessing the rates of clinical and radiographic resolution among these patients are limited.

**Aim:** To study the duration for clinical and radiological resolution of community acquired pneumonia and the factors leading on to delay in resolution.

**Design/methods:** A prospective observational clinical study conducted in the Department of Pulmonary Medicine during the period of one year from August 2009. The severity of symptoms in patients with CAP were recorded through structured questionnaires at 0, 3, 7, and 14 days of treatment and the scores tabulated. Serial chest radiographs taken at baseline and on days 7, 14, and 28. Radiographs were reviewed in sequence and the pattern and extent of opacities evaluated. Extent of opacity in the follow up X-rays were compared with the baseline film. Kappa statistics used to measure interobserver agreement on radiological clearance.  $\chi^2$  test was used to analyze qualitative variables. Quantitative variables between groups were compared using ANOVA and *t*-test.

**Results:** Of the total 51 patients, 46 (90%) were males. Clinical resolution occurred in 75% of patients at two weeks. Radiological resolution occurred in 43% by the end of 4 weeks and 78% at the end of 8 weeks. Females and those aged more than 60 years showed delay in resolution. Longer duration of symptoms prior to diagnosis and those with multilobar involvement showed delay in resolution.



**Figure** Radiological resolution. Interobserver agreement- kappa -0.723.

**Conclusion and recommendations:** Majority (75%) showed clinical resolution within a period of two weeks. Radiological resolution occurred in 43% at four weeks and in 78% at 8 weeks. Female sex, advanced age, longer duration of symptoms prior to diagnosis and multilobar involvement were associ-

ated with delay in resolution. Once clinical resolution has occurred, a delay in radiological resolution beyond 4 weeks doesn't require concern especially in resource limited settings.

### OP-125-15 Impact of concomitant pulmonary tuberculosis in treatment outcomes of hospitalized community-acquired pneumonia patients in Taiwan

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**Background and challenges to implementation:** Pulmonary tuberculosis (PTB) is an important infectious disease associated with high mortality and morbidity. In TB endemic areas, *Mycobacterium tuberculosis* is an important in community-acquired pneumonia (CAP). The impact of concomitant PTB in treatment outcome of CAP deserves investigation.

**Intervention or response:** This nationwide retrospective study recruited hospitalized CAP patients from six medical centers in Taiwan from January 2007 through December 2007. Concomitant PTB were defined as PTB diagnosed within 60 days of admission. The predictors for concomitant PTB and the impact of PTB in treatment outcome were investigated.

**Results and lessons learnt:** During the study period, a total of 934 hospitalized CAP patients were included in this study. The occurrence of concomitant PTB was 2.7% (25/934). Patients with concomitant PTB were more likely to have previous anti-TB treatment (16% vs. 5%,  $P = 0.015$ ), have malignancy (20% vs. 8.1%,  $P = 0.036$ ), and have higher PSI scores ( $140.3 \pm 36.1$  vs.  $126.1 \pm 31.5$ ,  $P = 0.033$ ). In multivariate analysis, previous anti-TB treatment (OR: 3.33, 95%CI: 1.09–10.22) and higher PSI score (OR: 1.013, 95%CI: 1.001–1.026) were independent predictors for occurrence of concomitant PTB. Regarding treatment outcomes, hospitalized CAP patients with concomitant PTB were associated with higher probability of ICU admission (44% vs. 19.7%,  $P = 0.003$ ) and longer length of hospital stay ( $32 \pm 27.4$  days vs.  $19 \pm 20.3$  days,  $P = 0.002$ ). Trend of higher in-hospital mortality ( $P = 0.06$ ) was also found in patients with concomitant PTB.

**Conclusions and key recommendations:** Concomitant PTB is not rare in hospitalized CAP patient and associated with worse treatment outcomes.

### OP-126-15 Validation of a new index to predict mortality from community-acquired pneumonia in Malawi: the SWAT-BP score

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**Background:** Community-acquired pneumonia (CAP) is an important cause of mortality in populations with a high rate of HIV. Currently there is no rapid method of assessment for use on admission to hospital enabling risk stratification and treatment prioritisation. In developed countries, severity scores have proven accuracy in stratifying patients according to mortality risk, but these scores exclude patients with HIV. This study aimed to validate our recently derived score in predicting mortality from CAP in adult patients admitted to a Malawian hospital.

**Design/methods:** The five variables constituting the SWAT-Bp score (male Sex, muscle Wasting, non-Ambulatory, Temperature (>38°C or <35°C) and Blood pressure (SP < 100 and/or DP < 60)) were recorded for all patients with a clinical presentation of CAP in Queen Elizabeth Central Hospital, Blantyre, Malawi, in February and March 2011 and October to November 2011. This data was correlated with in-hospital mortality. The sensitivity and specificity of the score were calculated to determine the accuracy at predicting mortality risk.

**Results:** 210 patients were enrolled. The median age was 35 years, HIV prevalence was 84.9% and mortality was 12.9%. A SWAT-Bp cut-off score of 2 has the optimal trade-off between sensitivity (55.6%) and specificity (77.0%) for predicting mortality risk. This test shows high accuracy (AUC = 0.746). A SWAT-Bp score of ≤2 indicates a relatively low mortality risk (7.8%) whereas a score of ≥3 indicates severe pneumonia with a higher mortality risk (26.3%).

**Conclusion and recommendations:** The SWAT-Bp score is a valid tool for rapid assessment of pneumonia severity on admission to hospital in Malawi. This aids clinicians in identification of high risk patients, enabling rapid prioritisation of treatment in a low-resource setting. Additionally, it will enhance the development of specific treatment pathways and protocols for those at high and low risk of death. Prior to use in other countries in sub-Saharan Africa, further validation is required.

### OP-127-15 Effectiveness of benzyl penicillin monotherapy for treatment of severe pneumonia among Kenyan children

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**Background:** While the policy for case management of severe pneumonia appears to be shifting towards the use of oral amoxicillin in place of injectable benzyl penicillin in many countries, there is little evidence on the effectiveness of these two antibiotics for the treatment of severe pneumonia in African populations. The aim of this study was to determine the effectiveness of benzyl penicillin monotherapy for the treatment of severe pneumonia among Kenyan children as a pilot to a randomised controlled trial that would compare the standard treatment (benzyl penicillin) with oral amoxicillin.

**Design/methods:** This was a pilot study to collect observational data from a consecutive cohort of children aged 2–59 months admitted for treatment of severe pneumonia at 7 primary referral hospitals across Kenya. Raw data from the OpenClinica database were extracted and exported to Stata for cleaning and analysis. Primary outcome was treatment failure at 48 hours.

**Results:** 820 children were screened. 220 (26.8%) fulfilled the eligibility criteria. Risk of treatment failure at 48 hours was estimated at 10.0% (95%CI 6.3–14.9%). Thresholds based on pre-defined criteria

Table 1: Treatment failure overall and by hospital among HIV-unexposed and unknown status

Endpoint	Bungoma	Enbu	Kerigoya	Mbagathi	Meru	New Nyanza	Kisumu	Total
48 hours								
Recruited	32	31	32	24	12	39	39	209
Recruited with outcome data	32	31	32	24	12	38	39	208
Treatment failure, n (%)	2(6.3)	2(6.5)	3(9.4)	2(8.3)	2(16.7)	4(10.5)	6(15.4)	21 (10.1)
95% CI	(0.8 - 20.8)	(0.8 - 21.4)	(2.0 - 25.6)	(1.0 - 27.0)	(2.1 - 48.4)	(5.3 - 30.5)	(6.4 - 15.0)	
Day 5/ discharge								
Recruited	32	31	32	24	12	39	39	209
Recruited with outcome data	32	31	32	24	11	38	39	207
Treatment failure, n (%)	2(6.3)	2(6.5)	3(9.4)	2(8.3)	3(27.3)	4(10.5)	9(23.1)	25 (11.9)
95% CI	(0.8 - 20.8)	(0.8 - 21.4)	(2.0 - 25.6)	(1.0 - 27.0)	(5.0 - 61.0)	(5.3 - 30.3)	(11.1 - 39.3)	(6.0-27.2)
Day 14								
Recruited	32	31	32	24	12	39	39	209
Recruited with outcome data	27	26	29	23	10	34	34	183
Treatment failure, n (%)	2(7.4)	2(7.8)	4(13.8)	2(8.7)	3(30.0)	4(11.8)	9(26.5)	27 (14.8)
95% CI	(0.9 - 24.1)	(0.9 - 25.1)	(3.9 - 31.7)	(1.1 - 28.0)	(6.7 - 65.2)	(11.1 - 27.5)	(12.9 - 44.4)	(10.0-20.7)

95% CIs are exact binomial confidence intervals around failure in the complete-case analysis, population (children with known outcome status at each time point).

were applied to the results of the pilot data to inform the feasibility of proceeding with the main trial (Treatment failure lower limit of 95%CI < 14% would proceed to intervention phase; lower limit of 95%CI  $\geq$  20% terminate trial).

**Conclusion and recommendations:** We conducted a three-month pilot study to establish the feasibility of conducting a randomised controlled trial at 7 hospitals across Kenya to investigate the effectiveness of amoxicillin versus benzyl penicillin for severe childhood pneumonia. All pre-defined thresholds for progressing to the trial phase of the study were achieved. Our findings suggest that benzyl penicillin monotherapy remains an effective treatment for severe pneumonia in the population studied. The main trial is currently on going at 6 selected sites. Results could potentially influence local policy towards use of oral amoxicillin for treatment of severe pneumonia in children.

#### OP-128-15 High mortality among adults presenting with pneumonia in Botswana

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**Background:** Pneumonia is a leading cause for admission to our referral center in Gaborone, Botswana, where HIV prevalence is an estimated 17.6%. Advanced HIV (defined as a CD4 count < 200 cells/ $\mu$ l) is a known risk factor for pneumonia. The prevalence of HIV among pneumonia cases is unknown after the rollout of Botswana's national antiretroviral therapy (ART) program in 2002. We describe HIV status and mortality for all adults presenting with pneumonia in our setting.

**Design/methods** We performed a retrospective chart review from April 2010 to December 2011 to identify adults  $\geq$  18 yrs with a diagnosis of pneumonia. We reviewed admissions to the Emergency Department and electronic medical records. The CD4 count closest to the time of presentation was accepted within one year prior or six months after presentation if ART was not initiated. Mortality data were collected from The Department of Civil and National Registration. We calculated pneumonia severity per IDSA-ATS criteria. Proportions were compared using the  $\chi^2$  test at the 95% confidence level.

**Results:** Of 1587 encounters identified with pneumonia, HIV status was positive for 62%, negative for 10%, and unknown for 28%. Among HIV+ cases, CD4 counts were available for 38%, and the median

CD4 count was 170 cells/ $\mu$ l. Stratifying by HIV status, we found no significant difference in pneumonia severity (HIV+: 8%; HIV-: 5%,  $P = 0.26$ ) or 30-day mortality (HIV+: 27%; HIV-: 20%,  $P = 0.09$ ). Of those eligible by national guidelines, 44% were on ART, and there was no significant difference in 30-day mortality based on ART status (On ART: 27%; Not on ART: 27%,  $P = 0.85$ ).

**Conclusion and recommendations:** Ten years after widespread implementation of a national ART program, a high proportion of pneumonia patients present with underlying advanced HIV disease. Mortality is high for all patients regardless of HIV status or ART, highlighting the importance of current efforts in Botswana to improve processes of care and understand the microbiologic causes of pneumonia.

#### OP-129-15 Respiratory symptoms and tuberculosis among HIV-positive children receiving care and treatment in Central Africa

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**Background:** Data describing respiratory symptoms and tuberculosis (TB) among children receiving HIV care in central Africa are limited.

**Design/Methods:** Data were obtained from a cohort study of 476 HIV+ children at 4 HIV treatment programs in Burundi, Cameroon and the Democratic Republic of Congo as part of the International Epidemiologic Databases to Evaluate AIDS (IeDEA). We examined respiratory and TB-related symptoms by antiretroviral therapy status (ARV+ vs. ARV-) at enrollment into the IeDEA database ( $n = 465$ ) and at <6 months ( $n = 233$ ), 6-11.9 months ( $n = 170$ ), and 12+ months ( $n = 123$ ).

**Results:** A larger proportion of ARV+ children as compared to ARV-children were classified as WHO clinical stage 3/4 at enrollment (67% vs. 51%) and during follow-up (64% vs. 45%, 63% vs. 32%, and 43% vs. 33%). History of pneumonia was reported among a larger proportion of ARV+ children at enrollment (32% vs. 28%) and during the first two follow-up periods (31% vs. 19%, 43% vs. 27%) and was approximately 30% for both groups at 12+ months. A larger proportion of ARV-children had symptoms such as wheezing, rales, and crepitations at baseline (21% vs. 4%), 6-11.9 months (18% vs. 13%) and 12+ months (33% vs. 18%) though the proportion was similar at <6 months (12% vs. 13%). Review of 72 chest X-rays at enrollment/follow-up revealed: pleural effusion ( $n = 5$ ), infiltrates ( $n = 12$ ),

diffusion (non-military  $n = 9$ ), cavitations ( $n = 1$ ). 23 children completed TB treatment before inclusion in the study and an additional 19 received TB treatment during the study. There were 20 reports of children in contact with family members on TB treatment at enrollment. Two children were placed on isoniazid prophylaxis during follow-up.

**Conclusion and recommendations:** Respiratory symptoms and TB are frequent in this cohort though TB may have been underestimated. Lung function tests are needed to better understand the underlying cause of chronic respiratory symptoms. Few children received TB prophylaxis.

## MONEY, MEETINGS AND TRAINING: BEST PRACTICES TO IMPROVE TUBERCULOSIS CARE

### OP-130-15 Identifying the contribution of community health workers to the treatment outcome of tuberculosis patients in four provinces of Afghanistan, 2010

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**Background:** Challenge in Afghanistan was poor treatment outcome for TB patients. In 2009, USAID supported TB CAP project launched community based DOTS that continued under TB CARE I in four provinces (Jowzjan, Hirat, Baghlan and Badakshan). This study assessed impact of DOT provided by CHWs in treatment adherence among new sputum smear positive TB patients.

**Intervention:** TB CARE I trained 3000 community health workers (CHWs) on TB-suspects identification, referral for diagnosis and provision of direct observed therapy (DOT). During Jan–Feb 2012, data collection encompassed gender and outcome variables, conducted. Sample size of 4053 (CI = 95%, power = 95%, RR and OR of 1.1 and 1.7, proportion of unexposed/exposed of 3.6) taken.

**Results:** Totally, during 2010, 853 (587 females, 266 males) new TB SS+-patients took DOT from CHWs (intervention) and 3200 TB patients received DOT from health facilities (control), recruited in study. Treatment outcome analysis for intervention group shows 97.65% (833,  $P < 0.00001$ , RR = 1.1) treatment-success rate, 822 (96%) cured, 10 (1.2%) completion rate, 11 (1.2%) died, 3 (0.4%) defaulted, 3 (0.4%) failure and 4 (0.4%) transferred out. Contrarily, values for control group shows 90.7% treatment success rate, 89% cure, 1.7% completion, 2%

default, 1.8% failure, 2% death, default and transfer out rates of 4%. Treatment outcome was equally distributed from gender perspective.

**Table** Comparison of treatment outcome among new TB SS+ cases in intervention and control groups, 2010

Variable	Result of DOT from CHWs, intervention group ( $n = 853$ ) $n$ (%)	Result of outcome in at four provinces, control group ( $n = 3200$ ) $n$ (%)	Treatment outcome national level ( $n = 12\,782$ ) $n$ (%)
Treatment success rate	833 (98)	2909 (90.7)	11 624 (91)
Cure rate	822 (96.4)	2855 (89)	11 175 (87)
Completion rate	10 (1.2)	54 (1.7)	449 (4)
Death rate	9 (1.1)	57 (1.8)	257 (2)
Default rate	3 (0.4)	54 (1.7)	244 (2)
Failure to treatment rate	3 (0.4)	25 (0.8)	122 (1)
Transfer out rate	3 (0.4)	160 (5)	550 (4)

**Conclusion:** DOT provision by CHWs resulted in significant improvement in treatment success/cure rate of TB SS+ patient and led to extreme decline in deaths, default and failure rates. The treatment outcomes are higher than national figures. Therefore, we strongly recommend its scale-up to similar settings.

### OP-131-15 Improving quality and access to care for tuberculosis patients through training of nurses in Russia

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**Background and challenges to implementation:** Nurses were to be trained as instructors and leaders of other health care professionals in delivering TB care based on best practice standards to improve quality and access to health care for patients.

**Intervention or response:** ‘Train the trainer’ approach (TOT) was applied—the TOT workshops were held in 10 regions of Russia; namely Tomsk, Omsk, Syktyvkar, St Petersburg, Moscow, Stavropol, Nizhni Novgorod, Kemerovo, Chita and Ulianovsk (4 days of training pro region), each workshop participant committed to train at least 20 other health care professionals in their respective regions.

**Results and lessons learnt:** Between 2006 and 2010 the 263 nurses trained at the 10 initial TOT workshops have successfully trained 4636 health care professionals in the regional TB and primary care services. As a result:

- Nurses developed the concept and established a network of Health Schools for TB patients in Stavropol, Tomsk, Omsk, Chita and Marii El Republic

- Nurses use their own initiative to develop and publish health education materials on TB for patients and communities in Kemerovo and Omsk
- Nurses in the regions where the training has taken place use the ICN standards of care to deliver best quality care for their patients
- TB nurses who have participated in the training have got better opportunities for personal, professional and career growth
- The network of nurses has been strengthened through better communication between regional offices and RNA, TB sections have been established inside nurses' organizations
- Patient compliance and commitment to treatment is steadily getting better in Tomsk region, St Petersburg and Stavropol Krai (area).

**Conclusions and key recommendations:** Training of nurses by using TOT methodology and best practice standards in TB care and control results in the better quality and access to care through the improvements in TB treatment, case management and case-finding, as well as TB prevention, health education and advocacy.

#### OP-132-15 Providing financial incentives to rural-to-urban tuberculosis migrants in Shanghai: an intervention study

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**Background:** In China, domestic migrants have limited access to public services and social security. Economic issues are a major barrier to migrants in accessing TB care. This study aims to evaluate the effectiveness of providing financial incentives to migrant TB patients on treatment results in Shanghai, China.

**Methods:** Financial incentives were provided to migrant TB patients in the intervention district. Every migrant TB patient in the intervention district received a monthly transportation incentive of RMB10 (US\$1.6). Those who were classified as 'poor' were allocated a financial subsidiary of RMB 1000 (US\$157) at intervals throughout treatment. A comparable control district was selected where no financial incentives were provided to migrant TB patients. Questionnaire survey was conducted to investigate patient expenditures in both districts.

**Results:** 90 and 93 migrant TB patients were registered in the intervention and control districts respectively. TB treatment completion rates significantly improved by 11% (from 78% to 89%) in the intervention district, compared with 3% increase (from

73 to 76%) in the control district ( $P < 0.05$ ). Default rates had significantly reduced in the intervention district by 11% (from 22% to 11%), compared with 1% reduction (from 24 to 23%) in the control district ( $P < 0.05$ ). Compared with the control district, each percent increase in treatment completion in the intervention district cost RMB6550 (US\$1031), while each percent reduction in default rate cost RMB5240 (US\$825).

**Conclusion:** Providing financial incentives to the migrant population was effective in improving treatment completion and reducing defaults in TB treatment among migrant TB patients in Shanghai.

#### OP-133-15 Care perceptions among tuberculosis patients in Burundi

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**Background and challenges to implementation:** Burundi, an enclosed country in central Africa, is characterized by a high relief which makes the access to health facilities very difficult. The Mount Heha, at the southeast of Bujumbura, culminates to 2670 meters. Access is specifically tough for tuberculosis case finding and treatment supervision.

**Intervention or response:** A socio-anthropological survey has been led in Burundi in 2011 in order to show perceptions, knowledge, attitudes and practices about tuberculosis in TB patients and general population. Data about the accessibility to health centers (HC) and Tuberculosis Centers (TC) had been collected among a sample of 2024 people from general population and TB patients.

**Results and lessons learnt:** About 48.6% of patients were complaining about a long time waiting before care in health facilities, 22.1% about the cost, 5.5% about diagnosis delay and 4.1% about bad greeting from health practitioners. Physicians repeatedly failed to take in account tuberculosis. This ignorance often appeared in the narrations of patients and contributed to increase the delay of diagnosis or treatment. The health system delay is characterized by ineffective visits to health facilities. This is added to the 'patient

**Table** Patients who mentioned some problems in health facilities

Indicators	
Patients who mentioned problems met in health facilities when they went for care (n = 72)	%
A long time of waiting	48.6
A long distance from home to health facility	18
It is expensive	22.1
Bad welcome from health workers	4.1
Delay to the diagnosis	5.5
Need to be present every day in health facility	1.3

delay' and can last until 2 years. After announcement of tuberculosis diagnosis, 26.6% of patients were happy and 25.4% had fear. Other reactions were great surprise (8.3%), a feeling of shame (7.1%), a shock (8.3%) and discouragement (5.9%). About 24.7% of the patients had declared to have been victim of a stigmatization.

**Conclusions and key recommendations:** The delay in TB diagnosis in Burundi is increased by patient's delay and especially by the delay from health practitioners to find tuberculosis. Some measures should be adapted by the NTP to reduce TB diagnosis delay.

### OP-134-15 Pharmaceutical care service for patients with tuberculosis and diabetes mellitus in Malaysia: issues and challenges

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**Background:** The increasing comorbid burden of tuberculosis (TB) and diabetes mellitus (DM) worldwide requires the management of all stakeholders including pharmacists. This raises the question whether current single disease management system fulfils patients' health needs and whether pharmacists could effectively play a role in enhancing the joint management of these two diseases. The aims of the study were to identify the pharmaceutical care issues in patients with TB and DM and the feasibility of providing a pharmaceutical care service.

**Design/methods:** Action research was conducted in one public hospital in Malaysia. We collaborated with the hospital pharmacist to provide the pharmaceutical care service. Thirty-five patients with TB and DM participated. The source of data varied from medical records, observational notes and interviews. Ethical approval was obtained from the Ministry of Health, Research and Ethics Committee, Malaysia.

**Results:** Pharmacists were able to integrate TB and DM management by identifying, communicating and resolving some medication-related problems. Pharmaceutical care issues identified include lack of medication adherence, poor management of DM, the need to manage adverse drug reactions, and the lack of frequent monitoring of certain clinical parameters. The barriers that impinged upon the provision of service include the lack of space with privacy to provide patient counselling; the lack of time to develop inter-professional relationships; and the pharmacist's hesitation in documenting pharmaceutical care plans in the patient's medical record.

**Conclusion and recommendations:** Despite the need

to address the challenges, this study showed that pharmacists have a role to play in integrating the management of TB and DM. Enhanced collaboration among health care professionals is vital in order to achieve mutual agreement in issues related to co-management, monitoring and access to clinical information.

### OP-135-15 Developing sustainable TB-HIV management capacity through training of pre-service education teachers in Zambia

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**Background and challenges to implementation:** Over time, there have been changes in the guidelines on management of TB-HIV. Transfer of this knowledge has relied mainly on in-service training, with providers attending off site group based trainings. This is not sustainable considering the limited resources available in Zambia. Pre-service education (PSE) offers an important opportunity to develop the necessary competences in the prevention, diagnosis, and management of TB. Zambia has close to 50 PSE institutions graduating about 1500 new health workers each year. The in-service model of training providers has often excluded PSE educators resulting in them lagging behind in knowledge on new guidelines and approaches, leading to new health workers graduating without necessary competencies in TB-HIV.

**Intervention or response:** Jhpiego, worked closely with the National TB program and General Nursing Council, to develop a program to build the capacity and improve the knowledge and skills of PSE teachers, focusing on new guidelines and approaches. The training included theory, field visits and clinical practicum. 40 educators from 20 institutions participated in the training.

**Results and lessons learnt:** The knowledge and skills acquired were assessed through pre/posttest and checklists. There was overall improvement in clinical skill competences and high level of knowledge on post-test. The mean pre and post test scores were 64% and 94.4% respectively.

**Conclusions and key recommendations:** Scaling up of PSE capacity development offers potential to improving the management of TB-HIV and other programs. PSE educators are responsible for developing future generation of health workers; they should not only be engaged in training, but also policy development and implementation.

**OP-136-15 The therapeutic meeting: a community-based strategy to reinforce information, education and communication among tuberculosis patients**

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**Background and challenges to implementation:** Community Based TB Organization (CBTO) is a non-governmental organization which have provided TB and TB-HIV treatment patients support since 1995 in community, Lusaka, Zambia. We have experienced high defaulter and death rates among TB patients around 2000. Those results might have been caused by high levels of stigma, myths and misconceptions regarding TB and TB-HIV in the community, and furthermore, the patients were not adequately prepared for treatment in those circumstances. Therefore, we have initiated monthly experience sharing meetings since 2001.

**Intervention:** In the Therapeutic Meetings, every TB patient had the opportunity to learn important information about TB and treatment. We provided a platform for patients and family members to ask questions, share challenges and learn from one another thus helping to deal with stigma and the many challenges associated with TB and TB treatment on that occasion. Focus group discussion was also conducted among same gender groups.

**Results and lessons learnt:** The percentage of all TB patients attending the meeting has reached to 86% after ten years. There was an increase in involvement of relatives' participating in the meeting from 4% to 58%. Furthermore, there was a reduction in missed appointments to collect TB drugs, from 76% to 15% after we have introduced this strategy. Treatment completion rate among TB patients has also moved from 30% to 70%. The meeting also helped all attendances to create relationships among themselves, so that in case one misses out from the meeting, colleagues are able to say what had happened to their friend.

**Conclusions and key recommendations:** Peer support is essential for the patients not only in order to maintain the adherence of treatment but also to access the information and knowledge. The Therapeutic Meetings works out as sensitization channel to motivate attendances for the successful treatment outcome.

**OP-137-15 Barriers to tuberculosis control in communities with poverty and high tuberculosis incidence, regardless of high treatment success rates**

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**Background:** TB rates are high in some communities, despite high treatment success rate and free access to health services. This study explored barriers to TB control and provided recommendations to improve TB control in high impact communities.

**Design/methods:** To identify TB control barriers, discussion and in-depth structured interviews were conducted with health volunteers, community leaders and residents including TB patients of villages with high TB rates in Sisaket, Thailand. Living arrangements were observed during home visits. Data were analyzed and shared with participants.

**Results:** Participants ( $n = 170$ ) had general knowledge of TB and family incomes below poverty line. More than two third of residents had an extended family. Almost all families had a one room house where all family members including active TB patients share the room and mosquito net. Housing ventilation was poor, especially in winter when houses were sealed from the cold putting family members in greater risk of TB infection. Community residents paid frequent visits to ill neighbors including bed ridden and infectious individuals to express their consideration. In doing so, people did not use protective devices or ignore TB patients to avoid stigma. They shared eating utensils, food, drink, and close environment. Participants were aware of TB risk. However, they did not protect themselves and child accompanies in order to keep close relationship with neighbors given that there is a cure for TB with free treatment. Those with TB symptoms sought services from several health facilities as they were not confident with the quality of medical care in the district.

**Conclusion and recommendations:** The major barriers to TB control were social and cultural concerns and quality of care, whereas the least barrier was access to care. To reduce these barriers, an integrated community and socio-cultural interventions tailored to community needs should be offered. Interventions for environmental control are suggested.

**MOTHERS, MIGRANTS, MILITARY AND MORE: TUBERCULOSIS IN SPECIAL POPULATIONS**

**OP-138-15 HIV positivity in tuberculosis patients accessing care in major Nigeria military health facilities**

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**Background:** Infection with the human immunodeficiency virus (HIV) is of major public health concern worldwide especially in sub-Saharan Africa. Reports have shown a close link between HIV and

pulmonary tuberculosis. There is paucity of data regarding the point prevalence of HIV among TB patients (civilians and military) attending military facilities in Nigeria. The objective of this study was to determine the positivity rate of HIV infection among tuberculosis patients attending six military hospitals in Nigeria, supported by NMOD-DOD WRP-N over a one year period.

**Methods:** This study is a retrospective data review and analysis based on the monthly program report submitted to NMOD-EPIC and DOD WRPN. The data are based on the national and PEPFAR reported indicators for monitoring TB-HIV services in Nigeria.

**Results:** Data analysis spanning 12 months from six high volume HIV and TB care and treatment centers cutting across the Nigerian Armed Forces and the three geographical zones of the country revealed an average HIV positivity rate of 16% among TB clients (406 HIV+ from 2605 TB clients), Defense Headquarters Medical Center, Asokoro, Abuja, had the highest positivity rate of 86%, followed by 45 NAFH Makurdi with 56%, while 445 NAFH Lagos had 4%. Fifty to seventy per cent of the patients were civilians and all received appropriate anti-TB therapy and anti-retroviral therapy.

**Conclusion:** There is a high positivity rate of TB-HIV co-infection amongst the patients accessing TB care in major Nigeria military hospitals. This is in contrast to the 30% estimated TB-HIV co-infection rate reported by the national program. Further studies will need to be conducted on the impact of these findings on morbidity and mortality.

#### **OP-139-15 Southern Health Improvement Samity efforts to serve the underprivileged and difficult-to-reach tuberculosis-affected people of the islands of Sundarban**

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**Background:** The contribution of Southern Health Improvement Samity (SHIS), a premier NGO of West Bengal India and partner of India's Revised Tuberculosis Control Program (RNTCP), to provide TB services to remote islands of Sundarban Delta region at the Southern most part of West Bengal, India, as part of country's ongoing efforts of Universal TB care.

**Method:** Inhabitants of 54 islands of Sundarban have extremely limited civic amenities like electricity, education and healthcare. Boats and launches are only modes of commutation. Working in TB control since 1982, SHIS has so far covered 39 islands which are home to 2.56 million people. The unique mobile boat dispensary services of SHIS have been reaching marooned villages of the islands, spreading awareness through local folk singers, screening TB suspects through sputum microscopy and chest X-ray as per

RNTCP guidelines and providing DOTS to TB patients through local community DOTS providers. SHIS has developed a network of 943 of providers across Sundarban who, are mostly cured TB cases and received TB services from the initiative of SHIS. SHIS claimed the distinction as the only NGO in India entrusted with the task of running 7 TUs in the RNTCP program of West Bengal.

**Results:** From 2009 to 2011, SHIS have screened 46866 TB suspects and detected 6707 TB cases with around 58% NSP cases in the islands. NSP case detection rate 67%, 62% and 62% in 2009, 2010 and 2011 respectively. The cure rate of the NSP is 94% in 2009, 99% in 2010 and 94% in 2011.

**Conclusion:** SHIS already achieved 85% cure rate and will soon achieve 70% NSP CDR through sustained and more intensified mobile boat dispensary services for the underprivileged islanders of Sundarban.

#### **OP-140-15 Reaching the unreachable: active tuberculosis case finding among the internally displaced population in six provinces of Afghanistan**

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**Background and challenges to implementation:** IDPs are at high risk of developing TB having poor access to TB services in Afghanistan. Under TB REACH project, ATA-AP initiated active case finding among IDPs in 6 provinces. Screening for TB was performed by mobile TB teams consist a doctor, a nurse and lab technician in each of target six provinces through door to door visits. Teams informed IDPs about TB, collected sputum samples from identified suspects and delivered the samples to the designated laboratory for microscopic examination. The mobile teams were responsible to start and follow the treatment of confirmed TB cases while DOT was provided by trained volunteers in camps. This study aimed to explore the magnitude of TB cases among IDPs and find feasible solution for IDPs access to TB services. A year data from Q4 2010 to Q4 2011 is analyzed.

**Results and lessons learnt:** Totally, 155 897 individuals were screened for TB, among them 5139 (3%) TB suspects were identified and 358 SS+ (0.2%) were diagnosed which shows high prevalence rate. The intervention cost high in some provinces since few numbers of IDPs existed and hence few SS+ cases were detected.

**Conclusions and key recommendations:** This review confirmed that there is higher prevalence among IDPs. Thus, these groups have to be addressed through active case findings and provide treatment and follow up. To reduce the cost and provide sustainable access to IDPs active case finding should be integrated in MoPH's mobile teams existed in provinces.

### OP-141-15 High prevalence of latent tuberculosis infection among attendees of a Malaysian Drug Rehabilitation Centre

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**Background:** Tuberculosis (TB) remains a leading cause of morbidity and mortality in low- and middle-income countries, including Malaysia. Though people who use drugs (PWUDs) have a higher risk of TB infection, screening for TB in drug rehabilitation centres in Malaysia is lacking. This study was conducted to assess the prevalence of latent TB infection (LTBI) among attendees of a voluntary-based Malaysian drug rehabilitation centre.

**Design/methods:** We assessed patients seeking care at a newly opened voluntary drug rehabilitation centre for risk factors associated with tuberculin skin test (TST) positivity. World Health Organization TB symptom scoring system was used to exclude those with suspected active TB. Asymptomatic participants were screened for LTBI using two-step TST, with TST being placed intradermally and read after 48–72 hours. Indurations of 10 mm and 5 mm were considered to be indicative of LTBI among HIV-negative and HIV-positive subjects, respectively.

**Results:** A total of 219 participants were screened,

of which 196 (89.5%) had complete data. Most (96%) were men, less than 40 years of age (mean age 37.9 years), with a history of previous incarceration (94%) and had injected drugs (67%). Three quarters had used heroin in the previous 30 days and nearly all (98%) smoked tobacco. Only 9 (4.6%) self-reported being HIV-infected. 172 (88%) had never been screened for active or latent TB before. The majority of participants (86.7%) were TST positive. Age range 26–45 years old (adjusted OR 12.89,  $P = 0.002$ ) was associated with TST+ on multivariate analysis after adjusting for other variables.

**Conclusion and recommendations:** The study revealed high prevalence of LTBI among PWUDs in Malaysia and highlighted the increased risk of TB infection in this group. Establishment of routine TST screening and introduction of isoniazid preventive therapy is crucial for TB control in drug rehabilitation centres and other settings where this high-risk group is concentrated.

### OP-142-15 The influence of gender and caste on knowledge, health seeking behaviour and social impact of tuberculosis

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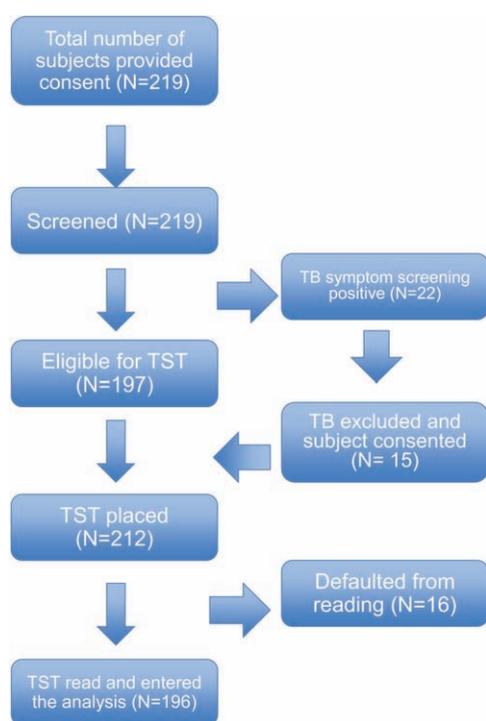
**Background:** Globally there is a growing body of evidence identifying gender differences in knowledge and health seeking behaviour for TB. There is less evidence of interactions between caste and gender on these aspects. The objective of this study was to assess differences by gender and caste in TB and HIV/AIDS knowledge, health service utilisation and social impacts.

**Design:** Mixed method study using a household survey and qualitative interviews and focus groups in 10 districts of Nepal.

**Participants:** 400 households were recruited for the survey.

**Qualitative study:** Six interviews with health care providers were conducted in each district and thirteen focus groups disaggregated by gender, caste and region (mountain, hill and Terai planes) were held with TB patients and their families. Descriptive statistics were used to analyse quantitative data and content analysis was used with the qualitative data.

**Results:** Both quantitative and qualitative data showed significant variations in TB knowledge, health seeking behaviour and social impact between caste groups and within this, by gender. These differences were further delineated by geographical location with women from lower castes in the hill districts having particularly poor knowledge and access to services,



**Figure** Disposition of the participants. TB = tuberculosis; TST = tuberculin skin test.

less than 13% of Dalit women from hill areas were aware that TB could be cured, compared to 95% among other caste groups. Women from all caste groups had lower awareness of TB-HIV co-infection compared to men. Decision making regarding treatment seeking was consistently lower among women with only 62% able to decide for themselves compared to 80% of men. 45% of men and 37% of women felt that those with TB should not marry illustrating the detrimental social impacts of TB.

**Conclusions:** Understanding these gender and caste differences is vital if services are to be maximise TB prevention, case finding and successful treatment.

### OP-143-15 Gender-related barriers to and delays in accessing tuberculosis diagnostic and treatment services: a systematic review of quantitative studies

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**Background:** TB is a significant cause of morbidity and mortality among women. Several studies have reported a variety of gender-associated differences in barriers to and delays in accessing TB services but a systematic review of published research has not been conducted.

**Design/methods:** We searched 12 electronic databases and limited our search to human and English-language articles that were published between 1953 and 2010. We excluded case reports, editorials, review articles, commentaries and practice guidelines. We examined associations between gender and individual-, provider- and system-level barriers to and delays in accessing TB services.

**Results:** Of 13448 papers reviewed, 139 studies were included: 1 (<1%) cluster-randomized trial, 8 (6%) cohort studies, 1 (<1%) case-control study and 129 (93%) cross-sectional studies (Table). About 75% of studies focused on diagnosed TB cases or TB suspects who had presented to health facilities. In 5 (26%) of 19 studies, a greater proportion of males than females reported financial barriers; 7 (37%) found that women faced greater financial barriers than men; and 4 (21%) showed no gender-related differences. The financial barriers faced by men included the opportunity cost of lost wages, while women were financially dependent on others. Of 24 studies assessing TB-related stigma, 11 (46%) found women experienced greater stigma than men; 11 (46%) found no difference; and 2 (8%) found men experienced greater stigma than women. 22 studies assessed the delay from presentation to TB diagnosis,

		Studies reporting greater barriers/delays among women than men	Studies reporting greater barriers/delays among men than women	Studies reporting no gender-related differences in barriers/delays	Total studies N
		n (%)	n (%)	n (%)	
Individual-level Barriers	Financial	9 (45%)	4 (20%)	7 (35%)	20
	Physical	2 (25%)		6 (75%)	8
	Stigma	12 (44%)	2 (7%)	13 (48%)	27
	Sub domain comparison*	1			
	Education and Health Literacy	18 (38%)	7 (15%)	22 (47%)	47
	Sub domain comparison*	1		2	
Provider-/ System-level Barriers	Socio-demographic	6 (86%)		1 (14%)	7
		7 (50%)		7 (50%)	14
Combined Patient-, Provider- and System-level Barrier		2 (40%)	1 (20%)	2 (40%)	5
Patient-level Delay		12 (21%)	7 (13%)	37 (66%)	56
Provider- and System-level Delays		9 (23%)	3 (8%)	27 (69%)	39
Combined Patient-, Provider- and System-level Delays		8 (32%)		17 (68%)	25
Multi-country studies*		1	1	1	

#### Patient-level Delay:

Delay between symptom onset and presentation to health care provider

#### Provider-/System-level Delay:

-Delay between presentation to ANY health care provider and diagnosis OR

-Delay between presentation to ANY health care provider and initiation of treatment OR

-Delay between diagnosis and treatment initiation

#### Combined Patient-, Provider- and System-level delay:

Delay between symptom onset and treatment initiation or delay between symptom onset and diagnosis

\*Some papers provided an overall score for gender comparisons of the impact of stigma and health literacy barriers as well as a comparison of sub domains of stigma (e.g. marital problems) and health literacy (e.g. mode of prevention, mode of transmission, causative agent, transmissibility of TB, etc). These papers appear in multiple cells in the table.

\*Multi-country study with reported gender differences differing from country to country.

of which 11 (50%) found that women experienced greater delays than men; 10 (45%) found no gender-related difference; and 1 (5%) found that men experienced greater delays than women.

**Conclusion and recommendations:** Overall, women face greater barriers than men in accessing TB services. Patients experiencing the greatest barriers to accessing TB services are also those least likely to present for care and/or be diagnosed with TB, and this group was underrepresented among the studies reviewed. Research must include all TB suspects, not just those presenting for care, and be designed from its inception to examine gender-related differences in barriers to and delays in accessing TB diagnosis and treatment services.

### OP-144-15 Does time since arrival affect site of tuberculosis disease in UK migrants?

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**Background:** By contrast to the epidemiology of tuberculosis globally, the UK and many low incidence countries have a high proportion of cases with extrapulmonary tuberculosis (ETB). Almost 70% of reported TB cases in the UK are among the non-UK born population, and many of these develop TB within the first five years after entry. A hypothesis that the distribution of the site of disease is influenced by time since arrival among migrants is evaluated.

**Design/methods:** All TB cases reported to the national surveillance scheme in the UK from 1999 to 2010 were included, using logistic regression analysis to investigate the association between time since entry and site of disease adjusting for confounders.

**Results:** Amongst UK born cases, pulmonary TB (PTB) was common (71.6%) and this pattern is similar in all ethnic groups. Amongst non-UK born persons PTB is common within the first two years of arrival (58.8%), but ETB was more common thereafter (52.2%). The logistic regression model showed that UK arrival >2 years ago (OR 1.53, 95%CI 1.46–1.6) and female gender (OR 1.26, 95%CI 1.21–1.3) were independently associated with ETB. Similarly, world region of birth (particularly South Asia, OR 2.5, 95%CI 2.13–2.94) and ethnicity (particularly Indian OR 2.48, 95%CI 2.15–2.86) were also significant predictors for ETB.

**Conclusion and recommendations:** Time since arrival significantly affects the site of disease increasing the likelihood of ETB compared with PTB amongst non-UK born persons. Conveying our findings to healthcare workers in the UK may improve early diagnosis of TB.

#### OP-145-15 Latent tuberculosis screening of HIV-negative women in pregnancy and post partum: comparing an interferon-gamma release assay with tuberculin skin testing in India

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**Background:** Immunological changes may increase the risk of reactivation of latent TB infection (LTBI) during pregnancy. The performance of immune-based LTBI screening tests (tuberculin skin test (TST) and interferon- $\gamma$  release assay (IGRA)) at different stages of pregnancy is not well described in high-endemic countries. The objectives of this study were to determine the peripartum concordance between the TST and an IGRA, the QuantiFERON® Gold-In-Tube (QGIT), and to estimate their conversion and reversion rates between pregnancy and delivery.

**Methods:** A cross-sectional LTBI screening study using TST and QGIT was performed in HIV-negative women presenting to the antepartum clinic (ANC) ( $n = 154$ ) or delivery ward ( $n = 148$ ) at a public government hospital in Pune, India. Women with active TB were excluded. Of the ANC group, 60 had repeat testing at delivery to estimate reversion and conver-

sion rates. Trained staff administered questionnaires to obtain sociodemographics and medical history. Agreement was measured using the kappa statistic and percent positivity with binomial exact confidence intervals was estimated.

**Results:** In the cross-sectional studies, 42 (14%) of 282 were TST+ versus 100 (33%) of 302 QGIT+. The stage of pregnancy impacted the proportion positive (Table). Percent agreement was 75% ( $\kappa = 0.4$ ) and 69% ( $\kappa = 0.26$ ) for the ANC and delivery groups, respectively. The predominant discordant group had TST-/QGIT+ results (ANC 18%, delivery 23%). Of those with repeat testing at delivery, the reversion rate for the TST was 9.5% versus 5% for QGIT. The conversion rate was 2.3% and 8.3% for the TST and QGIT, respectively.

**Table** Summary of TST results, IGRA results, and conversion/reversion rates among pregnant and postpartum women

	Total <i>n</i> (%)	Antenatal clinic ( <i>n</i> = 154) <i>n</i> (%)	Delivery ward ( <i>n</i> = 148) <i>n</i> (%)
TST read	282 (93)	140 (90)	142 (95)
TST positive	42 (14)	26 (18)	16 (11)
TST Conversion rate*	1 (2.3)		
TST reversion rate†	4 (9.5)		
QGIT positive	100 (33)	52 (33)	48 (33)
QGIT indeterminate	10 (3.3)	5 (3.2)	5 (3.3)
QGIT Conversion rate*	5 (8.3)		
QGIT reversion rate†	3 (5)		
TST+/QGIT+	34 (12)	21 (15)	13 (9.1)
TST+/QGIT-	7 (2.4)	5 (3.5)	2 (1.4)
TST-/QGIT+	59 (20)	26 (18)	33 (23)

\* Conversion from a negative test to a positive test between visits.

† Reversion from a positive test to a negative test between visits.

**Conclusions:** Between pregnancy and delivery, TST positivity decreased while QGIT was stable. The reversion rate was also higher in TST. These data suggest that TST performance is more vulnerable to the immune changes of pregnancy than QGIT. The clinical significance of the predominant TST negative/QGIT positive discordance deserves further attention.

## POSTER DISCUSSION SESSIONS

### TUBERCULOSIS DIAGNOSTICS: CULTURE AND RAPID DETECTION – 1

#### PC-213-15 Is fluorescent microscopy suitable for diagnosing tuberculosis in paucibacillary groups as in a prevalence survey?

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**Background:** Fluorescent microscopy (FM), especially using LED, is now widely used as direct smear examination due to its advantages. Cambodia and other countries adopted it to population-based survey. However, most data on the comparison between FM and conventional microscopy by Ziehl-Neelsen stain (ZN) have been collected in clinical settings, which are quite different from population-based settings in both disease prevalence and its severity. We compared smear results of a national prevalence survey (NPS) in Cambodia between FM and ZN to evaluate their performance in a paucibacillary group.

**Methods:** From 4612 subjects eligible for sputum for the NPS, 9221 specimens were submitted for smear and culture examinations. After a direct smear per specimen was examined with FM (400× magnification and 40 fields), slides from both 340 bacteriologically positive subjects and 455 bacteriologically negative subjects with chest radiography (CXR) suggestive of active TB including 6% of all the negative slides as negative control were re-examined with ZN (1000× magnification and 300 HPF if negative). All specimens were cultured with solid media.

**Results:** Out of 2108 slides obtaining the results with the two methods, 151 (7.2%) tested positive and 1868 (88.6%) tested negative by both FM and ZN with a 95.8% concordance rate. Out of 1921 negative slides with ZN, 53 (2.8%) were positive with FM, and out of 1904 negative slides with ZN, 36 (1.9%) were positive slides with FM ( $P < 0.001$ ). The rate of culture-positive specimens among scanty-positive with ZN was significantly higher than that with FM 69% (66/95) vs. 51% (44/86), respectively,  $P < 0.05$ .

**Conclusion:** FM showed higher sensitivity than ZN, but may include more false-positive, or MOTT cases. For diagnosing TB in paucibacillary group like a prevalence survey or active case detection, re-examination with ZN or combination with other diagnostic tool such CXR should be required.

#### PC-214-15 Evaluation of a novel concentration method for the microscopic detection of *Mycobacterium tuberculosis* from induced sputum

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Diagnosis of tuberculosis in developing countries relies on sputum smear microscopy, which has poor sensitivity for HIV-co-infected patients. Sputum induction can increase case detection but requires sample centrifugation. TB Beads can be used to concentrate mycobacteria from induced sputum as an alternative to centrifugation, and thus enable increased TB diagnosis in peripheral clinics. MSF runs a comprehensive HIV and TB clinic in a high HIV-prevalence setting in Zimbabwe. We compared the sensitivity and specificity of TB Beads with centrifugation, against culture on Löwenstein-Jensen medium as a reference standard. Direct smear-negative adult TB suspects (71% HIV-positive) were invited to undergo induction. Half of each sample was processed using TB Beads with fluorescent and Ziehl-Neelsen (ZN) microscopy; and half subjected to centrifugation, fluorescent microscopy, and culture on Löwenstein-Jensen medium. 134 (97%) of 138 patients produced an induced sputum sample. 133 patients had samples for full analysis. 26 (19%) patients were smear-positive, of whom 21/133 (16%) were positive by centrifugation, and 13 by TB Beads: 9/133 (7%) by ZN and 10/133 (8%) by fluorescent microscopy. Seven patients (5%) were culture-positive and 126 were culture negative. One patient was smear-negative and culture-positive. The sensitivity and specificity of microscopy compared with culture were 43% (3/7) and 95% (120/126) respectively for ZN and 43% (3/7) and 94% (119/126) for fluorescent microscopy. When ZN and fluorescent microscopy were combined the sensitivity was 57% (4/7). When centrifugation was used sensitivity increased to 86% (6/7). Our results show that TB Beads did not perform well enough to replace centrifugation.

### PC-215-15 Diagnostic utility of an enzyme-linked immunospot assay using induced sputum cells for pulmonary tuberculosis

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**Background:** The purpose of this study was to evaluate the diagnostic utility and predictors for determinate results of an enzyme linked immunospot assay using induced sputum cells (IS ELISPOT) for a rapid diagnosis of pulmonary tuberculosis (TB).

**Design/methods:** Subjects suspected of pulmonary TB who had either sputum acid fast bacilli smear-negative or not producing sputum spontaneously were prospectively enrolled in the study. ELISPOT assay was performed using cells from induced sputum.

**Results:** A total of 43 subjects, including 25 with TB (TB group) and 18 with non-TB disease (non-TB group) were enrolled in the study. Results of IS ELISPOT were determinate in only 17/43 (39%) subjects, but all of determinate results were consistent with the final diagnosis. Of the 43 sputum samples, 11 (26%) were inadequate to perform IS ELISPOT. Of 32 adequate sputum samples, the proportion of determinate results was significantly higher in the TB group (75%, 15/20) than in the non-TB group (17%, 2/12) ( $P = 0.002$ ) and diagnosis of TB was a unique predictor for the determinate results (odds ratio, 15.0; 95% confidence interval, 2.42–93.01). Smear positivity and extent of chest radiograph were not predictors for determinate results in the TB group.

**Conclusion and recommendations:** IS ELISPOT, in its current format, is not clinically useful because of the high proportion of inconclusive results. However, in the TB group, IS ELISPOT showed relatively high diagnostic value and accuracy regardless of smear positivity. IS ELISPOT may provide additional diagnostic yield for microbiological tools in the rapid diagnosis of smear-negative TB.

### PC-216-15 Comparative performance of thin layer agar and Löwenstein-Jensen culture for diagnosis of tuberculosis in Jogjakarta, Indonesia

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**Background:** Sputum smear microscopy is a cheap and simple method for the diagnosis of tuberculosis (TB) but the sensitivity is low. Culture on Löwenstein-Jensen (LJ) is more sensitive but takes 6–8 weeks to yield results. Thin-layer agar (TLA) culture has been

suggested as an equally sensitive and more rapid alternative. The objective of our study was to evaluate the performance of TLA for diagnosing TB in Jogjakarta, Indonesia.

**Design/methods:** All TB suspects presenting from July 2010 to July 2011 to the 2 lung clinics of the National TB Control Program (NTP) network of Jogjakarta municipality were eligible for inclusion. Following the NTP's protocol, TB suspects produced 3 sputum samples for smear microscopy. Their first sample was sent to the microbiology laboratory of Gadjah Mada University for decontamination, concentration, smearing and Ziehl-Neelsen (ZN) staining and culture on LJ and TLA. Blinded technicians read the results. The sensitivity of both cultures was evaluated against a composite reference standard (any positive culture or a 1+ to 3+ positive smear). Time to detection of Mycobacteria was recorded.

**Results:** Out of 1416 samples, 163 (12%) were smear positive, 99 (7%) scanty and 1154 (81%) smear negative. 168 (12%) and 149 (11%) samples were positive for TB on TLA and LJ respectively [Kappa coefficient 0.8 (95%CI 0.74–0.85)], while 72 (5%) and 32 (2%) cultures, respectively, were contaminated. The reference standard identified 199 (14%) TB cases. The sensitivity (95%CI) of TLA was 0.78 (0.73–0.84) vs. 0.69 (0.63–0.76) for LJ. The median (25th–75th percentile) time to detection was 44 days (36–52) for LJ and 12 days (9–19) for TLA.

**Table** Response pattern to smear microscopy, TLA and LJ culture in 1324 samples. Contaminated cultures were excluded

TLA	LJ	Smear	n (%)
+	+	+	92 (6.9)
+	+	–	28 (2.1)
+	–	–	19 (1.4)
–	+	+	7 (0.5)
+	–	+	17 (1.3)
–	+	–	11 (0.8)
–	–	+	25 (1.9)
–	–	–	1125
Total			1324 (100)

**Conclusion and recommendations:** TLA is a rapid and sensitive method for the diagnosis of TB. Implementation studies to evaluate the cost-effectiveness and impact of its introduction into programmatic settings are needed.

### PC-217-15 Cord formation in BacT Alert MP Medium: can it accord to more rapid diagnosis of *Mycobacterium tuberculosis* complex?

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**Background:** Serpentine cord formation in BacT Alert MP Medium was evaluated as a rapid method for the identification of *M. tuberculosis* complex.

**Material and methods:** A total of 919 clinical samples were processed for AFB culture using BacT Alert 3D system over a period of two years. AFB smears were prepared from 253 BacT Alert MP bottles flagged positive by the BacT Alert 3D instrument and stained by ZN method to examine the presence or absence of serpentine cording. The cord formation was compared with Accuprobe assay for the confirmation of *M. tuberculosis* complex.

**Results and discussion:** Of the 253 culture positives, 143 (56.5%) were identified as mycobacteria, of which 109 (76.2%) showed cording by smear microscopy out of which 3 isolates were identified as NTM by probe assay. In the remaining 34 (23.8%) cases, primary smear made from BacT Alert MP vial was negative for serpentine cord formation among these four cultures were confirmed as *M. tuberculosis* complex and 30 as NTM by Accuprobe culture identification kit. The sensitivity, specificity, positive and negative predictive values were found to be 97.2%, 88.2%, 96.4% and 90.9% respectively. An average detection time for Accuprobe assay was found to be around 2 days after the culture bottles was flagged positive by the BacT Alert 3D instrument as it requires sufficient growth for detection of *M. tuberculosis* complex, whereas cording results were available on the same day of culture positivity.

**Table** Showing comparison of cord formation and Accuprobe identification assay for MTB complex

(N = 143)	No. of samples positive for cording (109)	No. of samples negative for cording (34)	Final result
Accuprobe-positive (110)	106 (96.4%)	4 (3.6%)	MTB complex
negative (33)	3 (9.1%)	30 (90.9%)	NTM

**Conclusion:** As a highly sensitive, simple, rapid and cost effective method for the detection of *M. tuberculosis* complex, this test can be used for presumptive identification of *M. tuberculosis* complex and initiation of treatment in endemic countries. However, it should be supplemented with other tests for further confirmation.

#### PC-218-15 Evaluation of the performance of the PURE-LAMP test in China

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**Background:** Smear examination and solid media culture remain the major available tools to diagnose tuberculosis in China. The low sensitivity of ZN smear microscopy and long turn-around time of cul-

ture limit their performance on TB control. The PURE-LAMP Assay (Eiken, Japan) needs no high precision instrument, technical support and well-trained staff compared with traditional PCR. We aimed to evaluate the performance of PURE-LAMP implementation in peripheral labs of China.

**Methods:** 1164 initial patients were enrolled, and three qualified sputum specimens were obtained from each patient to complete smear, culture and PURE-LAMP test. The sensitivity, specificity, acceptable situation and report time of PURE-LAMP assay was analyzed.

**Findings:** We enrolled 1164 participants between March 15, 2011, and February 29, 2012, from two TB dispensaries in China. The reaction time by using PURE-LAMP was less than 40 minutes, and the total time of analysis including detection was less than 1.5 hour. The acceptable situation of eleven staffs reached 100%. The sensitivity of PURE-LAMP was 83% in smear-negative, culture-positive patients (147 of 177 patients) and 100% in smear-positive, culture-positive patients (149 of 149 patients), the specificity was 97% (811 of 838 non-tuberculosis patients).

**Conclusions:** The closed-tube system of PURE-LAMP minimized the risk of workspace contamination with amplicon, and the high sensitivity and specificity make the PURE-LAMP method as a prospected tool for molecular detection of TB in the peripheral laboratory with low-resource settings.

#### PC-219-15 Rapid sedimentation of acid-fast bacilli from non-aqueous solutions to improve sensitivity of tuberculosis microscopy

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**Background:** A variety of methods have been proposed to concentrate acid-fast bacilli (AFB) from specimens prior to microscopy to improve TB detection. Concentration by sedimentation is an attractive approach for widespread implementation because it is potentially simple and inexpensive and no additional equipment is needed. The rate of particle sedimentation from a liquid depends on the density and size of the particle and the density and viscosity of the liquid. Because TB bacilli are small and their density is only slightly higher than the density of water, the sedimentation rate from aqueous solutions is slow and often ineffective for AFB concentration. We hypothesized that if the liquid is chosen to have lower density and viscosity than water, the sedimentation rate may be increased, which could enable rapid and more sensitive AFB detection.

**Methods:** We assessed the sedimentation rate of AFB from smear-positive sputum specimens after processing in 4% sodium hydroxide in water or ethanol and neutralizing with hydrochloric acid in water, ethanol or acetone. The sedimentation efficiency was assessed

by determining the AFB density after a series of sedimentation times using AFB microscopy.

**Results:** AFB recovery after sedimentation from sputum processed with solutions of ethanol and acetone was significantly faster than that from sputum processed with aqueous solutions (see Table). Nearly all AFB were recovered after two hours of sedimentation from a processing solution with a final composition of 37.5% ethanol and 50% acetone.

Percentage of AFB recovered after sedimentation from representative sputum specimen processed with solutions containing varying amounts of water, ethanol, and acetone					
Solution		1	2	3	4
% of each solvent in final solution	water	100	50	12.5	12.5
	ethanol	0	50	87.5	37.5
	acetone	0	0	0	50
% of AFB from solution recovered after 2, 8 and 24 hours of sedimentation	2 hours	0	0	60	96
	8 hours	0	3	64	100
	24 hours	6	9	100	100

**Conclusion and recommendations:** Sedimentation from sputum processed using solutions containing the common solvents ethanol and acetone may enable rapid, safe, and potentially significant increases in AFB recovery for improved TB microscopy. Further evaluation is necessary to determine the sensitivity and feasibility of this approach for use in peripheral microscopy laboratories.

#### PC-220-15 Biopsy material studies by molecular-genetic methods in detection of tuberculosis in HIV-infected patients

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**Objective:** Confirming TB diagnosis in extra-pulmonary biopsy specimen from HIV-infected patients.

**Design:** As much as 56 patients were enrolled. All the patients were new TB cases and were HIV-positive. No one of them had obtained anti-retroviral therapy prior to detection of TB. Nineteen patients suffered with tuberculous pleural effusion (TPE) without pulmonary involvement. The other 37 had TB of lymph nodes (LN), with isolated non-pulmonary LN TB in eight cases, and multiorgan TB with extra pulmonary LN involvement in 29 patients. In all the cases, TB affection was confirmed with smears/cultures of the biopsy material positive for *Mycobacterium tuberculosis* and/or presence of caseating granulomas in biopsy specimen. To obtain the tissue samples, thoracoscopy

with pleural biopsy were made in the patients with TPE, and open biopsies were performed in the patients with LN affection. Real time polymerase chain reaction (PCR)—for *M. tuberculosis* complex identification in clinical specimens and DNA microarray analysis—TB biochip (TBCh)—for drug resistance (DR) testing were used directly in the specimens. TBCh identifies mutations in four *M. tuberculosis* genes associated with DR to rifampin (R)—*rpoB* and to isoniazid (H)—*katG*, *inhA*, *ahpC*.

**Results:** Sensitivity of PCR was 78.9% ( $n = 15$ ) for the pleura and 94.6% ( $n = 35$ ) for the LN. TBCh was made in 11 pleural and 25 LN specimens. Mutations in *rpoB* gene were found in seven (63.6%) pleural and in 16 (64.0%) LN samples. Mutations leading to DR to H were found in 15 (60.0%) samples from LN and in eight (72.7%) pleural biopsies. DR to H was associated with *KatG* mutations in seven pleural and 14 LN samples. Mutations confirming DR to H and R (multidrug-resistant TB) were present in 63.6% ( $n = 7$ ) pleural and in 56.0% ( $n = 14$ ) LN biopsy samples.

**Conclusions:** The study demonstrates that PCR and TB biochip of non-pulmonary biopsy material are highly effective for confirming TB affection and for rapid identification of drug-resistant TB in TB-HIV patients.

#### PC-221-15 Pulmonary tuberculosis diagnosis by *Mycobacterium tuberculosis* DNA amplification techniques: efficiency of blood tests

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**Background:** Prospective study to assess the diagnostic efficacy of peripheral blood tests by real time polymerase chain reaction (PCR-RT) for pulmonary TB (PTB).

**Design/methods:** Blood samples were collected from 648 suspected patients of PTB, all smear negative (S-). The patients were divided into 2 groups: HIV-negative (506 patients) and HIV positive (142 patients).

**Results:** Totally PCR-RT was positive in 34 (5.25%) cases. Average sensitivity and specificity was 2.2% and 100.0% for HIV negative and 26.3% and 98.7% for HIV positive cases, respectively ( $P < 0.01$ ). All HIV positive patients with mycobacteraemia CD4 levels less than 50. They all had fever, generalized lymphadenopathy, hepatomegaly, multiorgan dysfunction.

**Conclusion and recommendations:** Due to low sensitivity; negative *M. tuberculosis* PCR results for blood samples in S- cases cannot exclude the disease. However, this test may be helpful in cases when site of infection specimens are not available to confirm the diagnosis. PCR-RT blood analysis may play an important role for rapid diagnosis of TB especially in

the group of HIV-positive patients with high TB prevalence; disseminated, smear-negative and extra-pulmonary TB.

### PC-222-15 Evaluation of the loop-mediated isothermal amplification assay for the diagnosis of tuberculosis in a university teaching hospital, Zambia

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**Background:** The current diagnostic methods used to detect and differentiate pathogenic *Mycobacteria* in clinical samples and drug susceptibility tests are laborious. The main objective of this study is to establish a new diagnostic method based on LAMP (Loop mediated isothermal amplification) for the detection and differentiation of *Mycobacteria*. An in-house LAMP is being evaluated for its sensitivity and specificity in Zambia. This tool is rapid (1 hr), simple, does not require sophisticated equipment and cost-effective (US\$1 per test) compared to Gene Xpert costing US\$15 per test.

**Design/methods:** One to three routine decontaminated samples/suspect were used. Smear, decontamination, culture and identification tests were performed according to the standard. Two ml samples treated with NALC-NaOH, or concentrated by centrifugation were used for LAMP assay. Comparison was made between LAMP results and direct smear microscopy/culture using bactec MGIT 960 results and identification using Capillia TB.

**Results:** LAMP showed high sensitivity for all samples that were both smear and culture negative and for most of the samples that were both smear and culture positive. Although some smear negative and culture positive samples showed low sensitivity. To raise the sensitivity of LAMP, a concentration step by centrifugation was introduced into sample preparation. LAMP was positive for all samples that were both smear and culture positive and smear negative and culture positive samples. This exhibited high sensitivity of LAMP test on concentrated samples.

**Conclusion:** In this trial LAMP showed high sensitivity and specificity which can allow the actual study to be conducted.

### TUBERCULOSIS LABORATORY NETWORK: MANAGEMENT OF EXTERNAL QUALITY ASSESSMENT

#### PC-248-15 Probability matrix coupled with 24 loci MIRU-VNTR genotyping to determine cross contamination

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**Background:** The laboratory of the International Organization for Migration (IOM) in Nepal processes more than 200 specimens per day and cross-contamination is a serious consideration. Cost effective and reliable methods of detection of cross-contamination are needed.

**Design/methods:** Results of smears and cultures obtained over the period of 2008–2011, were analysed. Out of 297 culture-positive diagnostic cases, 78 (26%) had a single *M. tuberculosis* isolate. Specimens were labeled sequentially at all steps of processing and inoculation, therefore scrutinize of the processing sequence was performed. Specimens were decontaminated in batches of 10. Of the 78 specimens with a single positive culture, 18 specimens were processed after another culture positive ('source') specimen in the same batch. Cross-contamination probability matrix (CCPM) is based on the sequence and characteristics of the source specimen (Table). Selected specimens were referred for 24-loci MIRU-VNTR genotyping.

Table Cross-contamination probability matrix

Smear result	Position of the source specimen		
	≤3	4 and 5	≥6
AFB positive	High	Medium	Low
AFB negative	Medium	Low	Low

**Results:** 16 paired and one triplet isolate were identified for genotyping. According to CCPM, four pairs had high probability, three medium and 11 low. The genotyping showed all suspected cross-contaminants had different genetic makeup, representing true-positive results. The overall cross-contamination rate in this laboratory was 0% (one-sided 97.5% CI 0–1%).

**Conclusion and recommendations:** The study showed an extremely low level of cross-contamination in the IOM Nepal laboratory. The CCPM coupled with MIRU-VNTR is an invaluable indicator for laboratory quality assurance. Pre-screening cross-contamination with CCPM against a high MIRU-VNTR test cost is more cost effective. Further studies using genotyping are required to validate probability criteria.

### PC-249-15 Comparison of sputum microscopy and rapid tuberculosis antibody detection test kits for diagnosis of pulmonary tuberculosis in Abia State, Nigeria

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**Background:** Sputum smear microscopy (SSM) has variable sensitivity and the accuracy of new rapid immunochromatographic tuberculosis (TB) antibody detection tests (rapid TB tests) marketed in low-income countries like Nigeria is not known. The objective of the study was to compare the diagnostic performance characteristics of SSM and five rapid TB tests (DiaSpot TB, Spodex TB, SD Rapid TB, Clinotech TB Screen and Precious One-step TB).

**Design/methods:** A prospective cross-sectional study involving 150 TB suspects (male/female ratio of 0.81) was conducted at the Tuberculosis Referral Hospital, Uzuakoli, Abia State, Nigeria. Direct smears were stained by Ziehl-Neelsen technique and examined by light microscopy. Serological TB tests and HIV screening were performed using serum obtained from blood specimens. Culture on Löwenstein-Jensen slopes was used as the reference standard.

**Results:** Fifty-one patients were smear positive (smear positivity rate, 34%) and 91 were culture positive, 79 (86.8%) were due to *M. tuberculosis* and 12 (13.2%) to nontuberculous mycobacteria (NTM). Forty five (88.2%) of the smear positive cases were culture positive and 46 (55.4%) of 83 smear negative cases were culture positive. The diagnostic performances of SSM and the five rapid TB tests are presented in the Table.

**Table** Diagnostic performance of sputum smear microscopy (SSM) and five rapid TB test kits in culture positive TB patients in Abia State, Nigeria

Diagnostic tests	Sensitivity % (95%CI)	Specificity % (95%CI)	PPV % (95%CI)	NPV % (95%CI)
SSM	50 (39.0–61.0)	92.3 (86.4–98.2)	92.5 (86.7–98.3)	49.3 (38.3–60.3)
DiaSpot TB	39.2 (28.4–50.0)	78.4 (69.3–87.5)	83.8 (75.7–91.9)	42.2 (31.3–51.3)
Spodex TB	36.7 (26.1–47.3)	81.4 (72.8–90.0)	78.4 (69.3–87.5)	41.2 (30.3–52.1)
Precious One-step TB	32.9 (22.5–43.3)	82.9 (74.6–91.2)	78.8 (69.8–87.8)	39.1 (28.3–49.9)
SD Rapid TB	24.1 (14.7–33.5)	85.4 (77.8–93.2)	76.0 (66.6–85.4)	36.8 (26.2–47.4)
Clinotech TB Screen	24.1 (14.7–33.5)	87.8 (80.6–95.0)	79.2 (70.2–88.2)	37.5 (26.8–48.2)

SSM = sputum smear microscopy; CI = confidence interval; PPV = positive predictive value; NPV = negative predictive value.

**Conclusion and recommendations:** The sensitivity of SSM though moderate is inadequate for long term TB control in this setting. None of the five rapid TB tests had acceptable level of accuracy for diagnosis of active TB. There is need to improve the regulatory mechanism of rapid diagnostic tests in Nigeria.

### PC-250-15 A pilot line probe assay external quality assurance programme

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**Introduction:** Line Probe Assays (LiPA) are becoming widely used for rapid detection of isoniazid and rifampicin resistance in *Mycobacterium tuberculosis* (TB). Although the test is relatively easy to perform and interpret, multiple factors can affect the quality and lead to misinterpretation of results. In order to ensure the quality of the test, an external quality assurance program (QAP) was initiated to assess proficiency of TB laboratories in performing the test. Since 2010, a total of 4 rounds of QAP samples have been dispatched to 5 laboratories in 4 countries. We summarized the experiences gained on analysis on laboratory performance with this QAP.

**Methods:** Sets of six (6) *M. tuberculosis* DNA samples, including 2 blinded duplicates, were impregnated within pieces of filter paper, individually marked, and sent to participant laboratories. LiPA were performed blindly in participant laboratories and results returned to us for comparison and analysis. Reports on performance in the QAP with feedback/comments were returned to participants. Performance of the laboratories was reflected by their inter-laboratory and intra-laboratory comparison and reproducibility.

**Results:** Most laboratories performed well in the QAP with most of the hybridization band results read and interpreted correctly. Average inter-laboratory and intra-laboratory reproducibilities were both 96%. However, even though participants gave correct reading and interpretation of their test results, sharpness of bands on each of the strips did vary considerably. This appeared to be a major problem affecting laboratory performance in the QAP. Individual bands (e.g., *rpoB* WT8) that appeared weaker than the control were sometimes counted as positive by laboratories leading to erroneous interpretation of the susceptibility of the test sample.

**Conclusion:** An external LiPA QAP can help to ensure the quality and promote improvement in TB laboratory performance, especially in initial stages when the test is being set up.

### PC-251-15 Improving access to culture capability for smear-negative tuberculosis suspects in Western Kenya

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**Background:** Diagnosing smear-negative (SN) tuberculosis (TB) is a challenge in resource-limited settings due to limited access to sensitive diagnostics. In

Kenya, smear microscopy is the standard TB diagnostic method with culture reserved for retreatment or suspect MDR-TB patients. Early cases of TB and patients with TB-HIV co-infection often present as SN, experiencing delays in diagnosis until disease progresses to a smear-positive state. Patients informed that there was 'no TB' may not return for repeat screening. SN patients registered in TB programs experience poorer outcomes, whether due to poor adherence, or due to progression of an alternative undiagnosed, and therefore untreated, condition. As part of a TB REACH initiative, cultures were made available for SN suspects cared for at facilities within reach of the Mycobacteriology Reference Laboratory (MRL) situated on the grounds of Moi Teaching and Referral Hospital/AMPATH in Eldoret, Kenya.

**Intervention:** For 15 clinics in Western Kenya within 125 km of Eldoret, SN TB Suspects from outpatient facilities were provided with a free TB culture (MGIT 960). Either individual or pooled spot and morning specimens were transported in cooler boxes to the MRL within 7 days of collection. An SMS was sent to notify patients and providers that results were available; paper results were returned to facilities within 4–7 weeks of sputum collection.

**Results:** 287 SN patients were screened with culture. Of the 108 available result, 12 (11.1%) patients had *Mycobacterium tuberculosis*, 5 (4.6%) had non-tuberculous mycobacteria, 75 (69.5%) had negative cultures, and 16 (14.8%) had contaminated specimens.

**Conclusion:** Use of a central facility to provide culture for surrounding clinics diagnosed over 10% of SN patients who would otherwise remain untreated. Until a point of care TB diagnostic test can be established, addressing logistical barriers such as lab turn around times, specimen transport, and reporting can improve access to TB culture diagnosis.

#### PC-252-15 Improving the external quality assessment of AFB microscopy: impact of Global Fund tuberculosis projects in Nigeria

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**Background:** As a result of a weak external quality assessment (EQA) system, maintaining a quality assured AFB microscopy is a major challenge to peripheral microscopy centres in Nigeria.

**Intervention:** In order to improve the quality and coverage of service, the Global Fund Round 5 Phase 2 and Round 9 Phase 1 (October 2009 and June 2011) conducted training and retraining of AFB microscopist and the QA officers according to the na-

tional guidelines. Quarterly EQA activities at the states level and review meetings at each of the 36 states and the Federal Capital Territory (FCT) and the 6 geopolitical zones were financed.

**Results:** By the end of June 2011, a total of 900 AFB microscopists and 2 QA officers from each of the 36 states and the FCT were trained. The number of AFB microscopy centres participating in EQA increased from 110/975 (11.3%) in 2009 to 855/1080 (79.2%) in 2011. There was an increase in the reporting of EQA data to the NTBLCP from 10 states in 2009 to 36 reporting states and FCT in 2012. The average concordance rate increased significantly from 88.2% to 97.6%. The average FP decrease from 4 to 3.4%, while the average FN decreases from 7% to 4.7%.

**Conclusions:** The Global Fund TB Project in Nigeria has contributed to the strengthening of the AFB microscopy EQA system and enhancing the coverage and quality of the services in Nigeria. The government of Nigeria should commit more funding towards TB control.

#### PC-253-15 Trends in the quality indicators of AFB microscopy and tuberculosis case detection in Gombe State, Nigeria

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**Background:** The Gombe State TB Control Programme is implementing the external quality assessment (EQA) of acid fast bacilli (AFB) microscopy according to the Nigerian National Guidelines for TB control. We determine the trends of the quality of AFB microscopy services and its possible impact on the detection of TB cases in Gombe State, Nigeria.

**Methods:** Results of the 'blinded rechecking' EQA from the participating laboratories between April 2010 and March 2011 were analyzed. The EQA coverage per quarter, slide positivity rates, concordance rates, false positive (FP) and false negative (FN) rates of AFB microscopy reported quarterly were compared with the respective number of TB cases detected in the state in the period under review.

**Results:** Between April 2010 and March 2011, the proportion of laboratories participating in EQA increased from 84% to 100%. Slide positivity rate increased from 9.7% to 14.1%. Average concordance rate increased significantly from 52.9% to 86.6%. The proportion of laboratories attaining concordance rate > 95% ranged from 56.3% to 91.7%. The false positive and false negative rates decreased from 1.7% and 3.4%, respectively, to 0.6% each. The total number of TB cases detected in the period under review ranged from 272 to 488 per quarter, while the detection rate is 40%–45% per quarter.

**Conclusion:** An effective laboratory EQA system contributed significantly to the case finding in a TB control programme. The state TB Control Programme should sustain the AFB microscopy EQA system.

**PC-254-15 Sputum collection and transportation in tuberculosis control: experiences from a case study in Neemuch District, Madhya Pradesh, India**

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**Background and challenges to implementation:** There are several reasons why patients will not seek diagnosis when displaying symptoms for TB. These include: poor knowledge of TB symptoms and treatment programmes, poor infrastructure (roads and transport links) to local district medical centres and low motivation to seek help. A case study in Neemuch, Madhya Pradesh, India has shown sputum collection and transportation (SCT) to be a potentially effective grass roots intervention to solve the above issues.

**Intervention or response:** In order to improve TB services, NGOs associated with Project Axshya, involved the community in a Sputum Collection and Transportation program. These NGO volunteers are now involved in identifying TB symptomatics, collecting and delivering their sputum (to a certified microscopy centre) and any after care which is required upon diagnosis (such as: linking patient to DOTS provider, follow up samples, contact tracing, defaulter tracing and patient support).

**Results and lessons learnt:** Of 1256 TB suspects examined in Neemuch District between April and June 2011, 124 (9%) came from the sputum collection and transport mechanism implemented by the NGO. This further contributed to 13% of all sputum positive cases diagnosed in the same period.

**Conclusions and key recommendations:** In conclusion the sputum collection programme shows a lot of promise for TB control. This programme when properly evaluated for effectiveness could be used as a template for future programmes across India. What makes this programme so effective is that it targets the members of the population who would not have otherwise sought treatment. The programme allows challenging vulnerable and rural populations improved access to accredited microscopy centres for diagnosis.

**PC-255-15 Impact of long-term technical assistance for tuberculosis laboratory services**

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**Background:** Botswana has one of the highest rates of tuberculosis (TB), multi drug resistant TB, and TB-HIV co-infection. According to a CDC evaluation in 2005 TB laboratory services were inadequate and technical assistance (TA) was needed to build capacity to meet required standards for TB control in Botswana.

**Intervention:** Two full-time in-country TAs were provided to Botswana National Tuberculosis Reference Laboratory (NTRL) by TBCTA/TBCAP and TB CARE I, supported by PEPFAR through CDC Botswana for almost 4 years (2008–2011). Areas of support included QMS, training and EQA for microscopy; culture and drugs susceptibility testing (DST). Assistance for quality management systems (QMS) started in July 2009 and is still continuing. Additional short-term TA through ASM for microscopy and liquid culture complemented the technical support.

**Results and lessons learnt:** Recovery of *M. tuberculosis* increased with introduction of MGIT960 culture. Successive pass rates for culture and DST EQA were maintained. Reporting of results significantly improved due to improved workflow and development of MDR-TB surveillance system. Annual testing capacity increased from 1450 to 13 458 cultures and from 456 to 1732 DST between 2006 and 2010. TA is also provided for implementation of MGIT960 DST for first and second line drugs and rapid molecular tests. Microscopy EQA was implemented country-wide with 285 (90%) technicians trained. NTRL was accredited by SANAS and selected to become SRL for Southern Africa Development Committee Region in 2011. Implementation of the projects is challenged by high turnover of staff requiring continuous training. The achievements were possible due to day-to-day support of NTRL staff by both TAs.

**Conclusions and key recommendations:** Long-term technical support significantly contributed to improved capacity and quality of testing in Botswana NTRL. Joint technical and QMS assistance is highly advisable for successful and sustainable laboratory capacity building.

### PC-256-15 Sputum microscopy: evaluation of impact of standardised training courses conducted in 8 states of Sudan in 2010–2011

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**Background and challenges to implementation:** Effective control of tuberculosis (TB) is depended on a network of laboratories which provide accurate and reliable sputum microscopy testing for diagnosis and treatment monitoring. However, the results of previous study done on 2009 showed that TB laboratories provided very poor quality of services and a new training curriculum were developed then training was implemented in 14 out of 15 states. 107 tuberculosis management units (TBMUs) distributed in 8 states in Sudan applying panel testing method.

**Objectives:** To identify the impacts of standardized training course on sputum microscopy implemented in eight states and to make recommends for future services development.

**Methods:** Panel testing method was used before and after conducting training courses in 8 states. Reading of results were checked and given scores. Positive grading mode and quality of AFB staining were evaluated.

**Results and lessons learnt:** 107 TBMUs returned panel slides with results before training course started and 89 TBMUs after training course. Average scores in 8 states before and after training were 85.09% and 95.62% respectively. Number of TBMUs had errors (FP, FN) were 8 and 14 and percentage of TBMUs reported with acceptable positive grading mode were 1 and 5. Percentage of TBMUs returned slides which were adequate staining were 87.5% and 100%. There were statistically significant variation in acquiring skills and knowledge regarding to the mode of grading and staining technique and *P* value were *P* = 0.000 and 0.013 respectively.

**Conclusions and key recommendations:** Abilities of laboratory technicians who participated in AFB microscopy training course were obviously improved at reading, grading and staining techniques. It is concluded that standardized AFB microscopy training courses which were implemented had good impacts on the quality improvement of TB laboratory services at in Sudan. NTP need to continue on it.

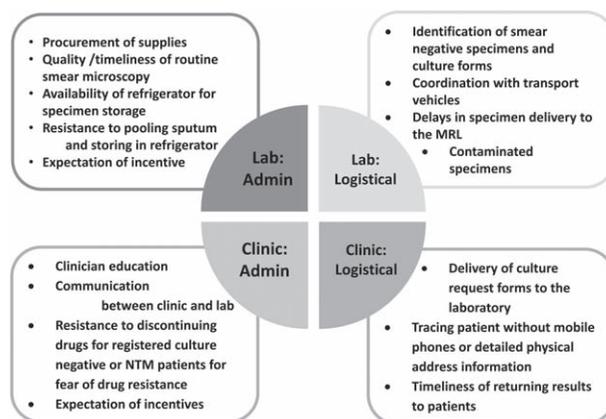
### PC-257-15 Challenges to providing tuberculosis laboratory-accessibility to patients in need: bridging the geographic gap from diagnostic facility to patient

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**Background:** As tuberculosis (TB) diagnostic capacity increases in resource-constrained countries, the challenge is to improve access to high-quality tools for people living at a distance from specialized diagnostic facilities. While the need for point-of-care diagnostics continues to be addressed, overcoming the barriers to accessing present capabilities remains a critical programmatic issue. As part of a TB REACH initiative, cultures were made available for smear-negative patients cared for at facilities within reach of the Mycobacteriology Reference Laboratory (MRL) situated on the grounds of Moi Teaching and Referral Hospital/AMPATH in Eldoret, Kenya.

**Intervention:** In North Rift and Western provinces, 15 clinics were identified based on patient volume, staff capacity, and ease of specimen transport. For each new smear-negative TB suspect, culture request forms were completed. Either individual or pooled spot and morning specimens were sent to the MRL. Specimens were kept in refrigerators until transfer to cooler boxes for transport by motorbike or the AMPATH vehicle system. Clinicians and patients were notified of the availability of results via SMS, and paper results were delivered to each facility.

**Results:** In the laboratory, challenges focused on resistance to packaging specimens (additional workload), storing in the lab refrigerator (fear of infection), supply shortages, turn around time of routine smear microscopy, and coordination with the specimen transport system. In the clinics, challenges included fostering communication between the lab and



**Figure** Operational challenges of culture diagnosis implementation in rural Western Kenya.

clinic, resistance to following results recommendations, and tracing patients without mobile phones.

**Conclusion:** While diagnosing patients within a specified distance from a central culture facility presented many logistical challenges, the greatest success was found with facilities with the most political will (engaged staff), that were closest to the MRL, and that had frequent transport schedules.

### PC-258-15 Validation of diagnosis of smear-positive tuberculosis in the Bangladesh National Tuberculosis Control Programme

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**Background:** Bangladesh held sixth position in the list of 22 high tuberculosis burden countries. Despite increasing coverage and improving quality of services, significant differences in case notification rates have been observed by performance areas. Challenges also have been raised as to how correctly diagnosis is made.

**Objective:** To assess validity of diagnosis of smear-positive TB cases.

**Materials and methods:** The cross-sectional study was conducted at 62 DOTS centers and categorized as high (>70%), medium (50% to 70%) and low (<50%) performing areas based on performance of case detection rate. Total 333 recently (in last ten days) diagnosed smear-positive cases from DOTS centers were included conveniently. Of each case, spot and early morning sputum was collected for microscopy and chest X-ray was done for case validity. Study findings were compared with findings of the DOTS centers.

**Results:** Among 333 cases, 302 (90.7%) were confirmed while 31 (9.3%) were detected smear negative by the validation study. Among smear negative, highest number (48.4%) of cases were detected from high performance areas whereas equal distribution was revealed from the medium and low performance areas. This difference could be due to poor quality of the sputum sample, poor smearing, staining or reading in the validation study or erroneous reporting by the DOTS centers. Virtually all cases had an X-ray finding compatible with TB.

**Conclusion:** The diagnosis of smear-positive TB could not be confirmed unless 10% of the cases rechecked. This may be due to over diagnosis of smear negative cases as smear-positive cases to reach the preset program target. However the nationwide drug stock-out may have provoked the DOTS centres for over case reporting.

**Key recommendations:** Special strategies should be designed to identify constraints and errors and to

ensure quality in AFB diagnosis process with close supervision, monitoring and evaluation must be ensured in all stages of case investigation.

### PC-259-15 Utility of combined solid and liquid culture in resource limited settings: is it worth the effort?

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**Background and challenges to implementation:** From November 2010 to September 2011, 5040 inmates were screened for TB during intensified case finding in six Zambian prisons. Inmate peer educators were trained to collect sputum specimens according to standard pre-analytical protocol. Due to prison restrictions, sputum collection was time-limited and unobserved. An average of 23 inmates was screened per day and only one specimen was cultured. We describe the *Mycobacterium tuberculosis* culture results of two laboratories supporting this programme.

**Intervention or response:** Sputum specimens were processed in one of two laboratories using different methodologies. The final concentration of NaOH/NALC was 1.5% and 2.0% in laboratories 1 and 2, respectively. A single processed sputum specimen was inoculated into two manual MGIT (BD BBL™ MGIT™) tubes in laboratory 1 and into one automated MGIT (BD BACTEC™ MGIT™ 960) tube and one Löwenstein-Jensen (LJ) tube in laboratory 2. Mycobacteria recovery and final contamination rates (both culture tubes contaminated) were evaluated. All procedures were performed according to good laboratory practice and international standards.

**Results and lessons learnt:** Laboratory 1 cultured 2721 specimens: 55 (2%) were identified as *Mycobacterium tuberculosis* and 250 (9%) as non-tuberculosis mycobacteria (NTM). The final contamination rate was 20%. Laboratory 2 cultured 2319 specimens: 90 (4%) were identified as *M. tuberculosis* and 133 (6%) as NTM. The final contamination rate for either MGIT or LJ alone was 15%, whereas cultures lost to contamination were reduced to 3% when both systems were combined.

**Conclusions and key recommendations:** In settings such as prisons, where the pre-analytic phase cannot be tightly controlled, the use of a combined MGIT-LJ culture system, although more labor intensive, may be a more reliable methodology to reduce contamination rates. Further analysis is ongoing to determine the clinical significance of NTM in this population.

### PC-260-15 Selection of supervising laboratories for peripheral facilities in the EQA programme for the Copperbelt Province of Zambia

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**Background:** Each supervising laboratory in Zambia should have the competency and capacity to plan and implement External Quality Assessment (EQA). Zambia has a total of 213 diagnostic facilities of which 136 (64%) are enrolled in the external quality assessment program. The district laboratories are responsible for effective implementation of quality assurance of smear microscopy service in peripheral laboratories.

**Intervention:** A structured questionnaire was used to assess 13 district laboratories in the Copperbelt province to determine which laboratories were qualified to supervise health center laboratories in the same province. Focus areas were; 1) staff capacity to conduct EQA 2) internal quality control (IQC) 3) slide positivity rate and turn around time. Review of laboratory registers and quality assurance records was done. Responses were analyzed using Statistical Package for Social Sciences (SPSS). The expected score was 80% and above.

**Results:** The average score for all facilities assessed was 61.8%. Only one facility had acceptable score. 8 (61.5%) had trained staff in smear microscopy. 11 (84.6%) had no false results in previous two quarters. 7 (53.8%) facilities had laboratory staff panel tested with acceptable scores. Adequate staffing levels and availability of transport was observed in 6 (46.1%) facilities. SOPs and up to date registers were available in 12 (92.3%) and 11 (84.6%) respectively. IQC measures were present in 5 (38.6%) laboratories.

**Conclusions:** The systematic use of a questionnaire in the selection of EQA supervisors is an important step in identifying laboratories with acceptable levels of competency and capacity to improve the performance of the peripheral laboratories in Zambia.

### PC-261-15 Impact of solid and liquid mycobacterial culture on diagnosis and management of HIV-positive, sputum smear-negative tuberculosis suspects in Kampala, Uganda

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**Background:** Solid- and liquid-culture techniques are reported to be highly sensitive for TB in HIV-seropositive, sputum smear-negative patients with chronic cough, but there is limited data on their yield, turn-around time, and clinical impact in high-burden countries.

**Methods:** We prospectively enrolled consecutive adults with cough  $\geq 2$  weeks at the Mulago-Mbarara Joint AIDS Program Clinic in Kampala, Uganda, from September 2009 to April 2010. We performed fluorescence microscopy on one spot and one early-morning sputum, and cultured the early-morning specimen on solid (LJ) and liquid (MGIT) media, using Capilia TB for speciation. We measured incremental yield of LJ and MGIT over smear; time to results; impact on treatment; and 6-month mortality.

**Results:** Of 337 eligible HIV-TB suspects, 24 were smear-positive and 113 failed to return to complete TB evaluation, leaving 200 enrolled smear-negative HIV-TB suspects. 191/200 (96%) had a negative 2nd smear, and 28/191 (15%) received empiric TB treatment. 26/200 (13%) had culture-confirmed TB: 24 (12%) by LJ and 4 (2%) by MGIT. Among culture-positives, median time to reporting was 92 days for LJ (IQR 69–148) and 106 days for MGIT (IQR 66–157). Among culture-negatives, median time to reporting was 121 days for LJ (IQR 73–165) and 104 days for MGIT (IQR 74–146). Treatment initiation after a positive LJ required a median of 31 days ( $n = 6$ , IQR 6–69); no MGIT-culture-positive patients started treatment. Treatment cessation after a negative result required a median of 176 days for LJ ( $n = 17$ , IQR 166–186) and 176 days for MGIT ( $n = 26$ , IQR 161–193). 6-month mortality was 4%.

**Discussion:** Culture showed a high TB prevalence among symptomatic smear-negative TB suspects in an HIV clinic, but we observed major delays in reporting results and little impact on patient management. One-third of patients failed to complete evaluation, emphasizing the critical need for sensitive, same-day diagnostic strategies for evaluating HIV-TB suspects.

## MOLECULAR GENETIC AND OTHER RAPID DRUG SUSCEPTIBILITY TESTING

### PC-282-15 Alcohol-based conservation of sputum: quantitative and qualitative impact among referred samples from distant centres for GeneXpert® MTB/RIF analysis

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**Background and challenges to implementation:** GeneXpert® MTB/RIF technology has been developed to

increase TB case detection in low-income and high-burden countries. These countries generally face major problems regarding the transportation of samples from peripheral centers to central labs due to biosafety issues, long distances and high temperatures. These issues could diminish the overall impact of the GeneXpert MTB/RIF technology in low income countries.

**Intervention or response:** To facilitate the transport of samples from peripheral health centers to central GeneXpert-equipped labs (TB Reach funding), we validated a protocol of alcohol-based conservation of the samples and implemented it in the South-Kivu Province.

**Results and lessons learnt:** Sputum conserved by a 1/1 dilution of 95° ethanol can be analyzed by GeneXpert even after 3 months and after spending 48 h at 37°C. The use of this protocol in the South-Kivu province permitted a considerable increase in term of efficiency of the GeneXpert technology.

**Conclusions and key recommendations:** A major problem faced by low income countries is the transportation of samples due to long distances and high temperatures. Alcohol-based conservation of samples permits to overcome bio-hazard, time and bad conservation issues. In addition, the spread of this protocol permits a considerable increase of the impact of the implementation of a GeneXpert MTB/RIF machine in the population.

#### PC-283-15 Development of a new format of the nitrate reductase assay for direct detection of MDR- and XDR-TB

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**Background:** Reports of *Mycobacterium tuberculosis* resistant to several drugs are increasing globally and routine laboratories are becoming increasingly aware of the need of drug susceptibility testing (DST), especially for treatment failures. During the last years, due to the long time required by conventional DST methods, new approaches have been proposed for faster detection of drug resistance, such as the nitrate reductase assay (NRA), which is considered fast and cheap, making it a good diagnostic tool for low-resource countries. In this study, we developed a phenotypic colorimetric plate assay as a direct DST method, in a multi-well format on solid medium and evaluated its performance in comparison to the proportion method (PM).

**Design/methods:** Sputum samples were decontaminated and processed by Petroff's method. The decon-

taminated suspension was used to perform direct NRA (DNRA) in 7H11 medium, using 1 µg/ml rifampicin (RMP), 0.2 µg/ml isoniazid (INH), 2 µg/ml ofloxacin (OFLO), 6 µg/ml kanamycin (KAN), 2 µg/ml amikacin (AMI) and 10 µg/ml capreomycin (CAP). The results were compared to those obtained with the PM.

**Results:** 84 samples were tested and the results for the most of the specimens were available within 21 days. This study showed an overall agreement of 98.4% between the DNRA and PM (496 of 504 individual susceptibility tests). The sensitivity and specificity, in comparison to PM, was 98.5% and 100% for INH, 98.3% and 96.2% for RMP, 91.7% and 100% for KAN, 78.8% and 97.3% for OFLO, 100% and 100% for AMI and CAP, respectively.

**Conclusion and recommendations:** The results demonstrate that DNRA, in this new multi-well format, is a rapid, accurate and inexpensive method for direct DST of *M. tuberculosis* and could become an appropriate alternative method for the resource limited settings.

#### PC-284-15 Strengthening DR-TB diagnosis capacity in Mozambique

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**Background:** Mozambique is ranking 16th in the list of 22 TB high burden countries. It is estimated that TB afflicts over 100 000 persons and causes about 27 000 deaths annually. TB case detection rate is estimated at 47%. TB culture and drug susceptibility testing (DST) was only available in Maputo National Tuberculosis Reference laboratory (NTRL).

**Intervention strategy:** In 2005 the NTP planned to increase DR-TB case detection rate by upgrading NTRL and expanding the TB culture capacity other parts of the country with the support of USAID through TB CAP from 2006 to 2010. A refurbishment of the NTRL was planned and executed to have a complete BSL3. The regional laboratory at Beira was renovated and become a BSL2 for TB culture. Training tools, guidelines, biosafety manuals, SOP's and mentorship sessions of staff were developed and implemented. 6 staffs receive an international training at Brazil and Portugal on new diagnostic technologies. A referral system of sample was implemented at the country level. TBCAP and NTP provided leadership and management capacity to support the upgrading of the TB diagnostic laboratories in Mozambique. Financial support from USAID and Global Funds was a critical ingredient to this success.

**Outcome:** Highly motivated staffs working in a safe environment and using newly introduced technologies MGIT and LED microscopy increased the quality of culture and DST results. Laboratory data is now readily available for decision making and have improved significantly over the past one year, see the table for details.

**Conclusions:** The expansion of TB culture and DST laboratories in Mozambique, staff training, adoption of new diagnostic technology and specimen referral system plan has increased the diagnosis of DR-TB and monitoring of MDR-TB treatment.

#### PC-285-15 Performance of the GeneXpert MTB/RIF assay on pooled sputum sediments

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**Background:** This study evaluated the sensitivity of the Xpert MTB/RIF assay for the detection of tuberculosis (TB) using pooled sediments of known smear-negative culture positive (SNCP) specimens.

**Design/methods:** Frozen processed sputum sediments from 75 SNCP TB patients, cultured the IOM laboratory in Nepal, were identified retrospectively. Each TB patient had submitted three sputum specimens for AFB microscopy and culture. Each specimen was processed using the standard NaOH-NALC method and the concentrated sediment was inoculated onto two LJ media and one MGIT culture. Aliquots of 300 µl from each of the three processed sputum sediments from each patient were pooled, regardless of culture results, and tested using the Xpert MTB/RIF assay. If Xpert MTB/RIF on a pooled specimen was negative, an additional test was performed on the sediment corresponding to positive culture.

**Results:** Xpert MTB/RIF was positive in 31 out of 75 pooled sediments (sensitivity—41%, 95CI 30–53%). Testing of additional culture-positive sediments yielded another eight Xpert MTB/RIF-positive results, bringing the sensitivity to 52% (95CI 40–63%). The Xpert MTB/RIF sensitivity was higher than sensitivity of a single LJ culture (37%, 95CI 26–49%), but lower than that of a single MGIT (59%, 95CI 47–70%) when compared to the same reference standard (at least one culture positive from a single sample).

**Conclusion and recommendations:** Pooling of sediments leads to the loss of sensitivity among AFB smear negative culture positive samples and should not be practiced. The overall sensitivity of a single Xpert MTB/RIF test on smear-negative specimens (pooled + individual) is higher than that of a single LJ and lower than of a single MGIT culture.

#### PC-286-15 GeneXpert MTB/RIF sensitivity and specificity for *Mycobacterium tuberculosis* and rifampicin resistance on direct sputum

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**Background:** Xpert MTB/RIF assay has shown promising results as an initial screening test for tuberculosis in several settings. The International Organization for Migration performs tuberculosis (TB) screening of Bhutanese refugees living in refugee camps in Nepal.

**Design/methods:** 249 TB suspects with radiological abnormalities on chest X-ray submitted sputum specimens for AFB bacteriology. Specimens were collected on four consecutive days. Three specimens were examined for AFB microscopy and culture using both solid and liquid culture. One specimen (in random order) was tested use the MTB/RIF assay. *Mycobacterium tuberculosis* identification and susceptibility testing was performed using the MGIT 960 system and the MTBDRplus Line Probe Assay (LPA).

**Results:** 31 individuals (12.45%) had positive cultures. 27 individuals were Xpert MTB/RIF-positive and culture-positive; and there were no MTB/RIF-positive culture-negative results. 25 individuals were smear-positive and culture-positive and there were 6 smear-positive and culture-negative results. Xpert MTB/RIF was positive in all cases of true smear-positives. Xpert MTB/RIF sensitivity was 87% (95CI 70–86%) and specificity—100% (95CI 89%–100%). In smears-positive specimens the Xpert MTB/RIF sensitivity was 100%. There were 3 rifampicin-resistant specimens, two of them confirmed by LPA and conventional DST. In the third case the isolate was phenotypically susceptible to rifampicin, but a rare mutation in *rpoB* was detected by gene sequencing. Xpert MTB/RIF-positivity did not depend on a specimen order.

**Conclusion and recommendations:** In this population with high smear positivity rate a single Xpert MTB/RIF assay had a very high sensitivity and specificity and could potentially replace sputum microscopy and chest X-ray as the initial diagnostic test.

#### PC-287-15 Use of GeneXpert MTB/RIF for diagnosis of smear-negative tuberculosis in remote health facilities in Western Kenya

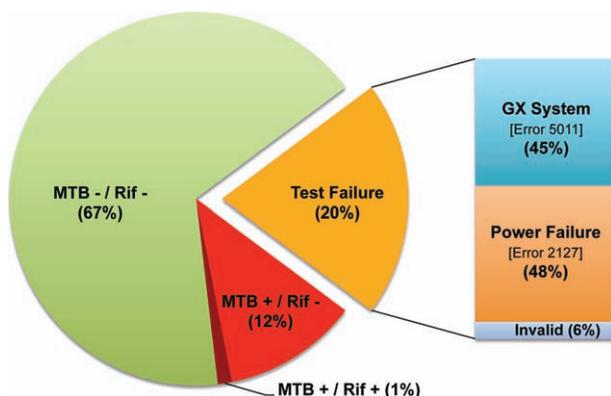
B Pederson,<sup>1,2</sup> L Kamule,<sup>2</sup> W Injera,<sup>2,3</sup> A Gardner,<sup>2,4</sup> E J Carter.<sup>2,4</sup> <sup>1</sup>Medical School, University of Minnesota, Minneapolis, MN, USA; <sup>2</sup>TB Care and Research Projects Office, USAID AMPATH Partnership, Eldoret, <sup>3</sup>Laboratory Medicine, Moi University School of Medicine, Eldoret, Kenya; <sup>4</sup>Medicine, The Warren Alpert Medical School of Brown University, Providence, RI, USA. e-mail: ben.pederson@gmail.com

**Background:** WHO recommended GeneXpert (GX) for use in the diagnosis of tuberculosis (TB) in De-

ember 2010. Kenya is 13th on the list of high-burden countries with a case rate of 305/100 000 and a TB-HIV co-infection rate of 44% in 2011. As part of a TB REACH initiative, GeneXpert laboratories were established to provide rapid testing for smear-negative patients, regardless of HIV status, at three peripheral public health facilities with high patient volumes.

**Design/methods:** One sub-district and two district level public health facilities were selected based on their relative high-volume TB patient load. Between December 2011 and February 2012, smear negative 'TB Suspects' were screened by GX with G3 assay cartridges upon request by their evaluating clinicians; beginning in March 2012, all new smear negative patients were automatically screened with GX. The second, morning smear negative sputum samples were analyzed with GX within 72 hours of collection. Tests were repeated when system errors occurred. All results were reported back to the clinicians and GX positive cases were specifically referred for treatment.

**Results:** During the first 17 weeks of the project a total of 162 GX tests were completed between all three sites on a total of 129 patients. Twenty-one cases of TB were detected, two of which were rifampin resistant. Technical test failure rate was 20%; nearly half were due to power failures and half due to GX system errors.



**Figure** TB REACH GeneXpert MTB/RIF (GX) data from three remote health facilities in Western Kenya (16/12/11–15/04/12). Total number of tests run = 162. MTB + = MTB detected; MTB - = MTB not detected; Rif + = rifampin resistance detected; Rif - = rifampin resistance not detected.

**Conclusions:** Institution of GX for the diagnosis of smear negative TB at a peripheral public health facility is feasible. Challenges to use in this setting include stability of the power grid that may be addressed by a back-up power supply technology. Institution of the updated G4 cartridges will reduce system error rates. These two technical interventions will decrease the need for repeat testing in our setting, thus reducing costs.

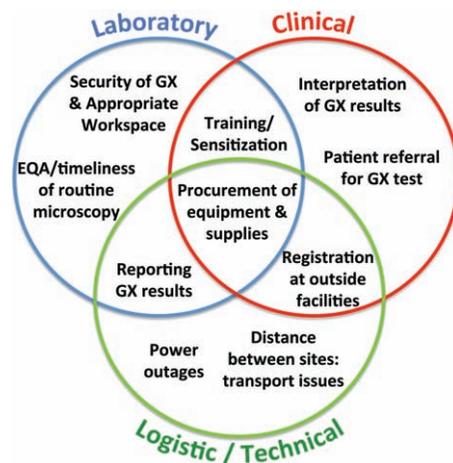
### PC-288-15 Operational challenges of GeneXpert MTB/RIF implementation at remote health facilities in Western Kenya

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**Background:** In Western Kenya, the diagnosis of tuberculosis (TB) has relied heavily on clinical evaluation and microscopy as culture remains largely unavailable. The GeneXpert MTB/RIF (GX) assay is specifically designed for use in resource-limited settings to diagnose TB and detect rifampin resistance. As part of a TB REACH initiative, GeneXpert laboratories were established to provide rapid testing for smear negative patients, regardless of HIV status, at three peripheral public health facilities.

**Intervention:** One sub-district and two district health facilities were selected based on patient volume, location, and availability of HIV and TB care services. GX technologists underwent a weeklong training and clinical staff were sensitized to the GX project. Two sites integrated the GX into the public hospital laboratory, and the other GX was installed in TB laboratory operated by a public/private partnership. All patients from outpatient clinics evaluated for TB who provided two smear negative sputum samples were eligible for GX evaluation.

**Results:** During the first 17 weeks of this project the primary implementation challenges included clinician interpretation of GX results, and improving the turn-around-time and quality of routine smear microscopy. Administrative challenges included staff sensitization, and procurement of supplies; technical challenges included power outages, security of equipment, and availability of appropriate workspace. The rural nature of each site led to logistic challenges of



**Figure** Operational challenges of GeneXpert MTB/RIF (GX) implementation in rural Western Kenya.

maintaining close project supervision and supply transport issues.

**Conclusions:** This project highlights important laboratory, clinical, logistic, and technical challenges that influence the operationalization of the GX in resource limited settings. Adequate GX training, staff sensitization, and efficient routine smear microscopy are essential to GX success. Integrating the GX into patient care requires focused clinician education on interpretation of laboratory tests results.

### PC-289-15 Multicenter study of the feasibility and effectiveness for Xpert® MTB/RIF in China

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**Background:** Smear examination, solid media culture and conventional DST remain the main available tools to diagnose tuberculosis in China. The low sensitivity of ZN smear microscopy and long turn-around time of culture and conventional DST limit their impact on TB control. The Xpert MTB/RIF test can detect tuberculosis and rifampicin-resistant with very high sensitivity and specificity in 2 hours. We aimed to assess the feasibility of Xpert MTB/RIF implementation in peripheral labs, provide experimental and management experience for broad scaling up in China.

**Methods:** We evaluated the performance of Xpert MTB/RIF in 2326 patients with suspected tuberculosis. Eligible patients in four county/district laboratories provided three sputum specimens. Each specimen was examined by smear examination, solid culture and Xpert MTB/RIF. Specie identification and conventional DST for RMP and INH were performed by PTRL and NTRL respectively. We assessed the performance, indeterminate rate, acceptable situation and report time of Xpert MTB/RIF that used in peripheral labs.

**Findings:** 2326 participants were enrolled between March 15, 2011, and December 31, 2011. 2034 patients were suspected cases of TB. In addition, 1 Xpert RIF indeterminate and 26 Xpert MTB negative but culture positive were also excluded. The sensitivity of Xpert MTB/RIF was 90% in smear-negative, culture-positive patients (221 of 246 patients), and the specificity was 90% (1374 of 1519 non-tuberculosis patients). 99 are culture positive from 292 suspected cases of MDR-TB. 6 Xpert MTB negative but culture positive were excluded. The sensitivity for rifampicin resistance was 86% (25 of 29 patients) and specificity was 91% (58/64), respectively. The indeterminate rate of MTB/RIF testing was 2.2% (162/7208) compared with 4.4% (627/14312) for cultures. Median time to detect tuberculosis for the MTB/RIF test was 2.5 hours. All fifteen laboratory staffs (100%) preferred this novel diagnosis tool rather than other traditional tools.

**Conclusion:** The MTB/RIF test can effectively be used in county level TB dispensary with the high sensitivity and specificity to detect tuberculosis and rifampicin resistance.

### PC-291-15 Discordance between the Hain MTBDRplus® assay and MGIT® culture in a highly drug-resistant population

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**Background:** Karakalpakstan is a semi-autonomous republic in Uzbekistan, with high rates of multi-drug resistant tuberculosis in new and retreatment cases. The Hain MTBDRplus® assay allows for the rapid detection of genotypic resistance to rifampicin and isoniazid from smear-positive sputum, and from culture isolates. We evaluated the performance of the assay on TB suspects between December 2010 and December 2011.

**Methods:** The Hain assay was performed directly on decontaminated sputum from microscopy-positive patients, and on isolates from smear-negative, culture-positive patients. MGIT® and/or LJ culture was the reference standard. The time to treatment (TTT) for the different test methods was also calculated.

**Results:** Hain and culture testing was performed on 1108 patients. Overall discordance was 9.2% (102/1108). Isoniazid showed 93.0% sensitivity, 92.2% specificity, 96.9% PPV, and 83.7% NPV, while rifampicin showed 97.4% sensitivity, 94.3% specificity, 96.8% PPV and 95.5% NPV. Discordance for sputum samples was 10.7% (86/801). Discordance for isolates was 5.52% (17/308). Average TTT was 8.8 days for Hain testing on sputum, 36.3 days for Hain testing on isolates, and 35.4 days for MGIT DST.

**Table** Performance of Hain MTBDRplus® assay according to sample and drug

	Smear-microscopy positive sputum %	Isolates %
Isoniazid		
Sensitivity	93.0	93.1
Specificity	88.5	100
PPV	95.8	100
NPV	81.4	88.1
Rifampicin		
Sensitivity	96.9	98.4
Specificity	92.5	98.4
PPV	96.0	98.9
NPV	94.2	97.6

**Conclusion:** In routine programme use, in a high MDR-TB prevalent setting, there was good agreement overall between the Hain assay and culture-based

DST. Discordance was lower on isolate testing, but as TTT was equivalent to MGIT DST, the relevance of the Hain test was limited on these samples. Rifampicin discordance caused most clinical difficulties, and more evidence is needed on the accuracy of genotypic versus phenotypic testing.

### PC-292-15 Introduction of Xpert MTB/RIF in National Tuberculosis Control Programmes of Nigeria and Indonesia: experiences with implementation under TB CARE I

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**Background:** Xpert MTB/RIF is a new molecular assay to rapidly detect *Mycobacterium tuberculosis* and rifampicin resistance. In March 2011, TB CARE I set out to support rapid implementation of this technique in routine laboratory services of national TB control programs (NTP) of Nigeria and Indonesia.

**Intervention:** Workshops were held with the NTP and local stakeholders to develop a national implementation strategy. Diagnostic algorithms and clinical guidelines were developed. Sites were assessed and selected based on agreed criteria. Registers, operating procedures and training material was developed. Local trainers were trained, who trained health staff on-site. Supply management and machines were set up: nine in Nigeria and five in Indonesia. Operator proficiency and challenges were assessed with supervision visits. Results continue to be monitored to evaluate impact.

**Results:** Many consultation meetings were needed to decide on diagnostic algorithms and site selection. Registration of equipment took several months, while

importation took a few days. Training of trainers was done within two weeks. On-site training, installation and operation showed minor problems with computer illiteracy, managing of error results, and occurrence of electricity interruptions. This was solved with retrainings and infrastructure improvements. Linking up with clinics for patient referral and follow up was challenging. Capacity to treat MDR-TB patients and availability of second-line drugs were limiting factors for rapid scale up.

**Conclusions:** Introduction of Xpert MTB/RIF into NTPs took longer than expected. Coordination by the Ministry of Health is needed to orchestrate implementation by in-country partners and donors. Clinicians and nurses should be trained simultaneously with laboratory staff. Implementation of Xpert MTB/RIF requires coordinated efforts to expand and enhance program management of MDR-TB and TB-HIV in order to ensure effective treatment for newly diagnosed cases.

### PC-293-15 Results from Xpert® MTB/RIF implementation in Médecins Sans Frontières field projects

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Between April–December 2011 Médecins Sans Frontières installed Xpert® MTB/RIF for routine use in 9 countries for a total of 16 sites. Thirteen instruments were used at the district and sub district level, 2 at the regional level, and 1 in prison. Fourteen sites implemented Xpert in parallel with smear microscopy, 7 using fluorescent (FM) and 7 Ziehl-Neelsen (ZN) microscopy. A total of 10 960 sputum samples were tested with G3 Xpert MTB/RIF cartridges. Out of the total specimens, overall positivity rate of Xpert MTB/RIF was 21%; compared to microscopy Xpert MTB/RIF increased laboratory detection by 48% (27% for FM and 54% for ZN). The proportion of rifampicin (RMP) resistance detected ranged from 3 to 45%. For an average rate of 7.3%, inconclusive results decreased from 10% during the initial period of implementation (April–Aug), to 5% during the follow-up period (Sept–Dec). During the second period, ‘error’ was the most common cause of inconclusive results, 63% (240/381), then ‘invalid’, 33.3% (127/381) and ‘no result’, 3.7% (14/381). The most frequent type of errors were 5011 (42.2%) and 2127 (15.3%). RMP indeterminate results were 1.4%. Xpert MTB/RIF in our experience significantly increased TB laboratory detection in sputum and



provided rapid screening for RMP resistance, decreasing delay to adequate treatment; empiric MDR-TB regimen was started upon receipt of Xpert RIF resistance results. Despite relative ease of use of the test, major constraints were high rates of inconclusive results, which required further training and replacement of 10 modules, and logistical and financial investment that limit Xpert MTB/RIF decentralization. Xpert MTB/RIF proved to be a valuable tool for a rapid diagnosis of TB and of RIF resistance, yet microscopy, culture and full line DST remain required for patient monitoring and confirmation of RMP resistance. Performances with new G4 Xpert MTB/RIF cartridge should be monitored. Studies on patients outcomes are essential.

#### PC-294-15 Microscopic observation of drug susceptibility testing for primary diagnosis of HIV-associated pulmonary tuberculosis in Indonesia

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**Background:** Diagnosis of pulmonary tuberculosis (PTB) in HIV-infected patients is difficult. Sputum microscopy has poor sensitivity, standard culture is slow, and molecular methods and liquid-culture are often too expensive to be implemented routinely. The recently developed 'microscopic observation drug susceptibility (MODS)' assay may be a good alternative. We evaluated the use of MODS for diagnosis of HIV-associated TB in an Indonesian setting.

**Design/methods:** Consecutive HIV-infected patients presenting with suspected pulmonary TB over a two-year period in a referral hospital in Indonesia were included. Sputum samples were analyzed using smear microscopy (ZN/FM), culture on solid medium (Ogawa), and MODS.

**Results:** A total of 184 patients were included in this study. MODS was positive in 59 patients (32%), compared with 55 using Ogawa (30%) solid culture, and 41 using sputum microscopy (22%). MODS was positive after a median of 7 days (range: 4–14 days), compared with 21 days (range: 18–28 days) for Ogawa solid culture. The running costs were \$4/patient for MODS compared with \$2/patient for solid culture. Laboratory staff were able to utilize MODS after 14 days of training. Contamination rate was reasonably accepted at 4% overall.

**Conclusion and recommendations:** We were able to implement MODS as a robust, rapid and quick method for diagnosing HIV-associated TB in Indonesia. MODS seems slightly more sensitive than standard culture. As such, MODS may be a useful diagnostic method for diagnosis of PTB in HIV patients, suitable for use in developing countries.

#### B.R.I.C. AND BEYOND: SPECIAL POPULATIONS IN EMERGING AND HIGH-INCOME COUNTRIES

##### PC-321-15 Tuberculosis in an urban area in China: differences between urban migrants and local residents

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**Background:** The increase in urban migrants has been one of major challenges for tuberculosis control in China. The different characteristics of tuberculosis between urban migrants and local residents in China have not been investigated before.

**Methods:** We performed a retrospective study of all pulmonary tuberculosis patients reported in Sojiang District, Shanghai, to determine the demographic, clinical and microbiological characteristics of tuberculosis cases between urban migrants and local residents. We calculated the odds ratios (OR) and performed multivariate logistic regression to the characteristics that were independently associated with tuberculosis among urban migrants.

**Results:** A total of 1366 pulmonary tuberculosis cases were reported during 2006–2008, among which 453 (33.2%) were local residents and 913 (66.8%) were urban migrants. Tuberculosis rates among urban migrants were higher than among local residents (67.0/100 000 vs. 27.7/100 000). Younger age (adjusted OR per additional year at risk = 0.92, 95%CI: 0.91–0.94,  $P < 0.001$ ), poor treatment outcome (adjusted OR = 4.12, 95%CI: 2.65–5.72,  $P < 0.001$ ), and lower frequency of any comorbidity at diagnosis (adjusted OR = 0.20, 95%CI: 0.13–0.26,  $P = 0.013$ ) were significantly associated with tuberculosis patients among urban migrants. There were poor treatment outcomes among urban migrants, mainly from transfers to another jurisdiction (19.3% of all tuberculosis patients).

**Conclusions:** A considerable proportion of tuberculosis cases occurred in urban migrants in Songjiang District, China, during 2006–2008. Our findings highlight the need to develop and implement specific tuberculosis control strategies for urban migrants, such as more exhaustive case finding, improved case management and follow-up, and use of directly observed therapy (DOT).

### PC-322-15 Correlation among women's high incidence of tuberculosis and reproductive health factors in Afghanistan

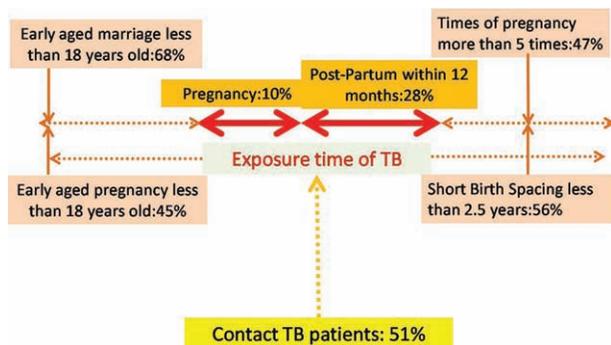
F Delawar,<sup>1</sup> H Ueki,<sup>2</sup> M Isono,<sup>2</sup> M Zafari,<sup>1</sup> H Manochehr,<sup>1</sup> H Akhgar,<sup>1</sup> M Seddiq,<sup>1</sup> S D Mahmoodi.<sup>1</sup> <sup>1</sup>National TB Control Program, Ministry of Public Health, Kabul, <sup>2</sup>TB Project, Japan International Cooperation Agency, Kabul, Afghanistan. e-mail: ntp.delawar@gmail.com

**Aim:** In Afghanistan, women of reproductive age (15–49 years) are the highest incidence of TB compare to men of same age. This is significant difference from other countries and remained unsolved question what risk factors are specific to this age and sex group.

**Objective:** Identifying correlated factors between women's reproductive health and TB incidence in Afghanistan.

**Methodology:** The study contained explorative with descriptive and comparative elements by combination of quantitative and qualitative methods. Triangulation methods such as semi-structured interview, in-depth interview and focus group discussion were used. TB female patients who were aged 15–49 years old, smear positive, and new registered in year 2011 were selected in 8 provinces with stratified and convenient sampling techniques.

**Result:** Totally 884 reproductive aged TB female patients were interviewed. The ratio of married to single was 2.5. Female patients of 68% (575) are ever-experienced pregnancy. One in 2.5 TB female patients who ever-experienced pregnancy exposed TB during pregnancy (10%) and exposed 12 months post-partum (28%). TB female patients' age at first marriage and first pregnancy less than 18 years old were 68% and 45% respectively. 47% had more than 5 times pregnancies and birth interval less than 2.5 years was 55%.



**Figure** Exposure time of TB among reproductive aged TB patients in Afghanistan.

**Conclusion:** The study revealed that there are significant risk factors of reproductive health to susceptible TB. Especially, early aged marriage, early aged pregnancy, prolificacy and short birth intervals are correlated to susceptible of tuberculosis among 15–

49-year-old women in Afghanistan. It suggests focus on policy makers for developing interventions to prevent TB.

### PC-323-15 Effectiveness of alcohol interventions among tuberculosis patients in Tomsk Oblast, Russia: randomized control trial, 2007–2011

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**Background:** We adapted two alcohol interventions to be delivered as an integrated component of tuberculosis treatment in Tomsk, Russia. Screening for alcohol use disorders and delivery of naltrexone with medical management and a Brief Counseling Intervention (BCI) were performed by tuberculosis providers as a part of routine care.

**Outcomes:** The primary TB endpoint was 'favorable outcome,' i.e., cure, completed treatment, or culture conversion, while 'poor outcomes' included treatment failure, death from any cause, or default. Our primary alcohol outcome was defined as the change in mean number of abstinent days in last month of study period compared with pre-hospitalization baseline.

**Results:** The study cohort for analysis includes 196 TB patients. There was a trend toward favorable TB outcomes among naltrexone versus no-naltrexone (87.0% versus 80.6%,  $P = 0.23$ ) but overall, TB outcomes did not significantly differ when comparing naltrexone versus no-naltrexone and BCI versus no-BCI. In terms of alcohol outcomes, mean abstinent days and heavy drinking days as well as average consumption per drinking day and per heavy drinking day did not differ by treatment arms.

**Conclusion:** Among TB patients with severe AUDs, we found that integrating evidence-based alcohol services into TB care did not have a significant impact on TB or alcohol outcomes. Possible explanations for this finding include the fact that individuals were not seeking treatment and may not have been interested in changing their drinking behavior. We suggest further exploration into integrated programmatic utilization of evidence-based interventions, particularly naltrexone, for individuals with co-occurring medical conditions such as TB.

### PC-324-15 Burden of tuberculosis in indigenous peoples globally: a systematic literature review

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**Background:** The burden of tuberculosis (TB) in the estimated 370 million indigenous peoples worldwide is not known. A literature review was conducted to summarize the TB burden in indigenous peoples, identify gaps in current knowledge, and provide the foundation for a research agenda prioritizing indigenous health within TB control.

**Design/methods:** A systematic literature review was conducted to identify articles published during January 1990–November 2011 that quantified the burden of TB disease in indigenous populations worldwide.

**Results:** Ninety-two articles from 19 countries were included. Limited published data exist on the TB burden among indigenous populations outside Australia, Canada, New Zealand, and the USA. Overall, indigenous groups were found to have higher TB incidence and prevalence than non-indigenous groups, though small studies from Africa, Asia, and Latin America showed mixed results (i.e., TB rates were equivalent or lower). Studies from the Amazon reported TB prevalence in indigenous groups up to 75-times national levels and the highest rates of TB incidence (>1000 cases per 100 000 population) in indigenous peoples globally. TB incidence rates in aboriginal and non-aboriginal Taiwanese were >100 and 50–70 per 100 000 population, respectively. In North America, the Inuit had the highest reported TB incidence (156 per 100 000 population), whereas the Metis of Canada and American Indians/Alaska Natives experienced rates of <10 per 100 000 population. Aboriginal Australians were approximately seven-times more at risk of developing TB compared to other Australians.

**Conclusion and recommendations:** There is a paucity of information on TB burden among the world's indigenous peoples. Where data are available, in general, indigenous peoples have higher rates of TB disease than non-indigenous peoples, but this burden varies greatly between groups and countries. Findings highlight the need to implement and improve TB surveillance in indigenous populations globally.

### PC-325-15 Excessive alcohol use and impact on tuberculosis treatment outcomes in a tuberculosis control programme

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**Background:** Excessive alcohol use is associated with TB disease progression and poor treatment outcomes, including relapse, treatment failure and default. The objective of the study is to evaluate the use of alcohol in active TB patients from central Ohio, and determine its impact on TB treatment outcome.

**Design/methods:** Retrospective review of demographic and clinical characteristics of patients diagnosed with active TB diseases in Franklin County (Columbus), Ohio, from 1994 to 2011 as reported to the Centers for Disease Control and Prevention (CDC) national surveillance database. Excessive alcohol use was defined by CDC reporting form as excessive use within the past year.

**Results:** A total of 995 active TB cases were reported during the study period. 13% (125/995) reported excessive alcohol use, 87% (862/995) denied alcohol use and the remainder of 8 were unknown. Patients with excessive alcohol use had a higher mean age and were more likely to be male, culture positive, have a pulmonary manifestation, be HIV positive, and have a history of homelessness, non-injection drug use and incarceration. Patients with excessive alcohol use were also less likely to complete treatment and had a higher death rate (see Table).

Characteristics	Alcohol use ( <i>n</i> = 125) <i>n</i> (%)	No alcohol use ( <i>n</i> = 862) <i>n</i> (%)	<i>P</i> value
Age, years, mean [median, range]	46 [44, 20–79]	37 [31, 3 mo–92]	<0.0001
Male	108 (86)	486 (56)	<0.0001
US-born	117 (94)	274 (32)	<0.0001
Culture confirmed diagnosis	112 (90)	657 (76)	<0.0001
Pulmonary	109 (87)	544 (63)	<0.0001
HIV status positive	16 (13)	35 (4)	<0.0001
Homelessness			<0.0001
Incarcerated	26 (21)	37 (4)	<0.0001
Non-injection drug use	7 (6)	6 (1)	<0.0001
	52 (42)	26 (3)	<0.0001
	( <i>n</i> = 118)	( <i>n</i> = 820)	
Completed treatment	94 (80)	715 (87)	0.026
Died	14 (12)	39 (5)	0.002
Other	10 (8)	66 (8)	0.875

**Conclusion and recommendations:** In our cohort, excessive alcohol use was associated with increased TB morbidity and mortality. A systematic alcohol assessment and intervention for this comorbidity should be incorporated into the current TB control program.

### PC-326-15 Tuberculosis disease among Somali and other foreign-born immigrants in Ohio, 1994–2011

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**Background:** Ohio is the second largest resettlement area for Somali refugees in the USA. The objective of the study was to compare cases of TB disease among Somali immigrants to US born and other foreign-born cases in central Ohio.

**Design/methods:** A retrospective review of all active TB cases in Franklin County (Columbus), Ohio from 1/1994 to 12/2011. Descriptive and geographic distribution analysis of the TB cases was performed using STATA and ArcGIS. Genotype groups were based on combination of a spoligotyping and MIRU analysis.

**Results:** A total of 995 active TB cases were reported during the study period: 66% (599/995) were foreign born and 38% (225/599) were Somali immigrants. A total of 66 countries of origin were observed, including 56 cases from India, 47 from Mexico, and 36 from Ethiopia. Somali cases were more likely to be younger in age, female, and had a higher percentage of extrapulmonary disease as compared to cases that were US born or foreign-born from other countries. The US born patients had a lower rate of completion and higher rate of death compared to foreign born patients despite higher rates of pan-drug susceptible *M. tuberculosis*. The majority of foreign-born cases were diagnosed less than four years after arrival to the US and were located in a smaller area that was geographically different than the US born cases. A total of 84% (83/99) of the Somali immigrant cases that were genotyped were clustered into 11 PCR groups (range 2 to 8 isolates).

Characteristic	US born	Foreign-born	Foreign-born
	(n = 396) n/N (%)	Somali (n = 225) n/N (%)	non-Somali (n = 374) n/N (%)
Age, years, mean [median, range]	46 [46, 3 mo–92]	28 [23, 2–74]	36 [30, 2–90]
Male	273 (69)	110 (49)	217 (58)
Extrapulmonary	65 (16)	98 (44)	114 (30)
Susceptible HRZE	301/313 (96)	128/145 (88)	251/287 (87)
Treatment completed	306 (77)	196 (87)	307 (82)
Died	43 (11)	2 (1)	11 (3)
Time from immigration to diagnosis, median, years	NA	2.25	3.5
Zip codes	28	25	35

**Conclusion and recommendations:** Characteristics of foreign-born and US born TB cases are different. Interestingly, clinical characteristics of Somali cases also differed from cases from other nations. Increased

cultural awareness and preventive TB therapy soon after immigration may decrease the development of active cases. Focused education and improved access to medical care in communities with high numbers of foreign-born cases are needed.

### PC-327-15 Multidrug resistance differences in permanent and floating population: a cross-sectional study in China

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**Background:** Population floating probably deteriorates the situation of drug-resistant tuberculosis. Careful monitoring of this patterns and its change trend should remain a priority. We aim to present the current situation of multi-drug resistant tuberculosis (MDR-TB) in permanent population and floating population in China.

**Methods:** A cross-sectional study was carried out in five representative cities with 28 million population. All sputum-smear positive tuberculosis patients diagnosed between July 2010 and June 2011 were enrolled. Data on drug resistance based on routine drug susceptibility testing (DST) and patient characteristics were collected.

**Results:** 2670 TB cases were enrolled in our study. Among 1786 cases reported result of strain identification, 1773 cases (99.3%) were identified to be mycobacterium tuberculosis and carried out DST. Among 1771 patients without missing data, 99 cases (5.6%) had MDR-TB, with 85 cases in permanent population and 14 cases in floating population. The overall prevalence of MDR-TB in floating population (9.5%) was higher than that in permanent population (5.2%) ( $P = 0.03$ ). The prevalence rates of MDR-TB for new TB patients were 3.0% and 5.5% in permanent population and floating population, respectively. And, the prevalence rate for treated TB patients in floating population (35.0%) dramatically increased compared with that in permanent population (22.8%).

**Conclusions:** Population floating has an impact on MDR-TB prevalence. Although there is no statistically significance for prevalence rates of MDR-TB in treated TB patients between two groups, our observation strongly implies the importance of TB case management in floating population for MDR-TB prevention and control. However, nation wide surveillance data on drug resistance is lack. We stress the necessity of continuous monitoring of drug resistance trends routinely, to assess the efficacy of case management in floating population and their impact on MDR-TB epidemic.

### PC-328-15 Higher death rate among socially vulnerable people with tuberculosis in Japan: evidence from tuberculosis surveillance

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**Background:** Tuberculosis (TB) research from high- and low-income countries consistently report that socially vulnerable populations (SVP) have high risk for TB, long patient delay and poor treatment outcome. In this study, we identified homeless, persons receiving welfare, and foreigners as SVP in Japan. We investigated whether or not patient characteristics, patient delay and treatment outcome, particularly death and default, of SVP differed from general population (non-SVP).

**Design/methods:** We conducted a cross-sectional study using the TB surveillance data from 2010. The study subjects were smear-positive pulmonary TB cases, aged 16–60. A cut off of one month was used to denote prolong patient delay. We analyzed the frequencies, and measures of central tendency to compare the proportions.

**Result:** The Table shows that foreign patients were younger and proportion of females was higher than males compared to other patient groups. MDR-TB rate in foreigners was obviously higher than other groups. Homeless and persons on welfare had similar

**Table** Characteristics of socially vulnerable population (SVP) with pulmonary TB smear positive (age 16–60) compared to non-SVP

Characteristic	Socially vulnerable population (SVP)			Non-SVP (n = 2081)
	Homeless (n = 116)	On welfare (n = 322)	Foreigners (n = 251)	
Sex				
Male	97%	89%	43%	70%
Female	3%	11%	57%	30%
Age				
Range	23–60	17–60	17–60	16–60
Median age	53	54	30	44
Address				
Metro	73%	68%	50%	42%
Non-metro	27%	32%	50%	58%
MDR-TB	0%	1%	5%	1%
X-ray (cavity)	83%	68%	58%	59%
Co-morbidity				
Diabetes	17%	17%	6%	13%
HIV				
Positive	0%	1%	1%	0.5%
Negative	48%	41%	46%	57%
Unknown	52%	58%	53%	43%
Patient delay				
More than 1 month	31%	31%	21%	30%
Treatment outcome				
Success	53%	56%	84%	69%
Death	6%	9%	0%	3%
Default	1%	2%	4%	3%

demographic characteristics. Although proportion of patients with delay is similar between homeless and non-SVP, the proportion of lung cavity in homeless is much higher than other groups. The coverage of HIV testing among non-SVP is higher than SVP although HIV infection rate is higher in foreigners and persons on welfare. Diabetes rate in homeless and persons on welfare is almost three times higher than foreigners. Default in all groups is quite low and did not significantly differ between SVP and non-SVP. However, death rate of persons on welfare is three times higher than non-SVP. Of the patients who died during TB treatment, 38%, 33% and 20% of homeless, welfare, and non-SVP had diabetes.

**Conclusion and recommendation:** Persons receiving welfare and homeless had higher death rates. Diabetes is a serious co-morbidity, especially among socially vulnerable patients, and active case-finding for TB among SVP should also screen for diabetes

### PC-329-15 Sex differences in tuberculosis diagnosis at private laboratories in Pakistan and Bangladesh

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**Background:** It remains unclear why more cases of tuberculosis (TB) are notified from males than females in the developing world. While data from DOTS centres shows an excess of male suspects and cases in most settings, gender dynamics in the private-sector have rarely been investigated. This study analyses sex differences at private laboratories (PLs) in Karachi, Pakistan and Dhaka, Bangladesh.

**Design/methods:** 6 PLs across Karachi and 4 across Dhaka were included in the study, based on their volume of TB suspects. Trained health workers screened all individuals attending participating PLs. TB suspects were identified based on reported symptoms, contact with a TB case or history of TB. All suspects were guided on sputum expectoration techniques; those providing a specimen were given a free smear-microscopy test and a chest X-ray. Suspects that were smear-negative but had a TB-suggestive X-ray were GeneXpert tested. Proportions of males and females at each stage of the diagnostic process were compared.

**Results:** From October 2011 to March 2012, 246 313 individuals were screened at participating PLs. While there was no notable sex difference at screening, significantly fewer females were identified as suspects in both cities ( $P < 0.001$ ). After guidance, sputum submission rates were similar in males and females. Smear-positivity rates were higher in females than males

across both sites (statistically significant in Karachi, 5.8% vs. 7.8%,  $P = 0.01$ ). In Karachi, smear-negative females were also more likely than males to have TB-suggestive X-rays (27.6% vs. 30.8%,  $P < 0.001$ ) and be Xpert positive (14.6% vs. 21.6%,  $P < 0.001$ ).

**Table** Sex differences along the TB diagnostic process at private laboratories in Karachi and Dhaka

	Karachi				Dhaka			
	M	F	p-value	M:F	M	F	p-value	M:F
A: Screened	103,790	97,163	n/a	1.07	23,060	22,743	r/a	1.01
B: Suspects identified (%B/A)	2,487 (2.4)	1,920 (2.0)	<0.001	1.30	1,052 (4.6)	629 (2.8)	<0.001	1.67
C: Suspects providing sputum for testing (%C/B)	2,056 (83.1)	1,567 (81.6)	0.21	1.32	775 (73.7)	443 (70.4)	0.14	1.75
D: Smear-positive suspects (%D/C)	119 (5.8)	123 (7.8)	0.01	0.97	25 (3.2)	18 (4.1)	0.45	1.39
E: Smear-negative suspects (%E/C)	1,949 (94.2)	1,444 (92.2)	0.01	1.35	750 (96.8)	425 (95.9)	0.45	1.76
F: Smear-negative and x-ray suggestive suspects (%F/E)	537 (27.6)	483 (30.8)	<0.001	1.11	143 (19.1)	83 (19.5)	0.85	1.72
G: Suspects Xpert tested	523	464	n/a	1.11	138	81	r/a	1.70
H: Xpert-positive suspects (%H/G)	74 (14.1)	99 (21.3)	<0.001	0.75	30 (23.3)	17 (22.7)	0.92	1.76
I: Bacteriologically-positive (%I/H)	193 (9.3)	222 (14.2)	<0.001	0.87	55 (5.2)	35 (5.6)	0.65	1.57

**Conclusion and recommendations:** Female suspects at PLs in both countries had higher smear-positivity rates than males. In Karachi, Xpert positivity was also higher in females. However, during screening fewer females than males were identified as suspects, particularly in Dhaka. This may be due to gender differences in symptoms experienced or communication of symptoms, and should be investigated further.

### PC-330-15 QuantiFERON®-TB Gold in-Tube for diagnosing latent tuberculosis infection in transplantation

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**Aim:** Tuberculosis (TB) is a feared complication in transplanted patients who need to use immune modulators. In Brazil, TB is up to 75 times more frequent among kidney and liver transplanted patients. The aim of the present study was to evaluate TST and QFT-GIT® for the diagnosis of LTBI in candidates to transplant in a reference hospital in Porto Alegre, in Southern Brazil.

**Methods:** Clinical and epidemiological data from patients in the waiting list for lung, kidney and liver transplant were collected using a standard questionnaire. Patients were submitted to TST as per routine (positive if >5 mm) and were invited to be QFT-GIT tested if they signed an informed consent. Those who were transplanted were submitted to consecutive QFT-GIT tests on the 3rd and 6th months after transplantation.

**Results:** A total of 100 patients were tested from February to December 2011, of whom 57 were QFT-/TST-, 22 were QFT+/TST+ and 20 were QFT+/TST-. One patient with an indeterminate QFT was TST negative. Eight patients deceased before they had the chance to be transplanted, 74 remain in the waiting list. Among the 18 transplanted patients (all under immunosuppressive therapy), five were initially QFT+/TST+, of whom four remained QFT+ and one became indeterminate; two were QFT+/TST-, of whom one became indeterminate and one remained QFT+; ten were QFT-/TST-, of whom nine remained QFT- and one became indeterminate and the one indeterminate became QFT-.

**Conclusions:** Initial discordance between TST and QFT was less frequent than in other populations (around 30%) considering a 5 mm cut-off for the TST. Although conversions and reversions were not observed, these preliminary results indicate that indeterminate QFT results may be frequent after starting immunosuppressive therapy, which suggests that those tests may be unreliable in these circumstances.

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### PC-331-15 Determinants of latent tuberculosis infection within an urban US setting, 2003–2011

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**Aim:** We examined the determinants for latent tuberculosis infection (LTBI) among an urban cohort using a mobile medical clinic (MMC) in New Haven, CT, USA.

**Methods:** Structured questionnaires were consecutively administered to 8261 unique patients accessing the MMC from 2003 to June 2011; tuberculin skin testing (TST) was routinely provided for clients not receiving prior TST within one year. Correlates of TST+ status were assessed using univariate and multivariate logistic regression analysis with AIC modeling.

**Results:** Of 8261 unique patients, 3937 (47.7%) were TST screened with 2386 (60.6%) TST's read. Prevalence of ever +TST was 8.9% ( $n = 733/8261$ ) with immigrant prevalence 4.2% ( $n = 346/8261$ ). Prevalence of newly +TST was 4.1% ( $n = 343/8261$ ) with immigrant prevalence of 2.7% ( $n = 220/8261$ ). Top countries of origin for newly +TST immigrants were Mexico ( $n = 52$ , OR 10.9), Ecuador ( $n = 43$ , OR 24.37), and Guatemala ( $n = 11$ , OR 12.03). Countries by WHO prevalence quintiles for newly +TST yielded OR 8.2 (CI 4.9–13.9) at highest prevalence

quintile. Immigrant status (aOR 6.06, CI 4.93–7.46), Hispanic ethnicity (aOR 1.52, CI 1.23–1.90), male gender (aOR 1.27, CI 1.07–1.52), ever cocaine use (aOR 1.61, CI 1.31–1.98), and transactional sex (aOR 1.41, CI 1.09–1.83) were significantly associated with ever +TST ( $P < 0.007$ ). Hispanic ethnicity (aOR 2.42, CI 1.86–3.16), male gender (aOR 2.01, CI 1.49–2.70), and a stable relationship (aOR 2.50, CI 1.86–3.34) were significantly associated with newly +TST ( $P < 0.001$ ).

**Conclusion:** LTBI is high among socially and medically marginalized individuals in urban settings, and innovative methods for screening and detection are urgently needed, especially for immigrant populations who may avoid traditional healthcare.

### PC-332-15 Flexi-time DOTS in Delhi slum, a 5-year experience: patient-provider perceptions and sustainability

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**Background and challenges to implementation:** Around 40% of the populations live in slums of Delhi. Most slum dwellers are daily wagers employed in factories or as food vendors, scrap collectors and other unorganised jobs. They lose their wages to avail supervised DOT delivered through fixed working hours. This was the cause of high default rate among slums. In collaboration with NTP Delhi, GLRA implemented a flexi-time community DOT project from September 2005 to March 2011 in 15 slums of Delhi. Community volunteers after TB training were encouraged to operate DOT centres within the slums at patients' convenient time. 2718 patients among total 2940 enrolled for DOT, completed treatment successfully during 5 years project with 32 patients reported defaulters. A retrospective review was conducted to understand the perception of the patients enrolled and the volunteers engaged in the project.

**Objective:** To review the patient and provider perception regarding provision of flexible timings of DOT therapy by community DOT volunteers.

**Methods:** Qualitative techniques were used to collect data from program managers, implementers and direct/indirect beneficiaries, i.e., treated patients, families of TB patients, and community members

**Results and lessons learnt:** Majority of DOT volunteers had contact with TB patient, self-motivated to become a community volunteer. They ensured 92% patients treatment completion. Most volunteers felt their social status improved in the slums. Case holding among drug addicts, alcoholics was a problem. GLRA transitioned this project in 2011 to NTP in a systematic way.

**Conclusions and key recommendations:** Flexi-time DOTS in urban slums improved treatment adherence and is a sustainable strategy.

### PC-333-15 Health care seeking behaviour of pulmonary tuberculosis patients in socio-economically depressed areas in the Philippines

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**Background:** Delay to tuberculosis (TB) diagnosis is hazardous both to TB patients and to community members. This study aims to describe the current health seeking behaviour on delay to TB diagnosis in socio-economically depressed areas in Metro Manila in the Philippines.

**Design/methods:** It is a cross-sectional study to describe possible attributable factors of TB patients to delays to TB diagnosis, i.e., patient, health system and total delays. Data were collected through data collection form during the intensive phase of the treatment course from each of the patients. All new smear-positive pulmonary TB patients, registered at DOTS facilities in District I in Tondo, Manila City, and in Payatas, Quezon City, in the Philippines from April 2010 to March 2011 were targeted. Wilcoxon's rank sum test or Kruskal-Wallis rank test were applied to compare medians.

**Results:** Among 824 new smear-positive pulmonary tuberculosis patients registered during the study period, 773 patients (94%) were successfully interviewed. Median patient delay of those who visited first to private clinics/hospitals tended to be short compared with that of those who visited first to health centers or NGO clinics (median 17 days vs. 30 or 37 days respectively, Kruskal-Wallis rank test,  $P = 0.00$ ). Median health system delay of those who consulted first either to health centers or NGO clinics showed significantly shorter than that of those who consulted first either to public hospitals or private clinics/hospitals ( $P = 0.00$ ).

**Conclusion and recommendations:** Shorter patient delays but longer health system delays of those who consulted first to private clinics/hospitals suggest that TB diagnosis practice at private clinics/hospitals needs to be improved in urban settings in the Philippines.

## TOBACCO CESSATION

### PC-364-15 An intervention study for tobacco control among children in college schools in Sousse, Tunisia

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**Background:** In Tunisia, young people start smoking at an early age. The mean age of smoking initiation is about 13 years among male smokers. The prevalence increases significantly with age among boys from 3.4% at 13 years to 32.3% at 19 years. Early preventive action against smoking can lead to the reduction of major smoking related chronic diseases in adults.

**Objective:** To implement and evaluate a school-based intervention program to prevent smoking habit among children.

**Design:** Pre-test post-test quasi experimental design with a control group.

**Setting:** 4 secondary schools in Sousse, Tunisia. A stratified and proportional sampling was used to include students who participated in the survey. Our population was composed of students aged 13–16 years attending colleges in the city of Sousse, Tunisia.

**Intervention:** The overall intervention program lasted for a school year and incorporated educative actions concerning tobacco use.

**Data collection procedure:** A pre-tested self-administered questionnaire in arabic and was distributed to students in the presence of pre-trained doctors.

**Results:** Globally, knowledge, behaviours and intentions concerning smoking improved in both groups between baseline and the end of the study, particularly in the intervention group. Changes from baseline in percentage of knowledge that smoking causes lung neoplasm were significantly different between intervention and control groups (+35.8% versus +7.3%;  $P < 10^{-3}$ ). The intention to smoke in the future decreased significantly in the intervention group (4.3% to 2.2%,  $P = 0.001$ ). The smoking behaviour decreased in both groups and the percentage of change wasn't statistically different between the two groups (−1.5% in the intervention group versus 1.8% in the control group;  $P = 0.62$ ).

**Conclusions:** This study has demonstrated the potential of school as a suitable setting for the promotion of non smoking habits in children. The study resulted in substantial improvements concerning knowledge, behaviours and intentions in the intervention group.

### PC-365-15 Depression and neuroticism and their association with smoking behaviour in a population-based survey in Egypt: implications in tobacco cessation

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**Background:** Cigarette smoking and other forms of tobacco use pose a large and growing public health burden globally and in Egypt. To better understand smoking behavior and addiction, researchers have recently focused on individual differences in personality and psychological traits; with the goal to inform policies and programs for smoking prevention and cessation, and ultimately improve interventions through personalized treatment.

**Methods:** We assessed associations between neuroticism and depression scores and smoking behavior among three groups of adult males randomly selected from five rural villages in Lower Egypt. Trained interviewers administered relevant questionnaires to 201, 278 and 120 never, current, and former smokers, respectively. CES-D (Center for Epidemiologic Studies Short Depression Scale), EPI (Eysenck Personality Inventory), FTND (Fagerström Test for Nicotine Dependence), and WISDM (Wisconsin Inventory of Smoking Dependence Motives) scales were used to generate different scores.

**Results:** The mean CES-D scores were higher among current (11.26) and former smokers (11.87) as compared to never smokers (10.42);  $P = 0.06$ . So were the EPI scores (5.34, 5.20, 4.71, respectively;  $P = 0.01$ ). Among current smokers, both CES-D and EPI scores were associated with FTND scores, albeit not statistically significant. Both CES-D and EPI scores were significantly associated with a variety of smoking motives. A moderate association was found between CES-D scores and quitting behavior ( $P = 0.05$ ).

**Conclusion and recommendations:** Neuroticism and depression were associated with several aspects of smoking behavior and motives. Therefore, in designing and implementing smoking cessation interventions, attention should be given to individuals and their personal needs for treatment. A combination of public policy and treatment strategies would help curb the smoking epidemic in Egypt.

### PC-366-15 Results of a low-intensity intra-workplace smoking cessation and predictors of sustained six months quitting success

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**Background:** This study aims to identify the predictors of a 6-month quitting success among employees involved in a low-intensity workplace smoking cessation.

**Design/methods:** A prospective cohort was introduced among employees from two different public universities. Interventions include three sessions of behavioral therapy sessions combined with free nicotine replacement therapy (NRT) for eight weeks. Participants were followed up for six months. Independent variables assessed were on sociodemographic and environmental tobacco smoke. Success was defined by self reported abstinence since started quitting with CO-oximetry (carbon monoxide < 6 ppm). Univariate and multivariate logistic regression analysis was performed to identify the predictors of success.

**Results:** One hundred and eighty five smokers volunteered to participate. Fifteen percent and 13% sustained quit at three months and six months respectively. Multivariate analysis revealed that at six months only two variables were predictive of success: attending all three behavioural sessions and being non-Malay. None of the environmental tobacco exposure variables were predictive of sustained cessation.

**Conclusion and recommendations:** Individuals who attended more cessation sessions had a higher probability of achieving success with combined medical and behavioural therapy. This result is similar to those in clinic-based smoking cessation. Furthermore, our study also demonstrated that in the case of a low-intensity workplace cessation programme with poor enforcement of smoke-free policy, environmental tobacco smoke does not contribute to long term cessation. Hence, future studies should concentrate on conducting and evaluating workplace programme with greater intensity (i.e., effective smoke-free policy and enforcement of smoking employees to enrol in cessation programme).

### PC-367-15 The challenges of reducing tobacco use among young Siddi women of Gujarat, India

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**Background:** In India, use of tobacco is three times as high for scheduled tribe women relative to non-scheduled tribe women. This study describes young (15–24 years) Siddi women's self-reported tobacco use and compares knowledge and attitudes of those who use and don't use tobacco.

**Design/methods:** Cross-sectional surveys with 182 young women in five villages of Junagadh District collected data on use of tobacco, health problems, risk knowledge, attitudes to smoking and sociodemographic characteristics. Multivariable logistic regression analyses assessed associations between knowledge and attitude variables and use of tobacco and health problems.

**Results:** Fifty-six per cent of the women ( $n = 103$ ) reported currently smoking. The majority (71%) who used tobacco reported quitting (14%). Relative to tobacco user, non tobacco user had more schooling ( $P = 0.001$ ), higher monthly income ( $P = 0.002$ ), lower parity ( $P = 0.001$ ), better understanding of tobacco related risks (cancer  $P = 0.01$ ; tuberculosis  $P = 0.002$ ; fever  $P < 0.001$ ; death  $P = 0.003$ ), and less frequently expressed attitudes indicating that quitting was very difficult given other problems they faced.

**Conclusion and recommendations:** Increasing awareness of tobacco-related risks to young mothers as well as children and the benefits of stopping may motivate Siddi women to attempt to stop. However, knowledge alone is unlikely to be sufficient considering the life circumstances of many women. Addressing the social environment and daily stressors, particularly those exacerbated by dual burden of production and reproduction, may be critical to supporting stop attempts.

### PC-368-15 Concept of tobacco-free village

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**Aim:** To reduce tobacco-users in India's north-east region (ASSAM) wherein tobacco consumption is a religious and social custom; higher than national average (GATS).

**Methods:** By upgrading 'anti-tobacco program' of schools of NTCP, India, to the community level with active support of students, parents, religious heads and political support. Observing social development of diverse religions and ethnic values of Assamese culture, we started in 'Sahpuria Village' (within 5 km radius, north-east of Jorhat town), wherein we conducted a school program and afterwards 5 de-addiction camps, 25 anti-tobacco awareness campaigns and street plays. Family history, tobacco consumption pattern of the villagers was surveyed. Youths, self-help and women groups were trained in counseling activity with participation in religious, social and community festivals injecting awareness at

all levels. Homes were visited imparting information on health and finances with personal interfaces with the un-yielding addicted. Nicotine replacement therapy was employed in two persons along with psychological support. Oath-taking ceremony was conducted in community sacred prayer hall. More villagers are getting aroused to join the active program. WNTD '2011 was celebrated in a festive manner. Active surveillance is going on to prevent any relapses for re-motivation.

**Village composition:** Families: 340, Population: 1240, Adults: 920, Children: 320, School going: 220, Religion: Hindu and a few Muslims. Prior activity: almost all adults used tobacco; Chewing: 80%. Smoking, 20% children were at risk of developing habit.

**Results:** Most of the adults gave up tobacco usage with 80% of success rate till date. Relapse rate is 0.5%. The risk of developing new tobacco user is reduced.



**Conclusion:** Presently we are developing more village projects. Tobacco-free villages can be effectively developed by creating a competitive environment amongst the schools. 'Anti-tobacco (swipe-out) community program's are possible beginning with simple school programs by generating sense of responsibility between govt. agencies, NGOs, social workers, students and guardians.

#### PC-369-15 Psychosocial factors associated with smoking status in a population of South African tuberculosis patients: a structural equation model

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**Background:** Tobacco smoking increases the risk of tuberculosis and of adverse tuberculosis outcomes. The aim of this study was to model how psychosocial factors, in particular low socio-economic position and social support, influence smoking status among recently diagnosed tuberculosis patients.

**Methods:** Data from structured questionnaires and medical records of 525 tuberculosis patients seeking treatment at 6 health facilities in Tshwane, South Africa were analyzed. Using structural equation modeling, the latent variable 'social support' was fitted first, where-after potential direct and indirect pathways with smoking status were determined. Models were tested and adjusted for model fit based on the modification indices obtained.

**Results:** The prevalence of current daily smoking, less than daily smoking and past smoking was 17.5%, 4.0% and 2.1% respectively. As hypothesized, the effect of low social support on current smoking was mediated through its effect on increased stress levels and problem-drinking (measured on cage scale). Stress in turn was linked to increased vulnerability to depression. The effect of low education on smoking was indirect through its relationship with social support. Low income, male sex, depression vulnerability and higher cage score exerted a significant direct effect on current smoking. The overall model fit was good ( $\chi^2$  goodness of fit index/degrees of freedom = 1.254, comparative fit index = 0.985, root mean square error of approximation = 0.022).

**Conclusion:** This study provides insight into mechanisms that may be linking low socio-economic position with smoking initiation and/or continuation. The findings highlight the importance of enrolling social support as part of interventions to aid TB patients with smoking cessation.

#### PC-370-15 Is the motivational Q-mat test useful to predict smoking cessation?

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**Background:** Smoking is one of the major causes of cancer, heart and pulmonary diseases. One of the essential steps in tobacco control is persuading the smokers to quit smoking. In this study we investigated abstinence rate after 6 months according to level of motivation to quit (Q-mat score) and level of nicotine dependency (Fagerstrom score).

**Material and method:** This cross-sectional study was conducted on the volunteers of smoking cessation clinic in Tehran. Their demographic information and cigarette status were assessed through a questionnaire. They underwent tests for nicotine dependency, motivation degree assessment by FT and Q-mat test respectively. Their quit rate was verified by telephone and through exhaled CO measurement after 6 months.

**Results:** 345 persons were studied from which 311 were (90.1%) male. After 6 months follow-up, abstinence rate was 39%. The mean Q-mat score was  $15.8 \pm 5.1$  (95%CI 14.9–16.7) in participants who

stopped smoking and  $15.4 \pm 5.1$  (95%CI 14.7–16.1) among participants who failed smoking cessation ( $P = 0.4$ ). The mean FT score was  $5.2 \pm 2.6$  (95%CI 4.7–5.6) in participants who stopped smoking and  $6 \pm 2.6$  (95%CI 5.7–6.4) among participants who continued smoking ( $P = 0.002$ ).

**Conclusion:** Q-mat score did not predict the success rate in the observed population. Lower Fagerstrom score is correlated with high quit rate. Thus in this regards attention should be paid on high nicotine dependent smokers.

### PC-371-15 Is physician's advice better than counselling to help tuberculosis patients quit smoking? A randomised pilot study in South India

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**Background:** Tobacco smoking has been identified as a risk factor for poor tuberculosis (TB) treatment outcomes, in addition to all its other health hazards.

**Aim:** To compare the efficacy of counselling provided by a counsellor and provision of a brochure containing smoking cessation information versus physician's advice in addition to these two interventions

**Design/methods:** The clinical trial was conducted at Madurai, South India, one hundred and sixty male patients with tuberculosis (80 HIV co-infected) were randomized, stratified by nicotine dependence (low/high by Fagerstrom scale). Abstinence at one month was assessed by self report and carbon monoxide breath analysis.

**Results:** Mean (SD) age was 39.5 (8.5) years. Overall, 35% had high dependence to nicotine. Most patients (45%) smoked both cigarettes and bidis. Quit rates were 42% of 67 patients in the physician group and 36% of 66 patients in standard counselling arm. No significant association was found between quit rate and type of tobacco smoked, past H/O quitting, number of cigarettes/bidis smoked, duration of smoking or educational status. There was no significant difference in quit rates between HIV-infected and uninfected patients.

**Conclusions and recommendations:** The data suggests that the physician's advice group has about 8% higher quit rates than counselling group in TB and HIV-TB smokers. However the difference was not significant as the sample size is small. Future studies should assess long term abstinence rate, and the efficacy of pharmacologic interventions in larger studies.

### PC-372-15 Preparedness for delivery of tobacco cessation service at primary care health facilities in India: results from STEPS health system intervention study

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**Background:** India with 275 million current tobacco users contributes to 1/5th global tobacco attributable mortality. The near-future tobacco mortality can be reduced with the provision of cost effective tobacco cessation (TC) service. The study examines preparedness for TC service delivery at primary health care settings.

**Method:** Cross sectional survey of 238 physicians using semi structured questionnaire was conducted in two Indian states—Andhra Pradesh and Gujarat—from January to April 2011.

**Results:** The preparedness for TC service delivery by physicians was defined as physician who (1) received training, (2) has TC knowledge and (3) is willing for providing TC services. The study revealed that 98% physicians are willing to be part of TC services. It is surprising that even though only 1/3rd of physicians have been trained during their professional training (29%) or during their service (16%) period; 2/3rd of physicians profess knowledge about TC services. The majority of 'on-job' training was of half to one day (46%) duration. This knowledge, however, does not seem to translate into practice as only 25% of physicians are practicing comprehensive TC services. The overall preparedness among physicians was 19% with significant ( $P = 0.006$ ) difference between the states. Age, gender and specialization have very little influence on preparedness.

**Conclusion:** There is inadequacy of skill-based training with need to review ongoing TC training programme and its duration. The integration of TC services at primary care health settings is plausible with skill-based training of adequate duration for all primary care physicians irrespective of their age, gender and specialization. Further study to assess state specific issues for TC service preparedness is required.

### PC-373-15 Implementing effective interventions for advancing tobacco use prevention and cessation among low socio-economic status youth in India

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**Background and challenges to implementation:** Tobacco use is an emerging threat to youth's health in India where 5500 youth initiate tobacco use every

day. Low socio-economic status (SES) is a strong determinant and is inextricably linked with tobacco use among youth. Need for low-cost, community-based tobacco use interventions for socio-economically disadvantaged youth have been recognized in India.

**Intervention or response:** Project ACTIVITY (Advancing Cessation of Tobacco In Vulnerable Indian Tobacco consuming Youth) is a community-based group randomized trial involving 14 communities (resettlement and JJ clusters), matched and randomized to intervention ( $n = 7$ ) and control ( $n = 7$ ) conditions to prevent the onset and reduce the prevalence of tobacco use among youth (10–19 years) in low SES communities in Delhi. Two year multi-component intervention was based on social cognitive theory and consisted of community-based interactive activities, tobacco cessation camps, m-health (SMS campaign) and outreach programmes. Surveys were conducted at baseline ( $n = 6023$ ), intermediate ( $n = 5473$ ) and endline ( $n = 4624$ ) to evaluate efficacy of the intervention. Outcomes measures included multiple forms of tobacco use. Growth curve analysis through mixed effects models was used to measure the difference in time trend of current tobacco use between two groups. Statistical analyses were conducted using LISREL 8.80.

**Results and lessons learnt:** Tobacco use significantly decreased in intervention group (slope =  $-0.69$ ) among youth from resettlement colonies, while it increased in control group (slope =  $0.24$ )  $P < 0.001$ . A significant decreasing trend in current smoking prevalence was observed in intervention group in resettlement colonies,  $P < 0.001$  (slope =  $-0.66$ ) than control group (slope =  $0.12$ ). Intention to smoke among 10–14-year-olds and susceptibility to smoke among 15–19-year-olds also decreased significantly in intervention group than in control group,  $P < 0.05$ .

**Conclusions and key recommendations:** Community based interventions that engage youth and utilize them as change agents are feasible, efficacious and sustainable for tobacco control particularly in low SES communities in resource deficient country like India.

#### **PC-374-15 Effectiveness of health promotional educational package on smoking cessation: raising awareness about respiratory morbidity and promoting smoking cessation**

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**Background:** Health professionals in their unique position can educate community on health effects of tobacco. In India, only 46.3% of smokers were advised to quit by health care provider, suggesting the need of involvement of health care professionals in providing tobacco cessation services to the community.

**Methods:** The study was a cross-sectional study conducted among 100 males belonging to 18–60 yrs of

age group in Pilani, Rajasthan. Participants were educated about the harmful effects of tobacco through health promotion package. Motivational interviewing was done using 5 As (Ask, Assess, Advice, Assist and Arrange) technique. The harmful effects of tobacco particularly respiratory effects were explained using flip-charts. Pre and post intervention knowledge on harmful effects of tobacco was compared using paired  $t$ -test after an intervention period of 4 months.

**Results:** Number of subjects who identified heart diseases, respiratory diseases, oral diseases, impotency, cancer and stroke had increased significantly ( $P = 0.01$ ). There was a significant decrease in the number of subjects with common misconceptions about tobacco smoking ( $P = 0.03$ ). Proportion of subjects who abstained from smoking for more than 7 days was 3.5% in the intervention area whereas none of the smokers quit in non intervention group. The mean number of per capita per day consumption of bidis and cigarettes decline significantly from 5.2 (SD = 9.7) to 1 (SD = 0.00).

**Conclusions and recommendations:** Health promotion package improved the quit rate in intervention group without use of any pharmacological treatment. Health promotion, health education package and brief advice can increase smoking cessation within the community.

#### **PC-375-15 What are the predictors of giving up smoking among patients suspected of tuberculosis? A sub-analysis of the ASSIST Pakistan trial**

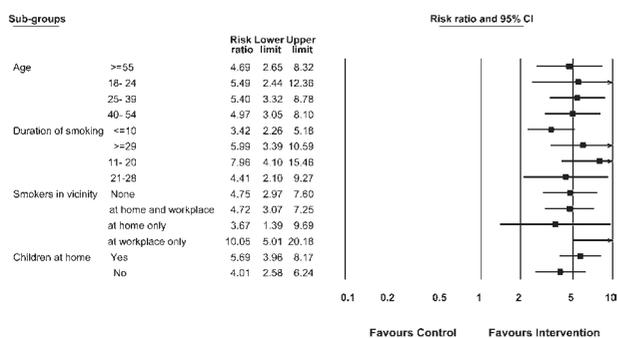
K Siddiqi,<sup>1</sup> O Dogar,<sup>2</sup> S Karam Shah,<sup>3</sup> A Khan,<sup>2</sup> N Safdar,<sup>2</sup> M Ahmad,<sup>4</sup> M A Khan.<sup>4</sup> <sup>1</sup>Health Sciences, University of York, York, UK; <sup>2</sup>Research and Development, Social and Health Inequalities Network, Islamabad, <sup>3</sup>RDD, Health Services Academy, Islamabad, <sup>4</sup>RDD, Association for Social Development, Islamabad, Pakistan. e-mail: omaradogar@hotmail.com

**Background:** The Action to Stop Smoking in Suspected Tuberculosis (ASSIST) is a cluster randomized trial designed to evaluate the effect of bupropion + behavioural support and behavioural support alone on six-month continuous abstinence compared to usual care, in Pakistan. Here, our aim is to identify individual-level predictors of smoking cessation among TB suspects in this trial, after, controlling for the intervention effect. In addition to generating hypothesis, this will help in understanding the characteristics that make individuals to either give up or continue to smoke.

**Design/methods:** 1949 participants were analysed using multivariate-binomial regression adjusting for clustering. A post-hoc exploratory analysis was further performed to assess the differential effect of intervention on six-month smoking abstinence by subgroups (age, smoking duration, smokers in vicinity

and children at home), using Breslow-day test for homogeneity.

**Results:** Quantity of tobacco (i.e., the number of hookah + cigarettes smoked per day) used per day was the only predictor of smoking abstinence [RR = 0.97; 95%CI: 0.96–0.98], after adjusting for the effect of intervention and all other covariates in the model. The Breslow-day test was not significant across sub-groups (all  $P > 0.1$ ).



**Figure** Effect of intervention on 6-month continuous smoking abstinence by sub-groups.

**Conclusion and recommendations:** These findings are consistent with previous studies on predictors of smoking cessation. Although Breslow-day test was non-significant, the effect of intervention (risk ratios) was higher among those having no other smokers at home (only at workplace) and presence of children (less than 12) at home. Effect of peer, social and family influence on the outcomes of smoking cessation interventions needs to be further explored by studies with bigger samples.

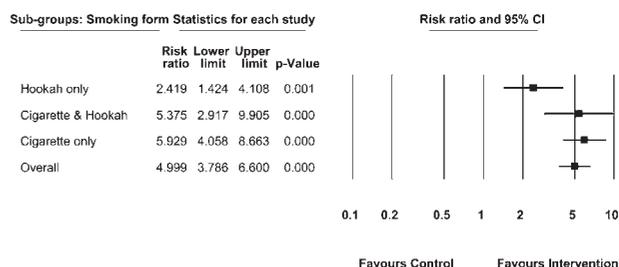
### PC-376-15 Effect of behavioural support intervention on six-month abstinence among hookah smokers: a sub-group analysis of the ASSIST Pakistan trial

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**Background:** Hookah smoking, a traditional form of tobacco use with water pipe, is prevalent in rural Pakistan with health hazards not much different to cigarette smoke. It is also the most popular and socially acceptable form of tobacco smoking among women. To our knowledge, smoking cessation trials targeting hookah smokers have not been conducted. We present findings of a post-hoc exploratory analysis of a smoking cessation cluster RCT assessing the effect of behavioural support intervention on six-month abstinence compared to usual care among hookah smokers.

**Design/methods:** A post-hoc exploratory analysis was done on 1290 smokers that participated in a smoking cessation RCT in Pakistan. Three sub-groups (based on smoking forms) were analysed, i.e., hookah smokers (188), hookah and cigarette smokers (312), and cigarette smokers (790) only. Sub-group specific risk ratios (RR) were computed for differential effects using the Breslow-Day test for homogeneity.

**Results:** Gender differences were observed with females comprising 19.3% of hookah smokers, 3.2% of hookah and cigarette smokers and 1.8% of exclusive cigarette smokers. The behavioural support intervention improved abstinence rates relative to usual care (RR = 4.99, 95%CI: 3.78–6.60). Specific risk ratios were 2.4 (1.42–4.11) for hookah smokers, 5.37 (2.92–9.90) for cigarette and hookah smokers and 5.93 (4.06–8.66) for cigarette smokers. The homogeneity test statistic across these three was not significant ( $P = 0.08$ ).



**Figure** Effect of behavioural support intervention on six-month smoking abstinence.

**Conclusion and recommendations:** The intervention appears less effective among hookah smokers compared to mix and cigarette smokers. This could be a type II error or that the intervention was more directed towards male cigarette smokers. More robust trials in future could build on the current behavioural support intervention to make the hookah smokers quit its use.

### PC-377-15 Action to Stop Smoking in Suspected Tuberculosis (ASSIST) in Pakistan: a cluster-randomised trial

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**Background:** There is a strong causal link between tobacco use and tuberculosis (TB) incidence. Almost 20% of the total disease burden due to TB is attributable to tobacco use. Pakistan is one of the top ten high burden countries for both TB and tobacco use. We carried out a cluster RCT to assess the effectiveness

of delivering smoking cessation interventions in achieving six-month continuous abstinence among adult smokers who are suspected of pulmonary TB.

**Methods:** 33 health centres (1957 participants) were randomised to three arms: (a) intervention arm I: behavioural support *plus* bupropion; (b) intervention arm II: behavioural support only; and (c) control arm: usual care and a self-help leaflet. Patients in all three arms were assessed for abstinence (verified by carbon monoxide test), one and six months after the quit date. To account for clustering, results were analysed using mixed-effects (multi-level) logistic regression.

**Results:** A total of 42.1% (275/654) of those offered behavioural support and bupropion achieved six months' abstinence compared with 39.8% (254/639) offered behavioural support alone, and 7.9% (52/656) offered usual care and a self-help leaflet. Both treatment conditions led to significantly improved abstinence rates relative to usual care (OR = 16.3, 95%CI: 5.6–47.8, and OR = 15.4, 95%CI: 5.2–45.2 for the behavioural plus pharmacological support condition and behavioural support condition respectively). After adjustment for potential confounders the effect measure estimates increased for both behavioural plus pharmacological support (OR = 22.8, 95%CI: 7.3–71.4) and behavioural support alone (OR = 20.6, 95%CI: 6.5–64.5). An approximate ICER for behavioural support plus bupropion was \$91.51 and for behavioural support alone was \$9.13 per smoking abstinence.

**Conclusion:** Behavioural support is effective in promoting cessation in smokers in Pakistan with suspected TB. Adding bupropion does not appear to increase abstinence rates.

### PC-378-15 Smoke-free health facilities and smoking cessation among tuberculosis patients in Bangladesh

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**Background and challenges to implementation:** In Bangladesh, about 44.7% of men and 1.5% of women currently smoke tobacco. Tobacco smoking is an important risk factor for TB and also contributes to poor treatment outcomes including increased mortality. BRAC is an NGO implementing community-based TB programme in two-thirds of country, with the support and guidance of National TB Control Programme. The objective of the intervention is to identify current smokers among TB patients and support them to quit smoking and to promote smoke-free health care facilities using the guidelines developed by the International Union Against Tuberculosis and Lung Disease (The Union).

**Intervention or response:** BRAC Dhaka urban TB

programme staff was trained on tobacco control with particular focus on the harmfulness of smoking, second-hand smoking and its impact on TB, introduce counseling methods and documentations using the Union smoking cessation and smokefree environments for tuberculosis patients guideline. The tools and contents of the Union guideline were translated in Bangla and shared with staff. Counseling is given to patients for smoking session during the initiation of treatment and subsequent visits to TB centre. The pilot phase started in 17 Dhaka City peri-urban TB centers that covers about 2.8 million population.

**Results and lessons learnt:** All the 17 health centers were declared as smoke-free and non-smoking signage was placed at the entrance of these centers. From May 8, 2011, to February 7, 2012, a total of 2266 patients were enrolled. Of them, 1216 (54%) were male and 1050 (46%) were female. 447 (36.8%) out of 1216 males and 5 (0.5%) out of 1050 females were smokers. Among 452 smokers, 339 (75%) quit smoking, 33 (7%) were lost to follow-up and 80 (18%) are still smokers.

**Conclusions and key recommendations:** Smoking cessation among TB patients is found to be effective. Thus the intervention will be expanded to other areas gradually.

## EPIDEMIOLOGY: TUBERCULOSIS IN HIGH- AND LOW-BURDEN COUNTRIES – 1

### PC-408-15 Cost incurred by patients attending tuberculosis diagnostic centres in Nigeria, Nepal, Ethiopia and Yemen, and risk factors for high expenditure

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**Background:** Patients attending TB diagnostic centres often come late and are unprepared for the need to attend several days. Patients often experience high expenses but high expenditure is unlikely to be homogeneous across the population. Here we describe the costs of individuals attending diagnostic services and identify risk factors for high expenditure.

**Design/methods:** Prospective survey using structured questionnaires in Nigeria, Nepal, Yemen and Ethiopia. Costs incurred the first/second day were quantified and, after a descriptive analysis of costs, grouped into quartiles. Participants were grouped as being  $\geq$ Q4 (i.e., >75%) and <Q4 for expenditure and defined as cases and controls. Multi-variate analysis was used to identify independent variables.

**Results:** 2225 (55.9% men) patients were enrolled. The majority attended with company and had a median travel time of 40 minutes. Very few paid for accommodation or food. About one third came from rural areas. Highest costs were observed in Yemen and lowest costs in Ethiopia. The main components of patient expenditure included diagnostic service charges, including clinic fees and sometimes undercover payments for services, and transport. The variables associated with high expenditure were age <50 years (OR 1.2, 1.0–1.5), rural residency (OR 2.8, 2.3–3.5), low education (OR 1.4, 1.2–1.7), attending with company (OR 2.5, 2.0–3.2), unemployment (OR 1.3, 1.1–1.6) and being a farmer, student, housewife or labourer (OR 1.6, 1.3–2.0). Rural residency and attending with company were the main independent variables associated with high expenditure in the multivariate analysis (aOR 2.5 [2.0–3.1] and 2.0 [1.6–2.6]).

**Conclusion and recommendations:** Costs for attending diagnostic services were substantial and certain population groups experienced higher costs (e.g., rural residents and those attending with company). Large components of the costs were service and transport related.

#### PC-409-15 Impact of community awareness on tuberculosis case notification in Panjsher Province

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**Background:** TB case notification is still a major challenge for National TB Control Program of Afghanistan. Panjsher is one of the provinces with lowest TB case notification rate the country. To tackle with this problem there is need for involvement of the community.

**Objective:** To encourage community to be involved in referring of TB suspects through out promoting their behaviour for seeking health services in case there are symptoms and signs of TB.

**Methodology:** 16 orientation workshops for 138 mul-lahs, 145 members of community health council and 201 school teachers were conducted in the year 2011. After intervention, the evaluation was conducted: 121 trainees randomly selected to assess degree of retaining knowledge after training. 58 school students' knowledge was assessed as beneficiaries. With 11 TB patients face to face interviews conducted.

**Result:** Trainees retained knowledge of TB up to 92% after training. 24 trainees referred TB suspected patients to TB diagnostic centers. After intervention by involvement of community, TB case notification rate increased from 26/100000 population in 2010

to 50/100000 (1.9 times) in 2011. Ten patients were referred by religious leaders, community health council members and teachers. However, mean of delay in diagnosis was 10 months among TB patients. Factors delays in diagnosis were avoiding health facilities and spending in private clinics due to social stigma and discrimination.

**Conclusion:** This intervention showed that awareness on TB for community key people has impact on TB case notification. Expanding of this approach is recommended for the provinces with low case notification.

#### PC-410-15 Molecular epidemiology, drug susceptibility and economic aspects of tuberculosis in Mubende District, Uganda

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**Background:** This study aimed at investigating genotypic characteristics, drug resistance profile and the geographical distribution of TB genotypes. Furthermore, aimed at determining prevalence associated risk and economic factors that could affect the control strategies. Samples were collected from 344 patients with either cervical lymphadenitis or cough that had persisted for at least two weeks between February and July 2011 at Mubende regional referral hospital. Mycobacteria in sputum and cervical lymph node aspirates were isolated and identified using standard culture procedures and identified as MTBC using Capilia Neo™. MTBC were subjected to first-line anti-TB drugs using MGIT. DNA were characterized using deletion analysis, spoligotyping and MIRU-VNTR techniques. Data were analyzed using MIRU-VNTR *plus*, SpolDB4.0 and multivariable regression models.

**Results:** 21% were TB infected, 65% HIV-TB co-infected, prior TB episodes (OR = 3; *P* = 0.01), HIV (OR = 2.7; *P* = 0.05) cigarette smoking (OR = 3.5; *P* = 0.003), and overcrowding (OR = 4.8; *P* = 0.002) were risk factors while medical related transport bills (OR = 13; *P* = 0.0001) was the salient economic factor. Predominantly genotypes were Uganda-II (36%), Uganda-I (22.3%), others CAS1-Delhi (2.9%), CAS1-KILI (2.9%), T1 (7.5%), X2 (1.5%) and LAM11-ZWE (4.5%). It was also the first reporting of an 'Ural' strain in this geographical area. The mono resistance to rifampicin, isoniazid and multidrug-resistance TB prevalence 5.7%, 11.4% and 3.7% was higher than the national and regional average.

**Conclusion and recommendations:** This study has shown a heterogeneous pool of *M. tuberculosis* genotypes circulating in this area, Uganda-II being the most predominant. Cigarette smoking, medical related transport bills and drug resistance to the predominantly circulating Uganda genotypes could undermine the usefulness of the current TB strategic interventions, thus the need for special attention towards TB control in Mubende District.

#### PC-411-15 Patient and health system delay for pulmonary tuberculosis care in Beira City, Mozambique

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**Background:** Tuberculosis (TB) remains an important public health problem in Mozambique. TB control is based on the rapid identification of cases and their effective treatment. However, many studies have shown that there are important delays in diagnosis and treatment of patients with TB. The purpose of this study was to assess the prevalence of and identify risk factors associated with patient and health system delay among newly diagnosed patients with pulmonary TB.

**Design:** A cross sectional study was carried out in Beira City, Mozambique, between September 2009 and February 2010. Data collection was done using a questionnaire prepared specifically for this study, but some data were also obtained from patients' files.

**Results:** A total of 622 patients were included in the study, with 43.7% (272/622) being female. The median age was equal to 32 years (interquartile range, 26–40). The total median delay, patient delay and health system delay were 150 days (interquartile range, 30–720), 61 days (28–113) and 62 days (35–120), respectively. The contribution of patient delay and health system delay to total delay was similar. Farming, seeking firstly care from a traditional healer, having coexisting chronic disease and low TB knowledge were associated with increased patient delay. Having had more than two visits to a health facility, farming and having coexisting chronic disease were associated with increased health system.

**Conclusion:** This study demonstrated the existence of patient and health system delays. A combination of interventions is required to facilitate timely and appropriate care of TB patients in Mozambique.

#### PC-412-15 DNA fingerprinting of *Mycobacterium tuberculosis* isolates of pulmonary tuberculosis patients in Iran by PGRS-RFLP

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**Background:** Molecular epidemiology has underlined the importance of recent tuberculosis (TB) transmission and has uncovered notable discrepancies compared with conventional epidemiology. The present study was conducted in order to analyze the current epidemiology of TB and interhuman transmission of *Mycobacterium tuberculosis*.

**Design/methods:** We conducted a descriptive analytical population-based study with genotyping of the isolates by using molecular typing, including restriction fragment length polymorphism with probe PGRS (polymorphic GC-rich sequence) to determine the incidence of and risk factors for clustering of *M. tuberculosis* isolates, indicative of recently transmitted infection, among patients with culture-proven tuberculosis diagnosed between February 2010 and August 2011 in Markazi Province of Iran.

**Results:** In consequence, from pulmonary tuberculosis patients during survey 95 *M. tuberculosis* isolates were collected and genotyping of the isolates by PGRS-RFLP with *PVU II* and *ALU I* displayed a wide range of genetic diversity as 50 and 48 genotypes were identified. 23 patients were infected with genetically different isolates, demonstrating the clonal heterogeneity of *M. tuberculosis* in these patients originating from various geographical areas. 72 patients were infected by strains clustered with identical fingerprints. Clustering was not more frequent among Iranian patients than among foreign ethnic patients and was independent to age, gender, residence, relapse and HIV infection as risk factors for clustering among patients.

**Conclusion and recommendations:** The RFLP typing of randomly collected strains provides a general picture of the strains involved in tuberculosis. The systematic study of limited areas where tuberculosis is endemic can provide evidence for the existence of persisting epidemics. This stresses the different problems which remain to be solved in order to improve the control of tuberculosis.

#### PC-413-15 A spatial clustering analysis of tuberculosis cases in eastern China

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**Objective:** To determine the spatial clustering and recent transmission of tuberculosis (TB) patients in Funing County, China.

**Methods:** Newly reported and retreat TB patients registered in Funing between June 1, 2009, and December 31, 2010, were successively recruited for research subjects. Geographic information system was applied to analysis the spatial clustering of TB patients. The mycobacterium tuberculosis (MTB) isolates were genotyped by mycobacterial interspersed repetitive units (MIRUs). Cluster was defined as two or more patients' MTB isolates harboring identical MIRU genotype.

**Results:** During the study period, there were a total of 681 TB patients reported. There was no statistical significance indicated both by global Moran's I value and local Moran's I value. Spatial scan statistics (SaTScan) shows that the patients in Guoshu town was statistically significant in spatial clustering (RR = 1.85, LogLR = 5.94,  $P = 0.036$ ). Spatial distribution of MIRU clusters showed, though there was certain geographically gathered trend, overall distribution of patients in clusters was scattered.

**Conclusion:** The result implies that sporadic transmission of TB may have played an important role in the epidemics of TB in high prevalence area.

#### PC-414-15 Transmission of tuberculosis among household cases from Karachi, Pakistan

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**Background:** Tuberculosis remains a serious threat to public health worldwide specifically in the South Asian region including Pakistan. Molecular typing methods are powerful tools for the detection of the transmission pattern of *M. tuberculosis* strains. Transmission rates are high and household contacts of cases are at risk of contracting disease. This study aimed to use MIRU-VNTR typing to understand tuberculosis transmission in a household-based population.

**Methods:** Forty seven different index cases and their household contacts ( $n = 60$ ) were recruited from patients in Karachi during 2006–2009. *M. tuberculosis* strains were genotyped using 15-loci based MIRU-VNTR methods. Clustering was determined using the Bionumerics software program.

**Results:** The most predominant spoligotype were CAS (including CAS1, CAS sub-families) = 58.9%, EAI = 8.4%, Beijing = 2.8%, Haarlem = 1.8%, T Clade = 6.5%, U Clade = 3.7%, Orphan cluster = 8.4% and Unique isolates = 9.3%. Spoligotyping analysis identified that shared types of three cases each in 4 households and two cases each in 12 households. MIRU-VNTR typing revealed that in four households, there were 2 strains each with identical patterns, with 3 identical isolates in a 5th household. Additionally, in four households 2 of 3 isolates had identical MIRU

types and in a 5th family, 3 of 4 isolates were the same. MIRU typing also revealed two clusters ( $n = 2$ ) which were from different households.

**Conclusion:** Overall, 26 clusters were identified and these data illustrate household transmission as a source of TB. While effective anti-tuberculous therapy remains a cornerstone of disease control it is important to have effective health awareness programs to protect at risk individuals in the community from contracting TB.

#### PC-415-15 Caracteristiques epidemiologiques des tuberculeux admis au régime de retraitement à Cotonou au Benin

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**Cadre :** Les cas en retraitement sont des situations à risque de pharmaco résistance. L'objectif de ce travail était de décrire les caractéristiques épidémiologiques des tuberculeux admis au régime de retraitement.

**Schéma/méthodes :** A partir des registres de la tuberculose et des dossiers des malades, une étude descriptive et rétrospective a été menée sur tous les cas de tuberculose pulmonaire à bacilloscopie positive admis au régime de retraitement du 1er janvier 2005 au 31 décembre 2009 à Cotonou.

**Résultats :** Les cas de retraitement représentaient 521/ 4545 (11,46%) des TPM+ enregistrés pour la période. Leur nombre était en régression au fil des ans passant de 126 cas en 2005 à 83 cas en 2009. 389/521 (74,66%) des dossiers étaient exploitables. Les proportions étaient respectivement, 62%, 21% et 17% pour les rechutes, les reprises et les échecs. La forme de tuberculose antérieure était dans la quasi-totalité pulmonaire. Le délai moyen entre le primo traitement et le retraitement était de 18 mois [3–58 mois] pour les reprises et de 30 mois [4–161 mois] pour les rechutes. La sex ratio était de 4 pour tous les types. Les moyennes d'âge étaient respectivement de 37 ans, 33 ans et 34 ans pour les rechutes, les reprises et les échecs, pS. La séroprévalence du VIH était respectivement de 26%, 12% et 12,5% pour les rechutes, les reprises et les échecs ( $P$  NS).

**Conclusion et recommandations :** Les cas de retraitement sont dominés par les cas de rechute. Une étude prospective, pourrait aider à élucider les facteurs associés à la rechute.

**PC-416-15 Molecular epidemiology of *Mycobacterium tuberculosis* isolates among pulmonary tuberculosis patients in Amhara Region, Ethiopia**

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**Background:** The burden of tuberculosis (TB) in Ethiopia is very high. Documenting the circulation of *Mycobacterium tuberculosis* strain families is necessary to better understand the TB epidemic in the country.

**Methods:** Sputum samples were collected from new pulmonary TB patients from selected hospitals and health centres in Amhara Region, Ethiopia, and subjected to mycobacterial culture. Genotyping of mycobacterial DNA was performed by spoligotyping and isolates were assigned to families and sub-families using the SpolDB4 and the model-based program 'Spotclust'.

**Results:** A high level of diversity was found among the 237 *M. tuberculosis* isolates. Sixty-five different spoligo-patterns were obtained of which 40% were in clusters of 2–34 strains. The T (30.8%), CAS (21.1%) and U (17.7%) families were the predominant isolates comprising 69.6% of the total strains. Eighty-five percent of the U lineage belonged to SIT 910 and SIT 1729. Only a few of these strains are included in SpolDB4 to date. Other genotypes identified included Haarlem, LAM and Beijing strain families. Of the total strains, 41 (17.3%) were unique and have not been described in SpolDB4 to date.

**Conclusions and recommendations:** The TB epidemic in Amhara Region, Ethiopia, is characterized by the circulation of numerous *M. tuberculosis* strain families. The strains, predominated by T, CAS and U families, exhibit a high degree of clustering. The high proportion of SIT 910 and SIT 1729 strains may indicate an increase in the importance of the U lineage in the transmission of TB in the study region.

**PC-417-15 A survey of nutrition and health knowledge and prevalence of diabetes among tuberculosis patients**

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**Background:** To investigate the level of awareness rate of nutrition and health knowledge and the influence factors and the prevalence of diabetes among tuberculosis patients in order to promote TB treatment and education.

**Methods:** 1713 tuberculosis patients (TB group) and

1879 matched group people were selected from Tancheng and Yishui, Linyi, China. Face-to-face questionnaires and medical examination including fasting blood glucose, blood lipid, etc were carried out by trained professional investigators.

**Results:** The prevalence of diabetes in TB group was higher than that in the matched group ( $P < 0.01$ ), which was 5.55% in TB group and 4.20% in the match group. The awareness rate of nutrition and health knowledge were 25.10% in the TB group and 37.36% in the matched group ( $P = 0.000$ ). TB group's awareness rate of 'how to eat is more healthy, where to see the doctor, whether tuberculosis can spread through cough and sneeze, whether tuberculosis can be cured, what to do feeling better in the course of treatment, whether tuberculosis patient is more likely to develop diabetes than normal' was higher than that in the matched group ( $P < 0.05$ ). The Logistic single factor analysis showed that education, marriage, age and physical exercise were the influencing factors of the rate of awareness among TB group with sex, education, marriage and age in the matched group.

**Conclusion:** The prevalence rate of diabetes in tuberculosis patients were higher than that in the matched group. The awareness rate of nutrition and Health knowledge lower in tuberculosis patients than in the matched group. So, there exists important linkage between TB and DM, which should be paid attention. And the health education about nutrition and hygiene habit should improved in TB patients.

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**PC-418-15 Spatial analysis of tuberculosis transmission dynamics in Lima: preliminary analysis of an ongoing population-based molecular epidemiological study**

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**Background:** Detailed characterization of the patterns of tuberculosis transmission within communities may inform the design of more effective control strategies.

**Methods:** In a large ongoing, population-based study of TB within Lima, Peru, we collected information on the spatial location of incident TB and the 24-loci MIRU-VNTR genotypes of *M. tuberculosis* isolated from each case. We used local tests of spatial association to identify areas in which there was a relatively high local risk of genotypically clustered and retreatment tuberculosis.

**Results:** Between September 2009 and April 2011, home spatial location and MIRU-VNTR genotypes were assigned for 999 individuals with incident tuberculosis. 22% of enrolled cases had previously been treated for tuberculosis and 50% had an exact 24-loci MIRU-VNTR match within our study database. We found a single shantytown settlement in which there was a concentration of individuals with incident TB who had a history of previous treatment and for whom we identified at least one other genetically clustered case. Further analysis revealed that the high genetic clustering of cases within this neighborhood was not the result of clonal dissemination of a single strain, but instead due to the circulation of multiple strains that were also found throughout the rest of the study area.

**Conclusions:** These preliminary results suggest that individuals with incident TB residing in this shantytown settlement are more likely than others within Lima to be members of active recent chains of TB transmission and to have also been previously treated for TB. A relatively high local risk of reinfection within this settlement would be consistent with this finding and might be explained by increased density of housing and increased density of individuals within houses in this hillside-settlement. Additional data is currently being collected to follow up these findings and to support decisions about how to better control disease within Lima.

#### PC-419-15 Standard of living of tuberculosis patients identified in a community-based survey in India

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**Background:** India is a high TB burden country in the world with an annual incidence of more than 2 million TB cases. A large Global Fund project is being implemented since 2010 in 374 out of the 650 districts of the country to supplement and support the National TB Programme (NTP) in enhancing the reach and visibility of TB control services in the community. A baseline survey was conducted to study the profile of TB patients in the community.

**Objectives:** The standard of living (SLI) of TB patients identified during the survey was assessed as a part of this survey.

**Methodology and results:** 609 TB patients were identified through door to door survey in 30 Global Fund project districts. The selection of districts and TB patients within the districts was done by multistage cluster sampling methodology. SLI index has been widely used in Indian context in demographic and health surveys to describe the living conditions of people in-

stead of household income. This index is calculated based on the housing type, ownership of house, main fuel used for cooking, source of drinking water, presence or absence of separate room for cooking, car, moped or scooter, tractor, bicycle, computer, telephone, mobile phone, refrigerator, television, radio or transistor, electric fan, sewing machine, mattress cot and bed, pressure cooker, chairs and table, clock, water pump, bullock cart and thresher. Numerical scores are given based on the presence or absence of each of these household amenities and added together to derive a composite score (range 0–60). A score of 0–17, 18–24 and 25–60 indicates low, medium and high SLI respectively. 55% of the TB patients belonged to low, 32% to medium and 13% to high SLI.

**Conclusions:** More than half of TB patients belonged to low SLI, reconfirming that a vast majority of TB patients live in extreme poverty with very poor housing and living conditions. Early detection of TB and curing vast majority of such people with free services under NTP may help partly in improving their quality of life.

#### PC-420-15 Condiciones de vida y acceso a los servicios de salud: factores asociados a la no adherencia al tratamiento de la tuberculosis

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**Introducción:** La administración completa del tratamiento de la tuberculosis constituye una de las principales herramientas para el control de la enfermedad. En Argentina la proporción de los casos nuevos que abandonó el tratamiento varió entre el 9,03% en 2005 y el 14,45% en 2007. El objetivo de este estudio fue identificar los factores relacionados con el paciente, su entorno y los servicios de salud que influyen sobre la adherencia a los tratamientos.

**Metodología:** Se realizó un estudio de caso-control en el Área Metropolitana de Buenos Aires, Argentina. Los casos ( $n = 38$ ) fueron los pacientes no-adherentes diagnosticados durante el año 2007, residentes y atendidos en hospitales de municipios seleccionados. Los controles ( $n = 85$ ) fueron los pacientes adherentes diagnosticados durante el mismo período, atendidos y residentes en los mismos municipios. El análisis de los factores predictivos de la no adherencia se llevó a cabo mediante regresión logística.

**Resultados:** Los hombres tuvieron 3 veces más probabilidades de no adherir al tratamiento que las mujeres (OR: 3,1; IC95% 1,3–7,7). Aquellos que realizaban los controles en un hospital tuvieron casi 4 veces más riesgo de no adherir al tratamiento que aquellos que los realizaban en los Centros de Atención Primaria (OR 4,3; IC95% 1,4–12,9). Asimismo los pacientes cuyos hogares tenían un ingreso mensual inferior a US\$123 tuvieron casi 4 veces más probabilidades de no adherencia que aquellos cuyos hogares

tenían ingresos mensuales superiores (OR: 3,8; IC95% 1,5–9,4).

**Conclusión:** Los resultados de este estudio permitieron delinear un perfil de paciente en riesgo de no adherencia, caracterizado por estar en condiciones de pobreza, contar con un bajo nivel de ingresos en el hogar y tener dificultades de acceso a los servicios de salud, y cuya tendencia a desertar el tratamiento aumenta conforme se incrementan esas condiciones.

#### PC-421-15 Evaluation of a tobacco cessation intervention for national tuberculosis control programme at Vadodara, Gujarat, India

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**Background:** India has the highest number of tuberculosis (TB) cases and second highest number of tobacco users globally. Active smoking is significantly associated with recurrent TB and TB mortality, yet tobacco cessation interventions (TCI) have not yet been integrated into the National Tuberculosis Control Programme (RNTCP) in India. This study assessed feasibility and impact of TCI integration for TB patients.

**Methods:** All TB patients registered under RNTCP from urban and rural districts of Vadodara from 1 October 2010 to 31 March 2011 ( $n = 2054$ ) were enrolled and followed for one year. TCI (brief counseling) was offered to all current tobacco users by trained health care providers as per standard guidelines (5As and 5Rs).

**Results:** TCI related data were successfully collected for 2020/2054 (98.3%) TB patients. Among 2020 TB patients, 837 (41.4%) reported ever tobacco usage in lifetime, while 607 (30%) reported current tobacco use at the beginning of treatment. Of 607 current tobacco users, 247 (41%) reported using smoked tobacco and 360 (59%) reported using smokeless tobacco. Nearly all individuals reported willingness to quit ( $n = 578$ , 95%), and 142 (58%) and 223 (62%) of the smoked and smokeless tobacco users, respectively, quit at least once for some duration during the course of follow-up. 40% of current tobacco users quit at the end of TB treatment. Successful TB treatment outcomes (treatment completed or cured) were more likely among patients who quit smokeless tobacco ( $P = 0.001$ ) or smoked tobacco ( $P < 0.0001$ ). Those who quit at some point during treatment also had a higher odds (OR = 3.2; 95%CI 1.7–6.3) of a successful TB treatment outcome after controlling for age, urban/rural residence, sex, HIV status, second-hand smoke exposure, TB case type, and treatment category.

**Conclusion and recommendations:** Integrating TCI into the RNTCP will increase successful TB treatment outcomes among tobacco users and tobacco related non-communicable disease burden.

#### PC-422-15 Analyse spatiale de l'incidence de la tuberculose et recours aux soins dans une grande ville d'Afrique centrale

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**Objectifs :** Décrire la distribution de l'incidence de la tuberculose à microscopie positive (TPM+) dans la ville de Douala (Cameroun) en 2011/12 et analyser les comportements des patients par rapport au recours aux soins.

**Méthodes :** Les résidences de tous les patients TPM+ consécutivement diagnostiqués dans un des centre de diagnostic et de traitement de la TB (CDT), résidant permanemment à Douala, et acceptant la participation à l'étude ont été recensés avec l'aide d'un GPS et reportés dans une carte géo-référenciée. Des données démographiques et socio-économiques des patients ont été collectées avec un questionnaire standardisé. Sept focus group ont été constitué (convenience sample) pour interviewer les patients par rapport au choix de leur CDT.

**Résultats :** Une partie sur-proportionnelle des environ 2500 patients recrutés (>80%) habitent dans les quartiers surpeuplés et/ou dans les quartiers spontanés ; ici se trouvent, également, les clusters identifiables. La fréquentation des CDT par des patients TB montre une distribution très inégale malgré un système fonctionnel de référence. Plus de 30% des patients ne se font pas traiter dans un CDT à proximité. Les causes évoquées par les patients sont variées : recommandation par un tiers, des mauvaises ou bonnes expériences antérieures, méconnaissance du système de santé et de l'offre de service de la TB ; réputation d'une structure ou d'un soignant.

**Conclusion :** Il existe des clusters d'incidence de la TB confirmée dans la ville de Douala. Ces clusters sont associés à la promiscuité et/ou la précarité socio-économique. L'offre du soins pour les malades de la TB n'est pas congruent avec la demande subjective.

#### PC-423-15 Tuberculosis in women, Brazil, 2008–2010

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**Background:** In Brazil, every year, around 20 000 women develop active tuberculosis (TB) and more than 1000 die because of that. TB is more frequent

among men. Few articles describe the profile of women affected. This study aims at comparing the profile of women and men who had TB.

**Design/methods:** By using the national information system for notification of diseases (Sinan), new cases notified from 2008 to 2010 were selected according sex. Data analyzed were stratified by age, race, level of education, TB type (pulmonary or extrapulmonary), HIV status and treatment outcomes (cure, dropout and mortality rate).

**Results:** A total of 74 593 women were studied (34.2% of all TB new cases). A significant number of them (62.1%) were aged 15 to 44 years. Most of the cases occurred among mixed color people (39.5% in women; 39.1% in men). The level of education more frequent was equal or lower than four years (22.8% in women; 25.4% in men). The pulmonary TB was more common (80.4% in women; 83.5% in men). TB-HIV co-infection rate was 8.3% in women and 9.9% in men. Cure among women was 74.9% (5.6% higher than among men) and the dropout was 7.7% (3.1% lower than among men). Mortality rate was nearly three times lower in women (1.3/100 000) than amid men (3.8/100 000).

**Conclusions and recommendations:** TB mainly affects people when they are in the most productive period of their lives. However, the TB social impact among women cannot to be designed taking as base only epidemiological indicators, once often in Brazil they are the responsible for raising child and providing their families. Though the cure and mortality rate are better among women, even in this group, Brazil did not reach fully the rates recommended by the World Health Organization. Women represent more than 30% of the total of cases notified in Brazil, so, in order to accelerate efforts against TB, the National TB Program should also them in the campaigns. More studies on this topic are desirable.

## TRAINING AND KNOWLEDGE ASSESSMENT

### PC-453-15 Assessing the impact of tuberculosis-related education and goal setting on knowledge retention and behavioral and structural change

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**Background:** The U.S. Centers for Disease Control and Prevention (CDC) is responsible for oversight of a worldwide network of panel physicians that conduct medical screening of U.S.-bound immigrants and refugees. CDC is currently phasing in updated

Tuberculosis Technical Instructions (TB TI), which require chest radiographs, sputum smears and cultures, and drug-susceptibility testing for diagnosis; directly observed therapy is required for cases. Panel physicians must understand the TB TI requirements and translate them into successful practice. CDC established Panel Physician Training Summits (PPTS); these 4-day educational events primarily focus on the TB TI. While assessments are used during the PPTS, little information is known about long-term knowledge retention, or whether PPTS results in positive practice changes.

**Intervention/method:** At the end of the Lima PPTS (August 2011), 24 attendees completed a knowledge assessment and 6-Month Goal Sheet, which documented goals for the next 6 months. In February 2012, an online knowledge and goal assessment survey was given to Lima PPTS attendees using MR Interview software. The mixed-methods survey assessed knowledge of tuberculosis, TB TI, and progress on 6-month goals.

**Results:** Seventy-five percent of PPTS attendees completed the survey. The average knowledge assessment score for respondents was 95% and 94.4% of respondents stated they had made progress on at least one of their 6-month goals. New goals were set by 66.7%. PPTS positively impacted clinical practice for 83.3%.

**Conclusions:** Lima PPTS results indicate that knowledge gain was sustained for at least 6 months and positive behavioral or structural change occurred in panel physicians' practice within 6 months. Continued longitudinal testing should be conducted to determine permanence of knowledge gain. Furthermore, research should be conducted to determine if goal-setting provides a stronger impetus to change.

### PC-454-15 Socio-demographic determinants of tuberculosis knowledge in three slum populations of Uganda

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**Background:** Knowledge of tuberculosis has been shown to influence health seeking behaviour; and urban slum dwellers are at a higher risk of acquiring tuberculosis than the general population. The study aim was to assess knowledge of tuberculosis and identify the associated socio-demographic determinants, in order to inform tailored interventions for advocacy, communication and social mobilisation in three urban-slum communities of Uganda.

**Methods:** A cross-sectional survey of 1361 adults between April and October 2011. Data was analyzed by descriptive statistics. Adjusted odds ratios (aOR) and 95% confidence intervals (95%CI) of potential determinants of tuberculosis (TB) knowledge were estimated by multivariable ordinal logistic regression using Stata 11.2 software.

**Results:** We found low knowledge of TB cause (26.7%); symptoms (46.8%), transmission (54.3%), prevention (34%) and free treatment (35%). Knowledge about TB treatment (69.4) and cure (85.1) was relatively high. Independent determinants of TB knowledge in the multivariable analysis included (aOR, 95%CI) older age (1.73; 1.30–2.29,  $P < 0.001$ ), lack of formal education (0.56; 0.38–0.83,  $P = 0.004$ ), unemployment (0.67; 0.49–0.90,  $P = 0.010$ ), never testing for HIV (0.69; 0.51–0.92,  $P < 0.012$ ) and residing in Lira Municipality (2.02; 1.50–2.72,  $P < 0.001$ ).

**Conclusion:** This study revealed deficiencies in the public health knowledge about TB diagnosis and treatment among urban-slum dwellers in Uganda. Tuberculosis control programmes in similar settings world over should consider innovative strategies for TB education, advocacy, communication and social mobilisation to reach the youth, the unemployed and less-educated; as well as those who have never tested for HIV.

#### **PC-455-15 Designated funding and improved qualifications: a shared responsibility between funding organisations and academic institutions?**

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**Background and challenges to implementation:** Capacity strengthening is something we all hold as a priority. This is equally true for research as it is for health services. The Desmond Tutu TB Centre (hereafter DTTC) seeks to obtain resources to improve the capacity and qualifications of research workers within DTTC. The aim of this study was to examine the association between designated funding for training and the improvement in academic qualification of DTTC staff.

**Intervention or response:** A cross-sectional study was done and all staff employed between 1 January 2004 and 31 December 2011 was included. The following data sources were used to collect data:

- Collective electronic data from Stellenbosch University
- Training statistics within the DTTC
- Information from the Human Resource hard copy files

Data collected included sex, age, qualification, date of employment, training received, type of training,

designated funding available and improvement in qualification. Improvement in qualification level was compared between those staff members who had dedicated funding available for training through specific studies and those who did not.

**Results and lessons learnt:** The total population was 323 research workers. Total population received training of which 310 (96%) had training supported by dedicated funding. 66 (21%) of those who received dedicated funding improved their qualifications, compared nil in the non-dedicated funding group. The risk ratio for those who had no designated funding was 1.27 (95%CI 1.20–1.35).

**Conclusions and key recommendations:** This study indicates the positive contributions of dedicated funds for training on the development and capacity strengthening of research workers. Funders are strongly advised to routinely include dedicated training funds in all research budgets.

#### **PC-456-15 Adapting MDR-TB patient education material to diverse settings and populations**

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**Background:** The programmatic management of MDR-TB expanded with the development of a number of DOTS-PLUS pilot projects. In Peru, a consortium of organizations (PARTNERS TB Control) developed a number of patient education materials using a systematic process including a patient education flipbook, video and brochure which were used at initiation and during treatment. As more countries began to detect and treat MDR-TB, the need for patient education materials grew significantly.

**Intervention:** After a formal needs assessment, development and field testing of the material in Peru, the final products used images that were simple and easy follow, targeting low literacy audiences. The products were widely used and presented in international forums as the first MDR-TB education materials developed using a systematic process. Other projects began to contact PARTNERS to adapt and use them. The products were available electronically and distributed free of cost. Technical assistance was provided as needed to adapt the material to local needs.

**Results:** The Peruvian materials have been translated, adapted, and reformulated for projects in Latvia, South Africa (Zulu), USA, Thailand (Hmong), Philippines, Romania and Pakistan. The new products used the initial design and content, saving time and costs and then were field tested and revised based on the local context to ensure acceptability. The materials have been used in diverse settings including refugee

camps, prisons, high risk groups, border TB control and for treatment scale-up and continue to be used in Peru.

**Conclusions:** Using adapting existing material to local contexts through formative evaluation provided valuable feedback, enhanced the usefulness of the material and save significant costs and time for product development. To continue to scale-up MRD-TB management, programmes should use already existing tools and adapt them to local conditions to ensure acceptability among the target audience.

### PC-457-15 Expanding continuing medical education for tuberculosis through online training in Indonesia

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**Background:** Indonesia ranks third among high-burden tuberculosis (TB) countries in the world. Strong efforts are underway to train TB providers, especially private sector providers, but it is difficult to reach all practitioners using classroom-based training. Working with the NTP and medical associations, the USAID funded Health Care Improvement (HCI) project developed a TB CD-ROM and computer-based training package in Bahasa Indonesia to improve diagnosis, management and referral of TB patients, targeting private sector providers with limited prior TB training.

**Intervention:** HCI conducted focus group discussions with providers to gain an understanding of existing TB knowledge and needs, and developed the content and format of the CD-ROM and accompanying materials. The structure of the modules mirrored the training already in use by NTP and the medical associations. Although the initial focus was on doctors, the project expanded in response to demand and separate versions were created for doctors and nurses/bidans. After pre-testing, dissemination began through the NTP and medical association networks.

**Results and lessons learnt:** Over 2500 CD-ROMs were distributed. The two computer based training packages have been launched by the Indonesian Nurses Association, the Indonesian Midwife Association, and Indonesian Medical Association where members can receive accreditation for successfully completing the course. The response is positive, with users finding the CD-ROM interactive, easy to use, and informative. It can be accessed by public and private TB service providers at their convenience.

**Conclusions:** The CD-ROM and online training filled a specific gap in continuing medical education for TB service providers. The format is accessible and convenient to use. The next steps are to further promote

the resources to TB service providers in Indonesia and elsewhere. The CD-ROM can also be easily adapted to the needs of other countries.

### PC-458-15 Involvement of pharmacists in tuberculosis care and control: experience from Maharashtra and Tamil Nadu States of India

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**Background:** Traditionally, private pharmacists in both rural and urban India are the first point of health care and dispense anti TB drugs based on self-reporting or private practitioner's prescription especially in lower socio economic settings. Many a time, the pharmacists are not aware that inappropriate use of anti-TB drugs is a potential risk factor for multi-drug-resistant (MDR) TB. The need and the potential of private pharmacist's participation in India's Revised National Tuberculosis and Control Program (RNTCP) were highlighted in many studies.

**Intervention:** The Union-led Project Axshya organised two sensitization programmes for pharmacists through Indian Pharmacists Association (IPA) in Maharashtra and Tamilnadu. The objective of the sensitization programme was to make pharmacists aware about tuberculosis and emphasizes their role in early detection and treatment.

**Results:** 90 pharmacists (43 from Maharashtra and 47 from Tamilnadu) were sensitised. Food and Drug Administrator (FDA) issued letters to trained pharmacists to function as DOT (Direct observation of treatment) provider under RNTCP. 84 Pharmacists agreed to serve as DOT provider and signed Memorandum of Understanding (MoU) with City/District TB Officer. Between February and March 2012, 23 TB suspects were referred by these trained pharmacists for sputum microscopy, of these 8 were found smear positive and 7 TB patients were put on treatment.

**Conclusion:** Private Pharmacists constitute an important role in health care setting in India as many times they are the first point of contact for primary health care. Maximizing their scope and potential and replicating similar approaches in other areas, will not only enhance the rates of early case detection and treatment but also prevent or reduce pharmacist induced MDR-TB in India. Training and involving more pharmacists and making them partners with RNTCP is the key towards achieving universal access for TB care.

**PC-459-15 'I have no difficult patients any more': lessons learned from the process of training trainers in effective health communication and patient empowerment**

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Of all short courses I have attended, never in my experience have I had training that positively impacted on me as this one. And never have I introspectively done an audit about myself until now

—participant in training of trainers

Training health professionals on how to communicate effectively with patients contributes to better results in TB control. Poor communication increases stigmatization, creates misunderstanding and decreases patient motivation to complete treatment. Good communication motivates patients to set and reach goals, creates an environment that promotes treatment and healing, decreases conflict with patients, reduces stress and improves working conditions. Learning basic communication skills, dealing with emotions and setting and reaching goals are part of the training. To increase the reach and sustainability, LHL started training trainers in 2011. This process includes developing a training manual, a facilitation guide, an eight months study period, two workshops, and several tools to measure the effect of training. A pool of trainers in each LHL partner country is now a reality and in-country trainings have started. The evaluation tools show that health workers report change in attitude and behaviour towards patients. From categorising patients as the 'problem' and being unaware how fear and emotions affect communication, to identifying the communication between health workers and patients as the problem. They experience increased awareness of own communication, taking responsibility for solving problems, better relationships with patients and colleagues, increased self-esteem and improved anger management. We will present lessons learned and results from this training process, including training material.

**PC-460-15 Online tuberculosis and MDR-TB training for physicians**

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**Background:** Expanded physician training is needed as diagnostic capabilities expand in MDR/XDR-TB. Due to human and financial resources shortages, in-person training is not always feasible. Two online courses have been developed by the World Medical Association and the Global TB Institute to address the growing challenge of MDR-TB management.

**Methods:** A *Tuberculosis Refresher Course for Physicians* (2011) and the *Course on Multidrug-resistant Tuberculosis* (2012) were developed using a systematic process. The Refresher Course was based on the International Standards for Tuberculosis Care, and both were consistent with the 2011 WHO guidelines and offer education credits. A 2008 needs assessment showed that desired topics included TB detection and treatment, MDR-TB and patient communication. Informants felt materials should be brief and include images to keep users' interest. A combination of learning styles was utilized; a brief multimedia clip starts each chapter and engages the user. Both courses employ a didactic approach, learning objectives, links and references to full information. Interactive components include moving graphics to demonstrate skills. The Refresher Course is a review of basic TB management principles, and complements the MDR-TB Course, an introduction to MDR-TB management.

**Results:** Physicians from many settings pilot tested the courses, allowing refinement of technical problems and content. Courses were shared on the TB Educate listserv and at international conferences. The MDR-TB course was presented at the global GLC meeting in 2012.

**Conclusions:** Online courses developed using sound educational methods are useful in TB training. The MDR-TB course may be useful as novel diagnostic tests for MDR-TB are scaled up globally. The course can serve as a prerequisite for onsite advanced skills training. Next steps may include updated print versions, a mobile app, or case studies to build MDR-TB management skills.

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**PC-461-15 Knowledge and practices regarding drug interaction between rifampicin and oral contraceptives among nurses and their clients in Fortaleza-Ceara, Brazil**

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**Background:** Brazil is one of the 22 high-burden TB countries and many Brazilian women in childbearing age are affected by it. We assessed nurses knowledge and practices with regards to drug interaction between rifampicin and oral contraceptives (OCs).

**Design/methods:** We identified a random sample of 12 of 41 health centres in Fortaleza City. A cross-sectional survey of all nurses providing TB treatment in the health centres and all (26) their female clients in reproductive years (10–49 years old). After consenting, nurses and clients were interviewed. Data was analyzed with SPSS® version 11.0.

**Results:** Most of the nurses (37.5%) had been qualified for 6 to 10 years and the majority of them had

also had training both in TB control (80%) and family planning (86.7%). Twelve (75%) nurses had knowledge about rifampicin and OCs drug interaction and half (8) of them reported prescribing barrier contraceptive methods to counteract this problem. Most women (73%) interviewed were between ages 21 to 49 and 25 (96%) were under TB treatment for less than 6 months. All of them were using rifampicin and half (12) of them were in use of hormonal contraceptives (6 on low-dose OCs and 2 on depot injection contraceptive). Only 9 (34.6%) reported having received information about rifampicin and OCs drug interaction and advised to use condoms during their TB treatment.

**Conclusion and recommendations:** Women in child-bearing age should always be informed about the risk of pregnancy during TB treatment when using hormonal contraceptives. Although 75% of nurses had knowledge about rifampicin and OCs drug interaction, only 34.6% of women reported being informed and advised about it. TB and family planning programs should look into strategies to overcome this problem, especially in high TB burden countries.

## MEDICAL MANAGEMENT OF TUBERCULOSIS–1

### PC-486-15 The impact of multidrug resistance on outcomes of the first-line anti-tuberculosis treatment in Georgia

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**Background:** MDR-TB has emerged as a serious public health problem in country of Georgia. The Drug Resistance Survey (DRS) which was performed during July 2005–May 2006 showed high prevalence of MDR-TB in Georgia (15% among all TB cases). All study participants were treated with first line anti-TB drugs based on WHO guidelines as the second line drugs for the treatment of MDR-TB were not available by then.

**Objective:** To assess the outcomes of the first line anti-TB treatment and risk factors for relapse and failure among patients enrolled in the population based DRS in Georgia.

**Design/methods:** Retrospective case-control study.

**Results:** Out of 1314 TB patients involved in the DRS, information on treatment outcomes was available for 1135 (86%) patients, 153 (14%) of which were MDR-TB cases. Overall, treatment outcomes were distributed as following: 51.4% (583/1135) cured, 10.9% (124/1135) treatment completed, 18.4% (209/1135)

defaulted, 9.6% (109/1135) failed, 4.7% (53/1135) died and 5% (57/1135) transferred out. The outcomes of first-line anti-TB treatment for MDR-TB group were as following: 23.5% (36/153) cured, 6.5% (10/153) completed, 19% (29/153) defaulted, 26.8% (41/153) failed, 15.7% (24/153) died and 8.5% (13/153) transferred out. In multivariable logistic regression analysis, having MDR-TB (aOR 4.87, 95%CI 3.33–7.13), previous TB treatment (aOR 3.8, 95%CI 2.9–4.9), male gender (aOR 1.70, 95%CI 1.2–2.4), being a former prisoner (aOR 1.8, 95%CI 1.2–2.5) and being unemployed (aOR 1.74, 95%CI 1.16–2.6) were independent risk factors for poor treatment outcomes.

**Conclusion and recommendations:** Patients with MDR-TB who were treated with WHO-recommended first line drug treatment regimens were significantly more likely to fail therapy. The study provided important information for the resource limited areas with no access to culture and DST where patients are treated with the first line treatment regimens.

### PC-487-15 Decentralised vs. centralised care for MDR-TB patients: a comparison of final treatment outcomes in KwaZulu-Natal, South Africa

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**Background:** KwaZulu-Natal, South Africa is a TB and HIV endemic setting, where prolonged hospitalisation for the treatment of the growing number of MDR-TB patients is no longer feasible or effective. To compare final treatment outcomes in patients with MDR-TB, with and without HIV co-infection, at four decentralised rural hospitals vs. care at a central, urban, specialised hospital.

**Design/methods:** An observational, field, prospective cohort study of MDR-TB patients over 18 years, starting treatment between 1 July 2008 and 30 July 2010. The primary study outcomes were treatment outcomes and survival. Secondary outcomes included culture conversion rate and time to culture conversion. Predictors of these outcomes were analysed.

**Results:** Of the 1567 patients with MDR-TB, 740 were at the decentralised sites and 827 at the central hospital. Overall, 76% were HIV co-infected. There was no significant difference in successful treatment outcomes between centralized and decentralised sites. Of the 1065 study participants who have finished

treatment to date (68%), successful treatment outcomes were recorded in 54% of the patients at the decentralised sites and 57% of the patients at the centralised site ( $P = 0.66$ ). No patients at the decentralised sites were lost to follow up. In comparison, 251 (30%) of the patients at the centralised site were lost to follow up. Present specific findings to date. Culture conversion rates of 79% were recorded at both the decentralised and centralised sites ( $P = 0.70$ ). However, the mean time-to-culture conversion was significantly shorter at the decentralised sites compared to the centralised hospital (90 days vs. 102 days) ( $P < 0.01$ ).

**Conclusion and recommendations:** The final treatment outcomes reported in this study suggest that decentralised care for MDR-TB patients is as effective as care in a centralised setting and fewer patients are lost to follow up.

#### PC-488-15 Does extended treatment of pyrazinamide benefit the treatment outcome of far-advanced pulmonary tuberculosis?

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**Background:** Standard regimen for new TB cases recommended by WHO is 2HERZ/4HER. According to the paper review, the successful rate was high and relapse rate was low with PZA used only for initial 2 months. But we wondered if there were any benefits in treatment outcomes if we extended the PZA treatment course more than 2 months.

**Design/methods:** Five hospitals engaged in TB treatment in Taiwan were enrolled in this retrospective study. Demographic data and treatment outcomes were collected with mycobacteria culture confirmed and HR sensitive TB cases between January 2006 and December 2007. Patients were divided into minimal, moderate-advanced and far-advanced pulmonary TB groups according to radiographic grade using the U.S. National Tuberculosis and Respiratory Disease Association scheme. Multivariate Statistical Analysis and survival analysis methods were applied to see if there were any benefit to extend the duration of PZA treatment.

**Results:** There were 295 minimal pulmonary TB cases, 323 moderate-advanced pulmonary TB cases and 182 far-advanced pulmonary TB cases enrolled. The median duration of PZA treatment in Far-advanced group was 75 days. So we divided the far-advanced TB patients into two groups according to less than and more than 75 days of PZA treat-

ment. There were no differences between these two groups in AFB stain conversion time (90 vs. 94 days). Sputum culture conversion time (74 vs. 79 days), complete treatment rate (96.8% vs. 98.9%) mortality rate (3.2% vs. 1.1%) and relapse rate followed 2 years (5.3% vs. 3.4%).

**Conclusion and recommendations:** It seemed to have no benefit to extend the duration of PZA treatment, even in far-advanced pulmonary tuberculosis. But because this was a retrospective study, the duration of PZA treatment were various. So we need to have a prospective study to confirm this conclusion.

#### PC-489-15 What had tuberculosis patients experienced in their previous course of anti-tuberculosis treatment in rural China?

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**Background:** In general, the acquired drug-resistant TB mainly results from irregular treatment and unqualified health services. This study aims to describe the treatment experiences of patients with multiple anti-TB treatment courses, and to find out the problems in TB medical services for the prevention of MDR-TB.

**Methods:** A cross-sectional study was carried out in 10 county/district TB clinics from 5 provinces of China. The study participants were TB patients with a history of at least two anti-TB treatment courses. Face-to-face interviews were given by trained investigators to the consented participants.

**Results:** Of the 328 TB patients, 231 (70.4%) had received two courses of anti-TB treatment before the investigation, and the others had 3 or more. The mean of out-of-pocket payments for previous anti-TB treatment was 12005CNY with a median of 3500CNY. About 63.1% and 67.1% of patients took the treatment at county TB dispensary for their 1st and 2nd treatment respectively. For the 206 patients having 1st treatment at county TB dispensary, 126 went back to the same health facility for the 2nd time. For those having their initial treatment in township and county general hospitals, 81.3% and 58.7% respectively would choose county TB dispensary for the 2nd anti-TB treatment. But when patients sought their 3rd time anti-TB treatment, half of them had went to city and up level comprehensive hospitals. Regarding the anti-TB therapy only 64.8% and 53.5% subjects were provided with the standardized anti-TB treatment, short course at their 1st and 2nd treatment course respectively. The more subsequent treatment, the more irregular therapy and self-treatment reported. The cure rate was decreased with the increased times of anti-tuberculosis treatment.

**Conclusion:** The county TB dispensary plays a major role in the provision of TB medical care in rural

China. Capacity building and advanced treatment training should be reinforced to improving the effects of anti-TB treatment.

### PC-490-15 Rational use of tuberculosis drugs to prevent the development of drug resistance

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**Background:** The tuberculosis (TB) drug pipeline has finally thickened and several new agents are under clinical development. We assessed how the currently available TB drugs are used and the risk for development of drug-resistance with the aim to support stakeholders when introducing new drugs and regimens in TB Programs.

**Methods:** Using standardised Cochrane and PRISMA Guidelines systematic reviews were conducted to assess: how often TB patients are prescribed inadequate drug regimens; the knowledge of healthcare workers (HCW) on TB regimens; the risk of developing multi-drug resistant TB (MDR-TB) when an inappropriate regimen was prescribed; and the risk of fluoroquinolone (FQ) resistant TB after FQ treatment for community acquired pneumonia.

**Results:** Between 0.4% and 100% of TB patients were prescribed an inadequate regimen. Between 8% and 100% of HCW reported having inappropriate knowledge of TB regimens. The risk for MDR-TB after being prescribed an inappropriate regimen increased by 27-fold (26.7, 95%CI 5.0–141.7). Treatment with FQ before TB diagnosis resulted in a three-fold higher risk of having FQ resistant TB (OR 2.81, 95%CI 1.47–5.39).

**Conclusions and recommendations:** These studies provide evidence that TB drugs are prescribed in inadequate regimens and that inadequate regimens, or the use of FQ for CAP, present an increased risk of drug-resistance. There is an urgency to strengthen guidelines and adherence to these to ensure a rational use of TB drugs and prevent the further development of resistant TB.

### PC-491-15 Initial smear examination as a predictor for positive tuberculosis treatment outcomes in Botswana: analysis of routine data

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**Background:** Acid fast bacilli detection by smear microscopy remains essential for tuberculosis diagnosis

and treatment monitoring. This analysis set out to determine if an initial smear examination predicted positive outcomes among TB patients.

**Methods:** Data for TB patients newly registered in Botswana in 2008 was extracted from the electronic TB register (ETR) and analyzed for the association between initial smear examination and treatment outcomes. Analysis was restricted to those with recorded treatment outcomes. Pre-treatment smear results were taken as a proxy of initial smear examination. Outcomes were categorized into positive (cured/completed) and negative (defaulted, failed or died) outcomes. Odds ratios, their confidence intervals were used as a measure of association. Multivariate analysis was used to control for potential confounders. Analysis was performed with STATA software version 10.

**Results:** A total of 6989 TB patients had treatment outcomes and initial smear results were available for 4005 (57.3%) of these cases. Re-treatment cases were more likely to get an initial smear (OR 1.28, 95%CI 1.09–1.49) and HIV-positive cases were less likely to get an initial smear (OR 0.67, 95%CI 0.59–0.76) compared to new cases and HIV-negative cases respectively. Initial smear examination was significantly associated with positive TB treatment outcomes (OR 1.60, 95%CI 1.43–1.80) and remained significant after adjusting for potential confounders (OR 1.56, 95%CI 1.39–1.75). Follow-up smear was a better predictor of treatment outcomes and showed a highly significant association with positive treatment TB outcomes (adjusted OR 5.26, 95%CI 4.52–6.22).

**Conclusion and recommendation:** Initial smear examination significantly predicted positive treatment outcomes. This association underscores that initial smear examination is indicative of timely diagnosis of TB, appropriate case management and increased encounters with health workers leading to favourable outcomes.

### PC-492-15 Factors affecting patients' adherence to anti-tuberculosis treatment in Yemen

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**Setting:** National tuberculosis control programme in 10 governorates, Yemen.

**Objectives:** To identify the risk factors (RF) associated with patient non-compliance to anti-tuberculosis (TB) treatment among positive pulmonary TB patients in Yemen DOTS programme.

**Methods:** This research was a prospective nested case-control study. Non-compliant cases ( $n = 133$ ) were recruited from a cohort of PTB patients registered between July 2007 and June 2008. Three controls per

case were randomly selected using the SPSS computerized sampling procedure from the list of compliant patients ( $n = 641$ ). Three forms were used for data collection that covered interviewing the participants and reviewing their medical cards and registers. Independent variables extracted from univariate logistic regression were analyzed in multivariate regression to identify independent RF for non-compliance.

**Results:** Non-compliance was reported in 133 of 774 TB patients (17.2%). Descriptive analysis showed that about 90% of respondents were at their most economically productive age (15–54) with a mean of 32.1 years ( $\pm 13.6$  SD). In the multivariate logistic regression analysis, factors that remained independently associated with non-compliance were literacy status (adjusted OR [aOR] = 1.87), travel time (aOR = 1.03), waiting time (aOR = 1.05), employment status (aOR = 2.19), living status (aOR = 6.72), family support (aOR = 4.05), stigma (aOR = 1.75), Khat chewing (aOR = 3.26) and patients' knowledge on TB (aOR = 0.84). Place of residence found also to be an important determinant of non-compliance where some rural governorates such as Hajjah (aOR = 42.13) and Mareb (aOR = 23.79) has higher risk compared to Metropolitan (aOR = 7.45).

**Conclusions:** The rate of non-compliance was high at 17.2%. Interventions to reduce it need to be institutionalized and patients on the continuous phase of treatment should be supported to continue taking medications. Policymakers should device strategies to improve socio-economic status of the general population and paying more attention to unemployed patients.

#### PC-493-15 Follow-up of DR-TB patients with co-infection after release from prison in the Republic of Azerbaijan

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**Aim:** Management of DR-TB with co-infections after discharge from prison and follow up their treatment with ensuring treatment adherence.

**Methods:** On the basis of Memorandum of Understanding signed on March 2009 between MOH, MoJ and ICRC the pilot project started for DR-TB patients after discharge from prison. The patients provided with continuation of treatment in civilian TB facilities. In order to strengthen treatment adherence among released DR-TB patients with high number of co-infections (Hepatitis B, C; HIV) social support is provided to the patients. The patients were followed up by the staff who had trained on management of TB co-infections.

**Results:** Since April 2009 up to January 2012, 72 DR-TB patients were released from prison. Majority

of them (65%) were drug users with different co-infections (HIV and hepatitis). 57 (79%) Hepatitis C, 8 (11%) HIV whose treatment need special care and management. Up to January 2012, 42 (58%) patients' treatment results were available. Out of 42 patients 25 (60%) were cured, 6 (14%) were treatment failure, 8 (19%) were defaulted, and 3 (7%) died. 30 patients are still under treatment.

**Conclusion:** Although the released DR-TB patients are very specific group of population with high number of drug users among which high level of co-infections observed the treatment adherence were achieved and treatment successful implemented due to DOT staff have good experience on management of such cases.

#### PC-494-15 Cost sharing procurement of second-line anti-tuberculosis drugs

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**Aim:** To document partnership in ensuring uninterrupted supply of second line anti-TB drugs to all drug resistant (DR) tuberculosis (TB) patients in Swaziland.

**Background:** Restricted capacity of Swaziland to fund all activities including procurement of second line drugs for all TB patients, the Green Light Committee (GLC) was requested to assist in the procurement of these drugs through the Global Drug Facility (GDF). Following assessment of programme capacity, a cohort of 50 patients was approved in the 1st year of the Global Fund (GF) TB grant whereas 175 TB patients needed treatment at the time. There was a gap that needed to be filled.

**Method:** The Ministry of Health and Finance funded the gap of patients needing treatment versus those that were provided treatment through the GF. The patients' already on treatment were identified and those that would require treatment were projected based on current diagnoses estimates with the assistance of partners involved in drug supply management. Drug estimates were made and projections for one year supply. Supplier was identified and direct procurement process initiated. Negotiations with central tender board were successfully done and upfront payment made.

**Results:** Drugs were made available for all TB patients on treatment whether a part of the GLC cohort or not. No patients were awaiting treatment because of unavailability of drugs.

**Conclusion:** Cost sharing greatly alleviates the burden on countries experiencing an economic meltdown and can greatly influence behaviour in seeking health care.

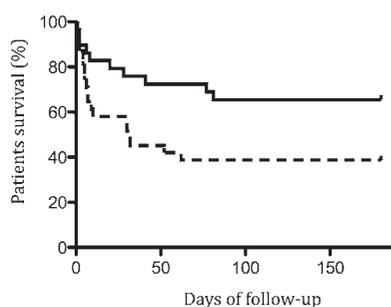
### PC-495-15 A randomised trial comparing pharmacokinetics, safety and clinical benefit of standard versus intensified antibiotic treatment for tuberculous meningitis

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**Background:** Intensified antibiotic treatment may improve outcome of TB meningitis (TBM). We examined pharmacokinetics (PK), safety and clinical benefit of treatment regimens including high-dose rifampicin and moxifloxacin for TBM in a hospital setting in Indonesia.

**Methods:** Sixty TBM patients were randomized to standard 10 mg/kg p.o. or 13 mg/kg rifampicin administered i.v., and (in a second randomization) to moxifloxacin 400 mg, moxifloxacin 800 mg, or ethambutol 750 mg QD. All patients received standard dose isoniazid, pyrazinamid and adjunctive corticosteroids. After 14 days of treatment all patients continued with standard TB treatment. Primary endpoints included pharmacokinetic (PK) assessments in blood and CSF within the first days of treatment, and adverse events attributable to TB treatment. This study is registered with ClinicalTrials.gov no. NCT 01158755.

**Results:** Sixty patients were randomized, most with BMRC grade 2 (82%) or 3 (12%) TBM, and 12% with concurrent HIV infection. Treatment with standard dose rifampicin was associated with low CSF rifampicin concentrations (geometric mean 0.27 mg/L). A 30% higher dose of rifampicin i.v. led to much higher AUC<sub>0-6</sub> (78.7 vs. 26.0 mg\*h/L), C<sub>max</sub> (22.1 vs. 6.3 mg/L), and CSF concentrations of rifampicin (0.62 vs. 0.27 mg/L). Moxifloxacin showed adequate plasma and CSF drug exposure. Hepatotoxicity and mild QTc prolongation were evenly distributed between groups. Mortality was substantially lower in patients receiving high dose rifampicin intravenously (Figure; HR 0.45, 95%CI 0.21–0.98), and



**Figure** Patient survival according to rifampicin treatment. Survival among TB meningitis patients treated with high dose i.v. (solid line) and standard dose oral (dashed line) rifampicin-containing treatment regimens during the first two weeks of treatment (adjusted HR 0.45, 95% 0.21–0.98). Two-week mortality was 17% resp 42%, six-month mortality 34% resp 61%.

not explained by HIV-status or GCS at time of presentation.

**Discussion:** Intensified antibiotic treatment for TBM leads to more favorable PK with acceptable toxicity. Our study, although not primarily designed for this purpose, suggests that high-dose rifampicin administered for the first two weeks i.v., improves survival of patients with severe TBM.

### PC-496-15 Laboratory findings of first and second cohort studies of drug-resistant tuberculosis in Azerbaijan

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**Background:** Treatment of drug-resistant tuberculosis (DR-TB) patients in the civilian sector has been started since August 2008 with financial support of the GFATM. It is fact that in the beginning of the project NRL was under construction and culture investigations and DST tests were realized in the laboratory (STIDT) of the Ministry of Justice then in the NRL. For laboratory investigations there have been used Löwenstein-Jensen method and Bactec MGIT 960 equipment.

**Purpose:** Laboratory analysis and evaluation of the first 2 cohort MDR-TB patients enrolled to treatment with 2nd line drugs in Azerbaijan.

**Materials and methods:** With this purpose there have been used data base (R8R) of the SRILD, the laboratory results of the NRL and Laboratory of Main Medical Department of the Ministry of Justice. Conversion of sputum smear according to the treatment period: 2 patients were negative from the beginning of treatment, 20 patients became negative after 6 months of treatment, 19 patients became negative after 12 months, 21 patients became negative during the 2nd year of treatment, and 3 patients became negative later, within 27–36 months of treatment.

N105	S	H	R	E	Z	Pt	Of	Cs	PAS	Cm	Am
R	90	94	84	77	55	39	49	5	7	30	32
%	85.7	89.5	80	73	52	37	46.6	4.7	6.6	28.5	30

**Conclusion:** As can be seen from the table, all of the 1st line of anti-TB drugs, and Z, Pt and Of from 2nd line TB drugs has highest resistance. Based on DST profile 3 (3%) diagnosed as PDR TB, 63 (60%) patients as MDR-TB, 39 (37%) patients as XDR-TB. 13 patients were sensitive to 3 drugs, 11 patients to 2 drugs and 1 patient to only one drug.

### PC-497-15 TB-HIV co-infection and outcome of tuberculosis treatment in Plateau State, Nigeria 2011

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**Background:** Tuberculosis (TB) and human immunodeficiency virus (HIV) are public health problems in Nigeria, with TB prevalence of 199/100 000 and HIV of 4.4% is one of the highest in the world. TB-HIV co-infection also rose from 2.2% in 1991 to 27% in 2010. This study was conducted to assess the prevalence of HIV and its effects on the outcomes of treatment of TB patients in Plateau state.

**Method:** We reviewed the medical records of all TB patients with known HIV status in Plateau State from January 2009 to December 2010. We used checklist to extract clinical and demographic information including outcomes of treatment. Univariate and bivariate analyses were performed using epiInfo software.

**Results:** Of 2564 records reviewed, 1417 (55.3%) were male; mean age was  $34.9 \pm 12.8$  year (male: 36.6, female: 32.9  $P$  value  $< 0.05$ ), 1439 (56.1%) of the patients were HIV-positive, 762 (53%) were females. More females (66.4) were HIV positive (OR: 2.16; 95%CI 1.84–2.55) including patients  $< 45$  years (OR 1.65; 95%CI 1.36–2.00). The overall treatment success rate was 79.4% (HIV negative: 81%, positive 77%), default rate 7.8% (HIV negative: 8.1%, positive: 7.7%) and death rate 7.7% (HIV negative: 5.2%, positive 9.6%). Deaths rate was higher among TB-HIV patients (OR 2.33, 95%CI 1.68–2.23) and TB-HIV females (OR 2.06; 95%CI 1.02–4.19).

**Conclusion:** TB-HIV co-infection is higher than national average and associated with high death rates in the state. Effective TB-HIV collaborative activities will reduce deaths among TB patients in the state.

### PC-498-15 Cost and cost-effectiveness of novel therapeutic regimens for tuberculosis

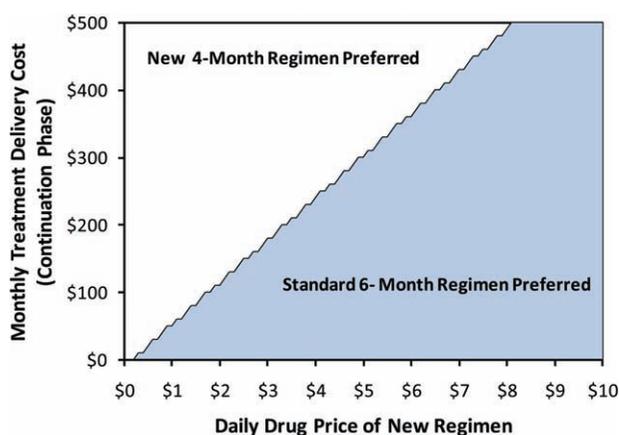
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**Background:** Shorter treatment regimens with equal efficacy against drug-sensitive tuberculosis (TB) may soon be available. The settings in which such regimens are likely to be cost-effective remains unclear.

**Design/methods:** We used decision analysis in a hypothetical cohort of patients with active, drug-sensitive TB to compare the costs and cost-effectiveness from the healthcare perspective of treatment with standard

6-month TB therapy against a hypothetical 4-month regimen (e.g., moxifloxacin-based) of equal efficacy. We obtained parameter estimates from published studies and performed sensitivity analysis across each parameter's widest reasonable range. Our reference case assumed a total standard treatment cost of \$304 per patient and a novel drug regimen cost of \$4.29 per day based on global prices for moxifloxacin.

**Results:** In the reference case, the novel regimen cost \$416 more per patient than standard therapy. In one-way sensitivity analysis, only two model parameters—the monthly cost of treatment delivery in the continuation phase and the daily price of the novel regimen—were capable of reducing this incremental cost below \$300. The Figure shows points at which the novel regimen becomes cost-saving relative to the standard regimen; for example, if the cost of the novel regimen were reduced to \$1/day, it would be cost-saving in settings where continuation-phase treatment delivery costs totaled \$50/month or more. Assuming that the novel regimen reduced mortality on treatment by 33%, it would avert an estimated 0.24 disability-adjusted life years (DALYs) per patient, for an incremental cost-effectiveness ratio of \$1700 per DALY averted in the reference case. Effects on transmission were minimal.



**Figure** Cost-minimizing TB therapeutic regimen, by treatment delivery cost and novel drug price.

**Conclusions:** If equal in efficacy, novel shorter-course regimens for TB are likely to be economically preferred to standard therapy in settings with high treatment delivery costs. Their applicability can be further expanded by lowering drug prices.

### PC-499-15 Death during tuberculosis treatment: who is at risk? Tuberculosis-associated and non tuberculosis-associated mortality during treatment in Israel, 2000–2010

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**Introduction:** Tuberculosis (TB)-related death may be preventable in developed countries. This study aims to identify risk-factors and estimate the mortality burden among treated TB patients in Israel.

**Methods:** Death certificates and/or last hospitalization records of all TB fatalities between 2000 and 2010 were divided into TB-associated and non-TB associated death to calculate the case fatality rate (CFR) and additional mortality measures.

**Results:** From 4555 TB patients reported, 447 died during treatment (average CFR = 9.8%, annual range: 4.7–14.3%). Comparing to TB-survivors, those who died during treatment were males (287,  $P = 0.03$ ), over 65 years (298,  $P < 0.01$ ), citizens (424  $P < 0.01$ ), non-Israeli born (393,  $P = 0.04$ ), HIV-co-infected (39,  $P < 0.01$ ) and had MDR-TB (34,  $P < 0.01$ ). In multivariate analysis, being male, older age, HIV-co-infection and MDR predicted all-causes mortality. From all fatalities, 336 (75.2%) were TB-associated (average CFR 7.0%, annual range: 5.2–10.3%). Of those, 203 (60.4%) were males, 227 (67.6%) over 65 years, 62 (18.6%) born in Europe/North America, 27 (8.0%) HIV-co-infected and 24 (7.2%) had MDR-TB. The respective CFR were 7.7%, 18.3%, 17.5%, 12.1% and 11.7%. In multivariate analysis, factors predicted TB-associated death were being male (OR = 1.4), every increase of 5-years of age (OR = 1.4), being HIV-infected (OR = 5.9) and having MDR-TB (OR = 2.8). The leading TB-associated mortality causes were septicemia ( $n = 113$ , 33.6%) and pneumonia ( $n = 55$ , 16.3%). Average proportional mortality rates (TB-death/all death in Israel) was 0.2% (annual range: 0.1–0.4%, in an increasing trend). Case specific mortality rate (TB deaths/Israeli population) was 2.1 per 100 000 population (annual range: 1.4–2.7).

**Conclusions:** The following risk factors were found in our study for TB mortality: male gender, older age, HIV-co-infection and MDR-TB. Most can be identified in the early stages of treatment—and followed up from start to lower mortality.

### PUBLIC POLICY– 1

#### PC-525-15 Modelling immigration-related approaches to controlling tuberculosis: could we meet the 2050 Millennium Development Goal?

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**Background:** Traditional strategies for reducing tuberculosis incidence rely primarily on interruption of transmission through effective detection, treatment and isolation. In low prevalence settings a dominant proportion of tuberculosis disease may relate to importation and reactivation of previously latent infection, without recent local transmission. We aimed to evaluate the potential impact in this setting of introducing immigration strategies targeting latent tuberculosis infection using a mathematical modelling approach, particularly with regards to achieving the 2050 Millennium Development Goal of <1 case TB/million population.

**Design/methods:** A stochastic individual-based model with discrete time intervals was used to simulate tuberculosis disease amongst immigrants to Victoria, Australia; a low-prevalence, low-transmission setting. A variety of immigration screening and treatment policies aimed at preventing reactivation of latent infection were imposed to consider the effect on overall tuberculosis incidence and rates of multidrug-resistant disease. Effectiveness thresholds for potential future treatments, particularly therapeutic vaccination, were also explored.

**Results:** No strategy was sufficiently effective to meet the target threshold of <1 case/million population by 2050, even in scenarios which assumed zero local transmission. The universal introduction of a 100% effective therapeutic vaccine for all immigrants to Victoria would be expected to reduce TB incidence from 70 to approximately 16 per million by 2050. The relative impact of different screening and treatment approaches are also explored.

**Conclusion and recommendations:** Public health strategies targeting latent tuberculosis infection in immigrants may substantially reduce tuberculosis incidence in a low prevalence region. However, projected reactivation rates from current residents with LTBI will continue to exceed targets, and no solely immigration-related strategy is likely to achieve the 2050 MDG.

**PC-526-15 Community knowledge levels about tuberculosis in 10 districts of Uganda: implications for the national tuberculosis control programme**

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**Background:** In 2009, Uganda was ranked 18th out of 22 tuberculosis (TB) high burden countries in the world. Uganda has a low TB case detection rate of 57%. Effective TB control requires considerable community contribution with high knowledge on its causes, symptoms, control and management. This study was part of a larger community health survey aimed at determining community TB knowledge levels and identifying areas with knowledge levels below national targets.

**Design/methods:** Lots quality assurance sampling methodology with standard questionnaires was used. The study had 3192 respondents categorized as youths aged 15–24 years, men (15–54 years), and women (15–49 years) from 10 districts of Uganda. Proportions were used to estimate knowledge levels by category per supervisory area and pooled data was used to determine overall estimates.

**Results:** TB knowledge levels were lower among the youth (15–24 years) and women (15–49 years) than men (15–54 years) by 5–10% for all indicators. Generally, 94% knew the risk of not completing treatment, 76.9% knew that TB is a curable disease, 50.3% knew at least 2 symptoms while 60% knew how TB is transmitted. However, 26% did not know the cause of TB. There was no major knowledge level variation across districts except for knowing at least 2 TB signs and symptoms and this ranged from 40.2% to 67%.

**Conclusion and recommendations:** Inadequate community knowledge about TB particularly on causes, signs and symptoms and transmission poses a major public health challenge in Uganda's TB control efforts. Knowledge on need to complete treatment is the only indicator above the national target of 80%. So as to realize the TB control targets, there is a need to review the current communication strategies for TB in the community and formulate an appropriate community led intensive health education campaign. The communication strategy developed should be gender and age sensitive if it is to be successful.

**PC-527-15 Harnessing the potentials of national Stop Tuberculosis Partnerships to improve mutual responsibility and sustainability: the Nigerian experience**

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**Background and challenges:** Eliminating TB is collective efforts of all stakeholders including government, development partners, civil society, private sector, academia etc. Mutual responsibility of all stakeholders is required for the effectiveness and sustainability of any TB program. One of such innovative platforms for improving the coordination and effectiveness of stakeholders is the National Stop TB Partnerships. Ensuring the effectiveness and sustainability of such a Partnership could be very challenging. Managing expectations and influence of members in the Partnership is very crucial to its viability.

**Intervention:** The outcome of the meeting held at the Union conference in Cape Town in 2007 by delegates from Nigeria led to series of interventions; and with active engagement and support of all stakeholders, culminated in the launching of the Nigeria Stop TB Partnership in 2009. This initiated a new phase to ensure the sustainability of the Partnership. Various stakeholders within and outside the country including the Global Stop TB Partnership Secretariat and the Global Fund had supported the improved effectiveness and sustainability of the Partnership with focus on mutual responsibility for sustainability.

**Results:** Since 2009, Nigeria Stop TB Partnership had achieved some success and also encountered many challenges. However the collective goal of working together to eliminate TB in the country still remains the same. Some of its achievements include: contribution to the National TB Strategic Plan, increased government funding, and innovative financing through mobilization of domestic resources.

**Lessons learnt:** An effective National Stop TB Partnership will contribute significantly to improve national plans, policies, services and funding for TB.

**Conclusion and recommendation:** The potentials of National Stop TB Partnerships are yet to be fully harnessed, adequate support should be given to establish and improve their effectiveness.

### PC-528-15 Is the new World Health Organization tuberculosis diagnosis strategy underestimating the issue of false-positive cases?

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**Background:** Before 2009, the World Health Organization (WHO) strategy for pulmonary cavity TB diagnosis was based on 3 sputum smears of which 2 had to be positive (i.e., 10 AFB/100 fields) to confirm a TB diagnosis. With the new WHO strategy based on 2 sputum smears, a TB patient is diagnosed if only 1 is positive (i.e., with only 1 AFB/100 fields). As stated by the WHO, the short reduction in specificity is supposed to be largely off-set by the gain in sensitivity. As it shortens diagnosis process, this new strategy is useful and decreases both patient's effort and workload of lab technicians. However, the question of false positives (FP) is problematic.

**Analysis:** A study of the WHO expert group showed a specificity of smear examinations of 98.6%, i.e., a FP rate of 1.4% due to technical issues. A further loss of specificity due to routine conditions and decentralization may be estimated between 1 and 2%. For each examination, the expected total FP rate would thus achieve 3%. Before 2009, the probability of having 2 FP smears for the same patient was less than 1 per 1000 (3% by 3%). However as the new strategy needs only 1 smear with only 1 AFB/100 fields to define a case, at least 3% of TB suspects will be wrongly classified as TB patients. Although this proportion seems low, field data may be very illustrative. In India, a research project showed that 162 true TB cases were confirmed by culture out of 2229 patients with discriminative symptoms (i.e., a TB prevalence of 7.3%). With the 1 smear new strategy, at least 62 (3%) out of the 2067 non TB patients will be treated needlessly with disastrous consequences (e.g., financial losses, emotional stress, stigma, treatment complications). The positive predictive value would be only 72% ( $162/(162 + 62)$ ).

**Conclusion:** With this new diagnosis strategy based on one positive smear, the risk of maximizing false positive cases is a real concern. The best alternative would be to confirm each positive smear by another one to decrease FP cases without affecting sensitivity.

### PC-529-15 Cost-burden of tuberculosis in rural Burkina Faso: illustration of a disease poverty trap

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**Background:** Tuberculosis-related costs incurred by patients constitute a severe economic burden for households especially in rural area where health expenditures and income loss threaten their ability to meet basic needs such as food, education and access to primary healthcare.

**Objective:** We aim at identifying the specific costs faced during pre-diagnosis, diagnosis and treatment of tuberculosis (TB) and then to define opportunities for improving the TB control strategy.

**Methods:** A cost-of-illness study was performed in rural Burkina Faso in 2008. 242 in-depth interviews were realised among smear-positive pulmonary tuberculosis cases enrolled into the DOTS program. We assessed cost-burden by collecting data on direct and indirect costs, family income and assets and coping strategies.

**Results:** Median direct costs were US\$104. In addition, median time lost due to health-seeking and treatment behavior, and inability to work as a result of the illness corresponded to 45 work days, representing high indirect costs. Median cost-burden was estimated to 3 months of household income and 75% of the patients faced catastrophic health expenditures (CHE). To deal with these CHE, households were forced to develop several coping strategies (using savings, selling goods or cattle, or borrowing money) that can seriously worsen their economical situation in the long run.

**Conclusion:** Failing to protect patients from CHE, the TB control strategy contributes to weak uptake and poor success of the national program and to household impoverishment. Decision-makers and managers must be aware of such evidences from field evaluations that may feed a relevant discussion on diverse ways to tackle adverse effects of social, economic and even system barriers to TB control (e.g., appropriate demand-side financing). To encourage this process, the future DOTS strategy must integrate these interrelated social and economic aspects in order to increase coverage and guarantee effective patient management.

### PC-530-15 Financial protection and effective coverage of the rural health insurance scheme in treating uncomplicated tuberculosis patients in China

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**Background:** China has achieved the universal coverage in rural areas since 2010. However, the rural health insurance scheme is pooled at the county level and does not have adequate coverage for outpatient care. Because of the free treatment policy for tuberculosis (TB), outpatient care at the TB dispensary is

covered by 45% schemes at the county levels in China.

**Aims:** To evaluate the contribution of rural health insurance in reducing medical burden of TB patients, and explore the measurement of effective coverage of the rural health insurance schemes for TB patients.

**Methods:** Zhejiang and Sichuan were study areas. In each province, two counties with insurance schemes covering TB outpatient treatment and another two counties without were selected. In each county, 50 uncomplicated new TB patients were randomly selected, and a total of 197 TB patients completed the questionnaire survey.

**Results:** TB patients paid generally high medical expenditure for TB care regardless of the coverage of their rural health insurance schemes. On average, medical expenditure per patient was US\$740 and US\$935 in the covered and uncovered groups in Zhejiang ( $P < 0.05$ ); while it was US\$660 and US\$616 per patient respectively in Sichuan ( $P < 0.05$ ). The medical costs accounted for 30–70% of their annual per capita income. Over half of medical expenditure was spent in general hospitals before TB diagnosis. During their treatment in TB dispensaries, 41% in Zhejiang received the reimbursement, with an average of US\$15 per person; while 84% in Sichuan received the reimbursement, with an average of US\$43. The amount covered by the rural health insurance scheme was far less than patient medical expenditure. The majority of medical expenditure during outpatient treatment was spent on auxiliary drugs such as liver function protection drugs.

**Conclusion:** A low protection and low effective coverage of the rural health insurance scheme for TB patients was found in China.

### PC-531-15 The importance of adhering to World Health Organization and National Infection Control guidelines in a resource-limited country

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**Background:** South Africa ranks third highest in the world in tuberculosis (TB) burden. Inadequate infection control (IC) leads to risky environments for the emergence and transmission of TB which is critically important for health care workers and persons at risk due to human immunodeficiency virus (HIV) infection. IC for TB requires and complements implementation of core activities in TB, HIV and TB-HIV control and health systems.

**Methods:** A cross-sectional survey was conducted in

2011 using a standard assessment instrument to assess 335 public health facilities, supported by non-governmental PEPFAR-funded organizations in South Africa. The instrument comprises three categories—administrative, environmental and personal risk reduction—based on the WHO guidelines for TB infection control in low-resource settings and the South African TB infection control guidelines. Criteria include the presence of a TB IC committee; a written site-specific TB IC plan; a TB IC focal person assigned to oversee facility infection control activities; recording of a facility TB IC risk assessment in the last six months; screening and triaging of coughing patients; open windows and directional airflow; medical surveillance of staff; signage of cough etiquette; appropriately ventilated designated areas for sputum-collection; and personal protective equipment with staff having received training on the proper fitting of respirators.

**Results:** Analysis of the 335 clinics assessed revealed that 218 (65%) had TB committees, 206 (61%) had written site-specific TB IC plans, and 218 (65%) had assigned focal persons to oversee TB IC activities. Of the facilities assessed, 102 (44%) reported at least one health care worker who contracted TB in the last year. The implementation of TB IC committees is significantly ( $P < 0.001$ ) associated with TB IC risk assessment recorded in the past six months, triaging of coughing patients, medical surveillance of staff, signage of cough etiquette, appropriately ventilated designated areas for sputum-collection, and protective personal equipment.

**Conclusions:** This study identified the importance of adhering to the WHO and national IC guidelines and the importance of the implementation of facility IC committees.

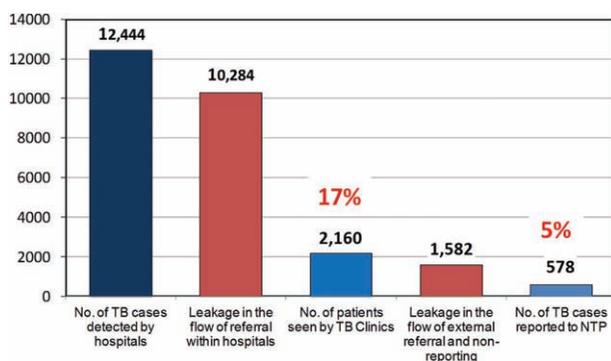
### PC-532-15 Assessing potential of large public hospitals to enhance tuberculosis case detection in Metro Manila, Philippines

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**Background:** The Department of Health (DOH) policy states that public hospitals must have TB clinics where all TB cases detected within the hospital should be referred for registration or referral to peripheral DOTS facilities. The DOH plan is to engage 90% of public hospitals by 2016. The NTP through the CATCH project supported by WHO-CIDA started with 14 public hospitals in Metro Manila in 2010. This study was done prior to project implementation to determine hospitals' potential to contribute to TB casefinding, and identify areas to be improved and supported.

**Design/methods:** A rapid assessment survey was done from December 2009 to January 2010. We reviewed the year 2008 records of the 14 public hospitals, and conducted key informant interview. Hospitals were classified into four quadrants: whether reporting/not reporting to NTP, and presence/absence of a two-way referral system to peripheral DOTS facilities. Hospital's potential was determined by the number of TB cases detected in 2008. Missing TB cases—those detected but not reported to NTP, were computed and 'leakages' in the flow of referrals and reporting process were identified.

**Results:** Thirteen were tertiary hospitals, eight owned by DOH. Bed capacity ranged from 150 to 4200. Eight hospitals have TB clinics, but only five were reporting to NTP. Of the five, three hospitals have a two-way referral system to peripheral DOTS facilities. In 2008, hospitals detected 12 444 TB cases, but only 2160 (17%) and 578 (5%) were seen by TB clinics and reported to NTP respectively (Figure). There were 11 866 missing cases, and 83% of these was due to 'leakage' in the flow of referrals to the TB clinics.



**Figure** Disposition of TB cases detected by 14 hospitals in 2008. Rapid assessment survey, December 2009–January 2010.

**Conclusion and recommendation:** Many TB cases detected were not reported because of the weak hospital referral system despite a national policy. Results of this study were used to design interventions for CATCH project, advocate to hospital management and allocate NTP resources. The study tool was also used in other hospitals.

### PC-533-15 The hidden costs of installing Xpert in a high-burden country: experiences from Nigeria

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**Background:** Since the development of GeneXpert, National TB Control Programmes have initiated its implementation. Supporting agencies often provide funds for the platform and cartridges but it is difficult to identify additional costs related to their installation.

**Design/methods:** Description of costs incurred when installing GeneXpert machines in the Federal Capital Territory (FCT) of Abuja, Nigeria.

**Results:** We installed new GeneXpert machines in April/May 2012 in 5 district hospitals at the local area councils (LAC) of the FCT as part of a TB-Reach funded project to increase case detection of TB in slum areas. The following hidden costs that had not been foreseen before initiating the project: 1. Custom clearance (machines and cartridges) required payment of a handler, even though they were duty free. 2. Laboratory staff required 3-day courses and several of them were not computer literate requiring extended support in the field. 3. Electricity supply is unstable and we had to purchase inverters, batteries, stabilisers and in two occasions generators, with their added running and security costs. 4. The GeneXpert machines, printers and computers plus the electrical equipment required 5 additional plugs and at least two lead extensions with electrical sockets. 5. Additional bench space for the equipment and processing specimens, which needs to be separate from each other. In one hospital we purchased a container due to lack of space. 6. Antivirus software and security cables for the computer. 7. Ink cartridges and paper for the printer. The bulky cartridges required large and secure cabinets for safekeeping and frequent transport from the base.

**Conclusion and recommendations:** Hidden costs for the installation of GeneXpert in a high burden TB country in Sub-Saharan Africa are substantial and should be considered when budgeting to introduce this new platform. Costs may vary by location but are not insubstantial.

### PC-534-15 Can linking the needy tuberculosis patients to social welfare schemes improve cure rates? A study from West Bengal, India

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**Background and challenges to implementation:** An Initiative to Manage People Centered Alliances in Control of Tuberculosis (IMPACT) to decrease the morbidity of tuberculosis in selected districts of West Bengal is being implemented by GLRA in collaboration with CARE India and Revised National TB Control Program. The project is supported by USAID and Eli Lilly. The important reason identified for high defaulters was difficulty in getting three meals a day due to inability to earn livelihood during their illness. The key objectives included strengthening of

case-holding and completion of treatment among retreatment and new smear positive TB cases living below poverty line (BPL) by linking with different social welfare schemes.

**Intervention or response:** In consultation with Gram Panchayats the needy TB patients were linked to social welfare schemes. They were monthly provision of food grains (cereals and pulses), cash assistance for nutritional support, snacks on DOT day and others. Among a total of 7501 patients, 1668 patients (1464 NSP and 204 retreatment cases) were linked with such schemes and ensured access to nutrition.

**Results and lessons learnt:** High cure rate (92%) was achieved among retreatment cases who were linked to social support scheme as against those who were not linked to schemes (59%)  $P < 0.01$ . Similarly high cure rates was seen among new smear positive cases also.

**Table** Treatment outcome of TB cases registered 2010–2011

Outcomes	Social support +		Social support –	
	NSP	Retreatment	NSP	Retreatment
Cured and treatment completed	1265	162	3272	811
Defaulted	44	10	327	348
Others	154	35	490	567
TB cases enrolled	1463	207	4089	1723

**Conclusions and key recommendations:** There is a significant relationship between access to nutrition (through linking to social support schemes) and treatment outcomes. The results show the benefits among NSP cases and more so among retreatment TB cases.

### PC-535-15 Estimates of incurred costs for different tuberculosis services in NGO schemes in India

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**Background and challenges to implementation:** The Revised National Tuberculosis Control Program (RNTCP) in India involves private sector in different initiatives to create an impact in TB control through schemes like ACSM, sputum collection and transport, microscopic services, treatment adherence, and others. A grant-in-aid is provided by RNTCP and it may be useful to understand the actual costing required to deliver different TB services.

**Objective:** To estimate the cost incurred in NGO settings for ACSM, sputum collection & transportation, DMC, and TB treatment unit (excluding drugs and lab reagents which are supplied free by RNTCP) services.

**Methods:** All relevant financial records for each service were verified for actual expenditure incurred by NGOs. The cost analysis was done for TB patients treated under DOTS in a period of one calendar year.

The exchange rate at the time study was US\$1 = 48 INR.

**Results and lessons learnt:** ACSM cost for 100 000 population is estimated to be INR 85 000 against INR 150 000 RNTCP grant for 1 million population; sputum collection and transportation cost is estimated to be INR 22 000 per center against RNTCP grant of INR 84 000 per center; sputum microscopy and treatment cost is estimated as INR 361 000 against RNTCP grant of INR 150 000 per DMC; TB Treatment Unit (TU) model cost is estimated as INR 750 000 against RNTCP grant of INR 530 000 per TU.

**Conclusions and key recommendations:** TB care requires considerable cost to provide quality services. This study data is vital for policy makers to allocate adequate budget to each RNTCP schemes.

### PC-536-15 Trends of tuberculosis notification rates in Rwanda and scale-up of antiretroviral therapy

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**Background:** Human immunodeficiency virus (HIV) is the most important risk factor of tuberculosis. Antiretroviral therapy (ART) is therefore anticipated to limit the occurrence of tuberculosis. In Africa, analyses of sub-national data showed potential impact of ART scale up on decline of tuberculosis notification rates (TNR).

**Methods:** We analysed surveillance data from tuberculosis (January 1995 to December 2011) and ARTs (January 2004 to December 2010). We compared trends of TNR (number of tuberculosis cases for a specific year by the estimated size of Rwanda population for the same year, reported to 100 000 populations), and trends of ART coverage (number of people on ART among those eligible), with stratifications by tuberculosis forms and HIV status.

**Results:** Between 1995 and 1999, all-forms TNR doubled from 44 to 85/100 000 (18% average annual increase). From 2000 to 2006, TNR remained stable between 66 and 90/100 000 (1% average annual increase). Since, a constant annual decline of –7% is observed, and started when a threshold of 58% as ART coverage was achieved. That decrease was more apparent for sputum smear negative (SS–) and extrapulmonary tuberculosis (EPTB) forms. TNR demonstrated rapid decline among HIV+ than in HIV– (respectively –15% against –2% when comparing 2005–2007 and 2008–2011 periods).

**Conclusions:** Our analyses demonstrated a potential impact of ART program on TNR decline, especially for SS– and EPTB forms and HIV+. There is

therefore need of an early HIV testing for an early start of ART. In Rwanda, this is achieved through systematic HIV testing for all persons with tuberculosis symptoms.

### PC-537-15 Uncovering Yemeni patient and family experiences of tuberculosis diagnostics

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**Background:** To date in Yemen the experiences of TB suspects and their families of the TB diagnostic pathway have remained untold. We aimed to identify and describe the barriers for the completion of diagnosis and registration for treatment with suspects attending a tuberculosis centre in Sana'a.

**Methods:** In-depth interviews were conducted with patients who completed and abandoned the diagnostic process (20; 11) and registered for treatment (21). Additional Focus Group Discussions (12) were held in sex and age segregated groups. A framework analysis was conducted within a 'contextualist' research paradigm.

**Results:** Poverty, insecure employment, low literacy, immigration and being female, shaped patients' perceptions and understanding of TB, and the ease or difficulty with which they completed the diagnostic process and registered for treatment. Barriers included lack of health information as multiple patients and their entourage entered the consulting room at the same time, the majority of patients travelling from outside Sana'a, missing work and women relying on male family members to accompany them. Other barriers included instances of preferential treatment. Combining public and private healthcare was also common. These barriers were more acute for patients who abandoned the diagnostic process, some of whom faced multiple barriers. A major reason for dropping out was being given a negative smear result and sometimes a clinical diagnosis on the first day of attendance. Patients also sought their own healthcare solutions in the private or informal sector.

**Conclusion:** Suspects/patients' lived experiences and perspectives are important to support the sustainability, equity and efficiency of the TB diagnostic process. To enhance case finding and reduce the direct and opportunity costs patients face, there is need to decentralise diagnosis and further develop tailored advocacy, communication and social mobilisation strategies.

### PC-538-15 Settling Community Advisory Boards in tuberculosis research: achievements, challenges and goals of a Brazilian initiative

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**Background:** The practice of constituting community advisory boards (CAB) around TB research is recent. The AIDS research practice is slowly being incorporated. REDE TB, in partnership with the Union, included CABs as a component of its PROVE IT/TREAT TB study in Brazil.

**Objectives:** CABs are created 1) to provide a social feedback for a study; 2) to create legitimacy around the study goals (practical use of the study); 3) to bring the perspective of the different stakeholders into the research design and development; 4) to generate advocacy for implementation of study results.

**Development:** PROVE IT in Brazil created five CABs for the different sites between November 2010 and August 2011. The CAB composition may vary, but in principle they are: community members (TB, TB-HIV advocates, people affected); local study coordinators and members; program managers. Each local CAB carries out regular meetings, according to its needs and in consonance with the projects' CAB coordination; this one provides technical, financial and logistical support.

**Results:** Significant contributions by community CAB members to the study development were achieved. In each site, community members brought unexpected suggestions, propositions or initiatives, e.g., meeting ethical committees requirements; indicating the proper partners in the local health programs to local project coordinators; organizing meetings with key local stakeholders; producing printed material to inform health care workers and MDR-TB suspects; strategizing to improving projects' recruitment; informing on patients' and health care workers' limitations. Community CAB members volunteered to helping directly overcoming the obstacles, by direct interventions/outreach activities.

**Conclusions:** Both researchers and program managers in TB field are yet to be convinced of the advantages of CAB initiatives. Nevertheless, the practice has shown the positive outcomes of bringing community into research and exercising shared responsibility.

## TB-HIV PHARMACOLOGY AND CLINICAL ISSUES

### PC-588-15 Hepatic tolerance among HIV-TB co-infected patients treated with antiretroviral and anti-tuberculosis drugs in a setting with high prevalence of HBV infection

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**Background:** The safety of non-nucleoside reverse transcriptase inhibitor (NNRTI) based antiretroviral therapy (ART) and anti-tuberculosis drugs co-administration is poorly documented in developing countries, especially in patients with hepatitis B (HBV) and C (HCV) co-infections.

**Design/methods:** HIV-TB co-infected individuals were enrolled in a randomized control trial (CARINEMO-ANRS 12146) comparing efficacy and safety of nevirapine (NVP, 400 mg without loading dose) and efavirenz (EFV, 600 mg daily) combined with lamivudine and stavudine/zidovudine during 48 weeks. TB treatment (2RHZE + 4RH) was started 4–6 weeks before ART initiation. Screening for HBV and HCV was performed at inclusion. Alanine-aminotransferase (ALT) and total bilirubin (BT) were measured before and after ART initiation.

**Results:** In 573 individuals enrolled (58% male), the median age, weight, CD4-count and HIV-1 viral load were 33 years, 52.2 kg, 89 cells/ $\mu$ l and 5.6 log, respectively. The prevalence of HBV and HCV was 21.5% (122/568) and 1.6% (9/573), respectively. ALT/BT grade  $\geq 2$  ( $>2.5$ – $5 \times$  UNL) was reported in 19.9% (114/573) and ALT/BT grade  $\geq 3$  ( $>5$ – $10 \times$  UNL) in 6.5% (37/573) of patients. ALT  $\geq$  grade 3 (severe hepatitis) was reported in 7.0% (20/285) and 5.9% (17/288) of patients in NVP and EFV arms, respectively. Severe hepatitis occurred in 3.5% and 3.0% of individuals on ART for 0–12 weeks and  $>12$  weeks, respectively. Occurrence of severe hepatitis was similar in individuals with (11/122, 9.0%) and without (26/443, 5.9%) HBV infection ( $P = 0.21$ ). After ART initiation, severe hepatitis was not associated with any of the baseline characteristics, including the ART regimen and CD4-count.

**Conclusion and recommendations:** Despite the high prevalence of HBV infection, the co-administration of NNRTI and anti-TB drugs was well tolerated. The use of NVP did not increase the risk of hepatitis.

### PC-589-15 Low body mass index as an important additional 'danger sign' in HIV-seropositive tuberculosis suspects: an observational cohort study

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**Background:** In 2007 WHO released revised recommendations for diagnosis of TB in people living with HIV. Included was a specific algorithm for reducing delay in TB diagnosis for seriously ill patients identified as at higher risk of mortality by presence of 'danger signs'. We investigate if the accuracy of these 'danger signs' at predicting mortality risk could be improved by inclusion of additional basic clinical indices available at time of first attendance at a rural antiretroviral (ARV) initiation clinic.

**Design/methods:** The setting was a rural district level clinic in KwaZulu Natal. Included were consecutive adult HIV seropositive patients attending for review prior to ARV initiation 18 June to 27 July 2010, who were considered TB suspects by the presence of 1 or more 'TB symptoms' (cough, weight loss, fever, night sweats). Variables collected prospectively for analysis included the 2007 WHO 'danger signs': pulse (HR)  $> 120$ , respiratory rate (RR)  $> 30$ , temperature  $> 39^\circ\text{C}$ , inability to walk independently. In addition other clinical variables previously associated with early mortality (identified through literature review) were analysed. Outcome variable was mortality at 12 months. Dependent variables were investigated for association with 12 month mortality. Significant variables were converted to clinical scores to allow the comparison of predictive accuracy of different combinations of variables using Receiver Operating Characteristic (ROC) curve analysis DeLong et al. method.

**Results:** Eighty-five TB suspects were included; 51/86 (59%) of these were treated for TB during the year of follow up, all were initiated on HAART, and the 12 month mortality was 16/86 (19%). Variables at first clinic visit significantly associated with 12 month mortality on univariate analysis included: inability to walk unaided, RR  $> 18$ , HR  $> 110$ , temperature  $> 38.6^\circ\text{C}$ , CD4  $< 100$  cells/ $\mu$ L, albumin  $< 30$  g/L, haemoglobin  $< 9.6$  g/dL, Karnofsky score  $< 70$ , BMI  $< 17.5$  kg/m<sup>2</sup>. A clinical score based on the 2007 WHO danger signs had AUC 0.63 on ROC curve analysis (95%CI 0.52 to 0.74,  $P = 0.075$ ), with a score  $> 0$  being associated with 60% sensitivity and 67% specificity. Addition of variable BMI  $< 17.5$  kg/m<sup>2</sup> improved AUC to 0.72 (95%CI 0.62 to 0.81,  $P = 0.0022$ ); presence of any WHO danger sign or BMI  $< 17.5$  kg/m<sup>2</sup> had 73% sensitivity and 60% specificity for 12 month mortality. Difference between AUC = 0.088 (95%CI 0.0067 to 0.17,  $P = 0.034$ ).

**Conclusions:** Addition of low BMI to 2007 WHO 'danger signs' may improve accuracy at predicting mortality risk. This could facilitate more sensitive patient selection for management by the seriously ill patient algorithm. The utility of the WHO danger signs and low BMI should be validated in additional settings.

### PC-590-15 Correlating chest radiographs and symptom presentation in HIV patients presenting for initial care at Connaught Hospital, Freetown, Sierra Leone

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**Background:** WHO recommends adult or adolescent with HIV, presenting with cough, fever, weight loss or night sweats be ruled out for active TB. In countries like Sierra Leone where Mycobacterial cultures are not available, symptom surveillance and sputum AFB smear play a more important role. The study objective was to evaluate the correlation of chest radiograph and symptom presentation in HIV patients presenting at their initial HIV clinic visit at Connaught Hospital, Freetown Sierra Leone.

**Methods:** We reviewed 384 charts from a retrospective cohort study analyzing medical records from Connaught Hospital, the largest government provider of HIV care in Freetown, Sierra Leone (January 2007–December 2007).

**Results:** Mean age of the 384 patients was 35 ± 9.95 years, 222 (57.8%) patients were female. 126 of 373 patients (33.8%) were asymptomatic and 115 (30.8%) of those with TB symptoms recorded, had two or more symptoms at initial clinic presentation. 207 patients (53.9%) had a chest radiograph performed, 87 (42.0%) were abnormal, 34 of 87 (39.1%) had cavitory disease. Of the 126 patients without symptoms, 15/59 (25.4%) had an abnormal chest radiograph, none were smear-positive. Of the 247 patients with symptoms, 71/135 (52.6%) had an abnormal chest radiograph. 9 patients had smear-positive disease and 8/9 (89%) were symptomatic at presentation (Table). In a logistic regression analysis, abnormal chest radiographs were significantly associated with symptomatic presentations (OR = 3.25, 1.65–6.40,  $P < 0.01$ ). Overall average CD4 cell count was 243 (SD ± 217). No significant difference noted in CD4 cell count among normal and abnormal chest radiograph ( $P = 0.88$ ) or asymptomatic and symptomatic patients ( $P = 0.69$ ).

**Table** Comparison of patients with and without TB symptoms at initial clinic presentation

Characteristic	Total <i>n</i> *	Asymptomatic <i>n</i> (%)	Symptomatic <i>n</i> (%)	<i>P</i> value
Age	35.25 ± 9.99	35.22 ± 10.25	35.3 ± 9.51	0.71
CD4 baseline	242.69 ± 217.76	234.04 ± 202.35	260.66 ± 246.83	0.39
Socio-demographic				
Marital status				0.06
Single	142	48 (34)	94 (66)	
Married	155	45 (29)	110 (71)	
Divorced	14	8 (57)	6 (43)	
Separated	9	3 (33)	6 (67)	
Cohabiting	9	6 (67)	3 (33)	
Widow(er)	34	11 (32)	23 (68)	
Unknown	6	4 (67)	2 (33)	
Education				0.11
Primary	58	13 (22)	45 (78)	
Junior secondary school (form 1–5)	93	37 (38)	56 (72)	
Senior secondary school (lower and upper 6)/trade/technical school	93	32 (34)	61 (66)	
Tertiary	28	13 (46)	15 (54)	
None	94	28 (30)	66 (70)	
Unknown	3	0	3 (100)	
Clinical				
Chest radiograph result				0.001
Normal	108	44 (41)	64 (59)	
Abnormal	86	15 (17)	71 (83)	
Abnormal chest radiograph				0.1
Non-cavitory	33	7 (21)	26 (79)	
Cavitory	33	7 (21)	26 (79)	
Sputum smear result				0.1
Negative	87	28 (32)	59 (68)	
Positive	8	0	8 (100)	

\* Note: One patient had no presenting symptom recorded.

**Conclusion:** Interestingly CD4 didn't predict chest radiography and TB symptom was independent of CD4 value. Despite presenting with TB symptoms, not all patients had a chest radiograph exam. With a large disparity between abnormal chest radiographs and sputum positivity, the need for additional diagnostic modalities is obvious. Improved training of clinicians for TB symptom recognition, will also lead to increased screening and diagnosis. This study calls for a closer more analysis of the remaining clinic data and a serious look at the recent WHO recommendation of using the GeneXpert system as an additional TB screening/diagnostic tool, especially in resource limited settings.

### PC-591-15 Factors associated with malnutrition in patients co-infected by tuberculosis and HIV/AIDS in Pretoria

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**Background:** Good nutritional status is important for the immune system to be able to fight and resist infections. Tuberculosis (TB) and HIV are infections that affect the immune system. The purpose of this

study was to evaluate the nutritional status of patients co-infected with TB/HIV treated at Pretoria West Hospital and identify the factors associated with inadequate nutritional status or malnutrition in patients treated at Pretoria West Hospital in 2011.

**Design/methods:** This was a cross-sectional study. Only patients that were admitted to the facility from January to June 2011 were included in the study. Data on nutritional status was collected using the Mini-Nutritional Assessment tool; while data on knowledge and practices about nutrition were collected using an interviewer-administered questionnaire. Clinical data were collected from patients' files. Patients were enrolled in the study upon giving their consent. Descriptive statistics were calculated and cross-tabulation was performed.

**Results:** In total 50 patients were enrolled in the study. Out of 50 participants, 62% were male, 38% female; their age ranged between 18 and 60 years. The mean age was 37.7 years. In line with the objectives of the study, 42% (21) of patients were found as having inadequate nutritional status or malnourished. The factors significantly associated malnutrition were, poor nutrition knowledge (60% vs. 41.4%,  $P = 0.013$ ), unhealthy practice of not eating snack between main meals (90.5% vs. 34.5%,  $P = 0.001$ ), unemployment (81% vs. 37.9%,  $P = 0.002$ ), relying of relatives as sources of income (71.4% vs. 31%,  $P = 0.09$ ), and being single (81% vs. 41.4%,  $P = 0.013$ ).

**Conclusion and recommendations:** The prevalence of inadequate nutritional status or malnutrition among TB and HIV co-infected patients admitted at Pretoria West Hospital was found to be high. Interventions are needed to address poverty and unemployment issues and improve their nutritional knowledge.

#### PC-592-15 Is non-attendance at health care facilities the reason for lack of regular CD4 testing?

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**Introduction:** There are limited data and few studies that evaluate linkage to care in people living with HIV (PLWH) prior to their initiating Antiretroviral therapy (ART). Opportunities to target this vulnerable group to access pre-ART care, including regular CD4 testing, need to be explored.

**Aim:** To determine the proportion of people living with HIV not having regular CD4 count testing who are accessing health care facilities.

**Methods:** A cross sectional community survey of self reported HIV positive people was conducted from January to April 2011 in the greater Cape Town area as part of a larger study to determine linkage to ap-

propriate HIV care. Participants who had taken part in the Zambia South Africa TB and AIDS reduction (ZAMSTAR) study were selectively sampled and completed a questionnaire detailing their attendance at routine health care facilities as well as their history of CD4 testing. Self reported PLWH who were not receiving ART were included in the analysis. Regular CD4 testing was defined as having had a CD4 test in the 6 months prior to the questionnaire.

**Results:** Of the 627 HIV positive participants interviewed 235 (37%) were not receiving ART (PreART) and of these, 137 (58%) had not had a recent CD4 test. Of those without a recent CD4 test, 95 (69%) had attended a health care facility for a medical reason in the previous 3 months. In this group women were 2.6 times more likely (95%CI 1.04–6.74) to attend a HCF than men.

**Conclusion:** There should be a mutual responsibility between a client and a health care facility to ensure regular CD4 testing. The majority of PreART participants had not had a recent CD4 test but had recently attended a health care facility. This subgroup of people needs further attention to understand why regular CD4 testing is not being done.

#### PC-593-15 Causes of death among HIV-positive tuberculosis patients in 2008–2011 in Bulawayo, Zimbabwe

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**Background:** Analysis of antiretroviral treatment (ART) outcomes for HIV-positive TB patients in Bulawayo has indicated that 10–12% of patients started on ART die by one year of ART. The objective of this retrospective record review was to assess available information on causes of death among these patients to reduce mortality.

**Method:** Clinic notes for adult patients for whom information on causes of death was available at two municipal clinics, Emakhandeni and Magwegwe, from 1 August 2008 to 31 December 2011 were reviewed. Epi Info (version 3.5.1) was used for data entry and analysis.

**Results:** A total of 172 patients had some information about cause of death in their notes. One-hundred and six (62%) were males and 141 (82%) were of 20–49 years of age. Only 36 (21%) had sputum-positive TB and 81 (47%) and 116 (67%) had a baseline CD4 lymphocyte cell count of <50 and <100 cells/mm<sup>3</sup>, respectively. Opportunistic infections were the most frequently reported causes of death: 19% of patients died from a central nervous system infection, 13% from gastro-enteritis, 12% from pneumonia and 10% from TB. Assuming that all reported cases of anemia (9), jaundice/hepatitis (6)

and lactic acidosis (3) were due to adverse drug effects and/or drug-drug interactions, 10% of patients died from these conditions. The cause of death remained unknown for 15% of patients in this setting where autopsies are not available.

**Conclusion and recommendations:** It is important that patients to be started on ART are examined carefully and co-morbidities are treated promptly to improve survival.

### PC-594-15 Tuberculosis treatment outcomes for patients on rifabutin and lopinavir/ritonavir-based antiretroviral therapy regimens

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**Background:** Tuberculosis and HIV are major public health concerns. Successful TB treatment and optimal retroviral suppression are critical determinants of the performance of TB-HIV programs. Interaction between rifampicin and lopinavir/ritonavir based antiretroviral regimens is a challenge in achieving TB-HIV treatment objectives. Rifabutin is better tolerated but not widely used in HIV prevalent settings. We describe the rollout of rifabutin in twenty six facilities across the country supported by the national TB and HIV programs, with patients on lopinavir/ritonavir based second line antiretroviral therapy regimen requiring treatment for active TB.

**Intervention:** Treatment guidelines and standard operative procedures were developed. Care providers sensitized on drug use and reporting requirements. Rifabutin was given under DOT at 150mg three times a week in combination with daily Isoniazid, ethambutol and pyrazinamide. Standard doses of lopinavir/ritonavir were prescribed. Data were collected by district TB coordinators using NTP reporting tools and analysed using Microsoft excel software.

**Results and lessons learnt:** Data for 43 patients were available. Of these, 31 (72%) pulmonary tuberculosis (PTB). Of the PTB cases 11 (33%) had smear positive TB. Treatment outcomes were available for 15 (35%) of the cases. Of the 3 smear positive cases; 1(33%) was cured, 1(33%) completed treatment while 1(33%) failed on treatment and developed Multi-drug resistant TB with resistance to all first line drugs. Eight (73%) of the remaining completed treatment 2(18%) died while 1(9%) was lost to follow-up. No adverse drug severe reactions warranting discontinuation of therapy were reported.

**Conclusions and key recommendations:** Rifabutin can be used in programmatic HIV prevalent settings to treat TB. Training is required to improve recording and reporting. Studies to determine rifabutin and rifampicin cross resistance are recommended.

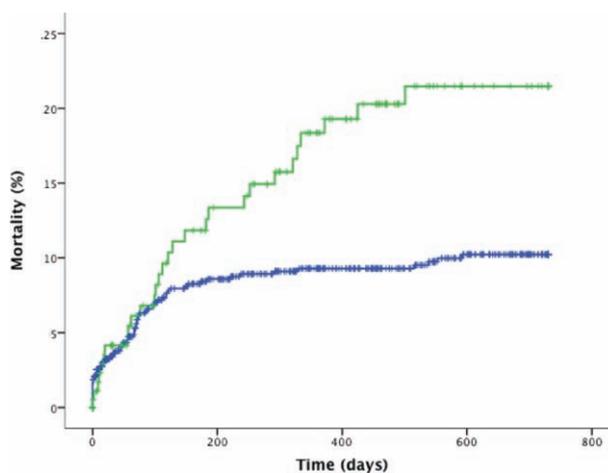
### PC-595-15 Burden of HIV-associated tuberculosis in Indonesia: a cohort study

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**Background:** Very little is known about HIV-associated tuberculosis in Indonesia, which has a rapidly growing HIV epidemic and a high burden of tuberculosis. We examined frequency and characteristics of HIV-associated tuberculosis in a referral hospital in West-Java, Indonesia.

**Design/methods:** We selected ART-naïve patients with information on tuberculosis. All HIV patients undergo regular interview, clinical examination and blood tests. Sputum examination and chest X-ray are done on indication. Tuberculosis incidence was based on tuberculosis treatment during follow-up. Using statistical methods, such as *t*-tests, Mann-Witney *U* and  $\chi^2$  tests we compared patients with and without confirmed tuberculosis. We also examined factors associated with tuberculosis as well as mortality using Kaplan Meier and Cox regression.

**Results:** We included 1348 unselected HIV patients, of whom 51% had symptoms suggestive for tuberculosis. Patients with symptoms had a lower CD4 cell count and more oral candidiasis. Sputum examination, done in 120 patients, (8.9%), confirmed tuberculosis in 67 patients (56%). Chest X-rays, done in 265 patients, suggested tuberculosis in 154 (58.1%). 229 patients (17%) were started on tuberculosis treatment and 778 on ART (57.7%), mostly within 3 months. Tuberculosis treatment was associated with low CD4 cell count (HR = 0.58), history of injecting drug use (HR = 1.87) and anemia (HR = 0.78). Mortality was higher among patients treated for tuberculosis (Figure; adjusted HR = 1.14).



**Figure** Mortality among HIV-infected patients, ART-naïve at enrollment who did (upper curve) or did not (lower curve) receive TB treatment during follow-up.

**Conclusion:** HIV-associated tuberculosis is often suspected but rarely confirmed in this setting. Tuberculosis is associated with increased mortality among HIV patients but further study is needed to examine the underlying causes.

## EXPANSION OF THE STOP TB STRATEGY-1

### PC-619-15 Quality tuberculosis care in Nigeria: using Smartphone technology for data-driven improvements

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**Background and challenges to implementation:** Nigeria ranks 10th among the 22 high TB burden countries in the world. Weak supportive supervision (SS) has been linked to poor treatment outcomes. Nigeria was open to exploring an improved SS program that assesses performance and immediately analyzes critical indicators to establish plans for quality improvement.

**Intervention or response:** The Nigerian Ministry of Health, the National Tuberculosis and Leprosy Control Program (NTBLCP) and Abt Associates improved the TB SS system with the introduction of Smartphone technology. Improving data quality with built in validation, skip patterns and calculations, the phone-based checklist provides immediate analysis, allowing supervisors to quickly identify performance issues and develop quality improvement (QI) plans at the facility level. Such QI plans include improved drug management and supply, external quality control on TB tests and defaulter tracing. The associated web-based database allows for an automated review process as well as aggregation and timely data sharing at all levels of the health system.

**Results and lessons learnt:** Rapid results indicators were created to highlight a facilities' performance at the time of supervision through repeated iteration. The web-based database houses data collected and aggregates and reports information to the national level immediately after supervision. Supervisors have indicated that the system is enabling them to monitor and assess performance of the TB health delivery system. For example, the rate of drug stock-outs has decreased, and external quality control is easily obtained for quality service with far less delay.

**Conclusions and key recommendations:** The use of Smartphones to collect data on TB has eliminated the need for printed forms, minimized human error in

data entry, reduced the lag time for getting data to policymakers and managers, and helped pinpoint ways to improve delivery of care.

### PC-620-15 An innovative approval to quality improvement of chest radiography in Cambodia: peer-review workshop approach

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**Background and challenges:** In Cambodia, the diagnosis of smear-negative pulmonary tuberculosis is made by chest radiography (CXR) as abnormalities consistent with active TB after at least six negative sputum specimens and no response to a course of broad spectrum of antibiotic. However, quality of CXR films in image and interpretation is limited. For improving it, the peer-review workshop (PRW) was adapted in eight rural district hospitals, with a population of 1476315 since September 2010.

**Intervention:** At the PRW, one CXR technician and two physicians, with three best normal films and five difficult interpretation films, from each hospital were invited. Each film was reviewed by themselves and further reviewed by Panel Team (PT). PT consists of the local and national CXR technicians and physicians. Quality of CXR was assessed by using the assessment sheet-HANBOOK-2008; as being graded as 'Excellent, Good, Fair and Poor'. Radiographic interpretation was assessed with the final decision of PT as gold standard 'True or False'. Data were collected from September 2010 to March 2012.

**Results and lessons learnt:** The numbers of CXR films assessed by PT were 28, 24, 27, 37, 29, 37 and 30 from the first PRW in September 2010 to sixth PRW in March 2012 respectively. The excellent or good quality CXR films increased from 64% in September 2010 to 77% in March 2012. Moreover, the true radiographic interpretation increased from 53% in September 2010 to 87% in March 2012. Three main factors were likely the key to success in this intervention: 1) well-organized effort of PRW, 2) leadership of Panel Team, 3) commitment of participants.

**Conclusion:** PRW is very effective to improve quality of CXR films in both image and interpretation for diagnosing tuberculosis. Thus National Tuberculosis Control Program should expand such intervention to other areas

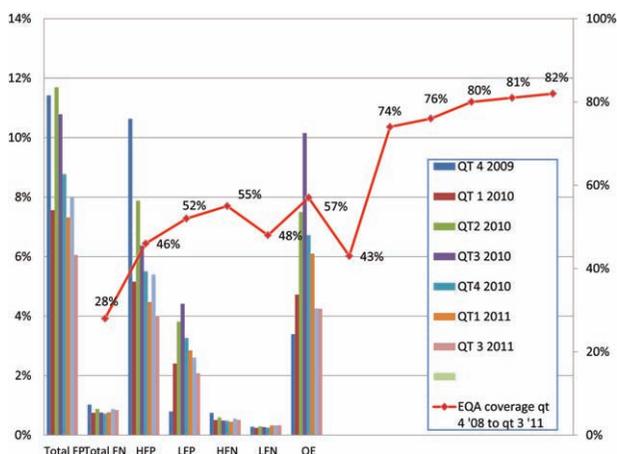
### PC-621-15 Acid-fast bacilli microscopy services in Kenya through strengthening of EQA systems

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**Background:** Improve the quality of AFB microscopy services in Kenya.

**Design/methods:** Supporting development and dissemination of AFB microscopy EQA guidelines, EQA forms, supervision checklist and standard operating procedures (SOPs) from October 2009 to September 2011. In addition we provided support at all levels for EQA feedback to the diagnostic centers after blinded rechecking of slides. The Provincial Medical Laboratory Technologists (PMLTs) and District Medical Laboratory Technologists (DMLTs) were supported to attend TB managers' quarterly review meetings. An EQA training package was adopted from TBCAP tools and used in training laboratory personnel.

**Results:** The EQA system has been strengthened as indicated by improved performance in the Figure. The EQA coverage gradually improved from less than 30% of 930 diagnostic centers in quarter 4, 2008 to 82% by September 2011. Annual cumulative coverage stands at 88% of 1581 diagnostic centers as of September 2011. There was also a great improvement in concordance and major errors from 74% and 14% in 2008 to 97% and 5% in September 2011 respectively. The participatory process that involves the laboratory health workers and their supervisors has been motivating to the health workers, thus enhancing their performance.



**Figure** Kenya EQA coverage and error rates, 2008–2011.

**Conclusion and recommendations:** Through development and dissemination of relevant documents, tools, training, effective feedback and consultative

meetings, TB CAP/TB CARE I and Global Fund has significantly strengthened the sputum smear microscopy services in Kenya.

**Challenge:** Reliance on District TB and Leprosy Coordinator (DTLCs) to sample the slides delays the process of blinded rechecking and feedback.

### PC-622-15 Driving sustainability through result-based management in Tuberculosis Control Programme in Nigeria

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**Background:** This study aims to demonstrate how Result Based Management (RBM) improved programme ownership, describe challenges and make recommendations for further improvement. In an effort to improve TB programme ownership through Government commitment and understanding among key stakeholders, the Netherlands Leprosy Relief supported 13 States it partners to transcend from 'activity based' to 'result based' planning of Project Documents (PD). This paper examines how RBM improved ownership and sustainability of the TB programmes in 2 States of Nigeria.

**Methods:** Advocacy visits were conducted to key stakeholders on the new PD. RBM Technical Committee (RTC) consisting of key stakeholders was constituted and a workplan was developed using the PD. A day's orientation training on RBM was given to all LGTBLS and other stakeholders. The RTC developed a supervisory itinerary and recording tools to capture specific tasks highlighted in the PD. Bi-monthly supervisory visits were conducted to facilities while monthly meetings of the committee were held.

**Results:** An improvement was observed in the quality of supervision; 90% of LGTBLS routinely use checklists during supervisions compared to 20% before the intervention. Quarterly planning and reporting of activities by LGTBLS also improved; 100% of LGTBLS draw their activities from the PD and report based on results compared to none before the intervention. Referrals of TB suspects by community members (community Volunteers) also improved; 7% of all cases notified in the programmes were through such referrals. There was an improvement in funding to the TB programme from 40% of approved budget to 80% after the intervention. Other areas observed to have improved include understanding of relevant results areas and indicators by LGTBLS and HWs, quality of data capturing and collation at the facility and LGA levels by HWs and LGTBLS.

**Conclusion and recommendations:** RBM could improve programme ownership, sustainability and government commitment.

### PC-623-15 Using innovative approaches to increase tuberculosis case detection in northern Tanzania

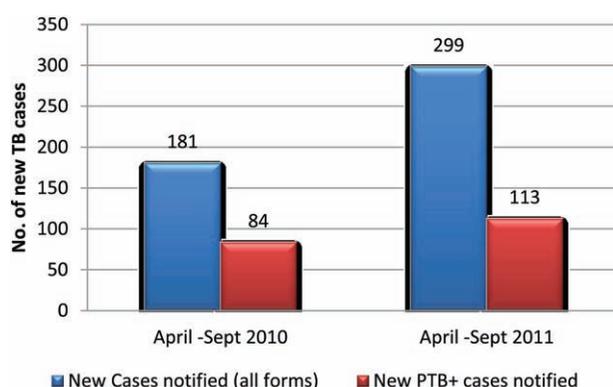
E Wandwalo,<sup>1</sup> I Myemba,<sup>1</sup> E Ntulwe,<sup>2</sup> S Egwaga,<sup>2</sup> Z H Mkomwa,<sup>3</sup> P G Suarez.<sup>4</sup> <sup>1</sup>Management Sciences for Health, Dar Es Salaam, <sup>2</sup>National TB and Leprosy Program, Ministry of Health and Social Welfare, Dar Es Salaam, <sup>3</sup>PATH, Dar Es Salaam, Tanzania; <sup>4</sup>Management Sciences for Health, Washington, DC, USA. e-mail: ewandwalo@hotmail.com

**Background and challenges to implementation:** The number of TB cases notified in Tanzania has stabilized in the last 10 years (2000–2010) with an average annual increase of about 1.6% compared to 10% in the period 1990 to 2000. Between 2005 and 2010, the country has notified an average decline of 0.2%. Since 2009, the country attained the WHO target of 70% case detection. Despite these achievements, there are still many TB patients who are not diagnosed. To address this challenge, NTLP and partners piloted an innovative approach to intensify facility based case detection in Arusha DC and Meru Districts in Arusha Region, Northern Tanzania.

**Interventions:** The approach focused on four main interventions; systematically improve the organization of TB case detection within health facilities; improve the knowledge and skills of staff from different departments on TB; use of standard operating procedures (SOPs) and job aides to improve case detection; improve recording and reporting including monitoring, mentoring and supervision. The intervention was piloted in 12 health facilities between April and September 2011.

**Results:** Evaluation was conducted in 8 major health facilities (representing 96% of TB patients) out of 12 piloted. TB cases increased by 65% (181 to 299) for all forms and 35% (84 to 133) for smear positives TB cases during intervention, April–Sept 2011, compared to the same period before intervention, April–Sept 2010.

**Conclusions and key recommendations:** The intervention has significantly improved TB case detection in piloted sites. The approach should be documented and scaled-up to other health facilities.



**Figure** TB notification in 8 health facilities before intervention, April–Sept 2010, and after intervention, April–Sept 2011.

### PC-624-15 Effectiveness and role of tuberculosis patient self-help groups in tuberculosis control activities in Myanmar: operational research

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**Background:** Previous studies in Myanmar showed that old TB patients influenced choice of treatment for TB suspects. It is essential to examine ways of facilitating TB patient's involvement in addressing TB, one of 6 Stop TB strategies, in Myanmar. The study aimed at describing the development of self-help groups (SHGs) and their roles in addressing TB.

**Methods:** Intervention with SHG strategy and intervention without SHG strategy were assigned to communities that were matched with demographic information in two townships. Baseline and end-line assessments were carried out in both areas through face-to-face interviews with 1020 TB patients and family members, document review, 14 focus group discussions, 28 key informant interviews and observations.

**Results:** Activities of 7 SHGs contributed to 23% of the total referral and 13% of the sputum positive TB cases of two townships for the first two quarter in 2011. The mean difference in knowledge and attitude scores between the baseline and endline measurements were significantly higher in the areas where the SHG strategy was used than the control area. (mean knowledge 3.01 v.s 1.76 and mean attitude 2.26 v.s 1.15) Main activities of SHGs were referral, health education and providing directly observed treatment. Moreover, SHG members gained self-reliance and confidence to carry out their activities over one year.

**Table** Activities of self-help groups for TB case detection for six months

	TB suspect referred	TB patients diagnosed	Sputum-positive TB
Total			
Thanbyuzayat Township	131	30 (22.9%)	6 (4.6%)
Hlaingtharyar Township	120	67 (55.8%)	17 (14%)
Total	251	97 (38.6%)	23 (9%)

**Conclusion:** Empowering TB patients through SHGs is an effective strategy for TB control. Consistent and systematic supervision and support to SHGs by the implementing organizations, appraising the role of SHGs by public sector and local authority and strong support from key stakeholders and donors are essential for yielding impact.

### PC-625-15 Tuberculosis surveillance and control in Germany: an application of the Berlin Declaration Monitoring and Evaluation Framework

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**Background:** In 2007, the 'Berlin Declaration on Tuberculosis' (BD) was signed by the Ministers of the WHO European Region Member States (MS) in order to address the re-emerging threat of tuberculosis (TB) by fully implementing the Stop TB strategy. WHO Euro developed a corresponding Monitoring and Evaluation (M&E) Framework using programmatic and epidemiological indicators to follow-up the BD from 2013 onwards.<sup>1</sup> We explored the Framework performance for Germany, a low-incidence country (5.3 TB cases/100 000 population in 2010).

**Methods:** M&E Framework outcome and output indicators were selected from a surveillance perspective focussing on country-specific indicators asked for all 53 MS. Investigated information sources included available guidelines, notification data and laboratory data by the National Reference Laboratory (NRL).

**Results:** As to national guidelines (indicator 1.1.1), up-to-date guidance documents are available covering all aspects for TB care. Regarding external quality assurance (indicator 3.2.1) proficiency testing performed by the NRL confirms high quality of culture and drug susceptibility testing. MDR- and XDR-TB prevention and control (indicator 4.1) is reflected by an MDR-TB rate of 1.7% among notified cases in 2010 and significantly decreasing MDR-TB notification rates from 2001 to 2010. As to treatment success (indicator 5), the WHO target of 85% is reached for all age groups despite the elderly >60 years. As required (indicator 5.2.2), Germany disposes of an electronic case-based surveillance providing evidence for TB policy and practices.

**Conclusions:** The selected M&E Framework indicators proved well applicable to a low-incidence country. The presented results suggest a well-functioning TB control in Germany.

<sup>1</sup> European Centre for Disease Prevention and Control/WHO Regional Office for Europe. Tuberculosis surveillance and monitoring in Europe 2012. Stockholm: European Centre for Disease Prevention and Control, 2012.

### PC-626-15 The effect of an incentive 'DOT & Shop' scheme on treatment outcome of low-income patients at the Singapore TB Control Unit

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**Background:** TB disproportionately afflicts the poor for whom financial and social factors may affect ad-

herence to treatment. An incentive 'DOT & Shop' scheme sponsored by SATA CommHealth, a local non-governmental organization, was implemented in July 2009 for low-income TB patients treated at the Singapore TB Control Unit. Eligible patients were given grocery vouchers on a monthly basis to encourage adherence to directly observed therapy (DOT).

**Methods:** We compared the treatment outcomes of 6 monthly cohorts of low-income patients treated at the TB Control Unit before (January 2007–June 2009) and after (July 2009–December 2010) implementation of the scheme using data from the National TB Registry. Residence in one- or two-room subsidized housing was taken as a surrogate for low income.

**Results:** 362 patients were enrolled into the scheme. Most recipients felt that the vouchers were helpful and saw it as an incentive to follow through with treatment. Treatment completion rate of the 6 monthly cohorts from January 2007 to July 2009 were 78%, 80.5%, 78.8%, 72.7% and 80%. This improved after the implementation of the scheme to 76.7%, 87% and 88.9% in the July 2009 to December 2010 cohorts respectively. The number and proportion of low-income patients who required legal action to complete treatment fell from 5 (10%), 5 (12.2%), 7 (13.5%), 9 (16.4%) to 5 (11.5%), 5 (10.9%), 5 (9.3%) after implementation of the scheme.

**Conclusion:** The 'DOT & Shop' scheme improved treatment outcomes in low-income patients. More support from the community to enable and incentivise TB patients to adhere to and complete treatment are needed.

### PC-627-15 Time delay and associated factors in diagnosis and treatment of pulmonary tuberculosis in Iran

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**Background and challenges to implementation:** Delay in the diagnosis of tuberculosis increase the risk of death and enhance tuberculosis transmission in the community. This study aims to determine patient and health service delay and factors affecting delays in tuberculosis diagnosis.

**Intervention or response:** A cross sectional survey that included all the public health centers was conducted in central province from May 2009 to Aug. 2011. Patients were interviewed after diagnosis by using structured questionnaire.

**Results and lessons learnt:** One hundred and sixty-six patients aged between 9 and 87 (median; 66) years were included in the study. They comprised 87 (52.4%, median 67 years) females and 79 (47.6%, median 64.5 years) males. The median patient delay was 35 days and mean 62 days, the median health system diagnosis delay was 34 days and mean 53 days,

the median health system treatment delay was 5 days and mean 6 days. The median total delays were 86 days and mean 121 days for all the patients. The main determinants of delay were non education ( $P$  value = 0/021), poor economic condition ( $P$  value = 0/005), private sector ( $P$  value = 0/008), first symptom of cough and hemoptysis ( $P$  value = 0/002), female gender ( $P$  value = 0/006) and age  $\geq 55$  ( $P$  value < 0/001).

**Conclusions and key recommendations:** The results of this review suggest that there is a need for revising case-finding strategies. The reported high treatment success rate of directly observed treatment may be supplemented by measures to shorten the delay in diagnosis and treatment. This may result in reduction of infectious cases and better tuberculosis control.

### PC-628-15 Potential impact of same-day diagnosis and treatment initiation for smear-positive tuberculosis in Africa

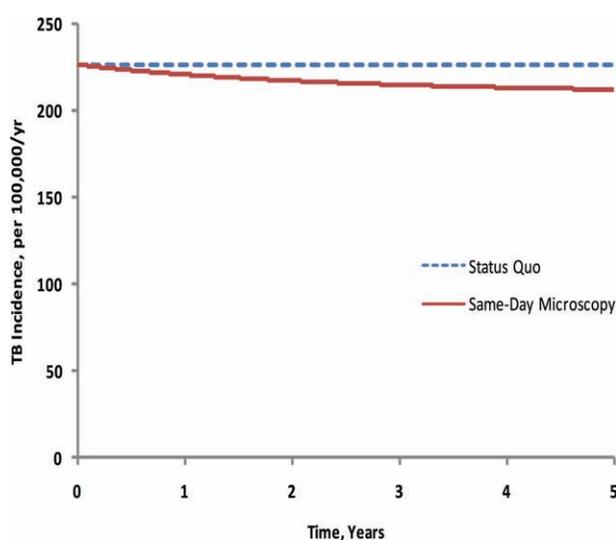
D W Dowdy,<sup>1,2</sup> L Davis,<sup>3</sup> S Den Boon,<sup>4</sup> N Walter,<sup>5</sup> A Katamba,<sup>6</sup> A Cattamanchi.<sup>2</sup> <sup>1</sup>Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, <sup>2</sup>Center for Tuberculosis Research, Johns Hopkins University School of Medicine, Baltimore, MD, <sup>3</sup>Pulmonary and Critical Care Medicine, University of California, San Francisco, SFGH, San Francisco, CA, USA; <sup>4</sup>Independent Consultant, Geneva, Switzerland; <sup>5</sup>Pulmonary Sciences and Critical Care Medicine, University of Colorado, Denver, CO, USA; <sup>6</sup>College of Health Sciences, Makerere University, Kampala, Uganda.  
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**Background:** The World Health Organization (WHO) has endorsed same-day diagnosis of tuberculosis (TB) by microscopy. Implementation of this policy has largely focused on same-day sputum collection, with less attention to the timing of reporting results or initiating treatment.

**Methods:** We linked decision analysis to a steady-state dynamic transmission model to quantify the potential impact if the WHO African Region adopted same-day microscopy (i.e., same-day sputum collection, results reporting and treatment initiation). We fit our model to the TB incidence and prevalence (including HIV-TB) of the African region. In comparison to routine microscopy (i.e., multi-day sputum collection), we estimated the incremental increase in TB treatments achievable with either same-day sputum collection alone (i.e., requiring an additional visit for reporting results and initiating treatment) or same-day microscopy, in which all steps are completed in one day.

**Results:** For every 1000 individuals with active pulmonary TB, same-day sputum collection alone resulted in 4 additional treatments initiated relative to standard microscopy. By contrast, full same-day microscopy generated 66 incremental treatments. If implemented for 5 years, same-day microscopy could reduce population-level TB prevalence by 6.3% and

mortality by 6.8% through averted transmission (Figure). If scaled-up throughout the African region, these reductions translate to 94 000 TB cases averted and 17 000 lives saved every year, suggesting that same-day microscopy could avert over 20% as many disability-adjusted life years (DALYs) as the entire existing delivery of antiretroviral therapy in the African region.



**Figure** Effect of same-day diagnosis and treatment initiation for smear-positive TB on incidence rates in Africa.

**Conclusion:** Same-day microscopy can avert substantial morbidity and mortality, with no requirement for expensive drugs or technology. Developing systems for same-day diagnosis of smear-positive TB, including reporting results and initiating treatment, should be an urgent priority for TB control in Africa.

### PC-629-15 Application du traitement supervisé de la tuberculose et attentes des patients dans le contexte des grandes villes comme Bujumbura au Burundi

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**Contexte et obstacles à la mise en route :** La répartition des cas de tuberculose n'est pas uniforme au Burundi. Les grandes villes semblent très affectées et un afflux important de la population des régions du pays pourrait contribuer à gonfler le nombre de cas et rendre la prise en charge plus complexe.

**Intervention ou réponse :** Dans la ville de Bujumbura ont été choisis six centres de dépistage et de traitement (CDT) afin de recueillir des opinions sur l'application du traitement supervisé et les attentes des malades. Au total, 202 malades ont été interviewés sur 603 inscrits dans le registre au moment de l'enquête.

**Résultats et leçons tirées :** Le diagnostic a été établi à la première consultation chez 23,3% de nos malades, 2 à 4 consultations chez 48% et plus de 4 consultations chez 28,7%. Seulement 40,6% de nos malades sont facilités la prise supervisée. Pour 11,4% elle ne facilite pas et pour 48%, il faut s'adapter à contre cœur. Pour la poursuite du traitement au quotidien, le retard des infirmiers est soulevé par 60,5% des répondants. Se présenter tous les jours au CDT est une difficulté soulevée par 21,1% des malades et la perte d'emploi par 10,5%. Les longues distances à parcourir, l'absence de collaboration des prestataires de santé et la longueur du traitement ont été évoqués moins fréquemment (7,8%). Pour faciliter la prise médicamenteuse, 33,8% des malades ont proposé la provision à domicile ou l'augmentation du nombre de CDT et 25,5% ont réclamé une aide alimentaire.

**Tableau** Répartition des propositions émises par les malades pour l'amélioration du traitement directement observé dans la ville de Bujumbura au Burundi

Proposition	Effectif (n = 145) n (%)
Aide alimentaire	37 (25.5)
Provision à domicile	49 (33.8)
Donner les médicaments à temps	30 (20.7)
Améliorer la collaboration malade-agent de santé	14 (9.7)
Multiplier les séances d'éducation pour la santé	6 (4.1)
Multiplier les centres de traitement de la tuberculose	9 (6.2)

**Conclusions et recommandations-clés :** Le diagnostic et la prise en charge de la tuberculose à Bujumbura sont caractérisés par des consultations médicales multiples avant le diagnostic et des difficultés à appliquer la prise médicamenteuse supervisée. Il convient d'adapter les stratégies au contexte afin de faciliter les prises de médicaments.

#### PC-630-15 Implementation of revolving loan activity and home gardening as incentives for tuberculosis support volunteers in Lusaka, Zambia

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**Background:** Retention of health volunteers was one of challenges for TB control in resource limited settings like Zambia, however, we believe regular salary is not the only solution. Since 2008, Japan Anti-Tuberculosis Association, Zambia (JATA Zambia) has been involved in TB control activities in Lusaka under national TB control programme. We have recruited 33 health volunteers for the activities of TB case detection and directly observed treatment in an

urban community with 65 000 population. We designed one model to encourage them to continue their roles for TB control in community.

**Interventions:** Two interventions we introduced were a revolving loan activity and a home gardening. For the revolving loan, we have provided trainings and seed money, supported a loan committee, and held regular meetings for supervision. For the home gardening, we conducted baseline survey, provided training, gardening tools and close supervision.

**Results:** All of 33 volunteers have been involved in the revolving loan activities since 2009, and currently 4th cycle of loan is undergoing. A loan committee was formed among them and periodical monitoring was done to ensure the repayment. The loan helped some volunteers to obtain food or school fees for their families. Twenty-two volunteers are currently benefitting from home gardening. Various kinds of nutritious vegetables were harvested and the advice of garden management was properly given to them in case of bad weather, theft and disease. Some of them could produce enough crops not only for their own consumption but to supply and sale to neighbors. After the three years, 96.9% of total volunteers are successfully retained.

**Conclusions and key recommendations:** Incorporating the revolving loan and home gardening activities are sources of motivation for the group as it gives the members a source of income to help to sustain their households. Hence, the values of these initiatives are seen in the high retention of the volunteers.

#### PC-631-15 Reaching the targets: lessons learnt in decentralisation of tuberculosis drug resistance testing using the Xpert® MTB/RIF assay in Nyanza Province, Kenya

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**Background and challenges to implementation:** Emergence of multiple drug-resistant tuberculosis (MDR-TB) threatens to reverse gains Kenya achieved with WHO TB control targets. The national MDR-TB surveillance policy stresses TB culture and drug susceptibility testing (TBC-DST) on sputum specimens for all re-treatment and treatment failure cases which contribute about 10% of notified TB cases annually. Nyanza Province with the highest HIV-driven TB burden, registered low TBC-DST coverage of 10% in 2007, 30% in 2008 and 50% in 2009 We share lessons on decentralizing and improving MDR-TB surveillance using Xpert® MTB/RIF assay in Nyanza Intervention or response The Kenya Division of Leprosy, TB, and Lung Disease (DLTLD) and KEMRI/CDC collaborated to decentralize MDR-TB testing using

the KEMRI/CDC TB laboratory in Kisumu. Sputum specimens from all retreatment patients in Nyanza were sent to the lab for the Xpert MTB/RIF assay, then liquid culture (MGIT) and for positive specimen first line DST testing for rifampin resistance.

**Results and lessons learnt:** From January to March 2012, 338 sputum specimens were tested, 128 (37.8%) confirmed *M. tuberculosis* positive, 20 (5.9%) had rifampin resistance and 8 (2.4%) were MDR-TB by DST, 1 (0.29%) rifampin mono-resistant, and >57 (16.8%) of the 338 sputum specimens were rejected. Results were relayed through email to district TB coordinators within 2 hours after testing, and hardcopies sent to facilities under 24 hours.

**Conclusions and key recommendations:** Eight MDR-TB cases detected within the 1st quarter of implementation, demonstrates untapped potential to increase MDR-TB detection and reduce turnaround time. Targeted efforts will be directed to address challenges with rejected specimen.

#### PC-632-15 Implementation of Xpert® in Pakistan: challenges and constraints

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**Background and challenges:** MTB/RIF for detection of TB and rifampicin resistance is recommended as the initial diagnostic test in individuals suspected of having MDR-TB or HIV-associated TB and as a follow-on test to microscopy in settings where MDR-TB or HIV is of lesser concern. Climatic temperature of Pakistan is harsh and in most part remains above 40°C for more than 9 months in a year. Pakistan is facing worst power crises and stable uninterrupted power supply for two hours is unusual. Power back up are not available for laboratories.

**Intervention:** Twelve 4-module Xpert® machine were implemented in Pakistan through financial support of US Govt. Diagnostic algorithm was developed to facilitate early diagnosis of rifampicin resistance. Sites were selected to provide maximum geographical coverage and TB Care. Installation of UPS, air-conditions and refrigerator for storage of KITS was included in plan but could not be implemented. 1500 Kits were received in single shipment and were stored in central air-conditioned office. Kits were delivered based on consumptions, transportation of KITS on average required 24 hours. Bulky packing kits posed a challenge for cold chain transportation. Reporting and recording forms were developed, dedicated trained were posted, guidelines provided to doctors. Referral of patients for Xpert testing remained low due to shortages of second line drugs.

**Results and lessons learnt:** Environmental limitations (stable and regular electricity, adequate room temperature) and difficulties involved in supply and

maintenance, lack of specimen transport system and availability of second line drugs are major obstacles in widespread and optimal use of Xpert.

**Conclusions and key recommendations:** Countries to develop sound plan for roll out of Xpert to match with PMDT plan and resources to meet operational need.

#### PC-633-15 Impact of IT reporting by the tuberculosis reference laboratory on MDR-TB management in Kenya

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**Background:** Kenya ranks 15th in the 22 TB high burden countries, reporting 105 781 cases in 2010, yet has only one TB reference laboratory to perform drug resistance surveillance testing on the over 10 000 patients with a history of pretreatment. For the last 50 years the NRL has been paper based in surveillance reporting. Hard copy reporting coupled with solid media culture methods resulted in turn around times (TAT) of 15 weeks.

**Design/methods:** New diagnostic testing was introduced into the laboratory including line probe assays as well as Liquid media growth methods and most recently GENE Xpert. A laboratory information management system was also introduced to improve tracking and allow for electronic transfer of reports. Data regarding TAT was collected every 3 months in 2010 and 2011. Comparisons were made between before and after the intervention of installing laboratory information management systems.

**Results:** Out of the twelve TB regions, 83% acknowledged shortening of the TAT for drug susceptibility tests; multidrug resistance in smear positives patients now occurs in 2 days. Culture negatives are reported in 21 days. The LIMS system has prevented missing patient records and reduced inaccurate results due to clerical errors. Infectious diseases physicians, infection control professionals, and microbiology laboratories have embraced electronic laboratory reporting using LIMS for appropriate public health interventions.

**Conclusion and recommendations:** The combination of the adoption of new diagnostics into the laboratory algorithm coupled with institution of LIMS markedly reduces TAT for TB laboratory services. Additional benefits include reduction of missing laboratory results. Improvement of laboratory infrastructure is critical to decreased laboratory TAT and institution of appropriate care.

## IMPROVING TUBERCULOSIS SURVEILLANCE IN CHILDREN

### PC-660-15 Screening for tuberculosis and HIV among children failing to thrive in Botswana

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**Background:** Failure to thrive (FTT) is a well-recognised feature of tuberculosis (TB) disease and human immunodeficiency virus (HIV) in children. In Botswana, despite high rates of TB and HIV, little is known about rates of TB and HIV in children presenting with FTT. We assessed the prevalence of TB and HIV in children with FTT encountered at one urban clinic in Botswana.

**Methods:** For one month in July 2010, we screened all children who attended a weighing clinic in Francistown, Botswana, for FTT. FTT was defined as no weight gain or weight loss over the previous 3 months, <-3 standard deviation (SD) weight-for-age, or moderate or severe acute malnutrition as per World Health Organization criteria. All children diagnosed with FTT were referred to a paediatrician who: (1) assessed causes of FTT; (2) evaluated for HIV and TB; and (3) reviewed the patient chart for prior evaluation for TB and HIV. TB evaluation included all of the following: a review of clinical symptoms, CXR findings, Mantoux testing, TB exposure and TB cultures.

**Results:** Of 919 children (53% female), screened, 19% ( $n = 176$ ) met criteria for FTT. The median age was 22 months (range of 0–64 months). Of those with FTT, 67% (118/176) presented to the paediatrician for review. TB was diagnosed in 6/118 (5%) of children. Of these, 3/6 (50%) had been evaluated for TB previously but none had been diagnosed with or treated for TB. Following paediatric review and 6 months of TB treatment, all 6 had resolution of symptoms and weight gain of more than 10%. Clinical screening excluded TB as a cause of FTT in 89/118 (75%) children, whereas 23/118 (20%) were lost to follow-up before an evaluation was completed. For HIV, 20% (23/118) of children with FTT had been tested for HIV prior to review by the paediatrician (3 HIV+, 20 HIV-). Of the 95 children with FTT and unknown HIV status, 50 (53%) were lost to follow-up. Of the remaining 45 (47%) tested, all tested HIV negative.

**Conclusion:** The yield of screening for TB and HIV in children with FTT in this high burden TB-HIV setting revealed newly diagnosed TB in 5% of cases but

no new HIV infections. Challenges included multiple visits required to diagnose TB, review HIV test results and a high lost to follow up rate.

### PC-661-15 Childhood tuberculosis at the main referral hospital in Lusaka, Zambia: a five-year review of registered child tuberculosis cases

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**Aim:** The burden of childhood TB in sub-Saharan African countries with high HIV infections rates is high. We aimed to determine the burden of TB in children as diagnosed and registered at the main referral hospital in Lusaka, Zambia over a five year period.

**Methods:** We retrospectively collected data on children diagnosed and registered with TB from 2007 to 2011 at the University Teaching Hospital, Lusaka. The main outcomes were annual TB notifications, age distribution, form of TB, and HIV co-infection rate. National TB program definition (Adapted from WHO) were used.

**Results:** In all, 2560 cases were registered, 1340 (52.3%) of whom were boys. The median age was 2 years (range: 1–7 years) and 1606 (62.7%) were under five years of age. On average, 512 ( $\pm 68$ ) cases were registered per year. The majority (99.2%) were new cases. Residents of low income/high density communities accounted for 1821 (71.1%) of the cases. The notifications rates declined after the 1st year (2007) remained stable over the next 3 years (2008–10) and then gradually increased in the fifth year of the review. There was no effect noted in the trends across gender, age and the types of TB reported. Pulmonary TB (PTB) accounted for 75.5 percent ( $n = 1931$ ) of the cases. Only 341 children had a documented smear result, 65 (19.1%) of whom were positive. Lymphadenitis and meningitis were the most commonly observed forms of extra-pulmonary TB (EPTB) accounting for 61.0% of the 234 cases with a documented site of the disease. Of the 2425 (94.7%) tested for HIV, 51.6% ( $n = 1251$ ) were positive. PTB was comparatively more commonly observed than EPTB ( $P < 0.001$ ) among HIV seropositive children. There were no differences in HIV co-infection rates between age groups ( $P = 0.83$ ) and gender ( $P = 0.41$ ). There were no significant changes in TB-HIV co-infection rates over the five year period.

**Conclusion:** The burden of TB and TB-HIV co-infection is high and has not significantly changed over the last five years. Infants and younger children

are predominantly affected reflecting the need for preventive treatment of household TB contacts. Further research is needed to determine the epidemiological profile of child TB country-wide in Zambia.

### PC-662-15 Management of paediatric tuberculosis in provincial and district hospitals of Afghanistan

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**Aim:** Childhood tuberculosis (TB) has low priority due to difficulties in diagnosis, lack of diagnostic tools and data on TB case management.

**Objective:** To evaluate the pediatric TB case management at those health facilities where all diagnostic processing are available.

**Methodology:** Conducting a retrospective observational study with 100% sampling from December 2010 till May 2011 at 8 provincial and 15 district hospitals of Afghanistan. Reviewing all data on TB management of children aged <15 years.

**Result:** The study found that 70% TB suspects referred to DOTs from Out Patients Departments (OPDs). TB suspected rate was 0.4% among OPD attendees; 5.8% were AFB positive. 14% of positive results were missed. Extrapulmonary TB formed 22.6% of all cases; of which respectively 36.1% lymphadenitis and 32.4% intestinal TB. 5.9% TB meningitis and 2.7% miliary TB. 19.2% BCG scar have been recorded. Successful TB treatment rate was 95%. Of 971 TB children under treatment 2.8% type of TB was unknown. Of 1039 pulmonary TB cases 760 children contacts were registered. 75.4% of children contacts >5 years old received INH prophylaxis. 26% of hospitals did not record TB contacts.

**Conclusion and recommendations:** This study suggests increased attention within hospitals on referring suspects and follow up of SS+ result. In addition screening of all child contacts should be implemented properly with consideration to recording system.

### PC-663-15 Integrating tuberculosis screening, diagnosis and treatment with HIV testing and counselling, and behavioral interventions: the Operation ARIFU experience

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**Background and challenges to implementation:** In 2011 the National Youth Service (NYS) College in Gilgil, a rural district in Kenya, recruited youth between ages 18 and 24. Evaluation for medical and physical fitness is a pre-requisite to the college admis-

sion but this does not routinely include HIV testing and comprehensive tuberculosis (TB) screening, only relying on radiology. These young people live in congregate settings, presenting a significant risk of TB infection.

**Intervention or response:** Operation-ARIFU implemented a comprehensive TB and HIV approach between April 11th and May 6th, 2011, in order to identify persons who would benefit from early treatment for TB and/or HIV. All the recruits, staff and members of the surrounding community received a rapid combination prevention education intervention on HIV and TB conducted in modular sessions of 30–35 persons daily. HIV counseling and testing services were offered voluntarily to those that consented. Those found HIV positive were referred for appropriate HIV care in the neighbouring district hospital. Further, all those found HIV positive, persons with ill-health, and contacts of TB patients were offered TB screening using a standardized symptom questionnaire; followed by appropriate referral for clinical tests and confirmation of TB diagnosis.

**Results and lessons learnt:** Nearly all consented to HIV counseling and all that were counseled consented to HIV testing. All clinical evaluations were negative for TB. Further, evaluation by radiography was done and those confirmed to have TB were started on treatment based on the standard protocol. This was the beginning of a TB treatment centre in this facility and they continue treating TB patients to date.

**Conclusions and key recommendations:** Integrating TB screening into HIV testing and behavioral interventions outreaches provides a comprehensive assessment and opportunity to diagnose and treat TB and HIV infections early.

### PC-664-15 How child-friendly is the Nigerian Tuberculosis Control Programme? Review of 12-year data

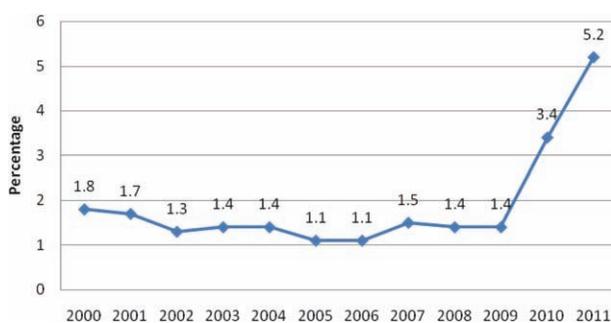
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**Background:** Infants and young children constitute a high risk group for TB infection, disease and death. It is estimated that TB in children accounts for a third of all TB cases. Despite this compelling statistic, many national TB control programmes appear not to pay sufficient attention to this problem.

**Objective:** To assess the level and trend of notification of childhood TB in southern Nigeria from 2000 to 2011.

**Methods:** This is a retrospective descriptive desk analysis of TB case notification data for all age groups (2000–2011) from 14 states in southern Nigeria supported by German Leprosy and TB Relief Association.

**Result/discussion:** (See Figure.) Proportion of children among all notified TB cases varies between and within countries. The median percentage of TB in children in this study is 1.4%. This is lower than observed in Thailand (2%), South Africa (39% and 21%), and 13% in Tanzania. The low notification rate in this study may not be unconnected with low index of suspicion among health staff and lack of focus on childhood TB by the National TB Programme (NTP). The NTP reserves diagnosis of TB for medical doctors who are often not available in rural areas/urban slums.



**Figure** Percentage childhood TB (0–14) among all cases notified in southern Nigeria, 2000–2012.

**Conclusion/recommendation:** The Nigerian TB control programme is grossly under-diagnosing TB in children. Orientation of doctors in secondary/tertiary health facilities on use of the score chart for diagnosis of childhood TB and task-shifting to nurses in primary health care facilities.

### PC-665-15 Childhood tuberculosis: trends, HIV prevalence and treatment outcomes in Tanzania

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**Background and challenges to implementation:** Tanzania ranks 18th among tuberculosis high-burden countries and is among the countries with generalized HIV/AIDS epidemic. Collaborative TB-HIV interventions have been implemented countrywide since 2006. We analyzed data of childhood TB for the period between 2007 and 2010 across 4 mainland regions of Tanzania to identify the burden, trends and outcomes of childhood TB and TB-HIV co-infection.

**Intervention:** Retrospective data from TB clinics were analyzed across 4 regions from 2007 to 2010.

**Results and lessons learnt:** A total of 2990 children below 15 years were analyzed; 51% smear negative, 34% extra pulmonary and 15% smear positive. A

continuous increase in pediatric enrollment has been observed with 22% of the assessed children enrolled in 2007, 23% in 2008, 26% in 2009 and 29% in 2010. HIV testing among children increased from 80% in 2007 to 97.5% in 2010. The HIV prevalence among enrolled children increased from 101 cases (31.7%) in 2007 to 223 cases (37.2%) in 2009. Generally, 33% of pediatric TB patients were found to be HIV positive, whereby age group of 7–9 had the highest HIV prevalence (38%) while the youngest age 1–3 years had the lowest prevalence of 29%. Among the HIV-positive children 74% had pulmonary TB and 26% had extra-pulmonary TB. Among smear positives, 82.5% completed TB treatment, 10.3% were cured, 4.8% died, 1.3% defaulted. There was high percentage of deaths among HIV positive patients (7%) as compared to the HIV negative patients (3.3%).

**Conclusions and key recommendations:** Our data suggest a continuous increase in notification of childhood TB, with greater risk of death among HIV co-infected children. Comprehensive interventions for prevention and management of childhood TB should be a priority for NTPs. Further studies to determine the annual risk of TB infection (ARTI) in young children and incidence and burden of childhood TB in different communities should be conducted.

### PC-666-15 Finding the vulnerable: is tuberculosis intensified case finding feasible for street children and youth in Kenya?

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**Background:** In Eldoret, Kenya, there are thought to be >1000 street children/youth (SC/Y). SC/Y are a vulnerable population with health problems including HIV/AIDS, tuberculosis (TB), and other respiratory conditions, but have minimal access to health-care. Minimal data exists on the rate of tuberculosis in this subpopulation, and TB screening among SC/Y is challenging and rarely performed. For 7 years, the Academic Model Providing Access to Healthcare (AMPATH) TB Projects office at the Moi Teaching and Referral Hospital has conducted intensified TB case finding using a cough monitor (CM) questionnaire model. The Tumaini Children's Drop-In Center (TCDIC) has become a trusted organization for SC/Y

and provides food, education, and basic healthcare services.

**Intervention:** AMPATH TB Projects office partnered with the TCDIC. A CM (lay individual trained in TB sensitization and symptom screening) was assigned to the center. The CM conducted two types of screening—at the center and in the street. The sensitization talk was adapted for this younger population. The CM was instructed to screen every willing SC/Y with a six-item validated case-finding questionnaire. Spot sputum samples (S1) were collected for SC/Y with a positive questionnaire. A second spot specimen (S2) was collected when possible.

**Results:** Three center screenings and four in the street screenings were conducted in an eight-month period. Seventy-nine individuals (72 males, 7 females) ages 10–30 (median age 17) were screened. Seventy-six (96%) had positive symptom screens. Seventy-two (91%) reported history of cough. There were 68 and 34 individuals who provided S1 and S2, respectively. One smear positive TB case was identified.

**Conclusions:** These data suggest that TB screening in SC/Y is feasible. A high incidence of symptoms (cough primarily) is present in this group subpopulation, potentially reducing the effectiveness of case-finding questionnaires and suggesting a need for access to primary healthcare services.

#### PC-667-15 Annual risk of tuberculous infection in Jhuggi-Jhopri colonies and slum areas in an urban setting

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**Background:** To ascertain the annual risk of tuberculous infection (ARTI) in marginalized population living in jhuggi-jhopri (JJ) and slum areas in the southern part of Delhi and comparing it with the ARTI of general population in the city.

**Design:** A community based tuberculin survey was conducted amongst children age 1–9 years residing in urban jhuggi-jhopri and slum areas in 1.5 million population of South Delhi. The 29 such colonies were listed randomly and the children were tested following this random list till the sample size of 5300 was completed. All children with or without BCG scar were tuberculin tested as earlier studies had shown that BCG did not influence the estimation of point prevalence of infection. 2 TU PPD RT 23 with Tween 80 was used for tuberculin testing and induration was measured after 72 hours.

**Results:** A total of 5767 households were visited to register the required number of children in 12 JJ colonies. Of the 6304 children tested, 5575 were satisfactory test-read (88.4%). BCG scar was observed in 40% of the test-read. Frequency distribution of the tuberculin reaction size in the overall study popula-

tion showed a clear cut anti mode at 7 mm and a mode at 12 mm. The prevalence of infection for the entire study group was estimated at 14.6% by the anti mode method and 16.6% by the mode method, giving a computed ARTI of 2.6% and 3.0% respectively. This was against the prevalence of infection of 5.9% and ARTI of 1.1% amongst the children 1–9 years in rest of Delhi as ascertained from the nationwide zonal survey 2008–2011.

**Conclusions and recommendations:** The prevalence and infection amongst the JJ colony and slum population was much more than the general community. Targeted interventions would be required in this marginalized population to prevent HOT SPOTS of TB infection and disease which may otherwise threaten the TB Control efforts of the country.

#### PC-668-15 Drug-resistant tuberculosis strains in HIV-infected and non-infected young children in India

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**Background:** India has among the world's highest burden of tuberculosis (TB). Diagnosis of TB is particularly challenging in young children in India—a vulnerable population, where lack of early detection/prevention of TB often have fatal consequences.

**Design/methods:** Children  $\leq$  5 years old with suspected TB were prospectively enrolled at Byramjee Jeejeebhoy Medical College (BJMC), Pune, India, from August 2010 to September 2011 and were followed for at least 6 months after enrollment. All children had detailed clinical evaluation, nutritional assessment (WAZ scores, WHO Anthro; reference India) HIV testing (ELISA or PCR if  $<$ 18 months old), mycobacterial cultures and drug-susceptibilities for isoniazid and rifampin. Children were classified into confirmed TB (culture-positive), probable TB (strict clinical definition), and no TB (TB reasonably ruled out). Children with confirmed and probable TB were grouped together for analyses.

**Results:** Median age of the enrolled patients ( $n = 175$ ) was 32 months (IQR 17 to 45 months). 96 (55%) were male, and 146 (84%) were found to have a BCG scar. Most children were malnourished and the median WAZ score was  $-2.2$  (IQR  $-3.3$  to  $-1.2$ ). HIV results were available for 172 patients and 14 (8%) were found to be HIV-positive. Seven (4%) children had confirmed TB, 67 (38%) had probable TB, 88 (50%) did not have TB, while 13 (7%) could not be classified appropriately. There were no significant differences between the age, sex, nutritional status and presence of BCG scar for children

with and without TB ( $P > 0.15$ ). Of children diagnosed with TB, 16 (22%) had extra-pulmonary disease, which was primarily central nervous system (CNS) TB ( $n = 10$ ). There were no significant differences between the age, sex, nutritional status and presence of BCG scar for children diagnosed with TB with or without HIV-co-infection ( $P > 0.20$ ). However, HIV-co-infected children were more likely to present with hepatosplenomegaly ( $P < 0.0001$ ). Of 7 children with culture-confirmed TB, 4 (57%) harbored drug-resistant (DR) strains of which 2 (50%) were multi-DR (MDR). Mortality by 6-months post entry for children diagnosed with TB was 5% (4 of 74), and 25% (1 of 4) among DR TB cases.

**Conclusions:** Diagnosis of TB is particularly challenging in young children in India, with high rates of extra-pulmonary and CNS TB. Though drug-susceptibilities could be performed only in a small proportion of patients, there is a high incidence of drug-resistant strains in this population.

#### PC-669-15 Improving access for diagnosis and treatment of childhood tuberculosis in Bangladesh

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**Background and challenges to implementation:** The access of child TB patients is limited to NTP services and also accurate disease burden among children is unknown. National Tuberculosis Control Programme (NTP) of Bangladesh intensified its efforts in early diagnosis and treatment of child TB cases in collaboration with NGO partners and professionals.

**Objective:** To explore progress in diagnosis and management of child TB under NTP services in Bangladesh.

**Intervention or response:** Simple symptom-based approach for diagnosis and treatment of child TB is recommended by NTP. The program involves specialized health institutions, hospitals and private practitioners specially the pediatricians in TB care. Six months isoniazid (INH) preventive chemotherapy is recommended for 5 yrs age, those who are in household contact with sputum smear positive index case.

**Results and lessons learnt:** In 2011, a total of 155 564 TB cases were identified under NTP. Of them, 4667 (3.15% of total cases) were child TB. Child TB diagnosis through NTP slightly increased from 2010 (4235 child TB cases which is 2.75% of total cases). Of the 4667 child TB cases diagnosed in 2011, 932 (20%) were new smear positive, and 3735 (80%) were smear negative and extra pulmonary. Of the smear positive child TB cases, 309 (7%) male and 623 (13%) female. While among the smear negative and extra pulmonary cases, 1904 (41%) were male and 1831 (39%) were female.

**Conclusions and key recommendations:** Accurate diagnosis of childhood TB still remains a major challenge. Strengthening of diagnostic facility, provision of preventive chemotherapy and involvement of pediatricians at different levels may increase the access of child TB diagnosis and management.

#### PC-670-15 Child and adolescent DR-TB case notification following a phased implementation of a paediatric tuberculosis project in Tajikistan

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**Background:** Tajikistan has the highest TB incidence in the WHO European region with 206 new cases per 100 000 population. Diagnosis of TB in children is mostly based on clinical and radiographic findings. An adult drug resistant TB (DR-TB) programme was started in 2009 but no children had been included before Médecins Sans Frontières opened a project to support the Ministry of Health in the diagnosis and treatment of DR-TB in children and adolescents. In this descriptive study we aim to share the early outcomes and lessons learned during phased implementation of the DR-TB project in Dushanbe, Tajikistan.

**Design/methods:** The initial phase of implementation involved clinical support and second-line TB drugs while using international paediatric DR-TB guidance. In the 2nd phase Tajikistan-specific paediatric DR-TB guidelines were implemented. The next phases will involve improved biological diagnosis with induced sputum and Xpert MTB/RIF followed by training staff across Tajikistan in paediatric DR-TB. We identified all patients < 20 years old registered in Dushanbe between October 2011 and April 2012; files of treatment failures or DR-TB adult contacts were reviewed. We determined the number of children and adolescents who started DR-TB treatment and the time from suspicion of TB to treatment commencement.

**Results:** By April 2012, phases 1 and 2 had been implemented. Nine patients were diagnosed and started DR-TB treatment. Median diagnostic delay was 106 days (range 7–206). Challenges included lack of adapted formulations of second-line drugs, no international guidance on their use in children and lack of adolescent dosage tables.

**Conclusion and recommendations:** Implementation of a child and adolescent focused project, even in its early stages, initiated paediatric DR-TB case notifications. International guidance on paediatric DR-TB diagnosis and treatment should be routinely included in national DR-TB guidelines to ensure that children are not neglected in the response to DR-TB.

### PC-671-15 Rising burden of tuberculosis in children in the African region

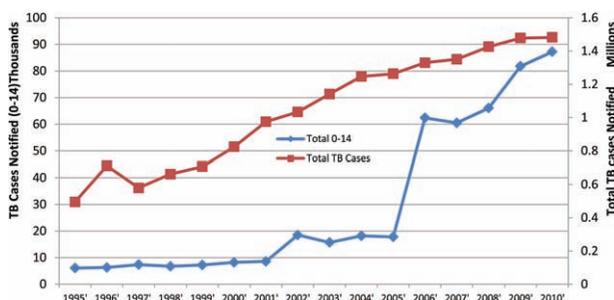
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**Background:** TB among children, is a top 10 cause of mortality. However children with TB are given low priority in most national health programs and thus are neglected group in this epidemic. This is because from a tuberculosis control point of view, they rarely transmit the disease and are perceived to contribute little to the maintenance of the tuberculosis epidemic.

**Objective:** To describe the trends of burden of TB in children (0–14) years notified in the African region.

**Methodology:** We review the notifications data for TB in children (0–14) who were notified between the years (1995–2010) in the African Region.

**Results:** African Region notified a total of 1 478 356 (24% of global notifications) in the year 2010 (Global TB Report 2011). The number of children notified in 2010 was 87 187 representing 6% of the TB case load in the region. It is evident that the TB epidemic seems to have stabilized in the African Region but the number of cases in children is still increasing. There is a 6 fold increase in children compared to 50% in adults between 2001 and 2010. The male:female proportions are the same in children and adults.



**Figure** Trend of TB cases notified and paediatric in the African Region.

**Conclusion:** While TB is stabilizing in Adults, it is on the rise in children in the African Region. The increase in children corresponds to increased disease in young adults 15–25 yrs.

**Recommendations:** Intensify contact tracing and INH prophylaxis in the 0–14 yr contacts of young adults. Strengthen pediatric TB care in national programmes.

### TOBACCO BURDEN AND SURVEILLANCE

#### PC-696-15 Comparison of cigarette and waterpipe smoking among pupils in the urban area of Sousse, Tunisia

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**Background:** Epidemiological and observational evidence suggests that waterpipe use is growing in popularity worldwide. The purpose of this study was to examine the prevalence of cigarette and waterpipe tobacco use among pupils aged 13–17 years in the urban area of Sousse, Tunisia, and to identify the factors which predict current cigarette and/or waterpipe smoking in this population.

**Design/methods:** A cross-sectional study was carried out on a representative sample of schoolchildren aged between 13 and 17 years in colleges and public secondary schools of the urban area of Sousse. Participants were recruited in randomly selected cluster samples. First cluster was constituted by the randomly selected classes within these establishments. The sample size should permit to estimate the prevalence of tobacco use with a precision of  $\pm 2.5\%$  and a confidence level of 95%, the needed sample size was 1600. We used a pre-tested and self-administered questionnaire to measure tobacco consumption. The significance level for all analyses was  $P < 0.05$ . Statistical analysis was conducted with SPSS 10.0 software. Appropriate ethical protocols were followed. Authorization was sought and obtained from the Ministry of Education and from the participants' schools, teachers and parents for their participation.

**Results:** Participants were 1569 youth. Fifty-two percent of them were male. The mean age of the sample was  $15 \pm 1.5$  years. Total cigarette smoking percentage for ever and current use were 33.1% and 7.6% respectively. Total waterpipe smoking percentage for ever and current use were 19.3% and 5.2% respectively. Overall, the total percentages of cigarette and waterpipe smoking (ever and current) were higher for male and aged pupils. In multivariate analysis, the odds of current cigarette smokers were higher among waterpipe smokers (OR = 7.39, IC [3.39–16.11]), males compared with females (OR = 2.71, IC [1.13–6.48]) and who ever consume alcoholic drinks (OR = 1.3, IC [1.16–1.46]).

**Conclusion and recommendations:** Despite the growing adoption of waterpipe smoking, there remains limited research in this area. Increased surveillance and additional research are necessary to address this growing threat to public health.

### PC-697-15 Relationship between cigarette smoking and latent tuberculosis infection among the US population, National Health and Nutrition Examination Survey

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**Background:** Cigarette smoking has been implicated as a risk factor for tuberculosis (TB) disease and TB-related mortality; however, fewer studies have examined the relationship between cigarette smoking and TB infection. We examined the relationship between cigarette smoking and latent TB infection (LTBI) among a representative sample of the civilian non-institutionalized US population.

**Methods:** Using 1999–2000 National Health and Nutrition Examination Survey (NHANES) data, participants aged  $\geq 20$  years were classified as having LTBI if they had a tuberculin skin test (TST) measurement of  $\geq 10$  mm. Smoking status was categorized into never/former/current cigarette smokers based on self-report and serum cotinine levels ( $\geq 10$  ng/ml for current smokers). Logistic regression was used to assess the odds of cigarette smokers having LTBI, adjusted for age, sex, race-ethnicity, country of birth, education, family poverty income ratio, household size, body mass index, history of diabetes, bacillus Calmette-Guerin (BCG) vaccination, and history of living in household with known TB disease.

**Results:** Of 4880 survey participants with TST measurements, 339 (5.3%) had LTBI, 1194 (33.7%) were current smokers and 963 (20.4%) were former smokers. LTBI was associated with current smoking (adjusted odd ratio [aOR] 2.1; 95% confidence interval [CI] 1.1–3.9), but not former smoking (aOR 1.6; 95%CI 0.7–3.6). LTBI was also associated with male sex (aOR 1.8; 95%CI 1.2–2.8), age  $\geq 50$  years (50–64 years aOR 2.4; 95%CI 1.3–4.3 and  $\geq 65$  years aOR 3.0; 95%CI 1.2–7.4), non-Hispanic black race (aOR 4.7; 95%CI 2.5–8.8), foreign-birth (aOR 7.3; 95%CI 4.3–12.4), larger household size (aOR 2.0; 95%CI 1.1–3.7), and residing in a household with a TB patient (aOR 4.2; 95%CI 2.0–8.9).

**Conclusion:** In this population-based sample, current cigarette smoking was associated with LTBI. Our findings suggest that tobacco control efforts could contribute to TB elimination strategies in the USA.

### PC-698-15 Socio-demographic determinants of smoking among women in Romania: implications for public health

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**Background:** After the change in the political regime in 1989, the consumption of tobacco in Romania increased dramatically. Although the rate for women smoking increased more, the tobacco control has not comprehensively addressed them.

**Aim:** To explore the profile of Romanian women who smoke for designing tailored tobacco control interventions.

**Design/methods:** This study is based on data gathered for GATS Romania 2011, a nationally representative household survey of persons 15 years of age or older. 2447 women have been interviewed. Complex data analysis was performed to obtain population estimates and their 95% confidence intervals. All the statistical analysis including sample weighting and computations of estimates and their confidence intervals were performed using the complex sample module of a statistical package, SPSS 17.

**Results:** In Romania women from urban area (20.1%) had a significantly higher prevalence of current smoking than their rural counterparts (12.2%) and those aged 25–44 years old smoked the most. The prevalence rate of current smoking was highest among those with secondary and high education (19.6% and 20.0%, respectively) and lowest among those with primary education or less (14.7%) but the proportion of ‘heavy smokers’ was largest among those less educated (46.8%). Of those who attempted to quit only 8.2% used nicotine replacement therapy and 1.2% prescription medication.

**Conclusion and recommendations:** The study showed that in Romania the prevalence of smoking is higher among women with secondary and high educational level from urban area. Still, the largest proportion of heavy smokers is noted in less educated women. Despite the high percentage of nicotine addicted women, pharmacological methods for cessation were used only in a very small proportion. These findings offer support to tailor tobacco control interventions and health education approach in Romania to specifically address women based on evidence.

### PC-699-15 The prevalence of smoking among type I and type II diabetic patients in the State of Penang, Malaysia

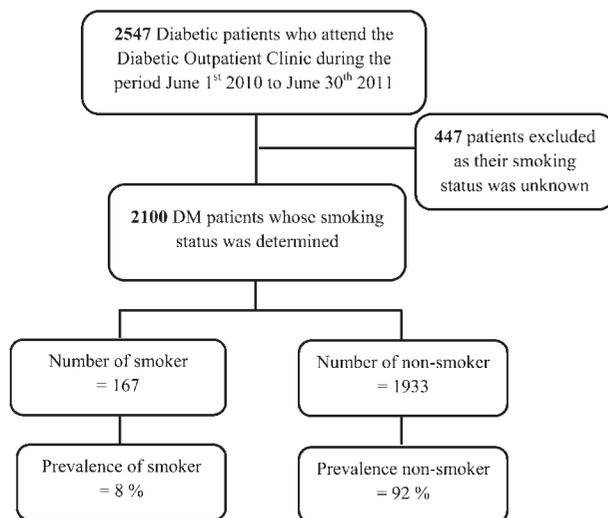
A Blebil,<sup>1</sup> S A S Sulaiman,<sup>1</sup> A Hassali,<sup>2</sup> J Dujaili,<sup>1</sup> K Subramaniam.<sup>3</sup> <sup>1</sup>Discipline of Clinical Pharmacy, School of Pharmaceutical Sciences, USM, Minden, <sup>2</sup>Discipline of Social and Administrative Pharmacy, School of Pharmaceutical Sciences, USM, Minden, <sup>3</sup>Department of Outpatient Clinic, Penang General Hospital, Jalan Residensi, Malaysia. e-mail: aliblebil@yahoo.com

**Background and objectives:** There is a dearth of information about the prevalence of smoking in patients who are at great risk of the complications due to smoking habit including diabetic patients. The current study aimed to determine the prevalence of

smoking among type I and type II diabetes mellitus (DM) patients who attended a diabetic outpatient clinic at tertiary Public hospital in the state of Penang, Malaysia.

**Design/methods:** A cross-sectional study was conducted to assess the smoking status of diabetic patients who attend Diabetic Outpatient Clinic between June 1st 2010 and June 30th 2011. The data were extracted from the patient's medical record in Penang General Hospital of Penang State, Malaysia.

**Results:** Between June 1st 2010 and June 30th 2011, 2547 type I and type II diabetic patients were registered for DM treatment. Of these, 447 (17.6%) subjects were excluded from analysis as their smoking status was unknown. The prevalence of smoking in 2100 diabetic patients whose smoking status was determined was 8%. Smoking was significantly associated with male gender ( $P = 0.007$ ) and younger age ( $P < 0.001$ ). Chinese patients were the most prevalent race among diabetic smokers compared with Malay and Indian (50.3% vs. 30.5% vs. 19.2%, respectively); however, the results were statistically not significant. Furthermore; diabetic smokers had significantly shorter duration of DM since diagnosis.



**Figure** Prevalence of smoking among DM patients in Penang, Malaysia.

**Conclusion and recommendations:** The prevalence of smoking among diabetic patients in Malaysia was low and did not reflect the prevalence in general population. On the other side, smoking status was inadequately documented and no information was available about the history of tobacco use in diabetic smokers. Smoking status should be evaluated as a routine care practice and advise those who are smoker to quit smoking and refer them for smoking cessation program.

### PC-700-15 Tobacco use and economic cost of treatment of cancer in Nigeria: a five-year study

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**Background and challenges to implementation:** As these medical evidences of the dangers of tobacco use continue to accumulate, the tobacco industry has shifted its position which was hitherto defensive to one based largely on economic arguments. Tobacco consumption as evidence proved entails a cacophony of adverse and often deadly effects on the smoker and also every fiber of the economy.

**Intervention or response:** The aim of this study was to analysis the economics of tobacco policy and critically evaluates the cost of treatment of tobacco related diseases in Nigeria, such as cancers, heart disease etc., a 5 years study. The prevalence-based attributable-risk approach is used to estimate economic cost using health care expenditure data from the State Sample Survey, a nationally representative household sample survey conducted.

**Results and lessons learnt:** A multistage stratified proportionate to size sampling technique was used to select the sample. The entire list of cases reported in a survey from 11 government owned hospitals in Lagos State reveals that at least two persons die every day from a tobacco related disease. To that end the state averred that it spent N222 000 subsidizing the cost of treatment of each tobacco related case. The study shown Nigeria spent N105, 339 000 000 on smoking-related illness for one year. Compare the N50billion paid by BATN as taxes for the period of five years.

**Conclusions and key recommendations:** This has generated various cost recovery and criminal suits against the industry by at least 10 state governments including the Federal Government in 2007.

### PC-701-15 Patterns of cigarette smoking, perception and media influence among medical students in a public university in Malaysia

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**Background:** Young medical students hold two important points in our system, as young adults as well as future healthcare professionals. Emphasizing on smooth transition from community to healthcare provision sector, we assess the patterns of cigarette smoking, perception and media influence among medical students in a public university in Malaysia.

**Design/methods:** Validated questionnaires adopted from the Global Youth Tobacco Survey were administered to all undergraduate medical students at three

branches of a medical faculty in a public university in Malaysia. Analyses and data entry were performed by using SPSS version 18.

**Results:** There were 875 medical students in the university. 522 (60%) responded and 23 students (4.4%) indicated they currently smoke tobacco at time of study. Out of those who smoke, 73.9% were male, 78% were in clinical years of study, 82.6% smoked at a younger age and had tried other types of tobacco products (21.7%) ( $P < 0.05$ ). 43.5% will smoke when offered by friends and will continue to smoke within a year (56.5%) but not in five years (69.6%) time ( $P < 0.001$ ). Out of total respondents, 18% had tried smoking and 3% had tried other methods of tobacco. Majority respondents (96%) agreed they will never attempt to smoke cigarettes even if offered by friends, within one year or five years time. They also agreed smoking gives bad impact on health and environment. Furthermore, smokers believed smoking reduces weight and make them more attractive despite knowing that it would lead to substantial health effects on diseases such as cancer, heart and lung disease, low birth weight and congenital anomaly ( $P < 0.05$ ). No associations between factors such as having knowledge about smoking rules in the campus, history of parents who smoke and family discussions on health hazards of smoking. Being a smoker, there was also no significant difference in the number and circle of friends compared to a non smoker. In regards to media influence and tobacco control efforts, 56.5% of smokers believed that antismoking messages through radio is more effective than printed materials, billboards, television and internet, but makes no difference in preventing or stopping smoking habit. Majority of students (96%) concurred an outlaw of sales and consumption of cigarette should be conducted, cigarette selling price should be increased, smoking in public places and work places should be prohibited and anti-smoking campaign should be organized. These perceptions were greater than the smokers ( $P < 0.001$ ). In addition, incentives by tobacco company and age limit for cigarette purchase were comprehended beneficial by both groups ( $P > 0.05$ ).

**Conclusion and recommendations:** Majority of medical students has positive attitudes and behavior against tobacco use and was supportive of the current tobacco control efforts. Nonetheless, this study highlights despite the low prevalence of smoking among medical students, false perceptions existed among them and the perceptions differ between smokers and non smokers. Media messages and anti-tobacco efforts should not only concentrate on preventing uptake of cigarette among non smokers, but should put a greater emphasis on changing the perception of smokers in tobacco related beliefs and quitting. An integrated teaching syllabus focusing on smoking under health promotion module is

highly recommended and should be incorporated earlier in medical undergraduate teaching program in Malaysia.

### PC-702-15 Public opinion poll about smoking and smoke-free legislation in a district of North India

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**Background:** A growing number of cities and counties across the globe are going smoke free. While an Indian national law namely Control of Tobacco Products Act exists since 2005 which aims at protecting all the people in our country; people still smoke in public places.

**Aims:** This study identified perception about smoking and in turn about COTPA among people residing in a district of India.

**Methods and material:** This cross-sectional study was conducted in Mohali District of Punjab, India. A sample size of 1600 people was obtained. Probability Proportional to Size technique was used for selecting the number of individuals to be interviewed from each block and also from urban and rural population.

**Statistical analysis used:** Data were coded, entered and analyzed using the Statistical Package for Social Sciences (SPSS), version 20.

**Results:** 25.4% were current smokers. Knowledge regarding harmful effects of smoking was very high. Most (84%) of the study participants were aware that smoking is banned in public places. However, very few knew about the enforcement agency (19%). More than three fourth participants perceived that effective COTPA implementation will save lives. They were quite supportive of the act.

**Conclusions and recommendations:** There was high knowledge about deleterious multi dimensional effects of smoking among residents and a high support for implementation of COTPA. Efforts should be made to make Mohali a 'smoke free district'. Such opinion poll should be conducted in different States of India to understand their perceptions about smoking and its related law. This will help in effective implementation of tobacco control law and shaping of public policies related to the act.

### PC-703-15 Behaviour, knowledge and attitudes of Iranian professional athletes towards smoking

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**Background:** This study aimed to assess the rate of tobacco consumption among professional athletes in Iran and assessing their knowledge and attitude in this regard.

**Materials and methods:** A total of 738 athletes from 10 different types of sports were evaluated. Athletes were all members of the priority leagues. After obtaining consent from the Physical Education Organization and coordination with the related federations, athletes were asked to fill out the standard questionnaire.

**Results:** All understudy subjects were males. The mean age was  $28.4 \pm 2.7$  yrs. A total of 46.7% had high school diploma. In general, 293 subjects (39.7%) were playing individual and 445 (60.3%) were playing team sports. The mean age of initiation of sport in these subjects was reported to be  $12.3 \pm 4.01$  yrs. A total of 178 (24.6%) subjects had experienced cigarette smoking and 308 (42.3%) had experienced hookah smoking. Sixty four subjects (9%) were current smokers (34 (59.6%) daily smokers, 20 (35.1%) occasional smokers). Twenty one cases (44.7%) were smoking less than 10 cigarettes a day. A total of 26 (66.7%) current smokers stated that smoking helps them in sport competitions. A total of 40 sportsmen from individual sports were current smokers, this rate was 24 (5.5%) among team players ( $P = 0.00$ ). The mean score of knowledge about hazards of smoking was  $7.65 \pm 0.91$  among those who had experienced smoking. This score was  $7.89 \pm 0.48$  among those with no smoking experience ( $P = 0.00$ ). The mean score of attitude was  $25.2 \pm 5.27$  in those with history of smoking and  $26.87 \pm 3.58$  in those with no history of smoking ( $P = 0.00$ ).

**Conclusion:** Rate of smoking among professional athletes is lower than general population average. So participation in organized sports may be a protective factor against tobacco use in people. Percentage of smoker athletes was significantly higher in individual sports compared to team sports. Experiencing hookah smoking was significantly higher than cigarette smoking among athletes. Athletes had good knowledge about hazards of smoking and had a positive attitude in this respect. Further studies are needed to evaluate reasons of cigarette and hookah smoking among athletes.

#### **PC-704-15 Environmental tobacco smoke as a risk factor for increased respiratory childhood infection and pneumonia in south-west region, Nigeria**

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**Background:** There is consistent evidence that children exposed to environmental tobacco smoke (ETS)

have higher incidence of asthma, ear- and throat disease, worsening of asthma symptoms and lung symptoms as cough, wheezing and pneumonia. A child exposed to ETS has about 30% higher risk of absence from school due to illness. Evidence clearly implicates (ETS) as a cause of lung cancer, excess respiratory disease, and cardiovascular disease mortality in non-smokers. Few studies have looked at the interaction of tobacco use or ETS exposure with occupational and ambient air pollution (both indoor and outdoor) in contributing to chronic obstructive pulmonary disorders in developing countries, or the importance of ETS as a risk factor for the already high burden of childhood respiratory infections.

**Method:** A descriptive cross sectional study was carried out in 5 states (Ogun, Lagos, Akure, Oyo and Ekiti). A multistage cluster random sampling was employed to select 450 families in each state. Data was collected using structured questionnaires by trained interviewers.

**Result:** About 2113 records were available for analysis. There were 1298 (60.7%) males and 815 (38.1%) females aged 10 and below. A majority, 807 (38.0%) live with both parents, 213 (10.0%) live with mother alone while 265 (12.5%) live with relatives. The prevalence of children exposed to ETS in the southwest region Nigeria was 73.2%, the study further revealed that 28.5% of children in this region with respiratory childhood infection are exposed to environmental tobacco smoke and 18.4% pneumonia cases are attributed to ETS.

**Conclusion:** Since Environmental Tobacco Smoke has this much negative effects on children in the south west region Nigeria. Efforts should be tailored towards protecting children from ETS to reduce the rate of children exposed to ETS, thereby curbing or reducing respiratory childhood infection and pneumonia in Nigeria.

#### **PC-705-15 Smokeless tobacco use and extrinsic teeth stains among tobacco farmers in South-West Nigeria: a cross-sectional study**

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**Background:** Extrinsic stains caused by substances, e.g., smokeless tobacco, are a constant source of concern for dentists and patients alike. Tobacco cultivation is on the rise in Nigeria with 60 000 farmers cultivating 120 000 acres of farmland. (D. Femi-Pearse, Aspects of smoking in developing countries in Africa, NY State J Med, 1983; 83: 1312–1313). Output has also increased from 2088 tons in 2004 to 2150 tons in 2009 (BATN).

**Methods:** A pilot cross-sectional study among tobacco farmers in Iseyin, Nigeria where BATIA (British American Tobacco Nigeria, Iseyin Agronomy) is situated. Sample size was 97 tobacco farmers (52 males,

45 females) selected randomly. Pre-tested, structured questionnaires were used with close ended questions.

**Results:** Forty-one (28 males, 13 females) of the subjects had used smokeless tobacco at least once before. Nine (5 males, 4 females) are regular users (at least once a week). Twenty-six (16 males, 10 females including all of the regular users) had extrinsic teeth stains that could be attributed to tobacco use. More of the females with stains were interested in having stain removal done (6 females, 5 males)

**Conclusion:** Almost 50% of the farmers have used smokeless tobacco in the past. More than half of this number had extrinsic stains attributable to tobacco use. Women with stains are more likely to seek help with stain removal (for cosmetic reasons?). There appears to be a correlation between growing tobacco, chewing tobacco and extrinsic stains. The economic costs of such stain removal would detract from profits made from growing tobacco. More studies need to be done on a large scale to examine relationship between teeth stains and chewing tobacco and the economic costs of removing same to tobacco farmers.

#### PC-706-15 Association between smokeless tobacco use by women and coronary artery disease

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**Background:** About 27.9% (13.4 million) women use smokeless tobacco (SLT) in Bangladesh. Relationship of use of SLT with coronary artery disease (CAD) is not yet clearly established. The present study was conducted to find out the relationship of SLT use by women and CAD diagnosed by coronary angiogram. **Design/methods:** Total 312 consecutive female non-smoker patients who underwent diagnostic coronary angiogram were included in the study. Tobacco use, anthropometric measurement and clinical information were collected using a questionnaire. Diagnosis of CAD was based on coronary angiogram findings. Rates of CAD were compared between ever SLT user and non user.

**Results:** Mean age of the respondents was 49.9 years. Out of 312 respondents 71.8% were hypertensive and 37.2% were diabetic. Among the respondents 40.6% were SLT user and 59.4% were non user, and 44.2% had positive and 55.8% had negative coronary angiogram. Among 137 SLT user 70 (51.1%) and among 175 non SLT user 68 (38.8%) had positive coronary angiogram ( $P < 0.05$  by  $\chi^2$  test). Among the patients aged less than 50 years 37.5% ever SLT user and only 25.8% never user had positive coronary angiogram, although among the patients with

age 50 years or more, 58.4% ever SLT user and 52.3% never user had positive coronary angiogram.

**Conclusion and recommendations:** Women who are SLT user had higher rate of positive coronary angiogram especially among the younger patents. Measures should be taken to reduce SLT use among women in Bangladesh.

#### PC-707-15 Tuberculosis: what to do with tobacco control

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**Background and challenges to implementation:** Tobacco has active relationship with occurrence of tuberculosis. Tobacco control has appeared to be the core issue to be addressed for global hazards like tuberculosis and other communicable and non-communicable diseases.

**Intervention or response:** The study was conducted to determine the relationship of tobacco consumption and pulmonary tuberculosis among 200 (100 ve+ and 100 ve-) respondents through face to face interview.

**Results and lessons learnt:** Data from the study showed that 55.5% of the respondents are currently using tobacco of any form. The most frequent form of tobacco use is smoking tobacco (41%) followed by chewing tobacco (27%). However, 12.5% using both smoking and chewing tobacco. Data showed that 44.5% are not using any form of tobacco. Data analysis revealed that the proportion of positive tuberculosis was found to be high among the respondents had habit of smoking tobacco (33%) and chewing tobacco (21%) than non-tobacco users (49%) and the difference was statistically significant ( $P < 0.05$ ). This indicated that tobacco use significantly associated with tuberculosis. However, a statistically significant association was found between knowledge against tobacco use and current disease status ( $P < 0.05$ ) indicating that though the respondents with positive tuberculosis had knowledge on bad effects of tuberculosis than the negative cases.

**Conclusions and key recommendations:** Based on the results, policy makers and public health personnel should consider addressing tobacco cessation as part of tuberculosis control. Introducing tobacco cessation advice may be feasible among TB patients, and an integrated approach has been proposed to monitor smoking cessation in TB care. From the perspective of prevention, the target of smoking cessation should aim beyond TB patients to reach high-risk populations who are likely to benefit most from cessation.

**PC-708-15 The association of smoking and household expenditure in low- and middle-income countries: a multi-country cross-sectional analysis**

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**Background:** The high prevalence of smoking, particularly among men in low- and middle-income countries (LMICs), is a global public health concern that may also pose a considerable economic burden on individual users and their families. In addition to the well-established adverse health consequences of secondhand smoke exposure, tobacco use could diminish the family's resources allocated for other key expenditures. This study investigated the association of tobacco use with household expenditures on food, education and health in LMICs.

**Design/methods:** Using data from the World Health Survey (WHS), this cross-sectional study included a sample of 86 682 adult males aged <60 years from 50 LMICs. Random-effects linear regression was used to determine the association between smoking and three categories of household expenditures, namely expenditures on food, education and health. The models controlled for age, level of education, marital status, and urban-rural setting.

**Results:** Smoking as reported by a male adult in the household was associated with reduced household expenditure on food, education and health by 2.3% [95% confidence interval (CI) 0.5%–4.0%], 20.8% [95%CI 16.0%–25.0%] and 7.3% [95%CI 2.6%–12.0%], respectively.

**Conclusion and recommendations:** Tobacco use in LMICs can lead to reduced household consumption on food, education and healthcare. These findings suggest that addressing the tobacco use problem in LMICs could benefit not just the health of smokers and their immediate families but also their economic well-being as well. Further analysis is required to improve the quality of these findings and to address the key methodological issues of this study.

**PC-709-15 Prevalence of tobacco smoking among newly diagnosed pulmonary tuberculosis patients attending DOTS clinics in Karachi, Pakistan**

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**Background:** There is strong evidence that tobacco smoking increases tuberculosis (TB) infection, disease and mortality.

**Objective:** The overall objective of this study was to investigate the prevalence of smoking among men

and women recently diagnosed with pulmonary TB in Karachi, Pakistan.

**Methods:** We conducted a cross-sectional survey, using a structured questionnaire modified from the CDC GATS survey, at four Directly Observed Therapy (DOTS) TB clinics in Karachi, Pakistan between October 2010 and March 2011. To reflect the smoking experience of patients who may stop smoking at onset of TB symptoms/diagnosis, current smokers included those who self-reported smoking at time of interview or quit smoking within 3 months of TB diagnosis.

**Results:** Among the 962 adult male and female pulmonary TB patients included in the study, 17% (95%CI 14, 19) were current smokers, and 18% (95%CI 16, 21) were former smokers who quit greater than three months prior to TB diagnosis. Using logistic regression, we found recent smoking among TB patients in Karachi, Pakistan to be associated with gender (odds ratio 9.2, 95%CI 4.5, 19); age (odds ratio 1.02, 95%CI 1.01, 1.04), and alcohol use (odds ratio 1.5, 95%CI 1.07, 2.15).

**Conclusion:** Estimates of smoking prevalence among the general population in Pakistan range from 16% to 19%, and from 7% to 10% in people from lower socioeconomic areas of Karachi. We observed smoking prevalence among TB patients in Karachi to be higher than previously seen among low income communities. These results provide preliminary data for future studies investigating treatment strategies for TB patients. Evaluation of tobacco smoking status and support for smoking cessation could be important in improving TB treatment outcomes in this population.

**MULTIDRUG-RESISTANT TUBERCULOSIS: CIVIL SOCIETY, COSTS, COUNSELLING AND CASE FATALITY**

**PC-739-15 Comparative analysis of WHO-recommended Category IV treatment cards versus updated forms to define missed dosages of anti-tuberculosis medicines in Kazakhstan**

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**Background and challenges to implementation:** Careful recording of every dose of each SLD in Cat IV regimen provides doctors with clinical and program tools aimed at improving collection of information on quality of DOT, drug tolerance, substance abuse

and to introduce measures to increase level of adherence, improve drug utilization and decrease risks of developing unfavorable outcome.

**Intervention or response:** In Q1 of 2011, 140 patients with confirmed MDR-TB started standardized Category IV treatment with CM, FQ, Pto, CS, PAS, Z in inpatient and outpatient settings in two pilot regions of Kazakhstan. In order to assess quality of DOT and to improve R&R we developed and tested the updated monthly Cat IV treatment card (Form 01) aimed at recording every dose of each SLD. Data collected by State Cat IV treatment cards (Form 01), which were developed in accordance with the WHO Guidelines on PMDT (2008), do not justify missed dosages of each particular medicine. During 2011, a comparative analysis of updated versus State treatment cards was conducted to identify the level of missed dosages of each SLD. Number of missed dosages was calculated at the end of each month in both cards by trained personnel.

**Results and lessons learnt:** Updated Cat IV treatment cards, when compared with State cards, yielded significant differences in number of missed dosages in following proportions: Z missed 18.8% more in updated forms, Cm 30.0%, FQ 7.8%, Cs 5.1%, Pto 25%, and PAS 74.1% more.

**Conclusions and key recommendations:** Updated Cat IV treatment cards allow the improved recording of missed dosages of SLD and provide health providers with important information on the quality of DOT and patient's adherence to treatment, drug tolerance and significantly decrease chances of further development of severe amplification of DR and unfavorable treatment outcome. As a result, updated Cat IV treatment cards were adopted by the NTP and scheduled for institutionalization in all of Kazakhstan in 2012.

#### PC-740-15 Prevalence of MDR-TB among DOTS attendees in rural Haryana, India

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**Background:** MDR-TB is posing a potential threat to tuberculosis control in the country. The available information are hospital-based and over certain region of the country. The present study estimates the prevalence of MDR-TB among DOTS attendees in Ballabgarh, Haryana, India.

**Methods:** The study was done in two DOTS centres of Ballabgarh Tehsil of district Faridabad, Haryana. It was a health facility based cross sectional survey. Data was collected from January 2007 to June 2008. Eligible subjects were informed about the study objectives and written consent was obtained and later

interviewed. Sputum was collected from patients belonging to Categories I and II, under Revised National TB Programme. Anti-TB sensitivity testing was done on randomly selected patients of Category 1 (50% of patients) and all of the Category 2 patients. Extra pulmonary and Category III patients were not included for sputum culture and sensitivity. Culture was done on BACTEC 460 and drug sensitivity for Isoniazid and Rifampicin was done by BACTEC 460 and Reverse Line Blot Assay (RLBA).

**Results:** Sputum collection was attempted for 211 subjects. Sputum was collected from 173 patients. 38 patients had difficulty in producing sputum. Of the 173 sputum samples 80 sputum sample were culture positive for *Mycobacterium tuberculosis*. All these 80 sputum samples were put for drug susceptibility test. Among the culture positive sputum, 9 samples were found to be multi drug resistant by RLBA. The prevalence of MDR among TB patients was 11.25% (95%CI 5.2–20.28).

Category	Patients n (%)
I	220 (53.3)
II	101 (24.5)
III	92 (22.2)
Total	413 (100)

**Conclusion:** Study subjects were from primary and secondary level public health facilities. The proportion of TB patients attending public health facility and the sample size of the current study is small, hence these results may not be generalized to all TB patients and to the entire area. However, the high prevalence of MDR-TB at primary and secondary health care facility requires a public health response. RNTCP needs to address this aspect in the program.

#### PC-741-15 Case fatality among patients who failed multidrug-resistant tuberculosis treatment in Tomsk, Russia

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**Background:** There are limited data available regarding MDR-TB patients' case fatality after registered failure in Russia.

**Design/methods:** We sought to analyze annual case fatality among patients failing MDR-TB treatment. The study included all MDR-TB patients with treatment failure who started MDR-TB treatment between September 10, 2000, and November 1, 2004. We retrospectively collected post-treatment follow-up data up to December 10, 2009 on sputum bacteriological

status, repeated TB treatment courses if any, date and cause of death if applicable, and the last date when the patient was known to be alive if available. Follow up time was calculated from the date of outcome until death, start of another MDR-TB treatment or the date the patient was last seen alive.

**Results:** Between 2000 and 2004, 47/613 (7.7%) patients failed treatment, however, 11 of them restarted another MDR-TB treatment within the first year of follow up and were excluded from analyses. Two more patients were lost to follow up. The final 34 patients were followed up for at least one year, with 15 (44%) TB deaths. Case fatality during the second year of follow up was 44%, the third year it was 43%. Four of 29 (14%) patients with five-year follow-up survived five years despite consistently positive smears and cultures.

Year	Number of patients				Proportion who died of TB
	Total at the beginning of year	Excluded/ lost to follow up	Survived by the end of the year	Died of TB	
1	47	13	19	15	15/34 (44)
2	19	3	9	7	7/16 (44)
3	9	2	4	3	3/7 (43)
4	4	0	4	0	0
5	4	0	4	0	0

**Conclusion and recommendations:** We found in our cohort that 44% of all patients with treatment failure died annually. However, the presence of patients with persistently positive sputum cultures for 5 and more years is challenging public infection control measures.

#### PC-742-15 Four-fold decrease in tuberculosis mortality in the Tomsk region of Russia due to successful patient-oriented MDR-TB treatment

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**Setting:** Russia's Tomsk region was one of the world's pilot territories for the DOTS-Plus MDR-TB project launched in 2000. Between 2000 and 2011, Tomsk TB Services, in collaboration with Partners In Health (PIH), enrolled more than 2262 patients in MDR-TB treatment in the civilian sector. In 2006 a new patient-centered approach was initiated with the aim of achieving universal MDR-TB coverage for the entire region (urban and rural areas) while focusing on the quality of the provided treatment. The vision was that every patient would like to be free of TB and that the TB program needs to accommodate all the needs of the patient. To achieve this vision, several activities such as the provision of daily food packages

for patients' motivation, treatment at home, inclusion of Red Cross volunteers, an anti-alcohol campaign, and the 'Sputnik' program were implemented.

**Results:** By 2001 the MDR-TB reservoir decreased from 823 patients (2002) to 89 (2011), and the overall TB notification rate among new cases (per 100 000) decreased from 116.7 to 75.5 (1.5 times decrease). The TB prevalence rate dropped from 224.7 to 104.9 (2.2 times decrease), while TB mortality fell from 21.9 to 5.8 (3.8 times). Comparing TB epidemiology in Siberia: in 2011 the TB notification rate of the Siberian region overall was 1.5 higher than that of Tomsk (also located in Siberia), TB prevalence was 2.7 time higher and TB mortality 4.7 times higher.

**Conclusion:** The patient-oriented approach and universal access to TB and MDR-TB treatment have significantly improved the TB situation in Tomsk Oblast when compared to neighboring Siberian regions.

#### PC-743-15 Portable room air cleaners to reduce MDR-TB transmission on a South African Hospital Ward

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**Background:** TB transmission in healthcare settings jeopardizes patient, health care worker, and other occupants' health. Easy to use, reliable, and evidence based strategies to reduce transmission are urgently needed. We investigated the efficacy of portable room air cleaners with HEPA filters in reducing MDR-TB transmission on an MDR-TB hospital ward in South Africa.

**Design/methods:** Over 3 months, we exposed 180 guinea pigs to the infectious aerosols generated by 21 culture proven, coughing, MDR-TB patients occupying a 6 bed hospital ward. Half the guinea pigs ( $n = 90$ ) were only exposed to ward air on alternate days when the room air cleaners were operational (intervention group). The other half ( $n = 90$ ) were only exposed to ward air on alternate days when the cleaners were off (control group). Guinea pig infections were assessed with a tuberculin skin test at monthly intervals and efficacy was calculated by comparing the proportion of guinea pigs becoming infected in each group. 5 room air cleaners were used, each operating in one of 4 rooms or corridor with an average volume of 1400 cubic feet. Clean air delivery rate through the room air cleaners was 480 cubic feet per minute per cleaner.

**Results:** The room air cleaners provided 18–22 air

changes per hour (ACH). There were 25/90 (27.7%, 95%CI 18.5%–37%) infections in the control group and 20/90 (22.2%, 95%CI 13.6%–30.8%) infections in the intervention group. This represented a 20% reduction (not statistically significant) in the risk of infection among guinea pigs exposed to air when the cleaners were on (hazard ratio 1.31 for transmission risk in the control group,  $P = 0.4$ ).

**Conclusion:** The use of portable room air cleaners with HEPA filters did not significantly reduce MDR-TB transmission on a hospital ward even though they provided 18–22 ACH. This may be due to patterns of airflow within the ward that prevented contaminated air from reaching the cleaners as we expected in a well-mixed room.

#### PC-744-15 The effectiveness of providing counselling and financial support to patients receiving treatment for multidrug-resistant tuberculosis

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**Background:** The DOTS+ strategy to address MDR-TB places a considerable burden on patients. This study identified problems experienced by patients in order to develop support strategies. The effects of these strategies were then assessed.

**Design/methods:** Qualitative and cohort study in 7 DOTS+ centres in the Kathmandu valley, Nepal. The cohort included three arms—counselling; combined counselling and financial support; and usual care (i.e., no support).

**Participants:** All MDR-TB patients starting treatment in 2008.

**Outcome:** Cure rate. Qualitative information on problems facing patients and their experiences of the interventions was collected from a purposive sample and analyzed using a thematic approach.

**Results:** Qualitative themes identified social impacts driven by stigma and isolation; financial impacts felt through employment loss and increased costs; and health beliefs of the ineffectiveness of treatment. The cohort study recruited 33 patients to counselling, 42 to combined support and 81 to no support. Cure rates for counselling, combined support and no support were 85%, 76% and 67% respectively. Compared with no support, the adjusted odds ratios of cure for counselling and combined support were 2.6 (95%CI 0.9 to 7.9) and 1.9 (95%CI 0.8 to 4.9) respectively.

**Conclusion and recommendations:** Both strategies were valued by patients. Those receiving combined support were more appreciative of counselling than those receiving counselling alone. Counselling appeared to be more effective than combined support.

Larger studies, preferably RCTs, may be required for conclusive results. In the absence of such evidence, we recommend that NTPs consider incorporating financial support and counselling into DOTS+.

#### PC-745-15 Can a single sputum specimen be used for follow-up culture monitoring of multidrug-resistant tuberculosis treatment?

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**Background:** The Indian Revised National Tuberculosis Control Programme (RNTCP) is scaling up multidrug-resistant (MDR) TB services nationwide. As part of treatment monitoring, two sputum specimens for mycobacterial culture are collected every 1–3 months. With laboratory capacity strained by MDR-TB service expansion, we considered how a single follow-up sputum specimen would affect patient care and laboratory work load.

**Methods:** We included 220 drug resistant TB patients with outcomes declared, registered at DOTS Plus sites of Andhra Pradesh, Gujarat and Rajasthan in 2008–09. Retrospective data of culture and treatment results were collected from laboratory and treatment registers. The sensitivity of a single follow-up to detect a positive final follow-up result (defined as culture positive results from either specimen) and its negative predictive value (NPV) was calculated. Clinical impact was estimated by considering the effect of any loss of culture information on patient management.

**Results:** Among the registered patients, 1794 follow-up culture examinations using two sputum specimens were done during their treatment period, and 464 (25%) overall examination results were culture-positive. Compared to two specimens, a single specimen detected 438 of 464 positive results (94% sensitivity) and predicted 1230 of 1253 negative results (98% NPV). The number of specimens needed to test for a positive culture result was 4.1 for the first specimen, and 69 additional second specimens were tested for each additional positive examination result. Among the 220 patients, 6 would have had durations of treatment shortened by 1–3 months, and no treatment outcomes would have been affected.

**Conclusion:** For nationwide scale-up of MDR-TB services, RNTCP may reduce laboratory workload by requiring only a single follow-up sputum specimen for culture monitoring, without meaningful loss of information or impact on patient care.

### PC-746-15 Health system strengthening interventions to implement community multidrug-resistant tuberculosis care in Gantsi District, Botswana

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**Background:** Botswana with 2 million inhabitants notified 7013 TB cases in 2010 and program indicators reveal the likelihood of an emerging MDR-TB epidemic. MDR-TB cases are initiated in 5 sites, Directly Observed Treatment (DOT) provided in wards and by clinics nurses; national Community TB Care program (CTBC) and Community Based Organizations (CBOs) are poorly involved in MDR-TB support, raising concerns about services accessibility, hence program performance. The Center for Diseases Control (CDC) funded University Research Corporation projects include supporting community MDR-TB care at national and district level.

**Intervention:** We conducted a multidisciplinary workshop (district management, hospital (MDR-TB site), clinics and posts staff, local CBO (Kuru), Central Medical Stores, National TB Reference Lab) to discuss MDR-TB, and identified HSS barriers liable of being overcome by simple and low cost interventions.

**Results:** Strengths include the pilot buy in by national level and district management, facilities staff, and Kuru, the provision of a GeneXpert® by CDC, clinics experience in DOT supervision and of Kuru in CTBC. Systems barriers include poor communication between levels of care, poor knowledge on DRTB programmatic management (PMDT) at district and clinical management at decentralized levels, and DRTB recording and report challenges. Solutions range from district management capacitation on PMDT (including communication systems and flows between levels of care) MDR-TB clinical training for decentralized staff (including intensified case findings and defaulter/contact tracing activation) and Kuru (prompt contact and defaulters' tracing, geographical patients' mapping) and quarterly collaborative evaluation of TB and DRTB programs.

**Conclusion:** This project shows that with political and stakeholders' will, simple and low cost interventions can make community MDR-TB care a reality.

### PC-747-15 Patient's experiences and perceptions in accessing MDR-TB diagnosis and treatment in Cape Town

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**Background:** Studies on the impact of new tests such as the MTBDR<sup>plus</sup> Line Probe Assay focus on test performance and clinical impact. Little is known of impact of these tests on patients accessing MDR-TB diagnosis and treatment.

**Aim:** To explore experience and perceptions of MDR-TB patients' in their pathway to diagnosis and treatment.

**Design/methods:** This qualitative study used in-depth interviews with eleven MDR-TB patients. Only smear-converted MDR-TB adults were included. The participants varied in MDR risk profiles, age and sex. Interviews were digitally recorded, transcribed. Thematic analysis done to identify the main trends of patient's illness pathway.

**Results:** High MDR risk (previous TB or with MDR contact) patients tended to recognise their recurring TB symptoms and access clinics early, with timely diagnosis. Low MDR risk patients often ignored symptoms, ascribing it to something less serious and arriving at an MDR diagnosis was often circuitous: patients typically sought care from pharmacists and private services on several occasions before visiting their local clinic. Some patients in this group were on initial drug sensitive treatment up to 3 months before diagnosis. Patients perceived process of getting the test done and receiving results as 'chaotic' with long waiting times, multiple visits to the clinic and results often not available on return. Other delays in starting treatment were due to personal circumstances such as having to travel up country. Patients felt relieved to have a final diagnosis and largely positive about starting treatment at clinics. They appreciated education about the disease. Some cited negative staff attitudes as a concern. They highlighted the negative impact of MDR-TB on their personal, social and work lives.

**Conclusion and recommendations:** This study highlights important challenges that need to be addressed to enable early MDR diagnosis and treatment.

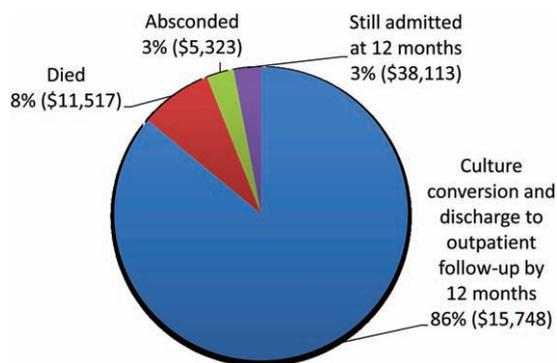
### PC-748-15 The cost of in-patient treatment for multidrug-resistant tuberculosis at a specialised hospital in South Africa

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**Background:** In South Africa, patients with multidrug resistant tuberculosis (MDR-TB) are hospitalized in specialized drug-resistant TB (DR-TB) hospitals from treatment initiation until culture conversion. To evaluate the potential savings from outpatient MDR-TB treatment, we estimated the cost of inpatient care.

**Methods:** All resources utilized by patients admitted to the DR-TB hospital with confirmed MDR-TB and initiating MDR-TB treatment on site from March 2009 to February 2010, excluding drugs for HIV and diabetes, were abstracted from patient records for up to 12 months following initial admission or until the earliest of discharge, abscondment, or death. Costs of hospital stay/day were collected from hospital expenditure records. Costs for drugs, laboratory tests, radiography, and surgery were collected from public sector databases. Costs are reported in USD 2011 prices (ZAR 7.17:\$1).

**Results:** Of 277 patients registered by the DR-TB hospital during the study period, 121 met study inclusion criteria and had complete resource utilization records. Mean age at admission was 40 years, 45% of patients were female, and 67% were HIV co-infected, of which 77% were on ART. Outcomes are shown in the Figure. The mean hospital stay was 108 days. The mean cost per patient was \$15 608, of which \$10 409 (67%) was for salaries and \$4320 (28%) for build-



**Figure** Patient outcomes 12 months after initial admission and mean cost/outcome (USD 2011) ( $n = 121$ ).

ings and other fixed costs. Mean costs for MDR-TB drugs and laboratory tests, including drug susceptibility testing, were \$363 (2%) and \$356 (2%), respectively. Costs for patients diagnosed smear positive or with any 2nd line resistance were 26% and 33% higher than for those who were smear-negative or had only 1st line resistance, respectively. Costs did not differ significantly by HIV status or weight <50 kg.

**Conclusions:** The high cost of inpatient MDR-TB treatment argues strongly for assessment of alternative approaches. Substantial resources could be invested in achieving good outpatient outcomes while reducing the overall cost of MDR-TB treatment.

### PC-749-15 Interrupting treatment among MDR-TB patients: exploratory study, Egypt 2012

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**Background:** Adherence to treatment regimens is pivotal to TB control in general and DR-TB in particular. This study aimed at exploring factors contributing to interrupting treatment among DR-TB patients.

**Design/methods:** In this cross sectional study, a questionnaire developed to explore the contributing causes of defaulting among 34 MDR-TB patients interrupted treatment during the last 3 years since MDR-TB management started in Egypt. Only 15 out of 34 defaulted patients (44%) could be reached and interviewed. Only one was a female and age ranged from 16 to 67 years old. Before starting Cat IV, 3 patients received more than 4 first line treatment courses (Cat I and Cat II), one patient received 4 courses, 4 patients received 3 courses, 6 patients received 2 courses, and one patient received only one course.

**Results:** Defaulting was the outcome in 27%, 53.3% and 25% of those patients in the first, second and third first line treatment courses respectively. Family and financial problems were the main cause of interruption. Second line drugs adverse effects were not a measure cause of interrupting treatment as might be expected. Long previous history of receiving many anti-TB treatment courses including Cat IV course played a crucial role. Attitude of care providers, unsatisfactory hospitalization conditions and lack of adequate health education and counseling played an important role.

**Conclusions and recommendations:** As early as possible ambulatory treatment with treatment supporters, can help increasing adherence to treatment. Stigma is still an important factor determining who could be the treatment supporter.

### PC-750-15 Mortality among MDR- and XDR-TB patients in a community-based programme in Karachi, Pakistan

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**Background:** Drug-resistant tuberculosis (DR-TB) is associated with higher mortality than susceptible TB, even when patients are on appropriate regimens. We studied baseline patient and disease characteristics associated with death as an outcome on patients in a community-based program in Karachi, Pakistan.

**Methods:** We conducted a retrospective analysis of all MDR-TB and XDR-TB patients enrolled between January 2008 and March 2012 in Indus Hospital's community-based DR-TB program.

**Results:** Of 153 MDR-TB and 2 XDR-TB patients with treatment outcomes, 42 (27%) had died during the course of treatment. 20 (49%) of MDR-TB patients died during the first six months of treatment, 8 (20%) of whom had died during the first month. One XDR case died after a month of treatment. 23 (55%) of the patients waited up to 6 months prior to treatment initiation, while 9 (21%) waited for longer than 6 months; 10 were enrolled within a month of diagnosis. 23 (55%) deaths reported were among females, and 41% were between 15 and 24 years old. At the time of registration, 60% had very low BMI (<16), 7% had low BMI (16–<18), 10 (24%) of normal BMI (18–24.9), and 2 were overweight. At the time of registration, 17 (41%) were re-treatment failure cases, 10 (23%) were failure cases and 7 (17%) were relapse cases. Four (10%) had diabetes (HbA1c > 6.5%), 2 (5%) were co-infected with Hepatitis C Virus and 3 (7%) with hepatitis B virus.

**Conclusion:** Most patients that died did so during the first six months of treatment, reflecting the long waiting times many of them had experienced between diagnosis in private laboratories in Karachi, and treatment initiation at Indus Hospital. Patients that died tended to be younger, and were more frequently females. In addition to likely having extensive disease at baseline, several patients that died had comorbidities such as diabetes and hepatitis C infection. Earlier initiation of treatment, and more aggressive nutritional support could help reduce deaths.

### PC-751-15 Addressing civic health literacy for the sustainability of tuberculosis treatment: a case of India

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**Background:** Tuberculosis (TB) is a problem in India now, with rising cases of drug-resistant strains. One

reason for drug-resistant TB is patients not completing treatments properly. A category of civic health literacy is the lack of awareness that individual health decisions impact the overall public health.

**Design/methods:** An exploratory study was carried out in Mumbai, India, regarding vaccination health literacy, competency and media usage and trust. The survey also examined sources trusted in obtaining information about TB and its symptoms, vaccination, treatment and diagnosis. A total of 238 participants took part in this survey.

**Results:** Two groups deduced based on income, lower and upper middle-of-the-pyramid (MOP), were compared. Only 15% of the lower MOP owned a computer with Internet access but 76.6% owned mobile phones. 41.2% of the upper MOP had Internet access and 87% owned mobile phones. The upper MOP know more about health issues in general compared to lower MOP, however, the lower MOP seemed to have a greater sense of civic health literacy such as encouraging other people to take BCG vaccination and feeling that immunization is important for family. But when it comes to further intentions to find out more about TB symptoms, the upper MOP was more willing.

**Conclusion and recommendations:** With high ownership of mobile phones in India, we propose the development of mobile solutions specific to various Indian MOP communities (as each have different needs) that foster and empower peoples' civic health literacy and the ability to make decisions with increased awareness of how a personal decision may contribute to a whole. On-going research investigates integrating factors of civic health literacy into the development of sustainable healthcare technologies for the treatment of TB in alerts, care and education.

### PC-752-15 Are multiple previous episodes of anti-tuberculosis treatment associated with multidrug-resistant disease?

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**Background:** Previous tuberculosis (TB) treatment is considered the strongest predictor of multidrug-resistant (MDR)-TB. This study was conducted in a high-incidence setting in South Africa with known high rates of disease recurrence. We aimed to investigate whether the risk of MDR-TB is associated with the number of previous treatment episodes.

**Design/methods:** Diagnostic sputum samples from all TB cases treated in the study area 1996–2008 were prospectively collected and stored in a sample bank. Treatment register data from the two local TB clinics

(same period) were captured in an electronic database. From this database, we selected all TB cases with at least one diagnostic sputum sample documented smear-positive. Corresponding samples were re-cultured and strain DNA sequencing was used to determine the presence of the *rpoB* gene of the mutant type, defined as MDR, or the wild type (non-MDR). Probabilistic record linkage and patient file searches were used to determine the number of previous treatment episodes among MDR- and non-MDR-TB cases.

**Results:** A total of 2613 smear-positive TB cases were selected from the treatment register database. *rpoB* genotype results were available in 1718/2613 (65.7%). The *rpoB* mutant type was found in 55/1718 (3.2%). It was found in 42 (2.9%) of 1460 cases without a previous treatment episode, 10 (4.7%) of 215 with one, and 3 (7.0%) of 43 with two or more previous episodes ( $P = 0.06$ ). The presence of the *rpoB* mutant type was linearly associated with the number of previous episodes of treatment default ( $P = 0.04$ ).

**Conclusion and recommendations:** The results of this study suggest that TB cases with multiple episodes of anti-TB treatment are at increased risk of MDR disease, especially when they defaulted from treatment multiple times. Our study underscores the importance of efficient treatment to prevent MDR-TB. The design of our study did not allow us to assess the potential of reverse causality.

### PC-753-15 New partnership model for improving access to multidrug-resistant tuberculosis treatment

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One of the greatest challenges in tuberculosis (TB) control is the limited arsenal of effective MDR-TB drugs. Moxifloxacin is not licensed for TB treatment but is included in the WHO MDR-TB treatment guidelines for use because of its demonstrated activity against *M. tuberculosis*. In a groundbreaking initiative, Bayer Pharma AG has agreed to make moxifloxacin available at a concessional price to patients in need through the Global Drug Facility (GDF), the drug procurement arm of the Stop TB Partnership. This agreement was signed following intensive consultations with GDF and the WHO Quality and Safety of Medicines (QSM) programme. Bayer, GDF and WHO have specified rules, procedures and responsibilities of all parties. The objective is to foster tight cooperation with all partners: Bayer, GDF, WHO and the recipient. These concern monitoring drug use and adverse event notification (ADR) and reporting. Organizations or government programmes

receiving moxifloxacin must sign a statement in which they commit to monitor, collect and send all serious ADRs and other relevant safety information to the Bayer affiliate in the country in which they are located. Recipient organizations are also advised to share this information with the national pharmacovigilance centre or the national drug regulatory authority. If necessary, the WHO QSM programme will provide special training in pharmacovigilance with Bayer's collaboration. It is anticipated that moxifloxacin will eventually become an important component of MDR-TB regimens. The new programme of collaboration between Bayer, GDF, WHO and recipient programmes will provide a platform for developing evidence for sustainable use of moxifloxacin. The new agreements will promote learning and shared responsibility while providing life-saving treatment.

### MULTIDRUG-RESISTANT TUBERCULOSIS: TREATMENT OUTCOMES

#### PC-782-15 Treatment outcomes in patients with XDR-TB in South Africa

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**Background:** Patients with XDR-TB have high but unclear mortality. We set out to determine treatment outcomes for patients with XDR-TB in an area of high HIV prevalence.

**Methods:** We retrospectively enrolled patients initiating treatment for XDR-TB in 2 provinces in South Africa, Eastern Cape (EC: 10/2006–6/2008) and KwaZulu-Natal Provinces (KZN: 10/2006–1/2008). We assigned patients to treatment outcomes 24 months after treatment initiation using standard MDR-TB 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, 385 patients initiated XDR-TB treatment (233 patients from EC and 152 patients from KZN). Of these, 11 patients had an unknown HIV status and an additional 20 patients had an unknown treatment outcome. In total, 237 patients (63.4%) were HIV positive, of whom 152 (64.1%) were on anti-retrovirals (ARVs). HIV negative patients were more likely to be male (60.6% vs. 38.4%,  $P < 0.001$ ) and less likely to be smear positive at treatment start (38.6% vs. 56.8%,  $P = 0.001$ ). HIV negative and positive patients had similar age at treatment start (mean 35.6 years  $\pm$  11.6), weight (50.2 kg  $\pm$  12.7), previous episodes of any TB (2.4  $\pm$  1.1) and MDR-TB

(59.7% with at least one MDR-TB episode). Treatment outcomes after 24 months of treatment were as follows: 39 patients (10.1%) cured, 13 patients (3.4%) completed treatment, 30 patients (7.8%) default, 227 patients (59.0%) died, 55 patients (14.3%) failed, and 1 patient transferred (0.3%). Among HIV positive patients, those patients not on ARVs at treatment start were 5.9 times more likely to have an unfavorable outcome ( $P = 0.009$ ; CI (1.4–25.9)).

**Conclusions:** Treatment outcomes were poor, though not as poor as first described. Further analysis will focus on the effect XDR-TB treatment and antiretroviral drugs, so as to examine predictors of treatment response.

### PC-783-15 High rate of successful and relapse-free outcome of short standardised treatment of multidrug-resistant tuberculosis in Niger

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**Background:** To evaluate the effectiveness of a short course standardized treatment for patients with proven MDR-TB previously untreated with second-line drugs in Niger.

**Methods:** Between July 2008 and December 2010, 92 consenting suspect patients were enrolled on a 12-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 every two months. Follow up after cure was continued for 24 months. The study was observational.

**Results:** A total of 92 patients started the treatment; 27 with non-proven MDR-TB were excluded from analysis (15 culture negative, 4 with poly resistant strains and 8 with other mycobacteria). 65 cases with proven MDR-TB (64 previously treated with first-line drugs and 1 new case) were analyzed for treatment outcome. Fifty-three (81.5%) were males; mean age was 32.7 years (range 16–66). Of 58 (89.2%) patients tested for HIV, 1 (1.7%) was positive. Twenty-eight (43.1%) started in severe clinical condition (inability to walk unaided or BMI  $\leq 16$ ). Culture conversion at 4 months was 92.3%. Only one patient had late culture conversion 2 months after intensive phase extension. Cure was obtained for 58 patients (89.2%; 95%CI 81.7–96.8), 6 died (9.2%) and 1 defaulted (1.6%). The major adverse event was vomit-

ing ( $n = 18$ ; 27.7%) during the first days of treatment and hearing impairment ( $n = 11$ ; 16.9%). No patient had to stop the treatment. All 45 patients completing 6 months follow up and the 35 with 12 months follow up after cure remained negative on smear and culture.

Status of cured patients at successive follow-up

	6 month follow-up <i>n</i> (%)	12 month follow-up <i>n</i> (%)	18 month follow-up <i>n</i> (%)	24 month follow-up <i>n</i> (%)
Culture-negative	45 (77.6)	35 (66.0)	29 (54.7)	19 (36.5)
Waiting for culture result	8 (13.8)	18 (34.0)	23 (43.4)	31 (59.6)
Relapse	0	0	0	0
Moved to other jurisdiction	3 (5.2)	0	1 (1.9)	0
Death	2 (3.4)	0	0	2 (3.8)
Total	58 (100.0)	53 (100.0)	53 (100.0)	52 (100.0)

**Conclusion:** A short course standardized treatment for MDR-TB appears to be very promising in a resource-constrained setting with low HIV prevalence and little exposure to second line drugs.

### PC-784-15 200 DR-TB patients enrolled on treatment with SLDs in Azerbaijan Penitentiary Sector: treatment results and risk factors

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**Aim:** Analysis of risk factors led to DR-TB patients' unsuccessful SLD treatment outcomes.

**Methodology:** Medical registration cards analysis of first 200 DR-TB patients enrolled to SLD treatment in Azerbaijan Penitentiary Sector performed according to WHO DR-TB Management guidelines.

**Results:** 200 DR-TB patients were enrolled to SLD treatment in penitentiary sector in 2007–2009 with following treatment outcomes: 'cured'–150 (75%); 'died'–15 (7.5%); 'failed'–18 (9%); 'defaulted'–17 (8.5%). 'Died', 'failed' and 'defaulted' are assumed as unsuccessful treatment outcomes. Average duration: treatment course—20 months; intensive phase—12 months. Statistical confidence evaluation through monovariant analysis of resistance rate on integration to treatment as risk factor for unsuccessful treatment outcome has revealed:

- Only H/R resistance:  $P$  value = 0.83
- H/R and additional resistance to SLD (excl. FQ and injections):  $P$  value = 0.53
- H/R and additional resistance to SLD (incl. FQ or injections)-pre-XDR:  $P$  value = 0.004

Statistical confidence evaluation through monovariant analysis of cavity in both lungs on integration to treatment as risk factor for unsuccessful treatment outcome has revealed  $P$  value = 0.0007. Statistical confidence evaluation through monovariant analysis

of hepatitis C co-infection (detected using express HCV test) on integration to treatment as risk factor for unsuccessful treatment outcome has revealed  $P$  value = 0.31.

#### Conclusion:

- 1 On integration to treatment: a) resistance to FQ and injections and b) TB process spread rate are significant risk factors for unsuccessful DR-TB treatment outcome.
- 2 To reach successful treatment outcomes critical is to perform in-patient treatment in case of long-term injections application during intensive phase.
- 3 it is important to proceed co-infection influence to unsuccessful treatment outcome investigations.

### PC-785-15 Treatment outcomes of MDR-TB patients enrolled in national tuberculosis control programmes in 2008

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**Background and challenges to implementation:** The World Health Organization (WHO) estimates that among TB patients notified worldwide each year about 290 000 are multidrug-resistant (MDR-TB). Treatment of MDR-TB is more demanding on patients and programmes and less effective than that for drug-susceptible TB. We describe the outcomes of enrolled patients using the most recent surveillance data.

**Intervention or response:** In 2011 countries reported data to WHO on MDR-TB patients started on treatment in 2008, allowing time for treatment completion. Treatment regimens varied between countries. Standardized definitions for outcomes were widely used.

**Results and lessons learnt:** 95 countries/territories reported outcomes for 15 565 MDR-TB cases—7% of estimated cases in 2008 (Table). More than 70% of cases reported were from the European Region and South Africa. Overall treatment success was 53%, 13% of cases died, 8% had treatment failure

**Table** Outcomes of MDR-TB patients started on treatment in 2008

Region	Countries reporting outcomes <i>n</i>	MDR-TB cases expected among TB cases notified in 2008 <i>n</i> *	Cases <i>n</i>	Outcome, %				
				Success	Death	Failure	Default/Unknown	
African	20	14 000	5 496	50	19	6	17	8
American	21	5 200	1 732	47	10	6	13	23
E. Mediterranean	11	1 600	262	56	9	3	10	22
European	26	70 000	6 904	56	9	11	14	9
S-E. Asian	6	61 000	413	63	11	9	16	1
W. Pacific	11	59 000	758	58	12	2	19	10
Global	95	210 000	15 565	53	13	8	15	11

\* Rounded estimates; limited to countries reporting outcome data.

and 26% defaulted or had no information. Success was highest in the South-East Asian (63%) and Western Pacific (58%) regions although the number of cases treated was modest. Success was low in the Americas (47%) owing to incomplete data, and in Africa (50%) as a result of high mortality (19%). Failures were highest in the European region (11%).

**Conclusions and key recommendations:** Many countries report outcomes for MDR-TB patients but for a small proportion of their caseload. Success remains low. Improving data completeness and patient adherence are crucial in most countries. In Africa, earlier diagnosis of drug-resistance, as well as improved access to anti-retrovirals in patients with HIV, are important. Rapid, adequate treatment of patients with severe and advanced drug-resistant disease is recommended in the European region.

### PC-786-15 Survival and predictors of mortality among patients on multidrug-resistant tuberculosis treatment in Ethiopia

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**Background:** The extent and burden of MDR-TB varies significantly from country to country. Survival of MDR-TB treatment is not described in Ethiopia. Therefore, the aim of this study is to assess survival and predictors of mortality among patients under MDR-TB treatment in Ethiopia: St Peter's Specialized TB Hospital, Addis Ababa, Ethiopia.

**Design/methods:** A cross sectional study was conducted from October 2011 to March 2012 among cohorts of MDR-TB patients in St. Peter's specialized TB hospital that starts treatment from February 2009. Data were collected and analyzed using STATA Statistical Package, Version 11.0. Sample size estimation for the assessment of survival time under the Cox-proportional hazards model is computed using STATA Statistical Package, Version 11.0. Risk was estimated for the entire follow-up time corresponding to each event occurrence using Kaplan-Meier method and the covariates are fitted to Cox proportional hazard regression model.

**Results:** Among the total 188 subjects, 87 (46.28%) are male and the rest 101 (53.72%) are female with median age of 27 years. There were 29 (15.43%) known deaths (incidence rate: 3.6 per 10 000 person-days). Survival rate at 6, 12, 18, and 24 months of treatment were 88.53%, 85.83%, 82.71% and 78.95% respectively. The mean survival time was 9.7 years. In multivariate Cox proportional hazard regression, factors independently associated with survival were smoking (HR: 4.01, 95%CI 1.42–11.37,

$P = 0.009$ ), therapeutic delay  $> 1$  month (HR: 3.61, 95%CI 1.41–9.20,  $P = 0.007$ ), HIV seropositive (HR: 5.94, 95%CI 2.40–14.72,  $P < 0.0001$ ) and clinical complication (HR: 1.90, 95%CI 1.52–2.39,  $P < 0.001$ ).

**Conclusion and recommendations:** Higher hazard of death was noted in patients who started treatment after a month of period diagnosed as MDR-TB, smokers, HIV positive and who have clinical complication during the treatment period. Therefore, reinforcing the existing treatment program to include all MDR-TB patients and urgent need for non-medical interventions are necessary to improve patients' survival in Ethiopia.

### PC-787-15 Good in vitro activity of trimethoprim-sulfamethoxazole against wild type and MDR-TB strains in Taiwan

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**Background:** Because the MDR-TB and XDR-TB had developed, more drug resistance strains had been isolated. So many previous medications should be tested again for clinical use. Trimethoprim-sulfamethoxazole was the first anti-tuberculosis agents in the world and had not been used for TB for decades. The study wanted to evaluate the in vitro drug susceptibility test of trimethoprim-sulfamethoxazole against wild type and MDR-TB strains.

**Design/methods:** Totally 44 clinical isolates of MDR-TB and 39 isolates of wild type *M. tuberculosis* were tested for the susceptibility of trimethoprim-sulfamethoxazole. The inhibitory activities of the drugs or solvents against tuberculosis isolates were determined by agar proportion method according to the Clinical and Laboratory Standards Institute (CLSI). The drug susceptibility tests of ofloxacin, levofloxacin, moxifloxacin, amikacin, kanamycin and capreomycin were also performed for the MDR-TB strains. Because no cutoff level was defined for trimethoprim-sulfamethoxazole, a tentative cutoff was used as MIC  $\leq 20$   $\mu\text{g/ml}$ .

**Results:** The MIC ranges for trimethoprim-sulfamethoxazole were 10–80  $\mu\text{g/ml}$  for MDR-TB and 10–40  $\mu\text{g/ml}$  for wild type TB. The MIC<sub>50</sub> for MDR-TB and wild type TB were 10  $\mu\text{g/ml}$  and the MIC<sub>90</sub> for MDR-TB and wild type TB were 40  $\mu\text{g/ml}$ . There were 77.3% of MDR-TB strains with MIC  $\leq 20$   $\mu\text{g/ml}$  and 78.4% of wild type TB with MIC  $\leq 20$   $\mu\text{g/ml}$ . Only one MDR-TB strain was found to have

MIC = 80  $\mu\text{g/ml}$ . The drug susceptibility rate of MDR-TB for ofloxacin (2  $\mu\text{g/ml}$ ), levofloxacin (1  $\mu\text{g/ml}$ ), moxifloxacin (1  $\mu\text{g/ml}$ ), moxifloxacin (2  $\mu\text{g/ml}$ ) were 70.4%, 81.8%, 79.5%, 84.1% respectively. For amikacin, kanamycin and capreomycin the susceptibility rate were 90.9%.

**Table** Drug susceptibility testing of trimethoprim-sulfamethoxazole against wild type and MDR-TB strains

Clinical strains	MIC ( $\mu\text{g/ml}$ )		Per cent of isolates		
	Range	50% 90%	$\leq 20$ $\mu\text{g/ml}$	40 $\mu\text{g/ml}$	80 $\mu\text{g/ml}$
<i>M. tuberculosis</i> ( $n = 37$ )	10–40	10 40	78.4 (29/37)	21.6 (8/37)	0 (0/37)
MDR-TB ( $n = 44$ )	10–80	10 40	77.3 (34/44)	20.4 (9/44)	2.3 (1/44)

**Conclusion and recommendations:** The in vitro activity of trimethoprim-sulfamethoxazole against MDR-TB and wild type TB was good. It might provide another alternative treatment choice for the MDR-TB or patients with liver toxicity.

### PC-788-15 Drug-resistant tuberculosis in the Tibetan population in India: epidemiological risk factors, resistance profile and treatment outcomes

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**Background:** Drug resistant TB is an emerging threat to the Tibetan refugee population in India. The overall incidence of TB in the Tibetan population in India has decreased from 632/100 000 in 2007 to 431/100 000 in 2010, but the incidence of multi-drug resistant TB rose from 57/100 000 in 2007 to 69/100 000 in 2010.

**Objective:** To study the epidemiological risk factors, drug resistance patterns and treatment outcomes for MDR-TB patients in the Tibetan population in India.

**Design/methods:** Treatment records of all patients registered for MDR-TB treatment from 2007 to 2011 at Tibetan Delek Hospital were retrospectively reviewed.

**Results:** Of 200 patients registered, 182 had MDR pulmonary TB confirmed by mycobacterial drug sensitivity test (DST). Of the 182, 171 (94%) had further resistance to streptomycin or ethambutol, and 70 (38.5%) had resistance to ofloxacin. Of the 200 patients, 91% are age 15 to 45 years, 71.5% are living in congregate or overcrowded settings, 79% are prone to migration and 74.5% are born in India. Female sex ( $P = 0.001$ ), age  $> 30$  ( $P = 0.001$ ) and

cavitary lesion ( $P = 0.003$ ) on chest X-ray are independently associated with resistance to ofloxacin. Of the treatment outcomes available for 127 patients from 2007 to 2010, 80.3% had successful outcome, 6.3% had failed, 6.3% had died and 7.1% had defaulted. 85.7% (7) of failures and 62.5% (5) of deaths are among the ofloxacin resistant group.

**Conclusion and recommendations:** Ongoing migration and living in congregate settings make TB control difficult in the Tibetan population. Given the significant rate of quinolone resistance, spread of primary drug resistant strains in congregate settings could have serious consequences. Aggressive contact tracing, sending sputum culture and sensitivity for every pulmonary TB patient and periodic TB education are potential solutions for the effective control of TB and drug resistant TB in this population. Overall treatment outcomes are excellent despite these challenges.

#### PC-789-15 Effectiveness of the standardised treatment regimens used in Tajikistan

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**Background:** The drug resistance survey (DRS) carried out during the period March 2008–April 2009, in Dushanbe City (1 000 000 population) and Rudaky rayon (296 000 population), Tajikistan, revealed 16.3% MDR-TB among new and 61.1% among previously treated patients. In 2009, the Green Light Committee approved first project for management of 52 MDR-TB patients diagnosed during the DRS. The aim of this study was to evaluate the effectiveness of the used standardized treatment regimen.

**Methodology:** The culture (Löwenstein-Jensen medium) was done in the National Reference Laboratory for isolates from sputum smear positive cases and sent for drug sensitivity testing to Supranational Reference Laboratory in Germany. The standard treatment regimen composed of pyrazinamid, second-line injectable; ofloxacin, prothionamide, cycloserine, and p-aminosalicylic acid were used. The data were recorded using the definitions of World Health Organization and analyzed.

**Results:** Total of 372 new and re-treatment cases were diagnosed, of them 26 new and 84 re-treatment had MDR-TB, of whom one new and 51 re-treatment cases were enrolled on treatment. Patients were between 15 and 35 years of age. Majority (53.8%), were resistant to four first-line drugs. Isolates were resistant to: kanamycin 46.2%, capreomycin 28.8%, amikacin 34.6%, ofloxacin 11.5%, prothionamide 38.5%, pyrazinamid 46.2%. Total of 71.2% were successfully treated, 11.5% failed, 13.5% died, and 3.8% defaulted.

**Conclusion:** The treatment success rate using stan-

dardized treatment regimens was at least as high as in published studies where individualized treatment regimens were used.

#### PC-790-15 Factors associated with treatment default among drug resistant tuberculosis patients in Yerevan, Armenia

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**Background and methods:** In Armenia, where multi-drug-resistant tuberculosis (MDR-TB) accounts for 14.5% of all TB cases, 24.7% of the patients default DRTB treatment. We performed a study to identify factors related with defaulting DRTB treatment in Yerevan using a quantitative (case-control study) and qualitative (focus group and individual semi-structured interviews in defaulters and staff) methodology. All patients who defaulted treatment since the beginning of the project were traced.

**Results:** From 2005 to 2011, out of 486 patients admitted to the MSF/NTP DRTB program in Yerevan, 100 were still on treatment, 193 had succeeded treatment, 27 died, 18 were transferred out, 51 failed the treatment and 97 defaulted. Out of 97 defaulters (66 MDR), 26 died and 27 moved out of Yerevan. Twelve individuals could be finally contacted and interviewed. The number of treatment interruptions (OR: 1.09; 95% CI: 1.04–1.14), rate of side effects (OR: 1.42; 95% CI: 1.12–1.80), treatment interruptions of longer duration (OR: 5.93; 95% CI: 2.39–14.72) and larger variability (OR: 3.73; 95% CI: 1.56–8.93), longer durations of the gaps between interruptions (OR: 0.22; 95% CI: 0.09–0.52), and culture-converting during intensive phase (OR: 0.34; 95% CI: 0.18–0.65) were independently associated with defaulting. In the qualitative study, poor treatment tolerance, perception that the treatment was harming, lack of medical information during treatment, and wrong feeling of being already cured, were identified as the main factors that influenced treatment default. The transition from in- to out-patient treatment was identified as a critical period for defaulting treatment.

**Conclusions:** Both the quantitative and qualitative analyses were consistent to show that poor tolerance and poor response to treatment were associated with defaulting treatment. Compliance to treatment before defaulting could predict the risk of defaulting.

### PC-791-15 Long-term outcomes of treatment of new pulmonary tuberculosis patients in view of MDR-TB treatment effectiveness

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**Background:** According to WHO guidelines (2006, 2009) and national rules, treatment failure outcome includes patient found to harbor a multidrug-resistant tuberculosis (MDR-TB) strain at any point of time during the treatment. For high MDR-TB level regions, this approach in assessing of treatment outcomes shows significant restrictions in TB treatment control analysis. Newly detected MDR-TB, as part of failure outcomes, distorts ratios' values and trends of treatment outcomes and impedes adequate analysis of TB treatment effectiveness.

**Design/methods:** The Russian TB patients' follow up system permits to provide a long-term analysis of the 'contribution' of MDR-TB treatment outcomes to the total treatment effectiveness. The 'total' outcomes' indicators were analyzed by summation of treatment outcomes of the initial and the first MDR-TB courses following switching to MDR-TB treatment regimen. The 'total' outcomes were considered two years after the cohort registration year (2009). The 'total' outcomes for ss+ new pulmonary TB cases were calculated for 5 Russian territories with different levels of MDR-TB prevalence, which had 90–98% failure outcomes defined by switching to MDR-TB treatment (5.2%–22.3% of all outcomes).

**Results:** All territories showed the same directions of changes of treatment outcomes' indicators after recalculation in 'total' outcomes. Values of successful rates increased by 11.3%, from 63.6% (95%CI, 60.5%–66.6%) to 70.8% (67.9%–73.6%), unsuccessful rates decreased by 54.3%, from 18.8% (16.5%–21.4%) to 8.6% (6.9%–10.5%), death rates increased by 7.5%, from 9.4 (7.7%–11.4%) to 10.1% (8.3%–12.2%) and lost follow up cases (default and unknown outcomes) increased by 39.7%, from 6.4% (4.9%–8.1%) to 8.9% (7.2%–10.7%). Less than 1.3% cases were 'treatment continuation'.

**Conclusion and recommendations:** Modified approach to generalized TB treatment outcomes calculation provides more adequate basis for decision making process comparing to traditional one.

### PC-792-15 Treatment outcomes of MDR-TB patients: cohort 2008 in Russian GLC approved projects within the Global Fund Round 4

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**Background and challenges to implementation:** To evaluate treatment outcomes of MDR-TB patients, enrolled for treatment in 18 Russian regional GLC-approved projects in 2008 within the Global Fund Round 4 (GF Round 4) project. GF Round 4 project in the Russian Federation was implemented in 2005–2010. Key task of the project was promotion of DR-TB programmatic management and strengthening the National TB Control Programme capacity for MDR-TB prevention and control. Russian Health Care Foundation as GF Round 4 Principal Recipient with WHO Country Office technical assistance managed implementation of GF Round 4 project activities.

**Intervention or response:** In 2008 within GF Round 4 project implementation 18 Russian GLC-approved projects enrolled 1352 MDR-TB patients for treatment. Treatment outcomes were evaluated in 24, 36 and 45 months after start of the treatment when the last patient in the cohort finished his treatment. 1104 (81.7%) patients were treated in civil sector and 248 (18.3%)—in prison sector. 37.0% MDR-TB patients were registered as new cases; 19.2% as relapses; 3.1% as after default; 10.9% and 8.9% as failure of Category I and II; 0.4% as extra-pulmonary cases; 20.5% as other.

**Results and lessons learnt:** Treatment success rate comprised 54.7%. 17.8% of patients defaulted treatment, 9.1% died; 15.7% had failure of treatment and 2.7% were transferred out and were lost for final evaluation. Treatment success rate in registered new cases was 59.0% against 43.3% in groups of re-treatment cases. There was no difference in treatment success rates between civil (54.6%) and prison (54.8%) sectors. Default rate in civil sector was 19.0% against 12.1% in prison sector. Prison health facilities reported about 23.4% of treatment failure against 13.9% in civil sector.

**Conclusions and key recommendations:** Treatment success rate in Russian MDR-TB cohort 2008 comprised 54.7%. High proportion of defaulters (17.8%) was the main limiter of treatment success rate.

### PC-793-15 Treatment outcomes in community versus inpatient initiation of multidrug-resistant tuberculosis treatment in a rural area of South Africa

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**Background:** Brooklyn Chest Hospital, the TB centre of excellence in Cape Town, has run a structured MDR-TB programme in the Western Cape since 1990. This included an outreach programme to some of the more rural areas of the province. Lack of beds, long

distances to the inpatient facilities as well as the many socio economic problems has led to community based treatment in the more rural areas.

**Design/methods:** A retrospective review was performed of all adults with a first MDR-TB sputum in the West Coast/Winelands region of the Western Cape from 2000 to 2005. Patients were excluded if they started MDR-TB treatment before their first MDR sputum, did not start an MDR-TB regimen (defined as 3 or more 2nd line drugs) or transferred out prior to a final outcome. Patients were stratified according to community-based versus inpatient treatment initiation.

**Results:** Of 474 patients with MDR-TB sputum, 162 were excluded. For the 312 included patients, median age was 35 years with 31.4% female; 175 (56.1%) initiated 2nd line regimens in an inpatient setting and 137 (43.9%) in the community. Community initiated patients were of similar age (34 vs. 36) but less likely to be female [70 (40.0%) vs. 28 (20.4%),  $P = 0.0002$ ]. Median days to initiation was lower in community-initiated patients [66 (49–93) vs. 79 (57–126),  $P = 0.0026$ ]. There was no significant difference in conversion rate (55.5% vs. 55.4%), days to conversion [115 (58.5–192.5) vs. 99 (63–160)], or cure/completion rate (42.3% vs. 34.3%). Community initiated patients showed a tendency towards lower default rates that was not significant (24.1% vs. 34.3%,  $P = 0.0507$ ). Treatment failure occurred in 23.1% of patients, and death in 9.0%.

**Conclusion and recommendations:** Conversion and treatment outcomes, while poor, were similar in community initiated and hospital initiated groups suggesting that community initiated and managed MDR-TB can be effectively implemented in resource poor settings. Strategies to strengthen adherence need to be implemented.

### PC-794-15 Analysis of the outcomes from use of second-line drugs for the treatment of isoniazid-resistant, rifampicin-susceptible tuberculosis in Karakalpakstan, Uzbekistan

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**Background:** The ideal drug regimen for patients with isoniazid resistant, rifampin susceptible, mono- and poly-drug resistant (HrRs) TB is not known. Standard DOTS therapy carries increased risk of failure and drug resistance. We sought to determine whether the use of 2nd line drugs was associated with improved clinical outcomes in the MSF-supported Karakalpakstan DOTS-plus TB programme.

**Design/methods:** We did a retrospective cohort study

of patients with HrRs pulmonary TB. Regimens were chosen based on drug susceptibility testing (DST) and treatment history. We compared treatment outcomes between three groups: patients on 1st line drugs; patients on 1st line and two 2nd line drugs; and patients on 1st line and  $\geq 3$  2nd line drugs. Multivariate regression was used to determine whether use of 2nd line drugs was associated with successful outcomes and lower risk of developing rifampin resistance.

**Results:** Between December 2003 and July 2010, 214 patients had HrRs on a diagnostic sputum sample of whom 165 met our inclusion criteria. Median time to treatment start from sputum submission was 44 days (IQR 6–93). 47% (16) of patients in the  $\geq 3$  2nd line group had a successful outcome compared with 79% (58) in the two 2nd line and 76% (44) in the 1st line group. The likelihood of an unsuccessful

**Table 1** Logistic regression model to assess factors associated with having successful TB treatment outcome vs. unsuccessful (MDR acquisition; failure without MDR documents, death or default) ( $n = 165$ )

	Unadjusted OR (95%CI)	P value	Adjusted OR (95%CI)	P value
Treatment received				
1st line drugs only	1		1	
Two 2nd line drugs	0.81 (0.35–1.86)	0.62	0.80 (0.32–1.98)	0.63
$\geq 3$ 2nd line drugs	3.54 (1.43–8.75)	0.006	3.21 (1.18–8.72)	0.022
Age at start of treatment (per 1 yr increase)	1.02 (0.99–1.05)	0.056	1.03 (1.00–1.06)	0.034
Sex				
Male	1		1	
Female	0.84 (0.43–1.66)	0.62	0.86 (0.41–1.83)	0.69
Body mass index at start of treatment (kg/m <sup>2</sup> )				
<18.5	1		1	
$\geq 18.5$	0.71 (0.35–1.43)	0.34	0.79 (0.35–1.80)	0.57
Smear				
Positive	1		1	
Negative	1.02 (0.34–3.08)	0.97	1.37 (0.41–4.55)	0.60
Prior TB treatment				
No	1		1	
Yes	1.17 (0.59–2.31)	0.66	1.09 (0.51–2.32)	0.82
Ethambutol DST				
Resistant	1		1	
Sensitive	0.26 (0.08–0.87)	0.029	0.48 (0.14–1.60)	0.23
Days between diagnostic sputum sample and treatment start (per 1 d increase)	1.00 (0.99–1.00)	0.58	1.00 (0.99–1.01)	0.98

outcome was highest in the  $\geq 3$  2nd line group (Table; adjusted OR 3.21, 95% CI 1.18–8.72). In the 1st line group 11 (19%) developed rifampin resistance compared with 9 (12%) in the two 2nd line group and 7 (21%) in the  $\geq 3$  2nd line group. Rates did not differ significantly between groups.

**Conclusion and recommendations:** A substantial proportion of patients with baseline isoniazid resistance developed rifampin resistance, despite the use of additional 2nd line drugs. Inadequate TB treatment while awaiting DST results may have contributed. Increased access to rapid DST and clinical trials with standardized treatment regimens are urgently needed.

### PC-795-15 Treatment outcome of MDR patients with fluoroquinolone (ofloxacin) resistance with standardised treatment regimen in Nepal

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**Background:** National Tuberculosis control program Nepal, has managed a Green Light Committee approved ambulatory DOTS plus project since Sep 2005. NTP, Nepal is providing MDR-TB treatment with a standardized second line drug regimen through 64 health facilities. The program offers MDR Treatment regimen to all cat 2 failures without the FLDST and SLDST and to FLDST confirmed MDR-TB without SLDST. The overall treatment outcome of MDR-TB patients in Nepal is 67% cured, 10.2% died, 6.4% failure and 14.6% defaulter (reported on 2010).

**Methods:** We retrospectively reviewed the treatment outcome of a total 199 MDR patients with SLDST examined in the duration of 5 yrs. Among them 54 (27.1%) were an ofloxacin resistance but susceptible to injectables, 13 (6.5%) were resistance to both ofloxacin and injectables and 132 (66.3%) were susceptible to both ofloxacin and injectables. These patients had the usual standardized treatment regimens kanamycin, cycloserine, ofloxacin, ethionomide and pyrazinamide in the intensive phase (8 months) and cycloserine, ofloxacin, ethionomide and pyrazinamide in the continuation phase (16 months).

**Results:** Among 132 susceptible cases 108 (81.8%) cured, 4 (3%) failure, 5 (3.8%) died and 15 (11.4%) defaulted. Out of 54 ofloxacin resistance cases, 23 (42.6%) cured, 19 (35.2%) were failure, 9 (16.6%) died and 3 (5.5%) defaulted and of 13 ofloxacin and injectable drug resistance cases 1 (7.7%) cured, 9 (69.2%) failure and 3 (23.1%) died.

**Conclusion:** Fluoroquinolone is an effective drugs in all empirical MDR-TB treatment regimens. Resistance to ofloxacin of MDR patients' strains threatens

to undermine the treatment success within the DR TB management program.

**Recommendation:** Timely, initial SLD testing for each enrolled MDR-TB cases and alternative treatment for patients with fluoroquinolone resistance should be considered.

### PC-796-15 Preliminary outcomes of a 12-month standardized regimen for the treatment of multidrug-resistant tuberculosis in Cameroon

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**Background:** The two specialized units for the treatment of MDR-TB patients in Cameroon. The objective was to assess the outcomes of patients with multidrug-resistant tuberculosis (MDR-TB) with a 12-month standardized regimen.

**Design:** Observational study of patients with laboratory confirmed MDR-TB disease put on a 12-month standardized treatment regimen during a period of 28 months (2008–10). The treatment regimen consisted of an intensive phase with 4 months of KmG-fxPtoHCfzEZ, followed by a continuation phase of 8 months with GfxPtoCfzEZ, given daily. Clinical and bacterial progress was monitored during treatment monthly until completion; follow-up was done clinically and with bacteriological control for up to one year.

**Results:** A total of 88 patients were put on treatment during the study period, 45 (51.1%) being male and 43 (48.9%) being female. The mean age of the patients was 33.6 years (range 17–68). The following anti-TB drug resistance patterns were identified: HR 32 patients; HRE 4 patients and HRS 24 patients, each; HRES 28 patients. 1 patient had taken any second-line drug. 18 (20.5%) of the patients were HIV-seropositive.

**Treatment outcomes were the following:** Cured 81 (92.0%); died 6 (6.8%); lost to follow-up 1 (1.1%); none of the patients defaulted or was referred. The most important treatment side effect was impairment of hearing in 10 patients. During a total of 636 patient-months follow-up no relapse occurred.

**Conclusions:** Preliminary results of our regimen appear to be very promising and underscore the fact that a standardized short-course regimen may be the best pragmatic alternative to the standardized WHO regimen or individualized treatment of MDR-TB in resource poor settings with little exposure to second-line anti-TB drugs.

### PC-797-15 High treatment success rates in Rwanda's national MDR-TB programme, 2005–2011

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**Background:** Rwanda reported 6780 new and relapse tuberculosis case notifications and an estimated notification rate of 63/100 000 in 2011. A national drug susceptibility survey in 2005 revealed multidrug resistance rates of 3.9% among new smear-positive case and 9.4% among retreatment cases.

**Methods:** Multidrug-resistant tuberculosis (MDR-TB) patients approved by Rwanda's national second-line selection committee were treated under directly observed therapy with a standardized 20-month regimen of ofloxacin-prothionamide-cycloserine (with an intensive phase of pyrazinamide and injectable kanamycin for at least six months). All patients received nutritional support and reimbursement for transportation fees for the duration of treatment.

**Results:** Between July 2005 and December 2009, 306 patients with confirmed MDR-TB (mean age 32.9 years, 51.8% female) were enrolled in Rwanda's national MDR-TB program. A treatment success rate of 88.2% (52.3% cured and 35.9% completed treatment) was achieved in this cohort, while 26 (9.2%) patients died, 6 (2.0%) defaulted, and 2 (0.7%) failed therapy. Among the 126 (41.2%) of patients who were HIV-positive, a success rate of 88.1% (49.2% cured and 38.9% completed treatment) was achieved. In 2006, 15.6% of enrolled patients died before initiating treatment; by 2011, this proportion had dropped to 6.2%. Mean turnaround time for drug susceptibility tests decreased from 86 days in 2006 to 13.5 days in 2009. Over the same period, mean duration of hospital admission decreased from 6.8 months to 3.3 months. Among the cohort initiating treatment in 2009, zero patients defaulted.

**Conclusion:** High MDR-TB treatment success rates can be achieved in national programs in sub-Saharan Africa, including in settings with large burdens of HIV. National ownership of the tuberculosis response, a robust drug supply, system readiness to harness advances in diagnostic technology, and comprehensive adherence support interventions are crucial.

### MULTIDRUG-RESISTANT TUBERCULOSIS: FOCUS ON SURVEILLANCE

#### PC-828-15 Epidemiology of pyrazinamide resistant tuberculosis in the USA, 1999–2009

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**Introduction:** PZA is essential in TB treatment and synergizes with new drugs currently in development. We describe the prevalence and identify predictors of initial resistance to PZA in the U.S.

**Methods:** We analyzed all culture-positive TB cases with reported drug susceptibility tests (DST) for PZA in 38 jurisdictions in the U.S. routinely testing for PZA resistance, 1999–2009.

**Results:** Of 79 321 cases with DST to four first-line drugs, 2167 (2.7%) had PZA-resistance: 1441 (66.5%) were PZA-mono-resistant, 312 (14.4%) poly-resistant, and 414 (19.1%) multidrug-resistant (MDR). PZA-mono-resistance (vs. drug-susceptible TB) was associated with age 0–24 years (adjusted prevalence ratio [aPR] = 1.50, 95%CI 1.31–1.71) vs. age 25–44, Hispanic ethnicity (aPR = 3.52, 2.96–4.18), Asian (aPR = 0.59, 0.47–0.73) and Black (aPR = 0.37, 0.29–0.49) race compared to non-Hispanic whites, positive HIV status (aPR = 1.43, 1.15–1.77), extrapulmonary disease (aPR = 3.02, 2.60–3.52), normal chest X-ray (aPR = 1.88, 1.63–2.16), and substance use (aPR = 0.80, 0.67–0.97). PZA-poly-resistance (compared to drug-susceptible TB) was associated with age  $\geq$  45 years (aPR = 0.72, 0.56–0.92), Hispanic ethnicity (aPR = 2.49, 1.67–3.71) and Asian race (aPR = 2.68, 1.82–3.96), previous TB diagnosis (aPR = 1.78, 1.15–2.75), and normal chest X-ray (aPR = 1.56, 1.17–2.08). PZA-resistance in MDR-TB cases was associated with female sex (aPR = 1.25, 1.08–1.46) and previous TB diagnosis (aPR = 1.37, 1.16–1.62).

**Conclusions:** Clinicians should be aware that patients with certain characteristics are more likely to have PZA-resistant TB. Predictors identified for PZA resistance likely reflect infection with different species within the *M. tuberculosis* complex (MTBc): PZA-mono-resistant TB conforms to the epidemiology of *M. bovis*, whereas TB resistant to additional drugs reflects *M. tuberculosis*. Although not typically available for initial case management, species identification is important to better understand these findings.

#### PC-829-15 Drug resistance pattern of *Mycobacterium tuberculosis* in Eastern Amhara Region, Ethiopia

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**Background:** Tuberculosis (TB) remains a serious public health problem, worsened by the emergence

and spread of drug resistance particularly multi-drug resistance. Information on drug susceptibility testing of *Mycobacterium tuberculosis* against anti-TB drugs is an important aspect of TB control especially in developing countries like Ethiopia which have a high tuberculosis burden and helps in detection, monitoring and prevention of transmission of resistance strain. so the aim of this study was to assess the magnitude of drug resistance pattern of *M. tuberculosis*, in Eastern Amhara Region, Ethiopia.

**Design/methods:** A cross sectional survey was conducted among new and re-treatment patients (age  $\geq$  18 years old) from September 2010 to February 2011. Sputum digestion and decontamination were carried out by modified petrofe method. Primary isolation and susceptibility were carried out on egg based LJ media using indirect proportion method.  $\chi^2$  and multivariate logistic regression was used.  $P < 0.05$  was statistically significant.

**Results:** Of 230 study participants for DST, 165 were new cases while 65 were previously treated cases. From these, 66.5% of isolates were sensitive and 4.4% resistance to four first line anti-tuberculosis drugs (HRSE) while the remaining 33.5% was resistance to at least for single drug. Among new cases primary drug resistance for one or more drugs was observed in 23.6% (39) cases. Primary MDR-TB was found in 3 (1.81%) cases. Similarly among previously treated cases resistance to any drug was found in 58.5% (38) cases. MDR-TB in previously treated cases was found in 18.46% (12) Cases; the highest being in failure cases 9.23% (6).

**Conclusion and recommendations:** Drug resistance TB is an emerging problem in new and re-treatment patients in our study area. so it is essential to address the problems of drug resistance TB through establishing good control program that encompass timely diagnosis, expansion and improving of DOTS and DOTS plus service to prevent further emergence of resistance strain.

#### PC-830-15 Implementing an electronic system in Nepal to manage data of drug-resistant tuberculosis patients

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**Background and challenges to implementation:** The treatment of drug-resistant tuberculosis (DR-TB) patients started in Nepal in 2005 and has since been rolled-out throughout the country. The decentralized nature of this programme presents challenges to monitor patient detection, enrolment and outcomes effectively. All data are handled on paper.

**Intervention or response:** In 2008, the National Tuberculosis Centre (NTC) successfully used the MDR-TB module of an open-source medical records software—OpenMRS (wiki.openmrs.org)—to enter data on all DR-TB patients placed on treatment. The data requirements for these patients were assessed in 2010 and recommendations made on the best-suited electronic solution. It was decided to keep using OpenMRS. The first phase of the implementation will last 6 months and cover the capital Kathmandu, including the laboratory performing drug-susceptibility testing in the country, and one other Region. Data transmission via cell-phones will be used in three sites in two Regions.

**Results and lessons learnt:** Implementation started in early 2012. NTC staff were trained and assigned duties in data management. Among the challenges which were successfully addressed were the provision of regular power, internet at an affordable price, the establishment of a server and software customization, including adaptation for the Nepalese calendar. Data entered using Open MRS when it had first been piloted in 2008 were transferred to the new version of the MDR-TB module.

**Conclusions and key recommendations:** Putting in place a functional electronic system for DR-TB patients in Nepal has proven to be challenging but feasible. The nationwide roll-out of the system and its extension to cover also drug-susceptible TB patients will depend upon experience gained during the initial implementation and whether additional funding is secured.

#### PC-831-15 Antituberculosis drug resistance in the Adamaoua Region of Cameroon

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**Background:** All tuberculosis diagnostic and treatment centers (DTC) of the Adamaoua Region of Cameroon. The objective was to identify *Mycobacterium tuberculosis* complex strains responsible for pulmonary tuberculosis in the Adamaoua Region and determine the prevalence of initial and acquired resistance to the main anti-tuberculosis drugs.

**Methods:** A total of 509 adults, consecutively admitted to the CDTs with sputum smear-positive pulmonary tuberculosis were systematically studied, sputum specimens collected from each patient were cultured on Löwenstein-Jensen medium. Identification of the cultured strains was based on their cultural aspects and standard biochemical tests. Testing for susceptibility to the major anti-tuberculosis drugs was performed by the indirect proportion method.

**Results:** Growth of *M. tuberculosis* complex strains was obtained from specimens of 445 (87.5%) of the 509 patients; 443 (97.3%) were identified as *M. tuberculosis*, 10 (2.3%) as *M. africanum* and 2 (0.4%) as *M. bovis*. Of the 445 patients with positive cultures, 108 (24.3%) were HIV positive. The overall resistance rate (one or more drugs) was 79% with initial resistance being 7.3% (31/426) and acquired resistance 21.1% (4/19). Initial resistance to isoniazid was the most common (4.2%) followed by streptomycin (3.3%), rifampicin (1.9%) and ethambutol (0.9%). Acquired resistance to isoniazid was 15.8%, to rifampicin 15.8%, and to streptomycin 5.3%. Of the 445 patients with positive cultures, 8 (1.8%) harboured multidrug-resistant (MDR) TB strains. Initial and acquired multidrug resistances were observed in 6 (1.4%) and 2 (10.5%) patients respectively.

**Conclusion:** *M. tuberculosis* is the main *M. tuberculosis* complex strain responsible for pulmonary tuberculosis in the Adamaoua Region of Cameroon. The proportion of resistant tuberculosis in the region is moderately high. This underscores the need for the improvement of the control program in the region by reinforcing the DOTS strategy.

#### PC-832-15 Anti-tuberculosis drug resistance in Tajikistan, 2010–2011

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**Background:** The Central Asian Republics are among the countries with the highest burden of multidrug-resistant tuberculosis (MDR-TB) in the world, yet to date few accurate estimates of the true prevalence MDR-TB are available.

**Objective:** To reliably estimate the national MDR-TB prevalence and describe the most common drug resistance patterns in Tajikistan.

**Methodology:** We conducted a population-based, cross-sectional survey of randomly selected *M. tuberculosis* isolates collected from all sputum smear-positive TB cases registered at all TB units (representative for the entire territory of Tajikistan) from June 2010 to May 2011. Drug susceptibility testing (DST) was conducted for isoniazid, rifampin, ethambutol, streptomycin, pyrazinamide, kanamycin, amikacin, capreomycin, moxifloxacin, and cycloserine. MDR-TB was defined as resistance to at least isoniazid and rifampin. Extensive drug resistance (XDR-TB), a subset of MDR-TB, had further resistance to at least one of three injectable second-line drugs (amikacin, kanamycin, or capreomycin) and fluoroquinolone.

**Results:** Out of a total of 917 cases that were enrolled, 544 (59.3%) were newly diagnosed and 373 (40.7%) were previously treated. Drug resistance to any first-line drugs were found in 419 (45.7%) of the TB cases; 160 (29.5%) among new and 259 (69.2%) among previously treated cases, respectively. Highest resistance rates were found for streptomycin (26.1%: new cases; 59.8%: previously treated) and for isoniazid (16.1%: new; 59.2%: previously treated). The overall MDR-TB rate was 29.2% (12.5% and 53.6% among new and previously treated cases respectively). Among the 368 MDR isolates, 133 (36.1%) were resistant to all first-line drugs, and 19 (5.2%) were XDR-TB.

**Conclusion:** High MDR and XDR-TB rates among TB patients remain a serious problem for TB in Tajikistan. Timely diagnosis and treatment of drug resistance should be one of the priorities of the TB program.

#### PC-833-15 Distribution of MDR-TB strains using molecular biology in the middle district of Taiwan

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**Background:** Primary resistant tuberculosis accounts for 35.2% of all multidrug-resistant tuberculosis (MDR-TB) cases in central Taiwan. Molecular genotyping has been utilized to determine distribution of MDR-TB strains and investigate any undisclosed transmission in the community.

**Design/methods:** All patients in the MDR-TB program from May 2007 to December 2010 were included to undergo molecular genotyping using spoligotyping and Miru-Vntr genotyping. Demographic information was collected and matched with the genotyping results to reveal any connection.

**Results:** A total of 168 MDR-TB patients were investigated and genotyping suggested a noticeable prevalence of the Beijing lineage ( $n = 79$ , 47.0%) followed by Haarlem lineage ( $n = 35$ , 20.8%), U ( $n = 9$ , 5.4%), T1 ( $n = 7$ , 4.2%), East-African Indian 2 Manilla (EAI2 Manila) ( $n = 6$ , 3.6%), T2–T4 ( $n = 3$ , 1.8%), T2 ( $n = 2$ , 1.2%), and Haarlem-like ( $n = 1$ , 0.6%). The remain isolates were undefined and failed to match any spoligotype in the SpoIDB4 database ( $n = 26$ , 15.6%). Patients who were 30 years old or younger comprised the highest (61.5%) ratio carrying Beijing genotype. Haarlemor Haarlem-like strains were found in 7 out of 15 Taiwanese native patients and the Taiwanese native mountain area had a higher proportion of Haarlem strain (35.7%) compared with other counties or cities. Nineteen clusters patterns were discovered and some were shown to have possible contagious transmission.

**Conclusion and recommendations:** Even though the incidence of tuberculosis has declined since the implementation of MDR-TB program and DOTs program, contagious transmission of tuberculosis still exists in the community. Beijing lineage is still the most predominant strain in Taiwan, however, Haarlem or Haarlem-like has a higher distribution among the Taiwanese natives. Future study can be directed to increase molecular genotyping and investigate more close contacts in order to disclose community transmission.

**PC-834-15 Continuous surveillance of *Mycobacterium tuberculosis* drug resistance in Hong Kong, 2001–2010: changes in a mature DOTS environment**

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**Background:** Directly observed treatment short-course chemotherapy (DOTS) has been implemented in Hong Kong since 1987. Survey in year 2000 showed that significant declines in drug resistances (DR) occurred from 1986 to 1999, including multi-drug resistance (MDR) tuberculosis (TB). With easy accessibility of most TB treatment centers and active follow up on all TB patients by the Hong Kong Department of Health, DOTS coverage and quality has been conducted in a very high standard. Continuous effects of 'good DOTS' on different DR rates were assessed in this survey.

**Methods:** Laboratory-based drug susceptibility testing data against streptomycin (S), isoniazid (H), rifampicin (R) and ethambutol (E) from year 2001 to 2010 were analyzed for new and previously treated (PT) patients.

**Results:** Of 37 549 non-duplicate isolates from new TB cases, 3979 (10.6%) were resistant to one or more drugs, 3040 (8.1%) were resistant to S, 1758 (4.7%) to H, 182 (0.5%) to E and 265 (0.7%) were MDR. Of 1935 isolates from PT patients, 447 (23.1%) were resistant to one or more drugs, 304 (15.7%) were resistant to S, 317 (16.4%) to H, 114 (5.9%) to E and 161 (8.3%) were MDR. MDR for PT cases was kept well below 10% in most years with a minimum of 5.3%. Compared with previous 1986–1999 data, resistance rates for all drugs in both new and PT cases, followed the previous slow declining trend and reached their minimum at around 2006 to 2008. However, for new cases: S, H and MDR resistance rates increased slightly in 2009 and 2010 while MDR rate (%) showed apparent slight increase from 2007 to 2010 were 0.5, 0.6, 1.0 and 1.0 respectively.

**Conclusion:** The overall low drug resistance rate, especially low MDR rate amongst PT cases confirmed the ability of 'good DOTS' in controlling drug resistance. However, in an area of high population flow

between TB endemic neighborhood of high drug resistances, the recent changing trend MDR rate in new cases requires prudent monitoring.

**PC-835-15 The surveillance of drug-resistant tuberculosis in Tak Province, Thailand, 2008–2010**

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**Aim:** The existence of multi-drug resistant tuberculosis (MDR-TB) has become a serious problem in Tak Province. The province's proximity to Myanmar and the regular movement of workers across the border between the two countries has contributed greatly to the problem. Increased knowledge of the situation and understanding of the trends of MDR-TB will greatly reduce the spread of the disease.

**Method:** This is a retrospective study of MDR-TB in Tak; the results of drug susceptibility testing (DST) for four drugs (isoniazid [INH], rifampicin [RFM], streptomycin [SM], and ethambutol [EMB]) from 1834 specimens collected in the province were assessed. The specimens were collected between 2008 and 2010 from a total of 13 agencies as follows: government hospitals (1102), private hospitals (46), and non-governmental organizations (686). Testing of all specimens was conducted at the National Tuberculosis Reference Laboratory (NTRL) located at the Tuberculosis Bureau in Bangkok.

**Result:** We identified 352 drug-resistant specimens from the original sample of 1834 (19.1%) and 162 poly-drug resistant specimens. Analysis of the data indicates that 106 patients (5.78%) had contracted multi-drug resistant TB; 17 patients (0.92%) were Thai and 89 (4.85%) were non-Thai. Mae-sot Hospital reported the majority of patients, followed by Médecins Sans Frontières (MSF), and TaksinMaharaj Hospital.

**Conclusion:** Our data suggests that the existence of multi-drug resistant tuberculosis in Thailand indicates a weakness of the national TB control program. We have also observed a failure in the quality of treatment of TB patients. These issues indicate a need for multidisciplinary collaboration to rectify the problem in Tak with an ultimate goal of applying the methods developed to minimize the effects of TB in Thailand for Thai and non-Thai patients.

**PC-836-15 Incidence of multidrug resistance in *Mycobacterium tuberculosis* patients, ongoing tuberculosis and trypanosomiasis research project in Lusaka, Zambia**

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**Background:** WHO estimated that the number of multidrug-resistant (MDR) TB cases in the world in 2010 was up to 650 000 out of 12 million prevalent TB cases (5.4%). According to the Zambia National TB Program, a total of 59 (1.2%) out of 4800 TB cases were MDR-TB in 2008, but extensively drug-resistant (XDR) TB cases have never been reported in Zambia.

**Design/methods:** Sputum samples were collected at the chest clinic in University Teaching Hospital (UTH). Two hundred forty-eight suspected TB patients submitted 1–3 sputum samples with informed consent and provided the following information: age, gender, education level, period of coughing, TB history, and HIV status. All the collected samples were examined using fluorescent microscope, MGIT culture, ID test and MGIT DST if ID test result was positive.

**Results:** The TB-ID test results were positive for 91 patients (36.7%). Three out of 91 patients (3.3%) had MDR-TB according to MGIT-DST results. Among the 3 MDR-TB patients, 1 was resistant to 2 drugs (INH and RMP), 1 was resistant to 3 drugs (INH, RMP and EMB), and 1 was resistant to 4 drugs (SM, INH, RMP, EMB).

**Conclusions:** The results of this ongoing study produced a higher than expected rate of MDR-TB cases in UTH although this could be due to the higher relapse rate (26.9%) among the patients with positive TB-ID tests. It also demonstrates the possibility of the existence of XDR-TB in Zambia. Establishing a facility in the country where routine second-line drug susceptibility tests can be conducted would prepare it for that possibility.

**PC-837-15 Multidrug-resistant tuberculosis in Somalia: results of a nationwide survey**

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**Background:** In Somalia, the prevalence of resistance to both rifampicin and isoniazid (multidrug-resistance; MDR-TB) among tuberculosis (TB) patients has not

been documented from past surveys. To better plan for future needs, the National TB Programme decided to undertake a first-ever direct measurement of drug-resistance prevalence among a representative sample of TB patients presenting for care.

**Methods:** A nationwide survey of pulmonary sputum smear positive TB cases from all three zones in the country was completed between March 2010 and October 2011. Sputum samples were tested at an overseas accredited laboratory for resistance to rifampicin and isoniazid using Genotype MTBDRPlus and liquid culture.

**Results:** A total of 946 patients were enrolled, of whom 96 had no results for drug-susceptibility testing. Among the 754 new and 96 previously treated cases retained in the analysis, the male to female ratio was 2.4:1 and median age was 30 years (range: 4–86 yrs). Resistance to isoniazid occurred in 12% of new and 55% of retreated cases. A total of 87 MDR-TB cases were detected by the survey. After weighting using data on TB cases notified in 2010, MDR-TB was estimated to occur in 5% of new (95%CI 2.7%–7.7%) and 41% of retreated cases (95%CI 23.3%–58.1%). TB cases from the south-central zones had higher likelihood of being MDR-TB.

**Conclusion:** The survey in Somalia showed high levels of MDR-TB compared to other countries in the region and in the African continent. Resistance was higher in those areas most affected by the volatile security situation. At the levels of resistance observed in this survey, one would expect that among pulmonary TB cases notified in Somalia in 2011, over 750 patients had MDR-TB detectable on sputum testing. The revised estimate will help the country measure better the TB caseload requiring drug-susceptibility testing, second-line medication, hospitalization, and their associated costs.

**PC-838-15 Increased burden of multidrug-resistant tuberculosis in Egypt: results of the anti-tuberculosis drug resistance survey, 2011**

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**Background:** The first anti-tuberculosis (TB) drug resistance survey conducted in Egypt in 2002 reported a prevalence of multidrug-resistant TB (MDR-TB) of 2.2% (95%CI 1.2–3.7) among new and 38% (95%CI 32–45) in retreated TB patients. A second survey was conducted in 2011 to assess the burden and time trends of MDR-TB.

**Design/methods:** A representative sample of new smear positive TB patients notified in 2011 was enrolled using probability proportionate to size sampling technique. All notified previously treated patients were enrolled. Sputum specimens were subjected to conventional culture and drug susceptibility testing (DST). Logistic regression analysis was carried out using STATA11 with adjustment for cluster design, sampling weight and imputation of missing values.

**Results:** Of the 1685 patients enrolled, 1198 (73.2%) were male. 1417 (84.1%) had positive culture and available DST results, 1047 (73.9%) were new and 370 (26.1%) retreated. The prevalence of MDR-TB was 3.4% (95%CI: 1.9–4.9) in new and 32.1% (95%CI: 24.4–39.9) in retreated cases. MDR-TB was detected in 66% of chronic cases, 37.2% of retreated after failure, 31.8% of relapsed cases, and 18.9% of retreated after default ( $P < 0.05$ ). The pattern of mono-drug resistance among new cases was: rifampicin (14.8%), isoniazid (10.8%), streptomycin (21.0%), ethambutol (2.6%).

**Conclusion and recommendations:** The prevalence of MDR-TB has increased in 2011 compared to the baseline in 2002, but not statistically significant. Strong measures should be taken to ensure adherence to treatment guidelines by private healthcare providers, and limit the sale of anti-TB drugs in the private pharmacies to prescribed medications.

#### PC-839-15 A nationwide survey of multidrug resistance among tuberculosis patients in Tunisia, 2011–2012

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**Background:** In Tunisia, the prevalence of resistance to both rifampicin and isoniazid (multidrug-resistance; MDR-TB) among tuberculosis (TB) patients was measured once in 2002 in a survey covering only part of the country. The National TB Programme executed a nationwide survey in 2011–2012 to derive a nationally representative estimate of MDR-TB prevalence.

**Methods:** The nationwide survey targeted TB patients cared for within the public health services, which are free of charge and which treat the majority of TB patients. A sample size of 570 cases (new and previously treated) was calculated based on an expected prevalence of 1.2% MDR-TB among new cases (95% confidence limits: 0.5%–1.9%). All new and retreated

sputum smear positive TB cases diagnosed during the study period were eligible for inclusion; cases who were sputum smear negative, extra-pulmonary, had already completed  $\geq 4$  weeks of treatment, and who had non-TB mycobacterial isolates were excluded. Sputum samples were tested by the National Reference Laboratory (NRL) for resistance to rifampicin and isoniazid using Löwenstein-Jensen media and molecular techniques (Genotype MTBDRPlus). All confirmed MDR-TB cases had drug-susceptibility testing (DST) to a fluoroquinolone and a second-line injectable agent performed.

**Results:** The survey started in August 2011, using 100% consecutive enrolment of eligible study subjects from the public sector TB treatment sites located in all of the country's 24 governorates. Sixty-four peripheral microscopy laboratories sent all their positive sputum samples to the NRL and another central laboratory for DST. DST quality assurance was performed by the supranational reference laboratory in Italy. To date, 504 cases have been recruited and 261 DSTs completed.

**Conclusion:** The survey in Tunisia will provide a national estimate of the prevalence of MDR-TB in TB patients and allow the study of associated risk factors. This will help to plan the expected needs for TB patient care and treatment.

#### PC-840-15 Improving drug-resistant tuberculosis surveillance in Nyanza, Province, Kenya

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**Background:** Drug-resistant tuberculosis (DR-TB) threatens to reverse gains Kenya has made to achieve WHO TB control targets. The national policy for DR-TB surveillance is to perform TB culture and drug susceptibility testing (TBC-DST) on sputum specimens for all re-treatments and treatment failures. Nyanza Province, a high TB burden setting, registered low TBC-DST coverage of 30% and 50% in 2008 and 2009, respectively. We report program interventions that led to improved DR-TB surveillance in this region.

**Interventions:** In 2010, ICAP Columbia University, a US Centers for Disease Control and Prevention partner, used routinely collected data to establish baseline TBC-DST coverage in 7 districts in Nyanza province. Technical assistance was provided to the Ministry of Health to identify obstacles to TBC-DST coverage during routine mentorship. Based on findings, ICAP engaged with TB and laboratory coordinators to provide refresher training, staff mentorship and sample

collection and packaging. Uninterrupted supply of culture bottles and improved sputum transport networks were established with the Central Reference Laboratory (CRL). To aid tracking results, a culture logbook was developed to improve documentation and communication with the CRL.

**Results:** Obstacles accounting for low baseline TBC-DST coverage included lack of culture bottles, inadequate staff orientation, poor documentation and communication with CRL. The TBC-DST coverage across the 7 districts improved from a mean of 63% (Rarieda 46%, Bondo 56%, Ugenya 66%, Gem 60%, Siaya 50%, Nyakach 63% and Nyando 100%) between July and September 2010 to 93% (Nyakach 94%, Gem 78%, Ugenya 88%, Bondo 91%, Rarieda 100%, Siaya 100%, Nyando 100%) over the same period in 2011.

**Conclusion:** The simple intervention of addressing logistical obstacles led to improved DR-TB surveillance. Continued staff mentorship, uninterrupted supply of commodities and MOH ownership are essential to sustaining improved DR-TB surveillance.

#### **PC-841-15 Scale-up of an electronic medical record system linked to mobile phone-based DOT for MDR-TB management in Sindh and Balochistan Provinces, Pakistan**

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**Background:** The Indus Hospital TB Control Program began treating drug-resistant tuberculosis (DR-TB) patients in 2007. Patient data were initially stored across paper records, Microsoft Excel files, and an older version of the open-source electronic medical record system OpenMRS. No single database allowed for managing patient treatment or for generating automated reports.

**Intervention:** We piloted the OpenMRS MDR-TB module during 2009 linked through a module we designed to enable collection of directly observed therapy (DOT) data by treatment supporters during home visits using mobile phones. We designed scripts to import legacy data into a newer version of OpenMRS from multiple databases and Excel sheets. The implementation consisted of three phases: data import and testing, integration of data collection through mobile phones for directly observed therapy, and expansion to two new treatment sites outside of Karachi.

**Results:** The expansion phase started in 2011, with program staff consulted extensively during the data import phase and trained in using the new OpenMRS MDR-TB module and our phone-based DOT system. We addressed multiple challenges, including

programming custom software to import legacy data directly into the new OpenMRS database, setting-up a dedicated server accessed by multiple remote sites, and providing reliable local power and internet connectivity.

**Conclusions:** The implementation of an electronic medical record system linked to mobile phones for treatment supporters of DR-TB patients in Sindh and Balochistan has been challenging but successful. The procedures followed and the software tools developed will facilitate rapid expansion to additional sites.

#### **PC-842-15 Evaluation of an MDR-TB data system in the State of Sao Paulo, Brazil, over nine years**

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**Background:** Multidrug resistance is a biological phenomenon resulting from inadequate treatments either by irregular drug intake or due to low potency therapeutic schedules. Drug resistance is escalating worldwide in the latest years, claiming for attention and effective measures for its monitoring and control. In 2000, the Brazilian Health Ministry introduced, a National System of Epidemiological Surveillance of Multidrug-resistant TB Resistance (MDR-TB), with the health care units generating information from notification and follow-up of MDR-TB cases. A standardized therapeutic schedule including amikacin, ethambutol, a quinolone, terizidone and pyrazinamide was also proposed.

**Intervention:** Study of clinical and epidemiological characteristics of cases notified and followed up in the MDR-TB system during the 2000–2009 period in the State of Sao Paulo, Brazil. Discovery of cases of resistance to isoniazide, rifampin and/or other drug resistances, according to susceptibility test results. All cases originated from MDR-TB reference centers in the State of Sao Paulo.

**Results:** During the 2000–2009 period, 762 cases were notified and started treatment, 509 (66.8%) of which were male and 82 (10.8%) were HIV+. The examined case contacts that developed disease were 15 (7.8%). The lower cover DOT was 52.4%. Regarding co-morbidities, stood alcoholism and diabetes. Treatment outcomes showed that mortality rates were very high, varying from 5 (7.7%) in 2000 to 11 (10.3% in 2009 while cure rates were low, between 30 (4.6%) in 2000 and 54 (50.5%) in 2009.

**Conclusions:** These results strongly highlight the necessity of diagnosis and susceptibility testing for early resistance identification and treatment supervision.

**Recommendation:** Strengthen surveillance over MDR-TB cases.

## TUBERCULOSIS MANAGEMENT: FOOD SECURITY AND COMMUNITY ISSUES

### PC-868-15 Identifying effective health education channels for tuberculosis control by community participation in rural and urban areas of Myanmar

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**Background:** Advocacy, Communication and Social Mobilization (ACSM) has an important role in the control of TB which is a major public health problem in Myanmar. It is necessary to identify ACSM strategies by involvement of local community.

**Objectives:** The study aims to identify effective health education channels for TB control according to different geographical regions in Myanmar.

**Methods:** Face-to-face interviews were conducted with 7519 community members in 50 townships. Preferable and effective methods for health education and their reasons were explored by 28 focus group discussions (FGDs) and pair wise ranking in rural and urban area of seven regions/states in Myanmar.

**Results:** About 93.9% have heard about TB and 45.9% heard about DOTS. The most common source of information about TB was from family members and friends (55.6%), television (TV) and video (45%), health workers (25.2%), and radio (17.9%) respectively. However, qualitative findings from FGDs showed TV was the least effective since majority did not watch TV. Survey findings showed 60.5% of community preferred health education talk although it had some limitations such as most men did not attend and less opportunity to ask questions. Majority of participants especially in rural areas of states highlighted that radio broadcasting through FM in the local language became popular and accessible for general public. It was suggested as the most practical way to disseminate health messages particularly for ethnic groups in rural areas.

**Conclusion:** The findings from this study were incorporated for developing ACSM tools and intensifying ACSM strategies for TB control in Myanmar.

### PC-869-15 Scaling up community DOTS for early detection and treatment of tuberculosis

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**Background:** In Cambodia, Community DOTS is a key component of the national TB programme (NTP), promoted as a means to improve access to TB services by engaging services of community volunteers to identify and refer TB suspects and ensure direct observation of treatment (DOT) close to the patient's homes.

**Intervention:** Starting in early 2009, the Health and Development Alliance implemented a project for scaling up community DOTS in 7 operational health districts of Kampong Chhnang and Prey Veng provinces covering a population of 1 155 907 people, 93 health centers and 1301 villages. Activities focused on key priorities of the NTP—to prevent multi-drug resistant TB through early detection and treatment under DOT; counseling and referrals of TB patients for HIV test; addressing vulnerable groups, especially children through contact tracing; implementing advocacy, communication and social mobilization through village awareness campaign and world TB day events; and building capacity through trainings, technical assistance and supervision of the project sites.

**Results:** From 2009 to 2011, community DOT watchers (DW) identified and successfully referred 23 233 TB suspects to the public health facilities. As a result of these referrals, 6793 new TB cases (all forms) were diagnosed, including 2829 new smear positive pulmonary TB cases. Community volunteers served as DOT watchers for 53% (3582/6793) of all registered patients. 96% of patients served by community volunteers completed their treatment successfully. 81% (5491/6793) of registered TB patients referred were tested for HIV.

**Conclusions and key recommendations:** Community volunteers play an important role in TB case finding, and are able to achieve high treatment success rates. Community DOTS project should be scaled up as a means to improve access for TB services.

### PC-870-15 Beyond drugs: tuberculosis patients in Bangladesh need urgent attention for nutrition support during convalescence

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**Background:** The study explored the nutritional status of TB patients in Bangladesh before, at two months, and after completion of TB treatment and the mean changes in body mass index (BMI) over the treatment period.

**Design/methods:** The study included 1066 TB patients at 10 DOTS centres from May 2009 to April 2010. The information on age, sex, duration of symptoms, TB types, school education, etc. were collected before treatment. The nutritional status indicators (weight in kg, height in cm, and mid upper arm circumference in cm (MUAC) were measured before

starting treatment from TB patients ( $n = 1066$ ) and healthy control ( $n = 910$ ). The measurements of patients were repeated at two months and after completion of treatment. BMI (calculated as wt (kg)/height  $m^2$ )  $< 18.5$   $kg/m^2$  and MUAC  $< 22.0$  cm were defined as malnutrition.

**Results:** About two-third of TB patients (67%) had low BMI ( $< 18.5$   $kg/m^2$ ) before starting TB treatment, whereas it was 23% among healthy control. At the end of treatment, half of patients (49.9%) had still low BMI. Among them, 12% had severe malnutrition (BMI  $\leq 16$   $kg/m^2$ ). We also found that the MUAC  $< 22.0$  cm was the highest among the patients before (42%), after two months (39%), and at the end of (34%) treatment compared to control group (9%). Poverty and lack of knowledge were identified as major barriers in accessing adequate food during treatment period.

**Conclusion and recommendations:** The study strongly suggests incorporating food supplementation intervention in TB control in Bangladesh to reduce the risk of mortality and morbidity from malnutrition in TB patients.

#### PC-871-15 Ultimate results of tuberculosis standard chemotherapy regimens depending on drug resistance patterns

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**Objective:** Study ultimate TB standard regimens chemotherapy results among 3187 pulmonary TB patients in dependence of drug resistance patterns.

**Materials and methods:** Retrospective cohort study of chemotherapy regimens results among 2733 new TB patients and among 454 patients with TB relapse from 5 Russian Federation regions was implemented. Patients were grouped according to their prescribed starting treatment regimen before receiving individual DST results by a method of absolute concentrations: 2448 new TB patients were treated by a 1st regimen (1st line drugs) and 285—by 2B regimen (combination of 1st and 2nd line drugs). 327 patients with TB relapse were treated by a 2nd regimen (1st line drugs) and 127—by 2B regimen. In 2–3 months after the beginning of chemotherapy regimens were corrected according to DST results. Ultimate results were assessed in 2–3 years after the beginning of chemotherapy. Ultimate result was considered favorable under stable cease of bacterioexcretion, confirmed by culture method and non active TB process according to X-ray and clinical data.

**Results:** Under drug sensitivity of *M. tuberculosis*

the share of patients with favorable ultimate results was 92.2% with 1st line drugs (1st and 2nd regimens) and 86.9%—with 2B regimen,  $P > 0.05$ . Patients with formerly mono- and polyresistant to isoniazid or rifampicin had favorable ultimate result in 90.4% of cases with 1st line drugs (1st and 2nd regimens) and 58.7%—with 2B regimen,  $P < 0.05$ . Patients with former MDR-TB who had favorable ultimate result were observed in 57.3% of cases and 34.7% correspondingly,  $P < 0.05$ . Amplification of drug resistance of *M. tuberculosis* was observed among 23.6% (35 out of 148) of patients treated by a 1st line drugs (1st and 2nd regimens) and having repeated DST results and 45.6% (31 out of 68),  $P < 0.05$ , treated by 2B regimen.

**Conclusion:** Efficacy of treatment among TB patients with drug sensitivity of *M. tuberculosis* is rather high and does not depend on a prescribed regimen. In case of drug resistance to isoniazid and/or rifampicin efficacy of treatment is decreasing as a result of amplification of drug resistance during the period of chemotherapy especially when combination of 1st and 2nd line drugs is prescribed.

#### PC-872-15 Comparison of nutritional status and food diversification level of tuberculosis patients and healthy adults in a rural area of China

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**Background:** Dietary nutrition can affect the development and prognosis of pulmonary tuberculosis (PTB), this article surveyed the dietary nutrients intake condition of PTB patients in order to provide a scientific basis for diet nutritional guidance and health promotion to PTB patients.

**Design/methods:** 1955 patients with PTB in rural areas in China were selected as the case group with 1955 healthy people as the control. FFQ (food frequency questionnaire) was used to investigate the consumption of food types and the recall method of 24-hour food intake was used to collect the dietary intake level of different nutrients. Dietary Diversity (9 kinds of food) Score (DDS) was used to evaluate the dietary diversity level.  $\chi^2$  test and the Student's *t*-test were used to analyze the difference between the two groups.

**Results:** The daily energy and protein intakes of PTB patients were 1712 kcal and 65.73 g separately, which were significantly lower than those in the control population ( $P < 0.001$ ); the intake of retinol and calcium in PTB patients were 320.59  $\mu g$  retinol

equivalent (RE) and 295.69 mg, only 40.08% and 36.96% of the RNIs (recommended nutrient intakes), which were significantly lower than those in the control group ( $P < 0.0001$ ). DDS result showed that 5.78% of PTB patients got 3 points (meaning three categories of food consumed), which was significantly higher than that in the control group (2.66%); 2.10% of PTB patients only got 2 points, also significantly higher than that in the control group (1.18%).

**Conclusions and recommendations:** Energy and nutrients intake of PTB patients were lower than those in the healthy population, especially for protein, retinol and calcium. As compared to the RNIs, inadequate intake existed in PTB and the healthy population. Dietary imbalance condition in PTB patients was more severe. Dietary education should be carried out in rural areas, especially in PTB patients.

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#### PC-873-15 Tuberculosis among HIV-infected persons in the country of Georgia

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**Objective:** We sought to evaluate rates of tuberculosis (TB) and estimate risk factors, including TB, for mortality among HIV patients in the country of Georgia.

**Methods:** Retrospective cohort study among newly diagnosed HIV patients entering clinical care at the National AIDS Center in Tbilisi, Georgia, between 1/2008 and 6/2009. Clinical data and laboratory information was obtained from medical records through 6/2011. A case was considered as having TB if there was culture confirmation and/or compatible clinical findings. Risk factors for mortality were assessed utilizing Cox proportional hazards model.

**Results:** 410 HIV-infected patients were included (71% male; mean age 40 years; average CD4 count 293 cells/ $\mu$ l). TB was the presenting opportunistic infection in 110 (27%); 91 pulmonary and 19 extrapulmonary. The mean baseline CD4 count was significantly lower in HIV-TB patients as compared to HIV patients without TB (157 vs. 340 cells/ $\mu$ l,  $P = < 0.05$ ). ART was initiated in 93 of 110 (85%) HIV-TB co-infected patients. There was a significantly higher risk of death among HIV-TB patients who never received or started ART  $> 2$  months after TB diagnosis compared to patients initiating ART within 2 months (HR 2.6 95%CI 1.03–6.75). Survival rates at 1 and

2 years after TB diagnosis were 77% and 75% in HIV-TB patients starting ART at any time compared to 15% and 0% in patients never receiving ART (log rank test,  $P < 0.05$ ). During follow up of the entire cohort (777 person-years), 4 new cases of TB were diagnosed for a TB incidence rate of 500/100000 person-years (95%CI 101–1200). After adjusting for covariates, initial presentation with TB was significantly associated with mortality among the whole cohort (HR 3.6 95%CI 2.02–6.52).

**Conclusion:** We found high TB prevalence and incidence rates among newly diagnosed HIV-infected persons in Georgia. Our findings confirm that the use of ART may help decrease mortality among co-infected patients.

#### PC-874-15 Characteristics and treatment outcomes of tuberculosis treatment defaulters legally compelled to undergo tuberculosis treatment in Singapore

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**Background:** Singapore has, since 2004, used the Infectious Diseases Act (IDA) to compel recalcitrant TB treatment defaulters to undergo directly observed therapy (DOT) until a successful outcome is reached. **Methods:** TB is a notifiable disease in Singapore. Data from the national notification registry of Singaporeans/permanent residents with pulmonary TB (pTB) notified between January 2004 and December 2008 was used for this study. Selected characteristics of patients for whom legal intervention was pursued was compared with the rest of the notified cohort to identify risk factors for recalcitrant defaulting. The treatment outcomes for these patients are also reported.

**Results:** 6124 pTB cases started TB treatment during the study period. Legal intervention was pursued in 135 (2.2%). Of these, 3.8% did not return for treatment despite being served the IDA, 80.5% completed treatment (of whom 55% completed within 9 months of being served the IDA), 5.3% died, 0.8% stopped treatment due to drug reaction and 9.8% were lost to follow-up. Persons for whom legal intervention was pursued were significantly more likely to be male, local-born, non-Chinese, single or divorced, living in 1–2 room public housing, and to have previous TB ( $P < 0.05$ ).

**Conclusion:** While legal intervention had worked for some, a significant minority did not return for treatment, defaulted after resuming treatment, or took longer than expected to reach completion. Further analysis will be done to describe the profile of these

highly recalcitrant defaulters, and to determine the underlying causes for their continued default despite legal intervention.

### PC-875-15 Identifying populations at risk for tuberculosis: policy and research gaps for care and control in Japan

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**Background:** Identifying populations at risk for tuberculosis (TB) has important implication to guide TB control and public health measures. Japan, a country with low HIV (0.02%) and middle-level TB prevalence had 23 261 TB cases or 19/100 000 notification in 2010. We studied clinical and social risk groups in Japan in terms of the size of and TB magnitude in the risk groups, and problems in TB care, current policy and research gaps in each risk group.

**Design/methods:** Fifteen TB-risk groups were identi-

**Table** List of populations at risk for TB in Japan: size, TB magnitude reported by TB surveillance, published and non-published literatures

Population at risk for TB and size in Japan	Magnitude of TB in risk group or magnitude of risk group in TB in Japan	
	TB surveillance data (2007–2010) N = 23261 - 25311	Data from literatures or other data-base
<b>HIV/AIDS</b> HIV=13667 AIDS=6266 (2011)	HIV in TB = 0.22–0.23%	TB in HIV = 6%
<b>Diabetes (DM)</b> 2,300,000 (2008)	DM in TB = 12.6– 13.3%	DM in TB = 14– 42.9%
<b>Rheumatoid arthritis (RA)</b> -336,000 (on treatment)	N/A	TB in RA = 0.3% and 9.6% RR = 3.21 (95%CI 1.21–8.55)
<b>Dialysis</b> 297,126 (2010)	N/A	Dialysis in TB = 1.3% TB in dialysis = 5%
<b>Gastrectomy</b> N/A	N/A	Gastrectomy in TB = 8.4 and 9.1% 3.8 times risk
<b>Mental illness</b> 3,233,000 (2008)	N/A	<ul style="list-style-type: none"> <li>Active TB = 0.13% (TB screening for 3194 psychiatric patients)</li> <li>TB incidence in schizophrenia = 26 and 140/100,000</li> <li>Homeless TB patients with mental problem = 15.6%</li> </ul>
<b>Malnutrition</b> (age > 20) BMI<18.5% men 4.6% women = 11% (2010)	N/A	TB patients with malnutrition = 69 – 100%
<b>Smokers</b> Men 32% Women 8.4% (2010)	N/A	TB patients with smoking = 14.5 – 69.2%
<b>Alcohol over consumption</b> Men 35.4% women = 6.9% (2010)	N/A	<ul style="list-style-type: none"> <li>TB patients with heavy alcohol = 38.8%–100%</li> <li>Alcohol is a risk factor for MDR-TB OR = 15.0(95%CI 2.34–96.1)</li> </ul>
<b>Elderly</b> >65 years ~ 28,980,000 (2010)	TB patients age > 65 years = 61.5 - 66.8%	N/A
<b>Children &lt; 5</b> 5,378,000 (2010)	TB patients age < 5 years = 0.13 - 0.19%	N/A
<b>Household and close Contact</b> (2010) 52,000 were screened for TB	TB in close contact = 0.8% (404/52,000)	<ul style="list-style-type: none"> <li>TB in household contacts = 1 - 4.8%</li> </ul>
<b>Prisoners</b> 74,232 (2010)	N/A	TB in prisoners: Sentenced = 1.1% (N = 15,634) Un sentenced = 3.5% (N = 774)
<b>Homeless</b> 10,890 (2011)	Homeless in TB = 1.2 – 1.4%	<ul style="list-style-type: none"> <li>TB screening in homeless - active TB 1.5% TB infection 50%</li> <li>-20-50 times risk</li> </ul>
<b>Foreigners</b> Entered Japan 9,443,696 Over stayed 78,488 (2011)	Foreigners in TB = 3.3 – 4.1%	<ul style="list-style-type: none"> <li>Active TB= 0.7% (TB screening for 2,370 migrant workers)</li> <li>Active TB = 0.2-0.5% (TB screening for students from language schools)</li> </ul>

**Note:** N/A=data not available. 2011 Population size in Japan = 126 million

fied for comprehensive review. We obtained data by analyzing TB surveillance, reviewing the literatures, policy and guidelines cited by PubMed, Ichushi-database, and international and Japanese professional organizations websites. A structured-review form was used to extract data from the literatures.

**Result:** Most research were hospital-based, observational studies employing medical record reviews, which provided limited evidences to compare with international risk magnitude. The Table shows elderly accounted for more than 60% of TB cases or 79/100 000 incidence, while incidence in young children under five-years was 0.6/100 000. Among the clinical risk groups, diabetes accounted for the highest proportion. For social risk groups, homeless had the highest incidence. Compare to Japanese TB patients, foreigners have higher proportions of drug resistance and TB in HIV-positive persons. There are pros and cons regarding universal BCG vaccination for infants in Japan. Professional societies including those of diabetes, nutrition, anti-alcohol and smoking organizations have not engaged in TB care and control. Several guidelines for risk groups are available, however state of implementation is not well studied.

**Conclusion and recommendation:** The high risk groups for TB in Japan are similar to those identified in other high-income countries, except the great proportion of the elderly. TB program needs to collaborate with other professional societies to reduce risks of TB.

### PC-876-15 Innovative community-based tuberculosis control interventions improved access, tuberculosis case notification and treatment outcome in southern Ethiopia

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**Background and challenges:** TB Control Program in Ethiopia uses passive case-finding to detect and treat TB cases. Notified cases remain low despite decentralization of services to health facility level. Geographic, socioeconomic and cultural barriers limit service access.

**Intervention:** An innovative community-based TB control intervention was implemented in Sidama zone. The package included advocacy, engaging stakeholders, communities and female Health Extension workers (HEWs) in TB control activities and training of staff. HEWs conduct house-to-house visits, identify TB suspects, collect sputum samples and prepare/fix smears. HEWs contact supervisors by phone to transport smears for microscopy. Supervisors

initiate treatment for confirmed cases (PTB+) in their community, screen contacts and initiate isoniazid (IPT) for asymptomatic children. Results were compared with that of the pre-project period and a control zone.

**Results and lessons learnt:** 1048 HEWs and 300 staff received training. Between October 2010 and December 2011, HEWs screened 49 857 TB suspects (60% women) and 2262 (4.5%) PTB+ cases (53% women) initiated treatment at community level. A total of 5090 cases with PTB+ and 7071 with all forms of TB were diagnosed in the zone and PTB+ case notification increased from 64 to 127/105 pop. 8005 contacts were visited, 897 symptomatic cases were screened of which 69 (7%) had TB. 1080 children age <5 years received IPT. Treatment success rate increased from 80% to 94% and defaulter rate decreased from 10% to 2% compared to the pre-project period.

**Conclusions and key recommendation:** The project decentralized TB diagnostic and treatment services to communities making them accessible to the poor, women and children. The interventions doubled TB case notification in the first year, improved treatment outcome and scaled-up contact tracing and IPT provision. This innovative approach could be implemented in resource constrained settings to maximize impact of TB control efforts.

#### PC-877-15 Active case finding by community health workers in one priority city for tuberculosis control: Ribeirão Preto, Brazil

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**Aim:** To analyze the active case finding (ACF) of tuberculosis (TB) according to Community Health Workers (CHW) perspective in one priority city for TB control.

**Methods:** Descriptive study conducted in 2009 using secondary data and an observational and structured questionnaire applied to 105 CHW. Indicators of structure, process and result were developed from the proportions of the items observed and from the mean scores of respondents' answers to items which contained Likert scale response. Indicators were assessed as unsatisfactory (values close to 1 and 2), regular (near 3) and satisfactory (near 4 and 5).

**Results:** According to observational forms, weaknesses in the structure of health services for the TB suspect case search were identified: lack of form for registering identification of TB suspects (42.6%), lack of professionals for patients care (30.7%), as well as for ACF and routine assistance for suspected cases

(38.5%). In the CHW inquiry, satisfactory scores have been identified related to training and prepare for TB control. There are weaknesses in detecting of cough during home visits and providing sputum pot in the territory, although scores have been found satisfactory for ACF in the community and into health services, as well as in the investigation of suspected cases from the index cases. We also identified weaknesses in partnerships with the community to ACF. The analysis of estimated TB suspect cases in the city showed that, only 6.2% of this population was examined with sputum smear.

**Conclusion:** The CHW work process brings out a reflection on their role as partners in tuberculosis control. Weaknesses were found in the structure of health services, which may have resulted in poor performance of the CHW for the ACF. The work also highlighted the need for an innovative work process capable of intervention on the real health problems of the community, improving permanent education actions and intersectoral coordination to increase case detection.

#### PC-878-15 Tuberculosis control in primary health care in Natal, Brazil: community health agents' perceptions

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**Background:** The community health agent (CHA) is a fundamental social actor for tuberculosis (TB) control strategies. The aim of the study is to analyze the attainment of active case finding (ACF) for TB, according to the CHAs' perception.

**Methods:** Cross-sectional study, conducted in Natal, Brazil, from June to September 2009, with 646 CHAs. The sample calculation was based on proportional division according to the number of CHAs by sanitary district and simple casual sampling was made. Data was collected using a questionnaire applied for CHA and formatted into three sections of health care evaluative components: structure, process and result. Each question was answered according to dichotomous, multiple answers and Likert scale (from 1 to 5) ranging. To analyze the scores observed, results from 1 to 2 were set as unsatisfactory, 3 as regular and 4 to 5 as satisfactory.

**Results:** Most CHAs were female, with an intermediate education level and employed at the health centers for an average of 122 ( $\pm 47.4$ ) months. The CHA assessed work in the community as good, wages as regular, and reported TB training always or almost always present. In the structure component, health

centers met satisfying conditions regarding register forms (mean = 4.90) and sputum pot (mean = 4.25) availability, despite some shortages (rated as regular) in refrigerators or thermal boxes (mean = 3.73) for storing the collected material. The CHA's sense of preparedness to identify a TB suspect (mean = 4.4), to give orientations about TB (4.7) and about sputum smear testing (mean = 4.2) were assessed as satisfactory, however, in many occasions they don't suspect cough as a TB symptom (mean = 3.4). Process component was rated as unsatisfactory (mean = 2.7), mainly for lack of performing sputum smear test to the patient (mean = 2.2). Only 11% of expected sputum smears tests were requested.

**Conclusions:** The performance of ACF is a complex action once it involves CHA training, health centers structure and organization.

#### **PC-879-15 Meeting DOTS implementation needs: developing a tool to ensure local success**

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**Background and challenges:** WHO reports that in 2010, 4% of new and 21% of retreatment cases were MDR-TB. While the National Center for Disease Prevention and Control released the Philippine Plan of Action to Control Tuberculosis (PhilPACT) in November 2010, tools to ensure implementation were needed.

**Intervention and response:** The DOTS Compliance and Assessment Tool (DCAT) was developed to facilitate uptake of PhilPACT, ensure TB control, and assess DOTS compliance within Local Government Units (LGUs). DCAT development included setting objectively verifiable indicators (OVIs) with the Department of Health National TB Program (DOH-NTP) and USAIDS TB LINC Project.

**Results and lessons learned:** Starting January 2010, a series of technical meetings examined the OVIs. In March, a draft was reviewed by a group including Regional NTP coordinators and refined using the Delphi process and a pretest. A 2011 DCAT baseline found that 12/13 LGUs scored below DOTS compliance standards. Scores will inform DOH-NTP allocation of performance-based grants to LGUs.

**Conclusions and key recommendations:** DCAT will ensure that at least 70% of provinces and highly organized cities (HUCs) include TB control plans and are DOTS compliant. Rollout will require careful monitoring.

#### **PC-880-15 Income generation activities assessment among tuberculosis Community-Based Organisations in the Zambian Copperbelt Province**

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**Background and challenges to implementation:** Copperbelt Health Education Program (CHEP) and Norwegian Heart and Lung Patient Organization (LHL) have since 2005 supported Treatment Supporters (TS) with DOTS training, organizational development and income generating activities (IGA). Income from these activities is aimed at addressing the food needs of TB. It also rewards and motivates the Treatment Supporters. To date, 29 groups have received seed funding for IGAs.

**Intervention or response AIM:** Assess factors that contribute to the success and failure of IGAs and recommend appropriate steps to enhance IGA success.

**Method:** Focus group discussions, desk review and key informant interviews.

**Results and lessons learnt:** The type of business activity has insignificant bearing on whether an IGA fail or succeed, however, ownership, planning, training, commitment and supervision play a critical role. Many TB treatment supporters had identified lack of food as a risk factor for defaulting, and it was found that groups often taking the decision to deal with urgent need of food, instead of investing in longer term initiatives. At the same time, smaller and individual IGAs, by treatment supporters, were found to be more successful, but these had less benefits for TB patients.

**Conclusions and key recommendations:** In order to foster high IGA success rate, the study recommends; sound setup conditions including signed contractual arrangements, training and skills development, diligent supervision and reporting of activities and sound financial management practices.

#### **PC-881-15 Community involvement in tuberculosis case finding among high-risk groups in Burkina Faso**

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**Background and challenges to implementation:** Burkina Faso is a country with high incidence of tuberculosis, 55 smear positive pulmonary tuberculosis per 100 000 2010. NTP is still faced to a low detection rate. Thus, the Support Program to association and community based organization NGOs in fight

against AIDS Tuberculosis and Malaria (PAMAC) through associations conducted outreach activities to increase the detection rate.

**Intervention or response:** The strategy of intervention was awareness (sensitization) with information, education and communication activities reference of the suspicious cases towards the CDT (center of diagnostic and treatment). Target group of the intervention was TB patients, people living with HIV, people living in slums areas of two big cities, nomads, prisoners, miners, clients of traditional healers, 180 associations produce talks, debates, theatres, proximity animations, film screenings/discussions, door to door sensitization.

**Results and lessons learnt:** During 2011, 180 associations were involved:

- 854 859 persons sensitized about 5.3% of the general population
- 5907 people referred to the CDT with card
- 368 smear positives detected (43 cases/100 000 habitants higher than the detection at the national level which is 24.2 cases/100 000 habitants).

The detection of TB among the group of people sensitized is approximately twice higher than non sensitized people group (the national rate of detection). The contribution of the reference made during sensitization activities to national detection is 9.3% (368/3934) in 2011.

**Conclusions and key recommendations:** The educational talks and outreach awareness (door to door) are more effective screening strategies. Awareness reduces geographical and socio-cultural accessibility barriers and increases the level of attendance at health centers. Awareness improve earlier cases detection of TB and detection rate at national level.

## TUBERCULOSIS MANAGEMENT: INNOVATIONS IN COMMUNICATION

### PC-905-15 Study of communication approaches to improve public awareness about tuberculosis

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**Background:** To increase public awareness on TB, improve treatment adherence and contribute to national efforts to fight MDR-TB, a comprehensive national-scale behavior change communication campaign has been designed and implemented. Two survey waves (before and after the campaign) were conducted among a 1000 person sample to reevaluate the media and methods selection for the project interventions.

**Design and methods:** The behaviour change activities included development of communication mate-

rials (print and video) for various audiences, community mobilizations (vulnerable groups, including refugees, and youth) and advocacy with the national policymakers. The main media for message distribution were national and regional TV channels, where two public service announcements were demonstrated. Two survey waves were conducted in eight regions of Azerbaijan among 1000 respondents. A structured questionnaire was used to define level of awareness on TB, recognition of the project materials and determining the best media for TB-related messages distribution.

**Results:** The first wave of the survey was conducted in June 2010, prior to the campaign and accounted for non-readers/viewers. Individuals who saw/read TB messages vs. those who did not were twice as likely (100 vs. 49%) to name ways of TB transmission correctly. The second wave was conducted in May 2011, after the communication campaign. 34% of respondents confirmed that they were exposed to TB-related messages over the last six months. 79% of all the respondents stated that if ever they received information on TB from TV/radio. 72% of respondents agreed that TV and radio are the most effective sources of information about TB.

**Conclusions and key recommendations:** The survey findings confirmed that the project selected the most effective means for communicating TB-related messages to big audiences. However, more aggressive interventions are needed to increase % of those who receive information on TB from TV/radio.

### PC-906-15 Enhanced case detection by integrated interventions (GPs and chest camps) for active case finding using new diagnostic tools, Sindh Province

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**Background:** NTP Pakistan has improved case detection from 2001 onwards but still high risk areas such as urban slums need to be focused. Around 24% of the smear positive estimated tuberculosis (TB) cases are not reported. NTP is running TB REACH Project since March 2011 with integrated interventions in periurban slums including chest camps, engaging private providers, introducing LED fluorescent microscope and front loaded sputum collection strategy.

**Design/methods:** The project was implemented in five intervention districts with comparison group of five control districts in Sindh Province. The activities included mapping and training of general practitioners, laboratories staff training, arranging Chest Camps, community awareness-raising, and developing health care service linkages of targeted population with District Health System.

**Results:** The result shows 2189 smear positive cases detected from 502 camps and 332 engaged GPs, 10537 suspects identified. The assessment shows 124% change from the historical baseline notification of evaluation population for smear positive cases. The GPs engaged have contributed significantly, i.e., 1167 smear positive cases, 55% of overall case detection. The florescent microscopy shows 16% slide positivity as compared to 13% by ZN microscope and the initial default is reduced in intervention districts to 10% as compared to 24% in control districts.

**Conclusion and recommendations:** The project is going on successfully with increasing number of engaged private GPs and arranging chest camps. The sustainability of the project after funds are over will be a challenge.

### PC-907-15 Reaching the underserved with tuberculosis diagnostic services in Mozambique

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**Background and challenges to implementation:** Tuberculosis (TB) is the leading cause of morbidity and mortality among adults in Mozambique, ranking 16th in the list of 22 TB high burden countries in the world. There are about 264 (1 lab/90000 pop) TB smear microscopy centers in Mozambique. TB microscopy centers are mainly concentrated in urban areas leaving most remote rural areas with no access to TB diagnostics. TB case detection rate has remained as low as 47%.

**Intervention:** Implementing partners (FHI and MSH), in collaboration with the Government of Mozambique, have developed a project of to increase access to TB smear microscopy, in 2010 under the TBCAP project. 192 nurses were trained on collection, smear preparation, fixation and transportation of sputum smears to microscopy centers. In order to support the trained nurses in the work place the following were provided SOPs manual, job aids, slide boxes, sputum containers and supplies.

**Results and lessons learnt:** The 169 new TB sputum collection sites increased the country's TB diagnosis centers from 264 to 433 sites. However, two years later TB diagnosis showed several challenges; unable to cope with increases work load, most 'nurse-manned TB diagnosis site' closed down due to transfer of trained nurses, running water, electricity, systematic stock-outs of reagents and consumables, and inadequate biosafety measures.

**Conclusions:** Involving well trained and supervised nurses to collect and send sputum samples to well

supported TB microscopy laboratories can improve case finding in resource challenged setting like Mozambique. Ownership by government is critical in order to sustain the system.

### PC-908-15 Mobile phone text messaging reminders to aid adherence to tuberculosis care in Eldoret, Kenya

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**Background:** Effective TB care requires adherence to a long course of medication and frequent clinic appointments. Support to adherence to anti-retroviral therapy using text messaging improves outcomes in resource-poor settings. We conducted a pilot program to determine the feasibility of reminder texts in enhancing clinic attendance among TB patients at Moi Teaching and Referral Hospital chest clinic.

**Methods:** The 187 TB patients with mobile phones at MTRH Chest clinic were informed that reminder texts will be sent to them in Ki-Swahili one day prior to their clinic appointments using the software Frontline SMS between April and May 2011. Rates of clinic attendance on scheduled days were recorded and compared between those receiving and not receiving (technical reasons) the text reminders. Each patient contributed 1 visit to the analysis.

**Results:** Text program patients had a mean age of 30.9, 42.2% female, 31.1% HIV infected, 8.8% re-treatment TB cases. 150 (80.2%) patients received at least one text; 37 did not. Those who received a text were 1.6 times (RR) ( $P < 0.007$ , 95%CI 1.06–2.29) more likely to adhere to scheduled clinic visits (see Table). Cost for sending all texts totaled USD35.

Table Clinic attendance among the various variables

	Received at least one text	Did not receive a text	Appointment-keeping relative risk	95%CI	Pearson $\chi^2$ P value
Total	101/150	16/37	1.56	1.06–2.29	<0.007
Males	56/85	45/65	1.17	0.79–1.72	<0.407
Females	13/23	3/14	3.23	1.17–8.92	<0.001
New TB	90/129	14/26	1.30	0.89–1.88	<0.115
Re-treatment TB	6/11	0/4	—	—	<0.057
HIV+	23/38	6/13	1.31	0.69–2.49	<0.366
HIV–	68/96	9/17	1.34	0.84–2.13	<0.144
0–18 years	18/26	3/4	0.92	0.50–1.72	<0.815
19–49 years	71/102	12/22	1.28	0.85–1.91	<0.173
≥50 years	6/12	0/5	—	—	<0.049
Intensive phase	48/70	6/15	1.74	0.90–3.25	<0.037
Continuation phase	48/71	9/16	1.202	0.76–1.91	<0.388

**Conclusions:** Text messaging is a potentially effective method to enhance adherence to TB clinic appointments. A carefully designed study can enumerate the full potential of this technology in improving TB treatment adherence.

### PC-909-15 Increasing tuberculosis awareness in South African schools: the Kick TB Awareness Campaign

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**Background and challenges to implementation:** South Africa, with the third highest TB incidence in the world, is one of the 22 high burden countries. Raising awareness and knowledge of TB is a key intervention in response to TB and HIV in the country.

**Intervention or response:** 'Kick TB' focuses on raising awareness and imparting knowledge among learners, contributing to the vision of South Africa's 20-year three zeros vision: (Zero new HIV, STI and TB infections, Zero deaths associated with HIV and TB, and Zero discrimination). It aims at increasing awareness and knowledge about TB, dispelling myths and misconceptions contributing to stigmatization, promoting behavioural change required to prevent TB infection, increasing TB case detection by encouraging uptake of services at different levels, increasing TB treatment adherence. The National Department of Health and Desmond Tutu TB Centre developed a campaign on TB linked to the 2010 FIFA World Cup in South Africa. 'Kick TB' links the spectacle of soccer, mass mobilization against TB, and linkages with facilities: a tool specifically conceptualized and designed for this campaign, the TB Passport, actively assist the latter with case findings.

**Results and lessons learnt:** Number of pupils reached, evaluation of post intervention knowledge and awareness of TB and number of new TB cases detected through the TB passport have been evaluated at six and nine months after intervention.

**Conclusions and key recommendations:** 'Kick TB' contributes to improved knowledge and awareness of learners; they take information home, contribute to increased disease knowledge and awareness among community members with its consequences of new infections reduced and increased adherence to TB treatment.

### PC-910-15 Initiative to make tuberculosis programme sustainable in Bangladesh through high school students

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**Aim:** Awareness raising is a key part to make any program successful and sustainable. In Bangladesh TB program is doing well but its sustainability is still a question. So NATAB wants to support the National TB Control Program to make it sustainable through awareness raising.

**Method:** NATAB worked with High School Students in all 64 districts. In the first phase 128 schools were covered. School students were oriented through one lecture on TB and then they received a simple questionnaire. Through that questionnaire they provided information of TB.

**Results:** Students per school are  $\geq 550$ . In total it was 71 000 students. These students oriented on TB Control Program and then they provide information on suspects of TB within their family. They covered their families and provided actual information about the situation on TB. Based on their information many new TB cases were included in national program. This activity helped NTP to raise coverage in urban set-up. This is also good information to creat new necessary actions.

**Conclusion:** Besides NATAB's regular advocacy program with Civil Society Member on TB control program we did this as pilot program. We only covered district Headquarters. We are confident that if we can continue this program in rural and hard-to-reach areas then we will be able to add many new TB cases in national program and this will help NTP to achieve MDG target on time. This program will facilitate TB Control Program of Bangladesh to make more success stories and sustainable program.

### PC-911-15 Use of mobile text messaging to improve tuberculosis treatment adherence in China

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**Introduction:** The mobile phone as an intervention of a cluster randomized trail was being used to improve TB treatment adherence. A web-based interface was established to automatically send SMS to patients and remind them to take drugs regularly by mobile phone. The SMS can also be sent to health care provider to monitor patients' drug-taken. Patients may receive the health promotion messages from mobile phones.

**Methods:** New smear positive and negative PTB patients were the study object. The routine process data were recorded and collected at enrolment and during follow-up, including failure of the system and withdrawal from study early due to problems with the mobile phone.

**Results:** 2405 patients were enrolled in the study from the 2861 eligible patients, and 456 patients (16%) who couldn't be enrolled because they couldn't

use the mobile phone or they had no any family available to help at home. Among those patients entering the study, 26% of them need a family member to assist them for using the phone. As of March 23rd 2012, 2423 patients started receiving SMS to improve TB adherence and there had been 11416 monthly follow-up visits. Some problems with the mobile phone were reported in 1086 (9.5%) visits. Only 27 patients (1.1%) discontinued the use of the mobile phone as part of the study.

**Conclusion:** Mobile text messaging is well accepted by patients as a means to monitor treatment adherence.

### PC-912-15 Use of mobile telephones for reporting referrals

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India has 407 million mobile users, with subscriptions more for rural than urban, i.e., 218.9 million versus 188.4, the use of mobile telephony for monitoring could be a good indicator for evaluation. In a project of The Union funded by Eli Lilly to train traditional healers on Tuberculosis and basic DOTS, one of the follow up mechanisms explored was the use of mobile telephony for recording referrals made by the trained traditional healers. A supervisor from the implementing NGO is entrusted to receive and send reminders to trained traditional healers (TH) on the number of referrals made by them to the nearest District Microscopy centre (DMC). The trained TH would message the supervisor informing him/her of the suspected patient he/she had encountered during their practice and the DMC referred to. The Supervisor notes and cross checks with the DMC on the referral. This ensures that the referred patient gets diagnosed and treated and recorded as referred by the TH thereby monitoring the engagement and motivation of the TH. This pilot trained 300 plus traditional healers across 4 districts, one in 4 states and 50% are using mobile telephony to stay in touch with the supervisor to inform them of the TB suspects referred to the DMC. In turn the supervisor is in contact with the lab technician of the various DMCs and updates on the referrals, diagnosis and treatment of the referred patient. In a short time the project have increased suspect referrals (472), case notification (36) and outpatient services, by about 25% in Uttar Pradesh and Tamil Nadu by engaging the largely untapped traditional healers who are often the first point of contact for people in the village for health seeking practices. Using mobile telephone is a motivational tool for engaging with trained THs thereby strengthening collaboration between NGOs and THs, establishing links between the NGOs and public system and maintaining the relationship built for future projects.

### PC-913-15 Use of tuberculosis helpline for increasing access to tuberculosis care services: a preliminary report from Chennai, India

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**Background:** Barriers to successful TB control such as lack of knowledge on availability of TB services and inadequate information about treatment result in delayed access to services and in diagnosis of TB. Increasing access to TB diagnostic and treatment services is very crucial to ensure early detection and appropriate treatment. An exploratory study was undertaken to examine the role of an exclusive TB helpline manned by trained staff in addressing barriers faced by patients. The study was undertaken in an urban setting of Chennai City in South India with a population of 6.2 million.

**Intervention or response:** The TB helpline (open from 8 AM to 8 PM on all 7 days a week) was manned by trained staff attuned to the specific needs and questions of different target groups. The helpline offered counseling services, basic information about tuberculosis, referral to nearest designated microscopy and TB treatment center and was popularized by advertising in billboards, advertisements on the public transport buses and at community meetings.

**Results and lessons learnt:** About 179 callers used the helpline for their TB related queries over 2 months period. Of 179 calls, most of them were TB symptomatics. 27.4% of callers expressed interest in knowing about the disease, 23.5% wanted information on symptoms of TB, 21.8% needed information on the treatment facilities available in their area. 22% of the callers were provided with basic information on TB while 63% were referred to appropriate TB center. Most of the callers had obtained the helpline from advertisements on bus-backs and hoardings.

**Conclusions and key recommendations:** This report highlights the feasibility of operationalizing a TB helpline and the use of mobile telephony as an important and low cost method of providing TB related information to the community, TB symptomatics and patients and also as a tool to link them with appropriate TB diagnosis and treatment centers thereby facilitating early diagnosis and treatment.

### PC-914-15 Emergency medical services: evaluation of health services for tuberculosis diagnosis, Ribeirão Preto, Brazil, 2009

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**Background:** Based on the National Tuberculosis Program Guidance and on the number (253 628) of patients who went to emergency medical services (EMS) in Ribeirão Preto in 2009, it was expected to screen 20 290 individuals for TB and identify 1476 cases in this kind of facility.

**Aim:** To analyze the performance of the EMS in tuberculosis (TB) diagnosis in Ribeirão Preto, Brazil.

**Methods:** A descriptive and exploratory study conducted in 2009 by interviews applied with 68 health professionals (medical doctors, nurses and nurses' auxiliaries) from 5 public EMS of Ribeirão Preto, priority city for TB control in Brazil. Indicators of structure-process were constructed by calculation of proportions (for dichotomous questions) and means (for Likert scale questions).

**Results:** Regarding physical resources (structure), more than 90.0% of health professionals related the availability of inputs (sputum smear requesting forms and sputum pots) and refrigerator for storage of exams. X-ray machine in the health service was informed by 63.5% of professionals. For human resources, availability and turnover of employees are regular, but with a high workload. 69.1% felt prepared to identify TB suspect cases. However, regarding the process of delivering care, only 10.3% of them related requesting sputum smear test. Though the nursing staff has the autonomy to perform this request, 69.6% of them refer the case to a doctor, which, in turn, require, in most cases, an X-ray (63.6%). Professionals evaluate as regular their time devoted to consult each user and deny difficulties to request sputum smear and to approach TB with patients. It was also found that the EMS screened only 3.6% of expected individuals and diagnosed 5.4% of expected cases.

**Conclusions:** The performance of EMS for TB diagnosis is incipient, despite the availability of inputs to identify TB suspects. It was also identified work overload and diagnosis focused on doctor decision, involving high technology features.

#### PC-915-15 Tuberculosis screening camps as a communication tool in Kenya

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**Background and challenges to implementation:** Recent national TB data suggests that urban centers in Kenya are disproportionately contributing to the burden of TB notified to the DLTL. Lack of knowledge, delay in diagnosis, limited or no resources to seek health services could be attributing to the disparity.

**Intervention or response:** KAPTLD sought to enhance TB case finding through community mobilization in form of screening camps, by screening resi-

dents of 11 urban districts in Kenya in the comfort of/near their homes and or place of work using music, dance, educational skits and one-on-one interactions. On the day of the screening camp, the music was used as a crowd puller with the magnet theatre group performing skits and dances as health care workers were screening the people for both TB and HIV. Those who were suspected of TB, the sputum specimen was collected by the laboratory personnel and examined at the nearest diagnostic facility. Smear positive results for the investigation were conveyed directly to the individual via mobile phone. Those who turned HIV positive were referred to the HIV care centre of their choice for comprehensive care.

**Results and lessons learnt:** 5708 people were screened at camps, 2290 were referred for further investigations from which 21 were PTB+ and were put on treatment. Though the yield of smear positive cases was low, the impact of the activity, as a communication tool was high.

**Conclusions and key recommendations:** Screening camps played a major role in intensified TB case finding by educating the community on TB disease

#### PC-916-15 Voices: understanding the experiences, challenges and factors supporting people affected by tuberculosis in Karachi, Pakistan, using Photovoice

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**Background:** In Pakistan, despite publically available free testing and treatment throughout the country, there were an estimated 58 000 deaths due to tuberculosis in 2010. Understanding the experiences of people affected by TB is essential in addressing barriers to effective treatment.

**Intervention:** The Indus Hospital conducted an exploratory study to understand the experiences of people affected by TB in Karachi. Participants included TB patients, their family members, and TB treatment supporters. We used Photovoice, a participatory research methodology in which participants were given cameras and asked to take photographs to represent their experiences, their challenges, and the factors that support them. Participants selected photos and contextualized them by introducing each image and relating it to the research questions. These discussions were transcribed and stories were developed to accompany each photograph. Participants then analyzed the photographs and stories with the project researchers to identify emergent themes.

**Results:** 230 photographs and stories were collected from 55 people affected by TB. Twelve themes emerged from the data. These included the challenges of physical difficulties, difficulties in taking

TB medication, stigma, loneliness, fear and guilt of infecting family members, financial difficulties and poverty and polluted environments that are detrimental to health. The photographs also highlighted the support received by patients from friends and family, welfare organizations, prayer, peaceful environments, and when they realized they were getting better. The photographs, stories, and a Call for Action were shared at a Gallery event with patients, practitioners, and policy-makers.

**Conclusion:** Photovoice is a very powerful tool for understanding TB. The study highlights that TB not only has physical impacts, but social, emotional, and financial impacts.

### PC-917-15 Impact of a low-cost mass communications campaign on tuberculosis awareness in Karachi, Pakistan

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**Background:** Mass media has been seen to be effective for raising awareness in TB and HIV. However, the high cost of air time on national or regional television channels is often prohibitive. We conducted a four-month long low-cost mass communications campaign to raise awareness on TB in a low to middle income area in Karachi, Pakistan with a population of approximately one million people. The campaign utilized three billboards at busy intersections, and low-cost TV spots on a local cable channel. We designed a study to identify the characteristics of people that had observed a mass communications campaign, and to determine whether any differences existed in knowledge about TB among those that had seen the campaign relative to those that had not.

**Methods:** We conducted a cross-sectional survey in three neighborhoods using systematic random sampling. We used multiple logistic regression to compare characteristics between those that had seen the advertisements and those that had not.

**Results:** We surveyed 541 individuals. Twenty-four percent had seen a campaign billboard, 24% a TV spot, 38% either a billboard or a TV spot, and 10% both a billboard and a TV spot. Respondents that had seen the ads were 1.7 times more likely to be male (95% CI 1.2–2.4) or have any schooling (95% CI 1.2–2.5), and 2.2 times more likely to be aged 15 to 18 (95% CI 1.1–4.5). After adjusting for gender, age and schooling, respondents were 1.8 times more likely to identify cough as a TB symptom (95% CI 1.3–2.7), 3.5 times more likely to state the need to complete a full course of TB treatment (95% CI 1.6–7.3), and 1.8 times more likely to have discussed TB, taken a TB test, or advised someone else to take a TB

test (95% CI 1.03–3.0). The total cost of the campaign was US\$6667.

**Table** Final multiple logistic regression model identifying differences in TB knowledge and action associated with having definitely seen at least one advertisement

	Ads not seen (n = 336)	Ads seen (n = 205)	Adj* POR†	95% CI
Identified cough as a symptom of TB				
Yes	204 (61%)	156 (76%)	1.8	1.1–2.7
No	131 (39%)	49 (24%)	Ref.	Ref.
Said that the full course of TB treatment must be completed				
Yes	282 (84%)	196 (96%)	3.5	1.6–7.3
No	54 (16%)	9 (4%)	Ref.	Ref.
Took an action related to TB				
Yes	34 (10%)	38 (19%)	1.8	1.03–3.0
No	302 (90%)	167 (81%)	Ref.	Ref.

\* Adjusted for age, gender, and schooling.

† Adjusted prevalence odds ratios.

**Conclusion:** Our low-cost communications campaign was successful in reaching a large proportion of the population and was associated with improved knowledge and action related to TB in this low-literacy setting.

### PC-918-15 Mass media survey in Tajikistan

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**Background:** During the last 10 years many health promotion interventions have been implemented to increase the population's awareness on Tuberculosis prevention in Tajikistan. Different mass media channels were used to spread TB information, however, no comprehensive research has been conducted to analyse sufficiency and effectiveness of their use. A study was conducted to identify and clarify the media habits and preferences of the general population of Tajikistan on exposure to media messages about TB.

**Design/methods:** Structured interviews were administered to 780 members of the general population from 11 districts of all regions of Tajikistan. Respondents were randomly sampled from population registers. The objective of the survey was to know the extent of people usage of mass media, the types of mass media that can be accessed by different demographic groups and what modes of mass media people prefer.

**Results:** The results showed that during the last 6 months 78% of respondents were exposed to TB messages through different mass media channels: 42% through TV, 23% health workers, 18% informational booklets, 8% volunteers, 4% radio, 5% through newspapers. 96% of respondents have access to TV,

23% to radio and 12% to newspapers. The urban population has access to all mass media channels while rural population mostly have access to TV. The preferred channels of getting TB information are: 52% TV, 18% health workers; 16% booklets, 3% newspapers, 2% radio and 9% volunteers.

**Conclusion and recommendations:** TV channels should be used to cover all demographic groups from urban and rural area with TB messages in Tajikistan. Health providers and volunteers can be used as a channel to spread TB information targeting adult population from rural area. Knowing the access of population to different mass media channels and their preferred channels can lead to more efficient use of resources and effective targeting of TB messages for the population.

#### **PC-919-15 Creation of evidence-based 'Balgam Bhai' 360 degree communication campaign for tuberculosis care and control in India**

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**Background and objectives:** Population Services International/India (PSI/I) conducted quantitative and qualitative research studies and developed a mass media campaign with BBC World Service Trust and the Union to raise awareness of TB and address gaps in diagnosis and treatment. Some of the key gaps identified were: simple cough was not perceived as a serious issue; people with a cough wasted time by going to chemists or unqualified health providers, getting ineffective tests, or using home remedies; people were not informed about TB testing services.

**Methodology:** Research showed a need to raise a person's self risk perception of TB. From the research PSI collaborated with BBC WST to develop a communication campaign to increase the awareness on TB among the target group. The communication message was 'A cough for two weeks or more could be TB' with a call to action to 'visit the nearest DMC (designated microscopy centre) for a sputum test'. A Mascot named 'Balgam Bhai' was co-created and the campaign intended to reach out to 360 million population which predominantly belonged to socio economic classification categories C and D. The campaign was on air for a month including TV and radio in the form of 3763 radio spots, 6163 TV spots supplemented by a toll free helpline.

**Results and conclusion:** The campaign has reached out to 360 million population in six states and also national coverage through the TVC. The reach of the campaign has been promising and recall of the same is recommended to be done.

## **ABSTRACT PRESENTATIONS FRIDAY 16 NOVEMBER 2012**

### **ORAL PRESENTATION SESSIONS**

#### **CO-LOCATION AND INTEGRATION OF TB-HIV SERVICES: BREAKING THE BARRIERS**

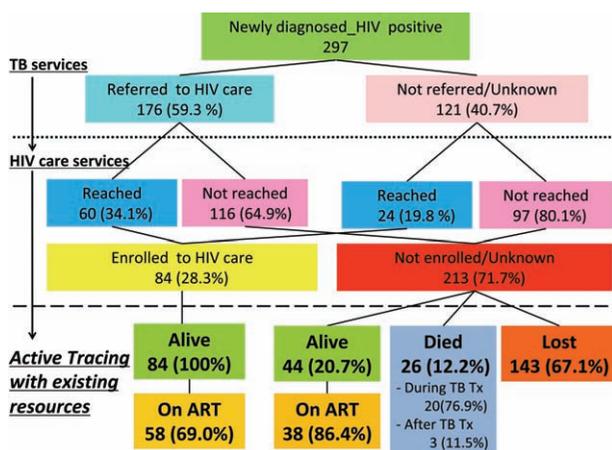
##### **OP-146-16 Retention between tuberculosis and HIV care in the field: an operational cohort study of TB-HIV co-infected patients in a resource-limited setting, Zambia**

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**Background:** The linkages between TB-HIV services remain as difficult issues to overcome especially in resource-limited settings. Our operational research aimed to evaluate the linkages between TB and HIV services for TB-HIV co-infected patients and to assess their final outcomes through active tracing with existing resources.

**Method:** All TB patients newly diagnosed as HIV positive in Chongwe District between 2009 and 2010 were included. The data from TB registers and records were reviewed. Their referral to HIV services and provision of ART were further examined through HIV registers and records. Those who were identified as 'not enrolled into HIV care/unknown' were actively traced by clinic staff and treatment supporters to ascertain their final outcomes.

**Result:** TB records indicated that 293 patients were newly diagnosed as HIV positive and 176 (59.3%) of them were referred to HIV care. When they were traced at HIV clinic to confirm their referrals, it was found that only 84 (28.3%) had actually been enrolled into HIV care and of which 58 (69.0%) had commenced ART. Fifty-five (91.4%) patients initiated ART during anti-TB treatment (mean time: 54.5 days). HIV records without TB information were more likely to start NVP-based regimen even though they were on TB treatment with RFP ( $P < 0.01$ ). Of 213 patients identified as 'not enrolled/unknown', 26 (12.2%) were dead. Of 44 patients, (20.7%) found to be alive, 38 (86.4%) were receiving ART. One hundred and forty-three patients (67.1%) could not be found despite active tracing. Those who were enrolled to HIV care showed significantly higher TB



success rate than those who were not enrolled ( $P = 0.036$ ).

**Conclusion:** Poor linkages between TB and HIV services affected patients' outcomes. Only one third of TB-HIV co-infected patients were retained on ART. Better referrals secured by good information sharing system between two services and more prompt follow-up of patients whose referrals are unclear are urgently required.

#### OP-147-16 Provision of antiretroviral treatment in tuberculosis facilities in Cape Town, South Africa: impact on tuberculosis treatment outcomes

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**Aim:** This study ascertained if integration of ART and TB services has impacted on TB treatment outcomes for all TB patients and those with HIV.

**Methods:** TB treatment outcomes were determined for new TB patients  $\geq 18$  years at 13 integrated ART/TB facilities (IFs) and 4 single service facilities (SSFs) using the electronic TB register from 1 Jan 2009 to 30 June 2010. Facilities with a TB case load  $>400$ /yr and a  $>50\%$  HIV coinfection rate were included. IFs provided both ART and TB treatment on-site and SSFs provided TB treatment with ART off-site. A random effects logistic regression model evaluated the effect of integration on TB treatment outcomes.

**Results:** Of 13 542 newly registered patients, 10 030 received TB treatment in IFs and 3 512 in SSFs. There was no difference in baseline characteristics between the two groups. HIV status was determined for 93.2% and 91.9% of whom 66.3% and 63.0% were HIV-positive in IFs and SSFs respectively. The median

CD4 count was 152 cells/mm<sup>3</sup> for IFs and 148 cells/mm<sup>3</sup> for SSFs. Cotrimoxazole was given to 95.6% HIV-positive patients in IFs and 95.7% in SSFs. TB treatment outcomes (see below) were similar ( $P = 0.56$ , all patients;  $P = 0.58$ , HIV-positive).

Outcome	All patients <i>n</i> (%)	IFs	SSFs
Cured	4 058 (30.0)	2 905 (29.0)	1 153 (32.8)
Completed	6 240 (46.1)	4 524 (45.1)	1 716 (48.9)
Failed	224 (1.7)	163 (1.6)	61 (1.7)
Died	825 (6.1)	644 (6.4)	181 (5.1)
Defaulted	1 391 (10.3)	1 081 (10.8)	310 (8.8)
Moved out	74 (0.5)	74 (0.5)	0
Transferred out	464 (3.4)	397 (4.0)	67 (1.9)
Not evaluated	266 (2.0)	242 (2.4)	24 (0.7)
Total	13 542	10 030	3 512

**Conclusions:** Provision of ART in TB facilities did not improve TB treatment outcomes however the direct effect of ART was not determined as uptake of ART and time to ART initiation was not recorded.

This research was supported by a USA Agency for International Development (USAID) Cooperative Agreement (TREAT TB-Agreement No. GHN-A-00-08-00004-00). The contents are the responsibility of the author(s) and do not necessarily reflect the views of USAID.

#### OP-148-16 Timing of initiation of antiretroviral treatment after diagnosis of tuberculosis: impact of the revised 2010 World Health Organization guidelines

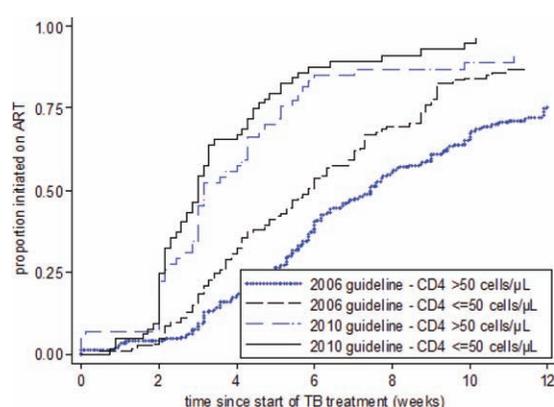
K Choun,<sup>1</sup> R Pe,<sup>1</sup> S Thai,<sup>1</sup> N Lorent,<sup>2</sup> L Lynen,<sup>2</sup> J Vangriens.<sup>2</sup> <sup>1</sup>Infectious Disease Department, Sihanouk Hospital Center of HOPE, Phnom Penh, Cambodia; <sup>2</sup>Infectious Disease, Institute of Tropical Medicine, Antwerp, Belgium. e-mail: kimchengarc@yahoo.com

**Background:** WHO 2010 ART guidelines recommend early initiation ( $\geq 2$  weeks) of ART after TB diagnosis, irrespective of CD4 count. Our main objective was to determine the change in ART delay concurrent with guideline implementation in real-life settings in low-income countries. Secondary outcomes included retention and toxicity-driven ARV drug substitutions.

**Methods:** Retrospective cohort study in a tertiary hospital in Phnom Penh, Cambodia. ART/TB diagnosis and treatment were done in line with WHO guidelines. We included all ARV-naive HIV-infected adult patients initiating TB treatment over 18 months post-intervention (WHO 2010 guideline implementation) and 18 months pre-intervention. Time to starting ART and determinants were analysed in a competing risk regression model.

**Results:** The post-intervention group consisted of 202 TB-HIV-coinfected patients (54% male, median age 38 yrs; median baseline CD4 count 43 cells/ $\mu$ l), 348 patients (54% male, median age 36 yrs, median baseline CD4 count 55 cells/ $\mu$ l) were included in the

pre-intervention group. Among ART initiators with baseline CD4 count  $<50$  cells/ $\mu$ L, median ART initiation delay declined from 5.1 weeks (IQR 4.1–6.6) pre-intervention to 2.8 weeks (IQR 2.4–3.1) post-intervention ( $P < 0.001$ ). With baseline CD4 count  $>50$  cells/ $\mu$ L, the interval changed from 6.4 (IQR 5.8–7.7) to 3.1 (IQR 3.0–4.1) weeks ( $P < 0.001$ ). Accounting for attrition, the estimated probability of ART initiation within 1 and 2 months after TB diagnosis increased from respectively 25% and 53% pre-intervention to 56% and 72% post-intervention. The intervention was independently shortened ART delay (adjusted sub-HR 2.1; 95%CI 1.6–2.8). A non-significant increase in 6-month retention of 17% and ARV substitution of 30% was seen post-intervention.



**Conclusion and recommendations:** Implementation of WHO 2010 recommendations in real-life settings was associated with shorter ART delay. Larger studies with longer follow-up are needed to assess the impact on patient outcomes.

#### OP-149-16 Barriers to implementing integrated TB-HIV service delivery in an antenatal care facility in Frances Baard District, Northern Cape, South Africa

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**Background:** South Africa is one of only 12 countries where maternal mortality has increased since the MDG baseline was set. TB and HIV have been driving problem. TB-HIV integrated service delivery—as part of maternal health services including antenatal care (ANC)—is recommended to reverse current trends. This study assessed levels of and barriers to TB-HIV integrated service delivery during ANC in a high TB-HIV burden setting.

**Methods:** 1) A retrospective descriptive analysis was done on a random sample of 308 pregnant women at

a day hospital ANC service between April 2011 and February 2012. Data on TB-HIV service uptake among participants were abstracted from ANC registers and corresponding patient case notes. Main outcomes assessed were proportion of women receiving HIV counseling and testing (HCT), CD4-counting, anti-retroviral treatment (ART), cotrimoxazole preventative treatment (CPT), TB screening, and isoniazide preventative treatment (IPT). 2) Interviews were done with 3 senior clinic staff on the implementation of the three tiers of WHO-recommended TB-HIV collaborative activities.

**Results:** All women underwent HCT; 80% of those testing HIV-positive received TB-screening and 86% of the eligible HIV-infected were offered a CD4 count. Thereafter service delivery was questionable: of the eligible only 36% received ART-prophylaxis on-site; only 11% were referred for ART-initiation; 0% received CPT; only 44% commenced IPT; and 0% of TB suspects underwent further investigation. Barriers identified included unawareness of WHO-recommended collaborative activities, shortage of up-to-date guidelines, -joint TB-HIV planning, -coordination/referral systems, -monitoring/evaluation, and poor infection control measures.

**Conclusions/recommendations:** Identification of the HIV-infected and TB suspects was good, but other activities were sub-optimal. Pilot studies are needed to see whether one-stop screening/diagnostic tests could improve current TB follow-up practices.

#### OP-150-16 The impact of HIV and ART on recurrent tuberculosis in northern Malawi

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**Background:** Antiretroviral therapy (ART) reduces the incidence of TB among HIV-positive patients, but the effect on incidence of recurrence in Africa is unknown. We report findings from a long-term cohort study in sub-Saharan Africa.

**Methods:** Patients who had completed treatment for laboratory-confirmed TB diagnosed since 1996 in Karonga District, northern Malawi, were visited annually to record vital status, ART use, and screen for TB. Survival analysis estimated the effect of HIV/ART status at completion of treatment on mortality and recurrence. Analyses were stratified by time since treatment completion to estimate the effects on relapse (predominates during first year) and reinfection disease (predominates after first year).

**Results:** Among 1133 index TB cases contributing 4353 person-years of follow-up, there were 307 deaths

and 146 recurrences, 103 of which were laboratory-confirmed (recurrence rate for confirmed TB 4.6/100 py). Over half (55/103) of the recurrences occurred in the first year since completing treatment. HIV infection increased the recurrence rate (rate ratio [RR] adjusted for age, sex, time period and TB type = 2.69, 95%CI 1.69–4.26), but with less effect in the first year (adjusted RR = 1.71, 0.87–3.35) than subsequently (adjusted RR = 4.2, 2.16–8.15). Recurrence rates on ART were intermediate between those of HIV-negative individuals and HIV-positive individuals without ART. Compared to HIV-positive individuals without ART the adjusted RR was 0.74 (0.27–2.06) in the first year, and 0.43 (0.1–1.73) later.

**Conclusion:** The increased mortality post-treatment and incidence of TB recurrence observed in HIV positive patients is reduced by timely ART. The effects are mostly on later (likely reinfection) disease so the impact of ART on reducing recurrence will be highest in high TB incidence settings.

#### **OP-151-16 Barriers to antiretroviral therapy initiation among Mozambican patients with active pulmonary tuberculosis co-infected with HIV**

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**Background:** In 2010, only 25% of TB patients co-infected with HIV were on ART in Mozambique. This qualitative study identifies factors self-perceived by TB patients with active pulmonary tuberculosis in anti-tuberculosis therapy and their TB health care providers as barriers to antiretroviral therapy (ART) initiation in rural and urban settings in Mozambique.

**Design/methods:** Data were collected through 16 focus groups discussions and 45 in-depth interviews to 183 TB patients co-infected with HIV, 6 TB health workers and 10 TB volunteers from November 2011 to March 2012. Data analysis was performed using both content and thematic analysis to build three thematic dimensions patient, professional and health network factors.

**Results:** Analyses revealed that fear of burden of both medications encouraged patients to decline initiating ART. Parallel, high workload due to community demand, competing tasks at TB care point and shortage of professionals in quantitative and qualitative issues were preventing ART initiation. Finally, domicile-health facilities network long distances, health facility-based ART services and lack of TB volunteers' involvement in ART training were barring ART initiation. Confounders may include lower edu-

cation, household tasks, lower income, poor road transportation network and financial constraints, poor incentives for TB volunteers and believe that working at TB care point is a punishment.

**Conclusion and recommendations:** We encourage stakeholders to consider these findings in their commitment, particularly during ART expansion efforts in rural settings.

#### **OP-152-16 Barriers and facilitators to accessing antiretroviral therapy among HIV-infected tuberculosis patients identified in tuberculosis clinics, Nyanza Province, Kenya**

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**Background:** HIV screening in tuberculosis (TB) clinics is a high priority. Once identified, HIV-positive TB patients may have difficulty accessing antiretroviral therapy (ART). In 2009, a study in Kenya assessing uptake of ART among newly HIV diagnosed adult TB patients at 50 sites determined that only 47% could be documented as starting ART.

**Objective:** To analyze qualitative data to understand barriers and facilitators to accessing ART from patient and provider perspectives.

**Design/methods:** In-depth interviews were conducted from October 2009 to April 2010 at 20 clinics (12 TB/ART co-located clinics and 8 TB treatment-only clinics). 60 patients (24 at TB treatment-only clinics, 36 at co-located clinics) and 32 providers (20 TB staff, 12 HIV staff) underwent interviews which were transcribed, translated and content analyzed.

**Results:** Of 60 co-infected patients, 48% were male and the median age was 35 years. At interview, 32 (89%) of 36 patients at co-located TB-HIV treatment clinics and 17 (63%) of 24 patients at TB treatment-only sites had initiated ART. Patient facilitators included family support and community role models; barriers included distance, transport, hunger, drug side effects, and time off work/school. Patients at TB treatment-only clinics noted unease at approaching unfamiliar HIV clinics. For providers, perceived facilitators were shared language of provider and community, and providing drugs on the same days; barriers included drug and staff shortages, stigma, pill burden, and weak referral systems. Both identified health education and friendly providers as key facilitators.

**Conclusions and recommendations:** Many patients at both co-located and TB treatment-only facilities were able to initiate ART despite barriers that could impact retention. Although challenging to influence, patient-provider interactions and involvement of peers should be emphasized in ART linkages.

### OP-153-16 The impact assessment of South Africa's ARV down referral system on AIDS patients and the health care system, February 2011–March 2012

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**Background:** Sub-Saharan Africa has severe health worker shortage and infrastructure challenges. About five million people are infected with HIV & AIDS in SA. There is an ever increasing demand of services, infrastructural challenges, relevant PHC and human resource constraints. Facilities remain congested and do not have sufficient capacity to handle the demand. The study was conducted with an aim to down refer all stable patients to PHC facilities to enhance management and scaling up of HIV infected patients as a means to address congestion in hospitals.

**Design/methods:** A cohort study on 1342 ART clients were prepared, counselled and referred to 30 primary health care facilities. Medicine was pre-packed and sent down on monthly basis for the patients. Suppressed viral load at 24 weeks and beyond so the clinical status was used as an indicator to determine who is to be down referred. Patients were deregistered if they developed side effects, failing on treatment and/or defaulted.

**Results:** The study findings show that 96.8% of the ART clients remained at PHC level. Only 3.2% needed up-referral to hospital care or lost to follow-up. New patients starting HAART were highly motivated to finish the 24 weeks treatment period so as to join the Down Referral (DR) Project. Patients save money and time as they are only seen after 6 months for renewal of scripts and check-ups and lead to low loss to follow-up. Patients remained with suppressed viral load and healthy on the DR Project.

**Conclusion and recommendations:** Stable patients need less attention and they do better on a DR programme. There was a shift of focus from a hospital-based ART to PHC-based implementation and is assisting in strengthening the systems. In this way the government has saved a lot of money through cost-efficient DR programme.

## CHILDHOOD TUBERCULOSIS IN HIGH-BURDEN SETTINGS

### OP-154-16 Active case finding to identify secondary tuberculosis cases among children, women and the elderly in Sana'a, Yemen

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**Background:** Currently Yemen does not have outreach services to screen household members for TB or monitor whether index cases bring household members to a health service facility, as advised. To enhance case finding amongst vulnerable groups, who may face barriers to accessing care, we conducted a study to assess the proportion of adults and children residing with adults diagnosed with TB that have symptoms and are later confirmed to have TB.

**Methods:** Adults attending the National Tuberculosis Institute in Sana'a with smear-positive TB and relatives at home were invited to participate. After obtaining informed consent and making an appointment, the household was visited by one male and one female trained worker to inquire after the presence of symptoms and collect specimens for examination. Two on the spot sputum specimens were collected from symptomatic adults and children unable to expectorate were taken to a hospital to obtain one gastric and one nasopharyngeal aspirate and one induced sputum. The study was funded by TB Reach.

**Results:** A total of 1142 adults were invited, 112 declined and 918 were enrolled. Among the 5059 relatives, 1859 were absent or refused to participate and 1818 adult and 1382 child relatives were identified. 837 (46%) adults and 520 (38%) children were symptomatic. 786 (94%) and 455 (88%) symptomatic adults and children submitted specimens. Among the symptomatic, 69/448 (15%) women, 53/338 (16%) men and 22/455 (5%) children were smear/culture positive, with 1 in 10 households having an additional case of TB.

**Conclusion:** A high proportion of household contacts of adults had symptoms and many of these had TB. Many women and men had not attended a health service for diagnosis. Further analysis will describe the cost effectiveness and sustainability of the approach.

### OP-155-16 Tuberculosis screening practices in HIV care and treatment settings in Tanzania

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**Background:** Intensified case finding (ICF) of TB is a cornerstone of TB-HIV care and treatment integration in high TB burdened countries. In Tanzania, national policy stipulates that all HIV-positive patients be screened for TB at every clinic visit. In support, the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) provides technical support through capacity building, mentorship, and supportive supervision on TB-HIV services in 165 antiretroviral therapy (ART) facilities since 2008.

**Methods:** EGPAF compared documented ICF services in some at-risk populations for TB such as children, women and patients on ART. Routinely collected TB data were abstracted from ART facilities between April 2010 and September 2011, and  $\chi^2$  analysis performed using STATA.

**Results:** 383 002 clinic visits forms were reviewed, 252 376 (66%) visits for women, 34 374 (9%) for children < 14 years and 246 397 (64%) for patients on ART. TB symptom screening was performed in 84% (322 435) with no significant difference between pediatric and adult visits (75.7% and 78.9%, respectively [ $P = 0.8$ ]); or between female and male visits (78.3% and 76.4%, respectively [ $P = 0.4$ ]); but differences in screening among those on ART compared to those not (87% and 74.1%, respectively [ $P < 0.001$ ]) was reported. TB symptoms were more often reported in children than adults (8% and 3.4%, respectively [ $P < 0.001$ ]); during visits involving men versus women (4.3% and 3.6%, respectively [ $P < 0.001$ ]), and during visits with patients not on ART versus those on ART (4.7% and 3%, respectively [ $P < 0.001$ ]). In all, 393 (13.3%) active TB cases were discovered among children, 1759 (45.3%) among women and 1745 (51.3%) among ART patients. ICF services were evenly delivered according to age and gender and yielded a high number of active TB cases.

**Conclusion:** It is not clear whether the higher proportion of active TB cases identified among patients not on ART was a function of a lower level of screening or a true higher TB incidence. While delivering TB-HIV services, programs shall consider delivery of equitable access to TB care including at-risk populations.

#### **OP-156-16 A successful tuberculosis contact investigation programme among children in northern Thailand**

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**Background:** Carrying out contact investigations among children who had contact with acid fast bacilli (AFB) smear-positive pulmonary tuberculosis (TB) patients is important since TB is still highly prevalent in Thailand.

**Intervention:** The study was conducted between 2009 and 2011 in 26 hospitals in 10 provinces in northern Thailand. We developed guidelines of how to carry out contact investigations among children under 18 years of age who had contact with both smear-positive and smear-negative pulmonary TB cases, and trained health care workers to use these guidelines as well as to perform tuberculin skin tests. We approached all eligible index cases. We took contact histories, did physical examinations, and took chest X-rays of all children before giving a diagnosis of either TB, latent tuberculosis infection (LTBI), or

normal condition. We followed all children up for at least 1 year after diagnosis.

**Results:** We collected data among 1676 index cases who had pulmonary TB (AFB smear-positive: 733 [44%]; AFB smear-negative: 943 [56%]). Six hundred twelve children (83%) were reported to have had contact with smear-positive index cases and 544 (89%) of these children came to the hospital for contact investigations. Twenty-four children (4%) had TB, 344 (63%) had LTBI, and 179 (33%) had a normal condition. Two hundred ninety-eight children (32%) were reported to have had contact with smear-negative index cases and 155 (52%) came to the hospital for contact investigations. Three children (2%) had TB, 74 (47%) had LTBI, and 79 (51%) had a normal condition. No children died during the follow-up period.

**Conclusion:** The contact investigations helped early diagnosis of TB and LTBI among children who had contact with both smear-positive and negative pulmonary TB patients. They enabled health care providers to provide timely treatment and prophylaxis for those children before the onset of severe TB illness.

#### **OP-157-16 Evaluating the roll-out of Lesotho's guidelines for intensified case finding for tuberculosis and isoniazid preventive therapy in maternal and child health clinics**

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**Background:** The Lesotho Ministry of Health and Social Welfare (MOHSW) issued guidelines on intensified case-finding (ICF) for TB and isoniazid preventive therapy (IPT) in April 2011. Provision of IPT to pregnant women has been controversial in some settings. Drug-induced hepatotoxicity is a rare but known side-effect of isoniazid. Furthermore, women may develop hepatobiliary disease, including the HELLP (hemolysis, elevated liver enzymes, low platelet count) syndrome, during pregnancy. Antiretrovirals for HIV infection may also cause hepatotoxicity; female sex and higher baseline CD4+ T-cell counts have been associated with an increased risk of nevirapine-related hepatotoxicity in some studies. It is unclear whether HIV-infected pregnant women receiving IPT with or without ART are at increased risk for hepatotoxicity compared with other patients. The Elizabeth Glaser Pediatric AIDS Foundation (EGPAF) and Johns Hopkins University Center for Tuberculosis Research (JHU-CTR) evaluated implementation of these guidelines

in the maternal and child clinics at Berea Hospital and St. Joseph's Hospital.

**Design/methods:** Routine program data were abstracted from clinic registers. Study participants included HIV-infected and -uninfected pregnant women presenting for their first antenatal (ANC) visit. Data were analyzed using the  $\chi^2$  or Wilcoxon rank-sum test for categorical and continuous variables respectively using STATA (v11).

**Results:** Between June 2011 and February 2012 we enrolled 160 HIV-infected and 640 HIV-uninfected women. The median gestational age was 24 weeks, and median CD4 count among 128 HIV-infected women was 409 cells/mm<sup>3</sup>. 799 women were screened for TB; 18 HIV-infected (11%) and 12 HIV-uninfected (2%) women were identified as TB suspects ( $P < 0.001$ ). 120 of 155 (77%) eligible HIV-infected women were started on IPT by March 2012. Of those eligible for IPT at Berea Hospital, 23 women (35%) were initiated on IPT at the first ANC visit, while at St Joseph's Hospital, 15 women (28%) were initiated on IPT at the first ANC visit. Among those initiated on IPT after the first ANC visit, 50% were initiated within 8 days at Berea Hospital and 64 days at St. Joseph's Hospital respectively. Women eligible for and receiving IPT presented for a median of three follow-up visits, with 106 (88%) having had at least one follow-up visit. None of the women reported side-effects potentially related to IPT (i.e., nausea/vomiting, jaundice, neuropathy, rash, convulsions) during 314 follow-up visits. Of those on IPT, 74 were on AZT prophylaxis for prevention of mother-to-child transmission of HIV, and 31 were on efavirenz-based and 14 on nevirapine-based antiretroviral therapy.

**Conclusion and recommendations:** Roll-out of the MOHSW ICF/IPT guidelines accompanied by implementation research identified site-level differences in IPT initiation due to drug availability. Ongoing research will assess TB case detection and IPT adherence and toxicity. Results will be instrumental to guide nationwide implementation of these guidelines.

### OP-158-16 Childhood tuberculosis: case notification, treatment outcome and INH preventive therapy for children in 26 countries supported by the Global Drug Facility

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**Background:** The World TB Day of 2012 emphasised the need to boost paediatric TB care in the context of global TB control. However, diagnosis of paediatric cases (0–15 years of age) and isoniazid preventive therapy (IPT) in children under 5 years of age remain major challenges. We present data from 26 countries

related to notification of paediatric cases, treatment outcome and IPT implementation.

**Methods:** Descriptive analysis of notified paediatric cases, treatment outcome and IPT implementation for children in 26 countries receiving GDF support, based on GDF country monitoring mission reports.

**Results:** In 2010, the percentage of paediatric cases over all cases ranged from 2.6% in Moldova to 23.6% in Myanmar; it was not reported in 7 of the 26 countries (Table). Ten countries reported treatment outcome of children; in countries where only the treatment outcome of smear-positive children was reported the sample size was very small. The treatment success rate was above 90% in 7 countries, 89% in one country and between 72% and 73% in two countries. By 2010, all countries had a policy to use IPT for children. In 5 countries, a tuberculin skin test was recommended before considering IPT. Ten of the 26 countries had no or minimal implementation of IPT. Only 10 countries could report on the number of children below 5 years of age put on IPT over a year: Lebanon, Jordan, Iraq, Afghanistan, Uzbekistan, Turkmenistan, Georgia, Zambia, Lesotho and Malawi.

**Table** Percentage and number of all notified cases below 15 years in 2010 in 26 GDF countries according to the estimated TB burden (TB incidence rate per 100 000)

TB incidence rate											
> 300	Zambia	Guinea	Lesotho	Cambodia	PNG	Djibouti	Myanmar				
%	no data available	4.2%	9.7%	11.1%	19.1%	20.9%	23.6%				
Number of children	no data available	479	1,276	4,613	2,733	878	32,471				
200 to 300	Haiti	Malawi	Mongolia	Pakistan	Somalia						
%	no data available	no data available	9.1%	9.2%	21.2%						
Number of children	no data available	no data available	438	24,474	2,217						
100 to 199	Nepal	Nigeria	Georgia	Moldova	Cape Verde	Afghanistan	Kyrgyzstan	Uzbekistan	North Sudan		
%	no data available	no data available	no data available	2.6%	3.0%	8.2%	9.2%	9.6%	14.0%		
Number of children	no data available	no data available	no data available	139	11	2,305	533	2,000	2,933		
< 100	Turkmenistan	Iraq	Morocco	Lebanon	Jordan						
%	no data available	7.1%	7.6%	8.3%	11.0%						
Number of children	no data available	714	22	43	39						

**Conclusions and recommendations:** In spite of GDF support over several years, not all countries reported for 2010 paediatric case registration. Full implementation of IPT for children was uncommon and unwarranted fear of producing INH-resistance was mentioned as a challenge. A better understanding of the real and perceived obstacles to adequate paediatric TB care will help to develop strategies for comprehensive paediatric TB care.

### OP-159-16 Risk of death during tuberculosis treatment in paediatric tuberculosis cases in Médecins Sans Frontières TB-HIV projects in Africa and Asia

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**Background:** Of 8.8 million estimated cases of TB in 2010 little is known about the burden borne by

**Table** Univariate and multivariate analysis of risk factors for death during TB treatment

Variable	Total n (%)	Died n (%)	P value $\chi^2$	Adjusted OR (95% CI)*
Overall	2451 (100)	8.6 (211)		
Sex				
Male	1256 (51)	9.2 (116)	0.26	
Female	1195 (49)	8.0 (95)		
Age group, years				
0–4	1026 (0.42)	10.7 (110)	0.002	1.70 (1.18–2.45)
5–15	1425 (58)	7.1 (101)		
Region				
Sub-Saharan Africa	1201 (49)	10.5 (126)	0.001	
Asia	1250 (51)	6.8 (85)		
Country				
Myanmar	1184 (48)	7.1 (84)	<0.001	
India	66 (3)	1.5 (1)		
Democratic Republic of Congo	412 (17)	7.3 (30)		
Zimbabwe	653 (27)	12.3 (80)		
Uganda	52 (2)	3.9 (2)		
Central African Republic	84 (3)	16.7 (14)		
Year of enrolment				
2007	819 (34)	9.0 (74)	0.07	
2008	825 (34)	6.7 (55)		0.56 (0.35–0.89)
2009	615 (25)	9.8 (60)		0.85 (0.40–1.82)
2010	192 (5)	11.5 (22)		0.77 (0.93–2.05)
Prior history of TB treatment†				
Yes	139 (6)	14.4 (20)	0.01	1.66 (0.94–2.93)
No	2232 (94)	8.2 (184)		
Site of disease				
Smear-positive PTB	158 (6)	5.1 (8)	0.008	
Smear-negative PTB	1223 (50)	9.6 (130)		
TB meningitis	50 (2)	18 (9)		2.64 (1.03–6.80)
TB adenitis	283 (12)	4.6 (13)		0.85 (0.40–1.82)
EPTB other site	139 (6)	8.6 (12)		1.51 (0.93–2.43)
EPTB site unspecified	468 (19)	8.3 (39)		
HIV status				
Positive	935 (38)	12.8 (120)	<0.001	2.57 (1.56–4.23)
Negative	578 (24)	5.2 (30)		
Unknown	938 (38)	6.5 (61)		—
HIV-positive children only (n = 935)				
ART status at time of TB diagnosis				
Receiving ART	137 (15)			1.62 (0.82–3.19)‡
Not receiving ART	415 (44)			
Unknown	383 (41)			—

\*Adjusted for HIV status (positive and negative only), site of disease, prior history of treatment, age, year of treatment and project clustering.

†Children transferred in excluded.

‡Adjusted for age, site of disease and project clustering.

PTB = pulmonary TB; EPTB = extra-pulmonary TB; ART = antiretroviral treatment; OR = odds ratio; CI = confidence interval.

children. In a retrospective analysis of programme data we reviewed the risks of death during treatment in paediatric TB patients in 13 Médecins Sans Frontières (MSF) projects providing integrated HIV care in 6 countries. This is the largest multi-national cohort of paediatric TB-HIV co-infection reported.

**Design/methods:** Paediatric TB data from 2007 to 2010 were analysed by descriptive statistics and logistic regression. TB diagnosis was by WHO algorithm and smear microscopy. Approval was given by MSF and LSHTM ethics committees.

**Results:** 2451 children, mean age 5.2 years (SD 3.9) were treated. 51% lived in Asia, the rest in sub-Saharan Africa. 56% had pulmonary TB. 6.4% were smear-positive. Overall, 211 (8.6%) died. Of the 1513 tested, 935 were HIV-positive of whom 120 (12.8%) died; 5.2% of HIV-negative children and 6.5% of those with unknown HIV status died. Antiretroviral treatment (ART) status was documented in 60% of HIV-positive children (552); 137 received ART at TB treatment initiation. In multivariate analysis, odds of death increased in those HIV-positive (OR 2.57; 95% CI 1.56–4.23), aged  $\leq 4$  years (1.70; 1.18–2.45) or with TB meningitis (2.64; 1.03–6.80). The odds of death were unchanged by ART in HIV-positive children. Children with unknown HIV status in Africa had higher risk of death than those confirmed HIV-negative (1.87; 1.07–3.28;  $P = 0.08$ ).

**Conclusion and recommendations:** Universal HIV testing in children with TB is vital. In Africa, children of unknown HIV status had higher odds of death than HIV-negative children, consistent with a proportion having undiagnosed HIV disease. Uncertainty around paediatric TB diagnosis may contribute to misdiagnosis of TB and mistreatment of alternative pathology, increasing mortality in HIV-positive children. The low proportion of microbiologically confirmed TB highlights the need for improved diagnostic tools in children.

### OP-160-16 Risk factors for mortality in Malawian children with HIV-TB co-infection

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**Background:** This study involved a cohort of patients from a large, urban pediatric HIV clinic in Lilongwe, Malawi over a period of time when national guidelines for the management of pediatric HIV and TB co-infection underwent significant revisions. Our objective was to describe this cohort in terms of clinical parameters including nutritional status, clinical and immunologic stage, and, secondarily, to identify risk

factors for mortality in children with HIV-TB co-infection.

**Design:** We conducted a retrospective cohort study of HIV-infected children (<18 years) enrolled between October 2004 and October 2010 with at least one current or historical TB diagnosis. Descriptive statistics and logistic regression analyses were performed to elucidate relationships between covariates.

**Results:** 1561 patients met inclusion criteria, representing 32% of patients ever enrolled. Median (IQR) age at TB diagnosis was 3.8 [1.5–7.4] years. 60.9% had severe immune suppression and 47.6% had some degree of acute malnutrition at the time of TB diagnosis. 77.8% of patients had started antiretroviral therapy (ART) at some point either before or after TB diagnosis. 225 (20.2%) of the 1113 patients with known outcomes had died (patients transferred to other facilities and lost-to-follow-up were excluded). Infants <12 months and those with advanced clinical stage and immune suppression were at increased risk for mortality. ART initiation at any time resulted in significant reduction of mortality risk (adjusted OR = 0.14, 95%CI 0.08–0.27).

**Conclusions:** Pediatric HIV-TB co-infection was common and mortality rates were high in this cohort. Recent national guideline changes recommending ART for any HIV-infected child with TB and more timely ART initiation in those already on TB treatment are supported by our findings. Clinic protocols should be designed to prioritize prompt initiation of ART and close follow-up of co-infected patients, particularly infants.

## CURES, DEATHS AND FAILURES: ISSUES IN THE MANAGEMENT OF TUBERCULOSIS

### OP-161-16 Study on curative effect and adverse reactions between different treatment approaches using fixed-dose anti-tuberculosis combination

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**Background:** National TB Control Programme (2010–2015) in China had put forward to the target that 100% of the counties will use anti-TB fixed-dose combination (FDC) till 2015. This study was supported by China-Gates Foundation TB Project, the findings will facilitate the development of promotion strategies on anti-TB FDC in China.

**Design/methods:** All new TB patients from 7 provinces and 41 counties were involved in this observational study. Anti-TB FDC were given to all the patients. One group was given 2HRZE (H75 mg,

R150 mg, Z400 mg, E275 mg)/4HR (H100 mg, R150 mg), and the other group used 2H3R3Z3E3 (H120 mg, R120 mg, Z400 mg, E250 mg)/4H3R3 (H200 mg, R200 mg). The  $\chi^2$  test was used for comparing the curative effect and adverse reaction between different treatment approach.

**Results:** Of 4907 patients, male accounted for 66.8% (3279/4907), farmers accounted for 75.6% (3711/4907), patients with junior high school education or less were 84.1% (4128/4907), average age was  $48.49 \pm 19.08$  years old, and their average weight was  $55.93 \pm 8.74$  kg. The total adverse reaction rate was 21.5% (1055/4907), the difference between the two treatment approaches are unnoticeable ( $\chi^2 = 1.713$ ,  $P = 0.190$ ), but the gastrointestinal adverse reaction rate was higher in the every other day treatment group ( $\chi^2 = 6.141$ ,  $P = 0.013$ ). The cure rate in new smear positive patients was 94.7% (2896/3059), and the every other day treatment group performed better than the daily treatment group ( $\chi^2 = 11.791$ ,  $P = 0.001$ ). The complete treatment rate in new smear negative patients was 95.1% (1758/1848) and there was no significant difference between the two treatment approaches ( $\chi^2 = 2.152$ ,  $P = 0.142$ ).

**Table** Side effects in different treatment approach

Group	n	Gastro-intestinal disturbance	Allergic reaction	Nervous system	Others	Total
Daily treatment	3559	390 (11.0)	122 (3.4)	101 (2.8)	169 (4.7)	782 (22.0)
Every other day treatment	1348	182 (13.5)	20 (1.5)	37 (2.7)	34 (2.5)	273 (20.3)
Total	4907	572 (11.7)	142 (2.9)	138 (2.8)	203 (4.1)	1055 (21.5)
$\chi^2$		6.141	13.152	0.031	12.219	1.714
P value		0.013	0.000	0.860	0.000	0.190

**Conclusion and recommendations:** The curative effect and adverse reaction were similar between different treatment approaches, but considering daily treatment can reduce the gastrointestinal side effects, and improve patients' compliance, it's more suitable to be used in the promotion of anti-TB FDC in China.

### OP-162-16 Time to consider failure for multidrug-resistant tuberculosis cases

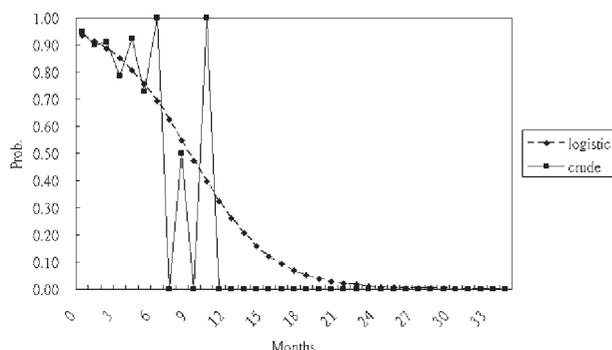
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**Background:** It has been debated for whether prolonged treatment for MDR-TB cases is beneficial. The aim of this study is to calculate sputum conversion

time and its relationship to treatment outcome in pulmonary MDR-TB patients.

**Design/methods:** Taiwan MDR-TB consortium (TMTTC) launched by Taiwan CDC started to provide MDR-TB care since May 2007. MDR-TB cases that were diagnosed during January 2007 and May 2009 were enrolled. They were followed up for at least 30 months after initial sputum collected. Vector Generalized Additive Model (VGAM) was used to predict the exact month after commencement of second-line anti-TB treatment. The analysis was done by R software (R Foundation for Statistical Computing, Vienna, Austria).

**Results:** A total of 272 cases experienced at least one time of culture conversion during the study period and 88% of them were successfully treated. Majority of first culture conversion occurred before 5 months so we took logarithmic of the converted month first. VGAM revealed that no conversion before the end of 2 months of treatment predicted worse treatment outcome. This point estimate had 65% predictive value (area under curve: 0.56–0.74). The Figure shows the prediction of initial culture conversion and treatment success estimated by logistic regression model. Treatment success decreased to < 85% if no conversion was noted after 3 months of treatment. Fifty percent probability of treatment success occurred between 8 and 9 months of treatment. We did another VGAM analysis by using culture conversion month defined by WHO criteria (at least 30 days with two consecutive negative culture result and no positive culture result until treatment completion). The result showed that no conversion before the end of 8 months of treatment predicted worse treatment outcome. This point estimate had 70% predictive value (area under curve: 0.62–0.79). Treatment success decreased to <85% if conversion defined by WHO was not achieved after 8 months of treatment.



**Conclusion and recommendations:** After quantitative analysis by VGAM, the relationship of conversion and treatment outcome could be well-visualized. Randomization study is warranted to testify whether sputum collected after 2 month of treatment could be a surrogate for adjustment of regimen or operation

evaluation. Sputum culture conversion between 8 and 9 months is a predictor for failure and the patient should be evaluated with caution.

### OP-163-16 A retrospective cohort study of clofazimine in the treatment of extensively drug-resistant tuberculosis in South Africa

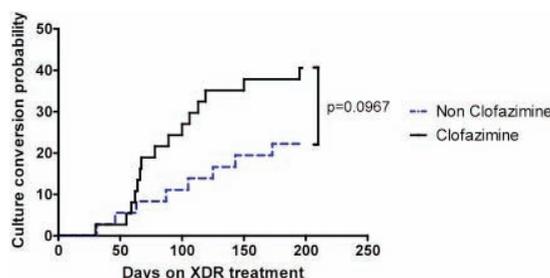
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**Background:** Clofazimine is a second line agent in the treatment of tuberculosis that has shown significant activity in in vitro studies against drug resistant strains of *Mycobacterium tuberculosis*. We performed this study to describe treatment outcomes in XDR-TB patients treated with clofazimine as part of their XDR-TB drug regimen in a high HIV prevalence setting.

**Design/methods:** From August 2009 to July 2011, 77 patients with XDR-TB at King George V Hospital in Durban, KwaZulu Natal, South Africa were evaluated, with 41 being initiated on clofazimine as part of their standard treatment regimen. Of this group of 77 patients, 85.7% were HIV positive. The outcome studied was the 6 month culture conversion rate with culture conversion being defined as two consecutive negative sputum cultures at least one month apart.

**Results:** We report a 42.1% 6 month culture conversion rate in the clofazimine regimen compared to 22.2% in the non-clofazimine regime. Our results in the clofazimine cohort are significantly higher than the 20% culture conversion rate previously reported in the same cohort in a 2009 study. The Figure shows a Kaplan Meier curve comparing the two cohorts with respect to 6 month culture conversion, showing a trend that patients on clofazimine were two times more likely to culture convert within 6 months compared to those not on clofazimine (HR 2.1, 95%CI 0.9–5.6). Significant predictors of outcome in the clofazimine cohort were age and HIV status. We did



**Figure** Six months culture conversion.

not find an association between ARVs, previous history of TB/MDR-TB and time to culture conversion. **Conclusion and recommendations:** Considering the trend towards a higher rate of culture conversion, we would like to make a recommendation to include clofazimine as part of the initial regimen in the treatment of XDR-TB. Further studies are required comparing regimens containing clofazimine to regimens not containing clofazimine.

### OP-164-16 How many sputum samples need to be examined for tuberculosis treatment management decisions during follow-up?

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**Background:** Response to TB treatment is monitored by follow-up sputum smear microscopy at periodic intervals with smear results guiding further clinical management decisions like extension of the intensive phase (IP) and declaration of treatment failure. Currently, two sputum samples (termed A & B) are examined at each follow-up which affects patient convenience and costs. We assessed the impact of reducing the number of specimens from two to one on the clinical decision making and the laboratory workload.

**Method:** We reviewed TB registers and laboratory registers to extract data on results of follow-up smear microscopy (A & B) for a cohort of pulmonary TB patients registered under the Revised National TB Control Program from July to September 2009, in 7 districts of Maharashtra, India, and related result of each of A & B specimen on clinical management decisions. We also collected data on total smears examined for the year 2010 to assess workload.

**Results:** Of 2301 pulmonary TB patients eligible to have 5273 follow-up sputum examinations, 4394 (83%) were done and 258 (6%) were positive. Discordance between A & B samples was noted in 0.57% (25/4394) cases, with 72% (18/25) having one sample graded 'scanty' and other sample negative. Using

**Table** Implications of considering results of single sample A or sample B smear examination during follow-up sputum examinations on TB patient management

	New Smear positive TB n=1076		Re-treatment Smear positive TB n=479		Smear negative TB n=746		Total Pulmonary TB n=2301	
	Sample A only	Sample B only	Sample A only	Sample B only	Sample A only	Sample B only	Sample A only	Sample B only
Extension of IP missed No. %	7 (0.65%)	6 (0.56%)	5 (1.04%)	0 (0%)	0 (0%)	0 (0%)	12 (0.52%)	6 (0.26%)
Identification of treatment failures missed No. (%)	0 (0%)	0 (0%)	1 (0.002%)	0 (0%)	0 (0%)	1 (0.001%)	1 (0.043%)	1 (0.043%)

results of single specimen would have led to non-extension of IP in 0.52% of pulmonary cases, while reducing laboratory workload by 12%.

**Conclusion:** There is no added advantage of examining two samples for microscopy as compared to one sample during follow-up of TB treatment. Other than missing IP extension in a negligible number of TB patients, it would have had no impact on clinical management. Rather, this would significantly reduce workload and improve patient convenience and program should consider revising the current guidelines.

### OP-165-16 The outcome of drug reintroduction after hepatitis during anti-tuberculosis treatment

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**Background:** Drug-induced hepatotoxicity (DIH) is the most common adverse effect leading to interruption of anti-tuberculosis (TB) treatment, but the best way to reintroduce first-line anti-tuberculosis medications after recovery of liver function was still unknown.

**Methods:** Randomized control prospective study.

**Results:** Between April 2011 and January 2012, a total of 4213 episodes of liver function tests were screened. Among 164 cases with abnormal liver function tests, 18 patients were randomized, with 9 into rapid reintroduction group and 9 into standard reintroduction group. The demographic data and severity of hepatitis were similarly between two groups. Isoniazid (INH) and rifampicin (RMP) were reintroduced successfully in 12 patients (66.7%). The successful INH-RMP reintroduction rate were similar in both groups (66.7% vs. 66.7%, respectively,  $P = 1.00$ ). Pyrazinamide (PZA) was reintroduced in 6 cases (3 in rapid reintroduction group and 3 in standard reintroduction group) and the successful PZA reintroduction rate were low and similar in both groups (33.3% vs. 33.3%, respectively,  $P = 1.00$ ). Among 18 cases with RMP reintroduction, 4 cases (22.2%) experienced non-hepatitis side effect requiring to stop reintroduction (3 with RMP-related jaundice and another with RMP-related skin rash). Among 18 cases with INH reintroduction, recurrent hepatitis due to INH developed in one case (5.6%). In contrast, among 6 patients who received PZA reintroduction, 4 (66.7%) failed to complete reintroduction due to side effect (recurrent hepatitis due to PZA in 3 cases and PZA-related jaundice in the other).

**Conclusions:** The incidence rate of adverse effects during reintroduction of anti-TB drugs was similar while using rapid or standard reintroduction protocols. INH and RMP could be reintroduced successfully in

two thirds and with few hepatitis recurrences (5.6%). In contrast, reintroduction of PZA was associated with high incidence rate of hepatitis recurrence.

#### OP-166-16 Serum CXCL10 levels in tuberculosis correlate with response to therapy

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**Objective:** To investigate the utility of serum CXCL10 levels as a biomarker of tuberculosis (TB) and subsequently to monitor response to anti-tuberculous.

**Study design:** Cross-sectional study.

**Place and duration of study:** The OJHA Institute for Chest Diseases, DOW University of Health Sciences, Karachi, and the Aga Khan University, Karachi, Pakistan. August 2009–July 2010.

**Methodology:** Patients with pulmonary TB ( $n = 120$ ) were recruited and classified according to a TB scoring system into severity classes I ( $n = 40$ ), II ( $n = 38$ ) or III ( $n = 42$ ). Healthy endemic controls individuals ( $n = 33$ ) were also recruited. Whole blood was collected upon recruitment and at 12 weeks post-treatment and CXCL10 levels were measured in serum samples of all patients by ELISA.

**Results:** Patients with untreated TB had significantly higher CXCL10 levels than healthy controls ( $P < 0.001$ ). Serum CXCL10 levels were compared in patients prior to treatment with those after 12 weeks of therapy. After 12 weeks of treatment it was observed that CXCL10 levels decreased significantly in all three TB severity groups.

**Conclusion:** Our data suggests CXCL10 as convenient serological marker of TB which can also be used to monitor response to treatment in TB patients.

#### OP-167-16 Treatment results of clofazimine used in the management of multidrug-resistant tuberculosis patients during the intensive phase of treatment

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**Setting:** According to WHO data clofazimine included into group of the drugs with unconfirmed anti-tuberculosis activity, it may be used in some cases. Clofazimine is in use in Donetsk Oblast for the treatment of XDR-TB cases and when it is impossible to compile full treatment scheme.

**Aim:** To assess pulmonary MDR-TB patients' treatment results after intensive treatment phase using clofazimine.

**Materials and methods:** 66 pulmonary MDR-TB patients have been treated, 48 males (73%) and 12 females (27%), with average age of 38 years old. Inclu-

sion criteria into this research were as follows: new and previously treated smear-positive and smear-negative MDR-TB cases with HRES resistance; resistance of MBT to Z was not checked. Patients of the first group ( $n = 30$ ) received treatment according to following treatment regimen Z Km Lfx Pt Pas Cfz, patients of the second group ( $n = 36$ ) received Z Km Lfx Pt Pas.

**Results:** Smear/culture conversion in 1 month of treatment was achieved in 13 (43%) patients of the first group and in 11 (31%) patients of the second group. Sputum conversion in 2 months was registered in 5 (83%) and 19 (53%) patients, after completion of intensive treatment phase (6 months)—in 26 (87%) and 7 (75%) patients correspondingly.

**Conclusion:** Using of clofazimine in treatment of MDR-TB patients helps to stop bacilli excretion in majority of patients for the shorter period of treatment.

#### OP-168-16 Increased risk of deaths in tuberculosis-hepatitis C virus co-infected patients in Karachi, Pakistan

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**Background:** Pakistan has a high prevalence of both TB (330 per 100 000) and hepatitis C virus (HCV) (4–5% of the general population). In areas of low-HIV prevalence, other co-morbid diseases are of increasing importance for the control and management of TB. Treatment outcomes in cohorts of co-infected (TB-HCV) cases have not been previously reported from Pakistan.

**Methods:** A retrospective, medical record abstraction was conducted on all adult drug-susceptible TB cases screened for HCV between January 2008 and March 2012 at the Indus Hospital TB Control Program.

**Results:** 1684 TB cases were screened for HCV infection and 221 (13%) were found to be co-infected. TB-HCV prevalence was significantly higher in males compared with females (17% vs. 10%,  $P < 0.0001$ ) and co-infected cases were significantly older than HCV negative TB cases (median age: 38 vs. 26,  $P < 0.0001$ ). Of those with treatment outcomes, TB-HCV cases were 2.2 (95%CI) times more likely to die during treatment than HCV-negative TB cases after adjustment for age and gender. The risk of default in co-infected cases was also higher, but only tended towards significance after adjustment. Treatment success was reported in 580 of 803 (72.2%) HCV negative patients as compared to 65 of 112 (58%) HCV co-infected patients.

**Table** Treatment outcomes in drug-susceptible tuberculosis (DS-TB) patients screened for hepatitis C

Outcomes	HCV- n (%)	HCV+ n (%)	Crude RR (95% CI)	Adjusted RR (95% CI)
Default, failure and death	223 (28)	47 (42)	1.73 (1.22–2.44)	0.84 (0.65–1.09)
Death	99 (11)	13 (28)	1.08 (1.01–1.16)	2.17 (1.13–4.16)
Default	75 (10)	24 (17)	1.01 (1.00–1.26)	1.60 (0.93–2.27)

**Conclusion:** HCV co-infection in drug-susceptible TB patients contributes significantly to observed death rates. In low-HIV settings, all TB cases should be screened for HCV prior to treatment initiation; those infected should have their baseline liver enzymes documented. Programs should consider conducting effectiveness trials of simultaneous treatment for hepatitis C and susceptible TB.

## NEW FRONTIERS IN THE MANAGEMENT OF MDR- AND XDR-TB

### OP-169-16 Novel therapeutic vaccines against tuberculosis and their synergistic efficacy using chemotherapy

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**Background:** Multidrug-resistant (MDR), especially extremely drug-resistant (XDR), *Mycobacterium tuberculosis* (MTB) is a big problem in the world. We have developed novel TB therapeutic vaccines, (HVJ-E/HSP65 +IL-12 DNA vaccine and granulysin vaccine), to eliminate XDR-TB.

**Design/methods:** DNA vaccine expressing MTB heat shock protein 65 and IL-12 was delivered by the hemagglutinating virus of Japan (HVJ)-envelope. MTB was intratracheally instilled into cynomolgus monkeys and then treated with the vaccine. Granulysin DNA was obtained from human CTL.

**Results:** HSP65+IL-12DNA 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 TB). This vaccine showed synergistic therapeutic efficacy by the addition of granulysin DNA vaccine in mice. This vaccine also exerted synergistic therapeutic effect by the combination of chemotherapy (INH). Furthermore, we extended our studies to a cynomolgus monkey model, which is currently the best animal model of human tuberculosis. HSP65+IL-12 DNA vaccine provided therapeutic efficacy of prolongation of survival time

(100% survival) and the augmentation of immune responses (IL-2 production) in TB-infected monkeys. Synergistic efficacies of this vaccine, granulysin DNA vaccine and chemotherapy (INH+RFP) are now being studied in monkeys.

**Conclusion and recommendations:** These data indicate that our novel vaccines might be useful against *Mycobacterium tuberculosis* including XDR-TB and MDR-TB for human therapeutic clinical applications. (Co-worker; Nishida Y, Nakatani H, Kano K, Kishigami C, Nakura K, Nagasawa T, McMurray D, Hayashi S, Saunderson P).

### OP-170-16 Treatment outcome of multidrug-resistant tuberculosis patients under modified DOTS-Plus, a new strategy: two year experience

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**Background:** Multidrug-resistant tuberculosis is a global problem and growing threat to human health with notoriously difficult and challenging treatment. This study has been framed to depict treatment outcome with second line drugs in patients of MDR-TB in modified DOTS-PLUS strategy.

**Design/methods:** A prospective cohort study analyzing 98 consecutive patients with MDR-TB attending the Dept of Pulmonary Medicine, CSMMU, between June 2009 and Feb 2010 with follow-up until February 2012. All the patients were given medications free of cost as per DOTS PLUS Protocol of Revised National Tuberculosis Control Programme (RNTCP). Treatment included monthly follow up, adherence check up, radiological and bacteriological assessment (sputum smear advised monthly till conversion then quarterly; culture for *M. tuberculosis* at 0, 4, 6, 12, 18, 24 months), intense health education and monitoring of adverse effects. Patients' outcome considered as cure when at least 2 of the last 3 cultures were negative and as failure when the same were positive.

**Results:** All the patients had resistance to at least isoniazid and rifampicin with mean no. of 3.02 drugs and were seronegative for HIV. Default rate and expiry rate at the completion of 24 months of treatment were observed to be 7 (7.1%) and 10 (10.2%) respectively. Mean smear and culture conversion time were  $3.4 \pm 2.1$  months (1–11) and  $4.6 \pm 2.5$  months (4–12) respectively. Sputum smear and culture conversion rate were 75/81 (92.5%) and 71/81 (87.7%) respectively with only 10 (10.2%) patients remained culture positive. Significant side effects were experienced in only 17.4% patients.

Outcome	Number of patients
Patients initiated on treatment	98
Lost to follow up/defaulted	7 (7.1%)
Expired	10 (10.2%)
Patients completed the treatment as planned	81 (82.7%)
Cured	71 (72.4%)
Failed	10 (10.2%)
Best scenario (excluding lost and expired patients)	71/81 (87.7%)
Worst scenario (lost & expired patients as failures)	71/98 (72.4%)
Mean duration of sputum conversion	3.4 ± 2.1 months (1–1)
Mean duration of culture conversion	4.6 ± 2.5 months (4–12)
Sputum conversion rate	75/81 (92.5%)
Culture conversion rate	71/81 (87.7%)
Patients experienced adverse effects	17 (17.4%)

**Conclusions and recommendations:** Culture conversion rate at the end of 24 months was 87.7%. Only 7.1% patients defaulted and 10.2% patients expired at the end of 24 months. MDR-TB can be cured successfully with appropriate combination of drugs for an adequate duration and requires much effort from both the patients and health care workers. Modified DOTS-PLUS strategy can be model for treatment of MDR-TB in private sector.

#### OP-171-16 Successful management of multidrug-resistant tuberculosis in Myanmar

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**Background:** The aim of this study was to evaluate the outcomes of the first MDR-TB patients treated according to World Health Organization guidelines in Myanmar.

**Methods:** Data on MDR-TB patients enrolled for treatment between July 2009 and March 2010 in 10 townships of Yangon and Mandalay were studied. A two-year standardized regimen of amikacin, levofloxacin, ethionamide, cycloserine, PAS and pyrazinamide was used for laboratory-confirmed MDR-TB patients that had undergone two TB treatment courses and had not received second-line anti-TB drugs for more than one month. Patients were hospitalized for the initial 2–3 months. Thereafter, home-based care was delivered by basic health staff. Diagnosis and treatment were provided free of charge, patients received socioeconomic support and patients and treatment providers received enablers.

**Results:** Of the 92 MDR-TB patients assessed, 58 (63%) were males. The average age and initial weight of the patients were 34.3 years (range 17–67) and 45.5 kg (range 26.8–88). Four patients (4.3%) were

co-infected with HIV (all were on antiretroviral therapy) and 10 patients (10.9%) had diabetes. The five most common adverse events were hypothyroidism (75.0%), nausea/vomiting (60.9%), arthralgia (59.8%), electrolyte disturbances (46.7%) and anorexia (44.6%) (Table). Cure was reported in 66 patients (71.7%), 18 died (19.6%), 7 defaulted (7.6%) and 1 failed (1.1%). The major causes of death were respiratory and renal failure (33.3% and 16.7%, respectively).

**Table** Frequency of adverse events among 92 patients receiving MDR-TB treatment in Yangon and Mandalay Regions

Adverse event	Affected <i>n</i> (%)
Hypothyroidism	69 (75.0)
Nausea/vomiting	56 (60.9)
Arthralgia	55 (59.8)
Electrolyte disturbances	43 (46.7)
Anorexia	41 (44.6)
Sleep disturbances	38 (41.3)
Gastritis	36 (39.1)
Dizziness/vertigo	28 (30.4)
Abdominal pain	26 (28.3)
Depression	25 (27.2)
Tinnitus	25 (27.2)
Hearing disturbances	19 (20.7)
Diarrhoea	13 (14.1)
Psychosis	10 (10.9)
Renal failure/nephrotoxicity	6 (6.5)
Rash	6 (6.5)
Peripheral neuropathy	4 (4.3)
Allergic reaction	3 (3.3)
Headache	2 (2.2)
Visual disturbances	2 (2.2)
Seizures	2 (2.2)
Hepatitis	0

**Conclusions:** The MDR-TB pilot project has been proven feasible with good cure rates, despite protracted disease among all patients and high frequencies of adverse events. Based on the overall results, MDR-TB diagnosis and treatment eligibility criteria are being expanded and the model of care refined. Earlier MDR-TB case detection and treatment should save additional lives and reduce transmission.

#### OP-172-16 Favorable outcomes for community-based extensively drug-resistant tuberculosis treatment

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**Introduction:** Extensively drug-resistant tuberculosis (XDR-TB, defined as TB resistant to isoniazid, rifampicin, one fluoroquinolone, and one of the second-line injectable drugs) in Peru is a serious public health problem with high social, economic, and political impact.

**Objective:** To analyze outcomes of a cohort of XDR-TB patients to better identify effective treatment

strategies, understand demographic and drug resistance trends, and inform the national TB program.

**Methodology:** Retrospective cohort study of 26 XDR-TB patients identified from records of 764 MDR-TB patients recruited between 1996 and 2005 at Sergio Bernales National Hospital in northern Lima, Peru. XDR-TB cases were confirmed with drug susceptibility tests (DST), treated with aggressive individualized regimens, and monitored with monthly smear and culture results. Treatment was administered using an intensive, community-based, DOTS-Plus strategy.

**Results:** Of 26 identified XDR patients, 17 (65%) were male and 9 (35%) were female. None of the patients were co-infected with HIV. Patients were generally young, with 73% of patients between 16 and 35 years of age (median age of 29). Treatment averaged 24.2 months, with 21 months of negative cultures. DST results are summarized in the Table. Outcomes were generally favorable among these 26 patients; 21 (80.8%) were cured (culture negative for  $\geq 18$  months), 1 (3.9%) defaulted (treatment interruption of  $\geq 30$  days), and 4 (15.38%) died.

Table Resistance in XDR cohort

Drug name	Resistant individuals (n=26)
Ethambutol	23 (88.46)
Streptomycin	22 (84.62)
Pyrazinamide	17 (65.38)
Kanamycin	20 (76.92)
Capreomycin	20 (76.92)
Ethionamide	15 (57.69)
Ciproflaxin	26 (100)
Cicloserine	1 (3.85)

**Conclusion:** Good outcomes in this small cohort demonstrate that, with appropriate care, XDR-TB can be effectively treated in this context. These high cure rates can be attributed to a number of factors ranging from the absence of HIV to the decentralized, highly individualized patient attention to the extensive socioeconomic interventions provided to patients. These data add to evidence that properly executed community-based interventions can effectively treat XDR-TB even in poorer contexts where HIV prevalence is low.

#### OP-173-16 Genomic characterisation of drug resistance mutations in extensively drug-resistant tuberculosis isolates from Delhi

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**Background:** MDR/p-XDR/XDR, the more severe drug-resistant form of tuberculosis is an increasing public health concern globally. The actual incidence and prevalence rate of XDR-TB in India is currently not available.

**Design/methods:** Six hundred and fifteen MDR-TB suspects were enrolled, and early morning sputum specimens collected, treated by NALC-NaOH method, cultured in MGIT 960 media and susceptibility testing to RIF and INH done for MDR-TB confirmation. Susceptibility testing to second line drugs (SLD) (amikacin, capreomycin, ofloxacin, and ethionamide) was performed for all MDR-TB isolates. DNA sequencing was done for the genes reportedly responsible for SLD resistance using ABI 3130 capillary sequencer. The sequences were analyzed using Gene-doc and Bio-edit softwares.

**Results:** Four hundred eighty-three MDR-TB isolates had 18 (3.72%) isolates resistant to ofloxacin or one of the second line injectable drug (either amikacin or capreomycin). Mutations were found primarily at position 1401 (A to G) in the *rrs* gene and at codon 94 (D to G and D to H) in the *gyrA* gene sequenced for detecting resistance to amikacin and ofloxacin respectively. The *thy* gene (for resistance to capreomycin) did not show any mutations in the 540bp region amplified for resistant isolates.

**Conclusion and recommendations:** There are a few scattered reports of XDR-TB in India. In the current study 3.7% of MDR-TB cases were XDR-TB. Our results clearly demonstrate the potential of sequence analyses of short regions of relatively few target genes for the rapid detection of resistance to second-line drugs among XDR-TB and pre-XDR-TB isolates and the ease of developing a rapid detection method. Reports of geographical predilection of drug resistant mutations call for a need to study prevalence of such mutant strains in different populations. Molecular detection utilising such data from world wide studies could eventually help in the design of a robust technique.

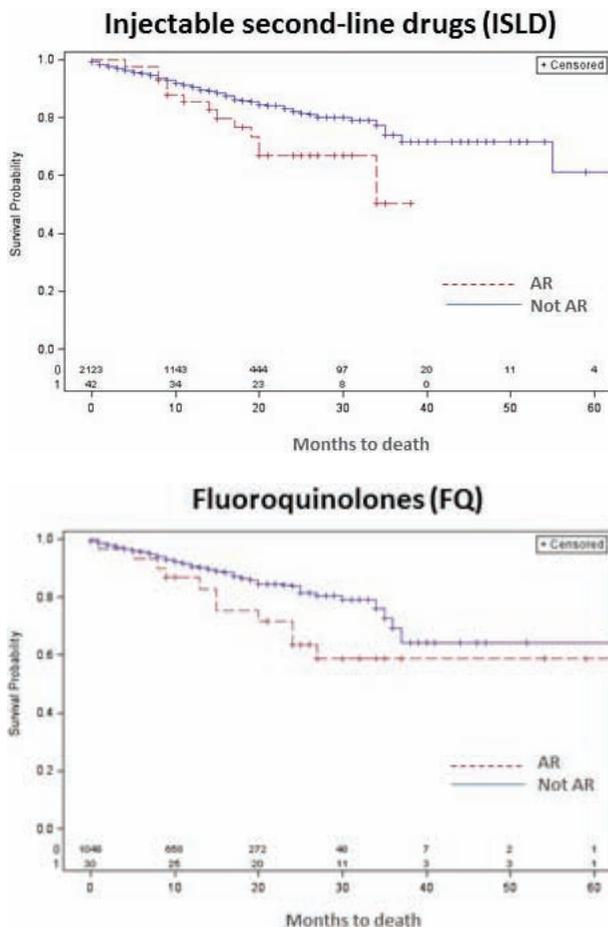
#### OP-174-16 Mortality among tuberculosis patients with acquired resistance to second-line anti-tuberculosis drugs in the US, 1993–2008

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**Background:** The emergence of extensively drug-resistant TB worldwide has raised concern about the impact of acquired resistance (AR) to SLD during treatment of drug-resistant TB. Our objectives were to assess the impact of AR to injectable second-line drugs (ISLD) and fluoroquinolones (FQ) on mortality among culture positive TB cases in the USA, 1993–2008.

**Design/methods:** We defined AR as drug resistance at the final drug susceptibility test (DST) but susceptibility to the same drug at the initial DST. We analyzed the impact of AR on all-cause mortality using Kaplan-Meier plots and extended Cox proportional hazards models.

**Results:** Of 2268 cases with both initial and final DST to ISLD, 49 (2.1%) acquired resistance; 13 (30%) of them died during treatment vs. 231 (11%) cases without AR to ISLD ( $P < 0.001$ ). Of 1138 cases with both initial and final DST to FQ, 32 (2.7%) acquired resistance; 12 (40%) of them died during treatment vs. 122 (12%) of those without AR to FQ ( $P < 0.001$ ). Probability of death was significantly higher among cases with AR to SLDs compared to cases without AR (HR = 2.4, 95%CI 1.3–4.6 for AR to ISLDs after 8 months of treatment, and HR = 2.0, 95%CI 1.1–3.6 for AR to FQs). MDR-TB at treatment initiation (HR (ISLD) = 1.4, 95%CI 1.1–1.8; HR (FQ) = 1.7, 95%CI 1.2–2.4), positive HIV status (HR (ISLD) = 7.6, 95%CI 5.4–10.8; HR (FQ) = 8.9, 95%CI 5.3–14.9), and extrapulmonary disease (HR (ISLD) = 2.6, 95%CI 1.9–3.4; HR (FQ) = 3.7, 95%CI 2.6–5.3) were also significantly associated with mortality among these cases.



**Figure** Kaplan-Meier survival curves of time to death.

**Conclusion and recommendations:** Mortality was significantly higher among TB cases with AR to SLD. Providers should consider AR to SLD and monitor DST results in cases with MDR-TB, positive HIV status, or extrapulmonary disease, especially if the patient's condition deteriorates during treatment.

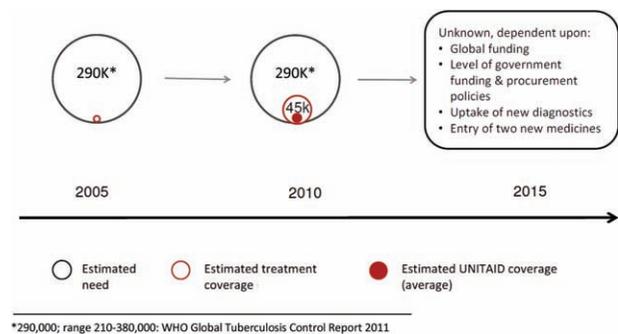
**OP-175-16 Market interventions to increase access to multidrug-resistant tuberculosis treatment: the UNITAID approach**

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**Background:** In 2012, ~45 000 patients were enrolled on MDR-TB treatment (only 16% of the estimated number globally). Sub-optimal treatment is driven by high prices, inadequate quality assurance (QA), lack of programmatic capacity to manage MDR-TB and limited laboratory capacity: less than 5% of TB patients were tested globally for MDR-TB in 2012.

**Intervention and results:** UNITAID financing, over the last 3 years, for MDR-TB treatment, expanded introduction of diagnostic technologies for DR TB and WHO prequalification of SLDs has achieved important public health gains: In 2011 an additional 11 000 MDR-TB patients were diagnosed in 13 countries (a 3-fold increase compared to 2010); MDR-TB treatment was scaled up in 18 countries (~10 500 additional treatments during 2008–2011); delivery lead-times were reduced through a Strategic Stockpile; and additional SLDs were prequalified.

**Lessons learnt:** UNITAID's market interventions are specifically designed to increase supply, improve quality, simulate the development of new products and reduce prices of medicines and diagnostics. On this count the success of its interventions to date has been important but limited. Critically, treatment with QA SLDs is still prohibitive at more than US\$2400 per course and the diagnostics introduced so far are only suitable for use at central/reference laboratory levels.



**Figure** Market evolution of second-line TB medicines.

**Conclusions:** The 'game-changer' for MDR-TB will be bringing high-quality diagnosis closer to the point-of-care, integrated with a medicines market approach driven by aggregation of global demand for current SLDs, coordinated global and national financing (particularly of BRICs and MICs) for MDR-TB commodities and the introduction of new medicines into treatment regimens.

**OP-176-16 The access pipeline: timelines for new drugs**

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For many in the TB community, the prospect of new drugs to treat TB, especially drug resistant TB, are a distant scientific endeavor not linked to today's treatment planning. The Working Group on New TB Drugs (WGND) has developed an informative drug pipeline that outlines the phases of study for new drugs. However, such a pipeline does not help to inform National TB Programs (NTPs), donors, providers or patients what treatments will be available for use and when. For specific populations, such as DR and pediatric patients, treatments may be available at different times from adult drug sensitive patients. Countries are not able to appropriately prepare to adopt new regimens based on the drug development pipeline alone. Using the WGND pipeline, the TB Alliance contacted drug developers and researchers to understand development timelines as they relate to specific target populations. Publicly funded clinical study programs and pharmaceutical company drug sponsors provided details on the anticipated product use and the estimated timeline for the product introduction, if approved. Publicly available information fed into the analysis. We have developed the first 'access pipeline' that details the timelines for introduction of new drugs for specific populations, including DR patients. The presentation of the pipeline allows NTPs and other planners to consider when, for whom, and how new drugs will radically change TB treatment, in cases such as a switch from today's multi-year MDR regimen with injections to a tablet-only four month regimen. Limitations are that timelines shift and clinical trials can fail to demonstrate efficacy. The access pipeline shifts the focus from clinical trial research to new drug adoption and implementation preparedness. NTPs are now able to plan using longer, practical timeframes rather than focusing on a 1–2 year timeline. Such planning is vital as implications for MDR treatment in terms of cost and scale-up are considerable.

**NEWER TUBERCULOSIS DIAGNOSTICS: ROLLING OUT AND THEIR IMPACT****OP-178-16 Improved tuberculosis case-finding and MDR-TB detection among Tibetan refugees in India**

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**Background:** The prevalence of tuberculosis among Tibetans-in-exile is among the highest in the world. In 2010, the prevalence was 420/100 000 among Tibetans living in India. Over half the TB cases occur among students, monks and nuns, who live in congregate settings, which contributes to high rates of TB and MDR-TB transmission. The main objective of this TB REACH project is to increase TB and MDR-TB case detection rates in Tibetan congregate living centers in India.

**Methods:** We conducted active case-finding for TB (ACF) in Tibetan schools, monasteries, and the reception center for new arrivals, where participants were screened for TB symptoms (cough, fever, night sweats or weight loss of any duration). Participants reporting any TB symptom were considered TB suspects, underwent a chest X-ray, and submitted sputum for smear microscopy or GeneXpert® MTB/RIF (GXP) rapid assay.

**Results:** Between September 2011 and March 2012, 10 522 people were screened and 1645 TB suspects underwent further testing at 8 Tibetan schools, 9 monasteries and the reception center. The overall prevalence of TB was 323/100 000 among those screened (37 cases). The prevalence of TB was 367/100 000 in Tibetan schools and 255/100 000 in monasteries. Among those cases identified by ACF, 38% (14 of 37) were sputum smear positive and 30% (11 of 37) were sputum smear negative and GXP positive. Three cases (8%) were rifampicin-resistant by GXP.

**Conclusions:** Implementation of ACF with the GXP test enabled early and rapid detection of undiagnosed TB cases in Tibetan congregate living settings and enabled diagnosis of additional cases of pulmonary TB not identified by routine sputum smear microscopy. However, the burden on laboratory personnel during ACF activities was substantial and will need to be addressed during ongoing ACF and GXP scale-up.

**OP-179-16 Global roll-out of Xpert® MTB/RIF**

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**Background:** Following WHO endorsement in December 2010 of the Xpert® MTB/RIF assay, a total of 611 GeneXpert instruments (2979 modules) and 863 790 Xpert MTB/RIF cartridges have been procured in 61 countries under concessional pricing, as of March 2012. Monitoring of procurements, coordination of partners, post-marketing surveillance, and collection of evidence on use of this tool were identified as essential actions required from WHO for the global roll-out.

**Methods:** The WHO Stop TB Department has launched initiatives to systematically collect information on country and partner procurements and

plans, on operational problems encountered, and on laboratory workload and results of testing using WHO-recommended algorithms (see [www.who.int/tb/laboratory/mtbrifrollout](http://www.who.int/tb/laboratory/mtbrifrollout)). A validation panel scheme was devised to check the performance of modules at the time of installation and recalibration. Global meetings of implementers and partners were organized in 2011 and 2012 to allow for knowledge exchange and improved coordination.

**Results:** As of April 2012, TB control programmes and/or partners in 48 countries have provided information on sites of machines and plans for procurements. A growing number of facilities have registered to provide information on operational problems, laboratory workload and Xpert MTB/RIF results; collaboration established with partners includes TB-CARE, TB REACH and the South Africa NHLS. Information from an increasing array of implementation sites is expected to be made available to WHO throughout 2012.

**Conclusions:** Global monitoring of procurement and implementation plans has facilitated coordination between country implementers, partners and donors. Post-marketing surveillance allows for the identification of any major recurring problem and aids in ensuring appropriate follow-up by the manufacturer. Collection of evidence on use will allow for the refining of guidance for implementers, enabling a more effective, wider global scale-up.

#### OP-180-16 The impact of the Xpert® MTB/RIF assay for detecting *Mycobacterium tuberculosis* among tuberculosis suspects in Cambodia

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**Background:** Xpert® MTB/RIF assay is a new diagnostic tool, which can provide TB diagnosis and detection of rifampicin resistance within 2 hours. It is user-friendly and easy to carry. Hence, we can use mobile GeneXpert testing for active case finding among high-risk groups. However, we face the challenge of 'ERROR, INVALID or NO RESULT', which decreases cost-efficiency of using this tool.

**Method:** We examined the records of Xpert assays for 2011–2012 in different settings: prison setting (284 tests), active case finding for drug resistant TB among high-risk groups for multi-drugs resistant tuberculosis (MDR-TB) (73 tests), routine MDR-TB finding (223 tests), and active case finding among close contacts of known TB patients (795 tests).

**Results:** We found that the National TB Program has conducted 1375 tests in these settings until now. Among these tests, we were unable to interpret 82 (5.96%) test results, which is slightly higher than the

acceptable limit of less than 5%. Of these, 41 (2.98%) were ERROR, 35 (2.55%) were INVALID, and 6 (0.44%) were NO RESULT; 348 (25.31%) tests showed *Mycobacterium tuberculosis* detected. Among these, 39 were rifampicin resistance, 304 were rifampicin sensitive, and 5 were rifampicin indeterminate. Remaining 945 (68.73%) tests did not detect *M. tuberculosis*.

**Conclusion:** Using GeneXpert tool, we can detect *M. tuberculosis* very fast and accurately. However, high rates of uninterpretable results can lead to waste of resources for the program and inconveniences to the patients. We need to study the types of uninterpretable results and train the staff on the reasons and solutions to minimize them. We should complement the training with on-site supervision for best results.

#### OP-181-16 Performance of the MTBDRs/ assay in the detection of extensively drug-resistant tuberculosis in the country of Georgia

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**Background:** The WHO has called for the implementation of rapid TB diagnostics to detect and help combat MDR- and XDR-TB. We sought to evaluate the performance of the commercially available Genotype MTBDRs/ assay, integrated into routine lab work, in the detection of *M. tuberculosis* resistance to aminoglycosides (AGs) and fluoroquinolones (FQs).

**Intervention:** From 11/2011 to 3/2012 consecutive AFB smear positive sputum specimens were obtained from patients referred to the Georgian National TB Program. Conventional cultures and drug susceptibility testing (DST) for the first line drugs along with the Genotype MTBDRplus assay were conducted. All samples identified as being MDR with MTBDRplus test were evaluated with MTBDRs/ tests along with conventional DST for second line drugs using the proportion method on Löwenstein-Jensen media. All tests were performed at the Georgian National TB Reference Laboratory.

**Results:** 47 patients with MDR-TB identified by the MTBDRplus assay had sputum further tested with the MTBDRs/ assay and had second line DST performed. Second line DST revealed 8 (17%) *M. tuberculosis* isolates with XDR. Amplification for the MTBDRs/ was adequate in 46 (98%) sputum samples. T MTBDRs/ identified XDR in 3 (6%) sputum samples. As compared to conventional DST, the MTBDRs/ had a 38% sensitivity (SENS), 100% specificity (SPEC), 100% PPV, and 88% NPV in detecting XDR. MTBDRs/ has a 67% SENS, 81% SPEC, 55% PPV, and 91% NPV in detecting FQ resistance and 50% SENS, 92% SPEC, 57% PPV, and 90% NPV in

detecting resistance to AGs. The average time from baseline sputum collection to second line DST results was 87 days as compared to 12 days for MTBDRs/ results.

**Conclusions:** The MTBDRs/ assay had a rapid turn around time; however results were not optimal as compared to conventional second line DST. Further AQ and FG molecular resistance mutations need to be included in the MTBDRs/ to improve test performance and clinical utility.

### OP-182-16 A rapid detection of extensively drug-resistant tuberculosis: comparison of the genotype MTBDRs/ assay with indirect second-line susceptibility testing

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**Background:** Extensively drug-resistant TB (XDR-TB) is a serious global health concern. Conventional indirect susceptibility testing for second-line drugs (ofloxacin, kanamycin) is constrained by the relatively slow growth of *M. tuberculosis*. Rapid molecular methods to detect drug resistance to second line drugs are necessary to optimize anti-tuberculosis treatment and to avoid the transmission of resistant strains. The Genotype MTBDRs/ assay was evaluated for its performance for the rapid detection of XDR-TB in MGIT cultures.

**Design/methods:** The Genotype MTBDRs/ assay was performed on 60 well characterised MGIT cultures comprising of XDR, MDR and mono-resistant strains of *M. tuberculosis*. The investigator performing the Genotype MTBDRs/ assay was blinded to the culture susceptibility results.

**Results:** Preliminary data: The Genotype MTBDRs/ identified XDR-MTB in 43 of the 60 MGIT cultures. In all 43 isolates the following mutations were identified: a single mutation (A90V) in the gyrase A subunit coding for fluoroquinolone resistance, a mutation in nucleic acid position 1401 (A1401G) of the *rrs* gene coding for an aminoglycoside/cyclic peptide resistance and a mutation in codon 306 of the *embB* gene coding for ethambutol resistance. The second-line indirect susceptibility testing confirmed XDR in all 43 MTB isolates with growths at 2 µg/ml for ofloxacin, 5 µg/ml for kanamycin and 7.5 µg/ml for ethambutol. Of the 17 non XDR-TB isolates, the assay detected no mutations in genes that code for fluoroquinolone, aminoglycoside and ethambutol resistance in 14 isolates. These were confirmed to be fully susceptible by the indirect susceptibility testing. The remaining 3 were found to be only resistant to a fluoroquinolone with a mutation in codon 91 (S91P). One of these three isolates was found to be susceptible to ofloxacin on the second-line susceptibility agar.

**Conclusion and recommendations:** Genotype MTBDRs/ assay allows for the rapid diagnosis of XDR-TB in cultures.

### OP-183-16 Responsible technology: success, challenges and key lessons from a novel Xpert® MTB/RIF deployment at a major public event in South Africa

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**Background:** At the 2012 South African World TB Day public event, an unprecedented deployment of Xpert® MTB/RIF testing was offered to TB symptomatic clients from gold mining and surrounding communities. Considerations included effective TB symptom screening; safe, effective sputum collection; ensuring uninterrupted electricity supply; client tracking and provision of on-site results.

**Intervention:** TB symptomatic clients screened from the presenting crowd were entered in a national 'TB suspect register' and given a barcoded sputum sample tracking pack and return time for results (3 hours later). Facilities were provided for mouth rinsing and sputum production in 8 private, ventilated gazebos. Ten GeneXpert (Gx16) instruments were placed in 5 mobile units around a central outdoor sample processing area. Each Gx was verified with a dried culture spot panel and standard of practice testing was performed. Results were printed and referral letters given; 46 clinical and laboratory staff were deployed.

**Results/lessons learnt:** 597 (36%) of 1661 clients screened were TB symptomatic. 532 of 591 (90%) specimens received were resulted: 12 (2.3%) were *Mycobacterium tuberculosis*-positive with one RIF resistant; all TB+ patients were appropriately referred. Of 59 specimens not resulted: 49 were due to power supply (switch failure) to two Gx16 instruments (9 clients were traced and samples repeated); 7 due to cartridge error; and 3 rejected (food contamination, incorrect labelling). Administratively, 95% (567/597) results were definitively linked to register entries. Some clients expected immediate TB results without the need to provide sputum.

**Conclusions and key recommendations:** Public event Xpert MTB/RIF testing is feasible but the case finding rate was low (2.3%). We recommend exploring enhanced symptom screening algorithms to improve pre-test probability, improved management of client expectations, cost effectiveness analysis, exploring alternate electrical fail-safes and on-site data connectivity.

### OP-184-16 Does the introduction of the Xpert® MTB/RIF test result in an increased tuberculosis diagnostic yield in a routine operational setting in Cape Town?

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**Background:** Xpert® MTB/RIF (Xpert) has been introduced in South Africa as a screening test for all tuberculosis (TB) suspects, replacing smear microscopy. Anticipated benefits include higher TB and multidrug resistant (MDR-TB) yields. This study aims to evaluate whether the introduction of Xpert increased TB and MDR-TB yields in a routine operational setting in Cape Town.

**Methods:** TB yields were compared for 28 primary health facilities using the Xpert algorithm and 48 facilities using the smear/culture algorithm during October–December 2011 (Algorithms in the Table). Electronic TB results were imported from the National Health Laboratory Services into an MS SQL database. Only pre-treatment sputum results were included in the analysis. Results were matched on name, surname and age/birth date to individual suspect level using Link Plus probabilistic software. Data was analysed using STATA 10.

**Results:** Preliminary results are presented in the Table. 5006 suspects were evaluated in the Xpert facilities: 19.1% had *Mycobacterium tuberculosis* (MTB) complex detected, 1.8% had a negative Xpert but positive culture. 1% of suspects had rifampicin resistance. 9886 suspects were evaluated in the smear/culture facilities: 10.8% were smear positive; 3.8% were smear negative/culture positive and 4.8% had no smear result but were culture positive. 0.6% were diagnosed with MDR-TB. The Xpert facilities had a TB yield of 20.9% compared to 19.3% for the smear/culture facilities (risk ratio 1.06, CI 1.0 1–1.12). Xpert facilities had RIF resistant yield of 1.0% compared to an MDR yield of 0.6% in the smear/culture facilities (risk ratio 1.35, CI 1.09–1.67).

**Table** Comparison of TB yields in the Xpert MTB/RIF algorithm and smear/culture algorithm

Xpert MTB/RIF Algorithm		Smear/Culture Algorithm	
<ul style="list-style-type: none"> <li>• 2 specimens for all TB suspects               <ul style="list-style-type: none"> <li>○ Xpert test on the first specimen</li> <li>○ If Mtbc complex detected, smear microscopy on the second specimen</li> <li>○ If rifampicin resistant, culture and DST on the second specimen</li> <li>○ If Xpert negative and HIV-infected culture on the 2<sup>nd</sup> specimen</li> </ul> </li> </ul>		<ul style="list-style-type: none"> <li>• 2 specimens for smear microscopy for all TB suspects               <ul style="list-style-type: none"> <li>○ Culture and DST on the second specimen for high MDR-TB risk suspects</li> </ul> </li> <li>• 3<sup>rd</sup> sputum specimen for culture if HIV-infected, smear negative, no previous culture low</li> </ul>	
Total suspects Xpert	5006	Total suspects (smear &/or culture)	9886
Mtb complex detected	958 19.1%	Smear positive	1066 10.8%
Xpert neg, culture pos	88 1.8%	Smear neg / culture pos	372 3.8%
		No smear / culture pos	472 4.8%
Total suspects with Xpert &/or culture positive	1046 20.9%	Total suspects with smear &/or culture positive	1910 19.3%
RIF R	48 1.0%	MDR	58 0.6%
Risk ratio 1.35 (95% CI 1.09–1.67)			

**Conclusion:** Whilst the introduction of Xpert MTB/RIF test has resulted in increased TB and RIF resistant yields, the operational significance of these increases is small; it may be of operational significance in settings without access to culture. Potential other benefits in reducing time to treatment initiation need to be explored.

### STIRRING IT UP: LABS, PHARMACIES AND MOTORCYCLE RIDERS IN THE PUBLIC-PRIVATE MIX

#### OP-185-16 Strengthening of TB-HIV coordination: involving NGOs through public-private partnership

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**Aim:** Tuberculosis is the most common cause of mortality in HIV infected individuals in high prevalence countries like India. Quality of life can be improved through early identification and improving access to care. A public-private partnership was designed to meet the objectives.

**Methods:** A three year public-private partnership project, funded by GFATM III, was implemented between 2006 and 2009, in four districts of Maharashtra, India, to improve access to public health facilities through community awareness and motivating referrals. PLHIV and TB patients were engaged to motivate patients attending integrated counseling and testing centers (VCCTCs) and designated microscopy centers (DMCs) for cross referrals and adherence to services. Community leaders and private health providers were sensitized to issues around TB and HIV/AIDS.

**Observations:** 357 outreach workers in four districts of the state referred 17200 individuals for voluntary HIV testing, 866 were detected seropositive for HIV (5.03%). During the same period, of the 32549 TB suspects referred for testing 4303 (13.2%) were diagnosed as TB.

**Lessons learnt:** NGOs, PLHIV and TB patients are motivated to improve access to health care. Public health facilities need to be fully operational; policies and guidelines need to be formulated before partnerships are formed. Sustainable funding is essential to effective implementation of projects and regular monitoring and evaluation with appropriate budget allocation should be inbuilt in the project.

**Conclusion:** Public-private partnerships can improve access to care for TB and HIV infected individuals. Constant dialogue between all stake holders is essential for successful implementation of such partnerships.

### OP-186-16 Tuberculosis management practices of private medical practitioners in Pune Municipal Corporation, India

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**Background:** Private practitioners (PP) are the primary source of health care for patients in India. Limited representative information is available on Indian PP's TB management practices, and the efficacy of India's Revised National Tuberculosis Control Programme (RNTCP) to improve the quality of TB management through PP sensitization/training.

**Methods:** We conducted a cross-sectional survey of a representative sample of PP in one urban area in western India (Pune, Maharashtra), using patient vignettes, and determined the proportions of PPs who reported practices consistent with international standards of TB care (ISTC). We examined the association between training and adherence to ISTC by calculating odds ratio and used 95% confidence intervals (CI) to assess significance.

**Results:** Of 3391 PPs practicing allopathic medicine, sample of 249 were interviewed, among whom 55% had been exposed to RNTCP PP sensitization/training. For the new pulmonary and previously-treated TB patient vignette, respectively 158/249 (63%) and 168/224 (75%) of provider responses were consistent with ISTC diagnostic practices, and 34% and 32% responses were consistent with ISTC treatment practices. In addition, 48% PP reported use of serological tests for TB diagnosis. In the new TB case vignette, 38% PP included at least one second line anti-TB drug in the treatment regimen. Sensitization/training was not associated with correct responses as per ISTC for diagnosis or treatment practices including use of serology and second line drugs.

**Conclusion:** In Pune, India, prior exposure to RNTCP training/sensitization was not associated with an improved quality of TB care, and disturbingly high proportions of providers resorted to TB serology for diagnosis and second-line anti-TB drug use in new TB patients. Efforts to achieve universal access to quality TB management must account for the low quality of care by PP and the ineffectiveness of current training efforts.

### OP-187-16 Improving tuberculosis case detection and quality of care in Kabul through implementation of Urban DOTS

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**Background:** Kabul has five million inhabitants and suffers from overcrowding; population density, poor sanitary facilities that resulted in poor TB indicators. In 2009, USAID/TB CAP developed an Urban DOTS approach, and engaged public-private sectors in DOTS implementation to address this gap. In 2009, 106 public and private HFs existed in Kabul, 22 implemented DOTS without a system for public health interventions. TB case-notification rate was 26%, conversion rate 43% and success rate was 46%. Urban DOTS encompasses, engaging private-public health facilities in DOTS, training health staff, improving communication/coordination and regulating monitoring/supervision visits to health facilities. Aim of this assessment was to identify the role of Urban DOTS in TB control activities in Kabul.

**Intervention:** In February 2012, the TB technical team reviewed 2011 data from 56 health facilities and compared to data from 2009 to 2010, using standard NTP recording-reporting tools. More public-private health facilities involved.

**Results:** In 2011, Urban DOTS coverage reached 56 (8 private) public-private health facilities while in 2009 only 22 public facilities provided TB services. In 2011, 11 900 TB suspects identified, 2728 TB cases (554 by private) diagnosed. Also, 1083 new TB SS+ cases (220 by private) notified, which denotes 33% increase compare to 2009 (only 814 new TB SS+ cases in 2009). Moreover, the conversion rate reached 70% in 2011, and the success rate increased to 70%.

**Table** Urban DOTS' public-private mix performance in TB control services, 2009–2011

Explanation	2009	2010	2011
HFs, <i>n</i>	106	111	111
HFs covered by DOTS (diagnostic and treatment), <i>n</i>	22	48	56
TB suspects identified/examined, <i>n</i>	2856	10 150	11 900
All TB cases notified, <i>n</i>	1934	2 738	2 728
New TB SS+ cases notified, <i>n</i>	814	1 022	1 083
TB sputum smear conversion rate, %	43	62	70
New TB SS+ success rate, %	46	62	70*

\* 1st Q 2011.

**Conclusion:** It is evident that Urban DOTS contributed significantly on TB services and improved case notification, sputum conversion and treatment success rate. Thus, we recommend the scale-up of Urban DOTS to other urban settings.

### OP-188-16 Improving primary health care access to laboratory-based tuberculosis diagnosis and HIV monitoring in Lesotho via Riders for Health's sample transport system

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In 2008 the Ministry of Health and Social Welfare (MoHSW) and Clinton Health Access Initiative (CHAI) identified a barrier to TB and HIV treatment in Lesotho, a country where 76% of TB patients were HIV-positive in 2008 (source: WHO). Laboratory-based TB diagnosis and HIV monitoring were only available in district-level laboratories, which were difficult to reach given terrain and distance.

In 2009 in partnership with CHAI and MoHSW, Riders for Health (Riders) started a national sample transport (ST) programme based on Riders' preventive maintenance system, employing 26 motorcycle couriers to transport samples/results between 155 health centres and 17 district laboratories weekly. Riders interviewed staff at 35% of health centres served to examine referral methods and estimated result turnaround time (TAT) pre- and post-ST. Based on courier logsheet data, Riders also estimated the number of samples/results transported.

Prior to ST, 16% of health centres interviewed did not collect samples; instead they referred patients for testing. Post-ST, Riders serves 93% of health centres nationally. The average TAT from collection to return of result to health centre (for those originally referring samples) decreased from 15 to 7 days with ST. The estimated number of samples transported by Riders increased from 126 800 in 2009 to 241 900 in 2011, of which 29 200 were sputum for TB diagnosis.

Riders improved access to laboratory-based TB diagnosis and HIV monitoring at health centres through a weekly ST system that increased sample volumes sent to laboratories and decreased TATs, which is critical to faster linkages to care/treatment. Riders since expanded the programme to Zambia then Zimbabwe, where Riders transported 34 400 sputum samples in 2011 for the International Union Against Tuberculosis and Lung Disease. Riders is exploring new regions for scale-up and opportunities for other ways to improve TB care, such as distribution of medicines and laboratory consumables.

### OP-189-16 Engaging non-qualified rural health care providers for tuberculosis control services: experience from India

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**Background:** Non-qualified RHCPs serve as the first point of care for most of the rural and semi-urban population. Despite their lack of knowledge and potentially harmful practices they enjoy the confidence of the community. The NTP has not taken any steps to involve these healthcare providers. Under the Global Fund supported 'Project Axshya' RHCPs are being systematically trained to identify and refer TB symptomatics for sputum microscopy to the nearest NTP diagnostic facilities. They are also encouraged to become DOT Providers. In the first year of implementation of the project 2700 RHCPs from 90 districts have been trained.

This study tries to assess the impact of this intervention measured by referral of TB symptomatics by the trained RHCPs during the quarter July–September 2011 and key reasons for not referring TB symptomatics. The study also assesses the proportion of trained RHCPs who became DOT Providers.

**Design/methods:** Cross-sectional study under which 92 trained RHCPs (selected randomly from 2700 trained) from 20 districts (selected randomly from 90 districts) were interviewed using a semi-structured questionnaire.

**Results:** During the quarter the 92 RHCPs identified 1283 symptomatics (mean = 14; range 0–159) of which 1067 (mean = 12; range 0–159) were referred for sputum microscopy to NTP facilities. 292 (mean = 3; range 0–52) were found to be smear positive. 23 RHCPs (25%) were providing DOT services. 12 RHCPs (12%) did not refer any TB symptomatics. The key reasons for not referring were fear of losing patients and unwillingness of patients to go to microscopy centres.

**Conclusion and recommendations:** The study shows that 78% of the trained RHCPs were identifying and referring TB symptomatics for smear microscopy to NTP facilities and 25% were providing DOT services. On an average each RHCP referred 12 TB symptomatics and contributed to detection of 3 smear positive cases in a quarter. The study highlights that RHCPs could be effectively involved in TB control.

### OP-190-16 Engaging private laboratories in tuberculosis diagnosis and treatment: experience from Pakistan and Bangladesh

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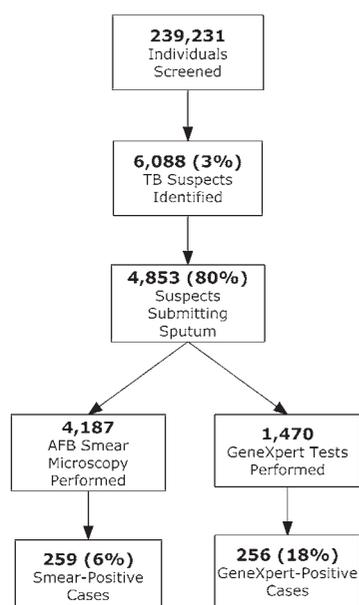
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**Background:** In South Asia approximately 80% of patients choose the private sector for healthcare. While progress has been made on linking private doctors with National TB Control Programmes (NTPs), strat-

egies to engage private laboratories (PLs) have not been tested.

**Intervention:** The following steps were taken to engage 6 PLs across Karachi and 4 across Dhaka: health workers (HWs) were stationed in each lab to aid in screening, registering and notification of TB suspects; microscopy quality was improved through training and external quality assurance; GeneXpert systems were placed in PLs; suspects identified were offered a free smear-microscopy test, chest X-ray and Xpert test (for suspects with history of TB treatment or negative smear and TB suggestive X-ray) on the initial visit. An advertising campaign was run to inform private doctors, pharmacies and mosque leaders about availability of free TB tests at the PLs. Diagnosed patients were counselled by HWs when they came to collect results at the PL, and provided free treatment at the PL or through a collaborating DOTs centre.

**Results:** The PL-collaboration system took 2 months to set up. From October 2011 to March 2012, 239 231 individuals were screened at participating PLs and 6088 suspects were identified. 4853 (81%) suspects submitted sputum. Of 4187 smear-microscopy tests performed, 259 (6%) positive cases were diagnosed and of 1460 Xpert tests performed 256 (18%) were positive. Thus 515 new bacteriologically-positive cases were diagnosed in 6 months of operation.



**Conclusions:** In settings with a strong private-sector, working with high volume PLs is an effective way to diagnose and treat a large number of TB cases that would otherwise be missed by NTPs. The system piloted was effective in engaging PLs as they benefited financially from an increased volume of suspects tested and improved TB diagnostic services. Placing project HWs in PLs ensured timely reporting without burdening labs with data compilation.

### OP-191-16 The role of the PSI Sun Quality Health Clinics network in increasing tuberculosis diagnosis and treatment in Myanmar

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**Issue:** According to Myanmar TB prevalence survey (2009), the estimated number of TB patients in Myanmar is 116 160. Estimated case detection rates have increased from 52% in 2004 to 71% in 2011, with a success rate of 85% in 2009.

**Program description:** In March 2004, Population Services International (PSI) Myanmar started a franchising network—the Sun Quality Health Clinic (SQHC)—for TB diagnosis and treatment using Directly Observed Therapy (DOTS). The PSI network has grown from 102 TB trained providers in 2004 to 944 in 2011.

The franchisees (Sun Quality Health Clinics) are responsible for diagnosis and treatment of TB cases following the national guidelines. PSI is responsible for training and supervising the providers. Patients pay a low fee and TB drug are given free of charge if patients found to be TB-infected. Analysis conducted on monitoring and MIS data examines the uptake of TB diagnosis and treatment through the franchising network, and estimates the contribution of the PSI program to the reduction of TB related burden of disease in Myanmar.

**Findings:** By 2011, a total of 338 717 cases of TB had been detected by SQHC providers. The average number of new cases detected per SQH provider increased from 53 in 2004 to 79 in 2011. In 2004, SQHC providers were contributing an estimated 1.9% of the total estimated TB burden in Myanmar. This has increased to an estimated 18% in 2011. In 2004, 1047 patients with smear positive had successful treatment—completion of 6 month course or cured at the end; a rate of 78%. The success rate had increased to 84% by 2010.

**Conclusion and next steps:** PSI SQHC has contributed significantly to fight against TB in Myanmar. Improved efficiency was found between 2004 and 2011, with an increase in the average number of cases detected per provider, and an increase in the success rate of those found to be TB positive. Findings of the SHQC should be shared and the network should be expanded to other similar settings.

### OP-192-16 Achieving universal access through engaging community pharmacists in India

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**Introduction:** Indian Pharmaceutical Association (IPA) with the help of chemist associations and the

local TB program managers in Mumbai, India, established a partnership of engaging community pharmacists in Revised National Tuberculosis Control Program (RNTCP) in India, The Elli-Lilly Funded project of IPA & SEARPharm Forum undertook training of community pharmacists in identifying TB suspects, doing community awareness and delivering Directly Observed Treatment (DOT). Taking lessons from this experience IPA took advocacy initiatives with RNTCP to scale up this initiative to 500 000 pharmacies in a phased manner, to achieve Universal Access.

**Interventions:** The findings of the initial projects were disseminated to the National Program Managers in a workshop and followed up with the policy makers. Documentary depicting the experiences of pharmacists and patients was shown in the workshop, supported with the data from the project site showing improvement in case detection and case holding. More than 70 project pharmacists have cured 225 patients and positive case detection rate among the referred cases was 16%.

**Results:** RNTCP signed a Memorandum of Understanding with IPA and All India Organization of Chemists and Druggists to carry forward the pharmacists' engagement to all over India. Three states were selected as pilot states to initiate the activities and the program expressed the commitment to scale up in a phased manner.

**Conclusion:** Utilizing evidences from pilot project and focused persistent advocacy efforts influence the policy change for strengthening the TB care and control in India, to achieve the Universal Access.

## POSTER DISCUSSION SESSIONS

### MOLECULAR EPIDEMIOLOGY – 1

#### PC-236-16 Genetic diversity of *Mycobacterium tuberculosis* isolates obtained from patients with pulmonary tuberculosis in Beira City, Mozambique

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**Background:** Tuberculosis (TB) represents a serious public health problem in Mozambique, with an estimated incidence rate of 544 cases per 100 000 population in 2010. Information on the molecular epidemiology of *Mycobacterium tuberculosis* strains

circulating in Mozambique is limited, with data only available for some regions. This study provides the first description of the genetic diversity of *M. tuberculosis* strains circulating in Beira City, the second largest town in Mozambique.

**Results:** The genetic lineages of 67 *M. tuberculosis* isolates, were determined using real-time PCR. Results indicated that only three of the 6 major lineages were represented, with 41 (61%) strains belonging to lineage 1, 25 (37%) belonging to lineage 4 and the remaining isolate to lineage 3. No lineage 2 strains (containing the Beijing family) were identified. A high degree of diversity, based on the mycobacterial interspersed repetitive unit-variable numbers of tandem repeat (MIRU-VNTR) profiles, was observed amongst the strains from both lineage 1 and 4. Comparison of the profiles of representative strains with those of reference strains in the MIRU-VNTRplus database revealed that whilst all the lineage 1 isolates clustered with the Eastern African Indian (EAI) 5 sub-family, the lineage 4 strains clustered with a variety of different sub-family strains, including the Latin-American-Mediterranean (LAM) 1 sub-family, the Haarlem, Uganda 1 and Cameroon sub-families and the T2-S sub-family.

**Conclusions:** The TB epidemic in Beira City is caused by a diverse group of *M. tuberculosis* strains predominantly belonging to lineages 1 and 4.

#### PC-237-16 Evaluation of *Mycobacterium tuberculosis* Beijing family in Kaliningrad Oblast Russia

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**Aim:** The study of MBT genetic identity in pulmonary TB patients in the Kaliningrad Oblast.

**Methods:** Sputum of 90 pulmonary tuberculosis patients by culture and drug sensitivity test was studied and MBT strain genetic study was carried out.

**Results:** All patients were smear and culture positive, 67.8% was recorded in cavities in the lungs. The main clinical form was infiltrative pulmonary tuberculosis (46–51.1%), followed by disseminated process (35–38.9%), 5 patients had chronic tuberculosis with the development of fibrotic cavities. The study of MBT drug sensitivity revealed multidrug resistance in 30 patients (33.3%), including a two XDR cases. Genotyping of the MBT found in 57 cases variants of the Beijing family (63.3%), LAM-17 (18.9%), 4 strains belonged to the Harlem family and the 5 to an unknown family. 30 patients excreted MDR MBT 28 (93.3%) had Beijing family. 24 out of 35 (80%) of patients with disseminated tuberculosis had Beijing isolates. The study of MDR-represented in each of the families found that the Harlem family had only two polyresistant cases (resistant to SH). LAM family

was also mainly drug-susceptible (15 of 17, 88.2%), only in two cases of MBT LAM family multidrug resistance, and polyresistance were identified. Unknown strains of MBT found in 5 patients were drug-sensitive in all cases. But in 49.1% of MBT by Beijing family (28 from 57) were MDR. TB outcomes showed that most adverse outcomes were in patients suffering from tuberculosis due to the MBT Beijing family: deaths registered in 17 (29.8%) patients, significantly more than deaths of LAM family MBT cases (17.6%,  $P = 0.03$ ).

**Conclusion:** In Kaliningrad Oblast the most common genetic variant of MBT is Beijing family. Pulmonary TB caused by Beijing MBT, accompanied by the frequent occurrence of disseminated forms, the formation of multi-drug resistance and adverse outcome of the disease.

#### PC-238-16 Rapid detection of rifampin and isoniazid resistance of *Mycobacterium tuberculosis* complex in positive liquid cultures by an oligonucleotide array

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**Aim:** Early diagnosis of tuberculosis (TB) and drug resistance are important for TB control. A combination of solid and liquid media is currently regarded as the 'gold standard' for mycobacterial culture. The Bactec Mycobacteria Growth Indicator Tube (MGIT) system (Becton Dickinson) is a sensitive, safe, and automated liquid culture system widely used in the world. Moreover, due to the increase of drug-resistant *Mycobacterium tuberculosis* complex (MTBC), it is imperative to develop rapid molecular methods for diagnosing antibiotic resistance of MTBC. Rifampin (RIF) and isoniazid (INH) resistance are caused by point mutations in *rpoB*, *katG* and the *mabA* promoter of MTBC strains. This study aimed to develop an oligonucleotide array to rapidly detect point mutations of these genes in positive MGIT cultures that might contain MTBC.

**Method:** The method consisted of multiplex PCR amplification of *rpoB*, *katG*, and the *mabA* promoter, followed by hybridization of the PCR products to oligonucleotide probes immobilized on nylon membrane.

**Results:** A total of 483 positive liquid cultures contained MTBC were analyzed. The sensitivities of the array were 100% (RIF) and 86.2% (INH), respectively, while the specificities were 99.8% (RIF) and

99.5% (INH), respectively. The positive predictive values were 95% (RIF) and 96.6% (INH), respectively, and the negative predictive values were, respectively, 100% (RIF) and 97.9% (INH). The method can be completed within a working day.

**Conclusion:** The array could rapidly and effectively detect RIF and INH resistance of MTBC in positive MGIT cultures.

#### PC-239-16 Targeted screening of multidrug-resistant tuberculosis among high-risk populations using a line-probe assay

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**Aim:** Approximately 150 new multidrug-resistant tuberculosis (MDR-TB) cases were notified annually in Taiwan. For timely diagnosis of MDR-TB cases in high-risk populations, sputa were tested directly using a line-probe assay.

**Methods:** The GenoType®MTBDRplus assay was used for screening high-risk TB populations in 2011. A modified PCR protocol was used for smear-negative and scanty sputa. Of the 1242 cases tested, 344 cases were treatment after failure, 43 were treatment after default, 613 were relapse, 35 were MDR-TB contacts, and 207 were aboriginal villagers (Table).

**Results:** In this study, 527 (42.4%) cases were AFB-smear positive, 45 (3.6%) scanty, 668 (53.8%) negative, and 2 (0.2%) unknown. Of the 1242 cases, 39.5% (490/1242) had positive results of *Mycobacterium tuberculosis* complex (MTBC) by the GenoType®MTBDRplus assay. Even through the assay is only recommended for testing smear-positive samples, we still can successfully detect MTBC in 97 (14.5%) smear-negative cases. Of the 490 MTBC positive cases, 53.8% were treatment after failure, 41.9% were treatment after default, 36.5% were relapse, 37.1% were MDR-TB contacts, and 24.2% were aboriginal villagers. Of the 29 MDR-TB identified, 86.2% were

**Table** Screening results of 1242 high-risk tuberculosis cases using a line-probe assay

Case category	Case no.	Positive	No. (%) of MTBC				
			MDR by smear category		Mono-RIF resistance	Mono-INH resistance	
			Negative	Scanty			Positive
Treatment after failure	344	185 (53.8)	1		6	8	11
Treatment after default	43	18 (41.9)			1	2	1
Relapse	613	224 (36.5)		1	14	17	17
Multidrug-resistant TB contacts	35	13 (37.1)	2		4	1	
Aboriginal villagers	207	50 (24.2)				3	4
Total	1242	490 (39.5)	3	1	25	31	33

from smear-positive cases, 3.4% from scanty, and 10.3% were from smear-negative. Notably, we observed the highest MDR-TB detection rate (46.2%, 6/13) among contacts of MDR-TB. In addition, we found 6.3% and 6.7% were mono-rifampicin resistance (probable MDR-TB) and mono-isoniazid resistance, respectively. Overall, approximately 40% of MDT-TB and probable MDR-TB cases can be rapidly identified.

**Conclusion:** Intensified and early diagnosis of MDR-TB can be achieved by using a line-probe assay to facilitate proper management.

### PC-240-16 Spoligotyping study on the population structure of *Mycobacterium tuberculosis* in Rwanda, Nepal, Nigeria and Yemen

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**Background:** Studying changes in the population structure of *Mycobacterium tuberculosis* is important to understand its adaptation to control measures. It is conceivable that measures such as BCG vaccination and treatment by anti-tuberculosis drugs may select for strains that are better adapted to acquire resistance and to circumvent BCG-induced immunity. If so, it is important to test the efficacy of new candidate vaccines against emerging genotypes in the current epidemic.

**Design/methods:** We investigated possible associations of *M. tuberculosis* genotypes with patients' age and BCG vaccination status in Nepal ( $n = 82$ ), Nigeria ( $n = 212$ ) and Yemen ( $n = 417$ ). To investigate whether particular *M. tuberculosis* genotypes are associated with the spread of MDR-TB in Rwanda, a case-control study was performed ( $n = 90$ ).

**Results:** The Beijing and CAS genotypes were predominant in Nepal, representing 22% and 40% respectively. The CAS genotype was more frequent among patients younger than 30 years compared to older patients ( $P = 0.035$ ). The LAM genotype predominated in Nigeria (67%). The T (52%) and CAS (27%) genotypes were predominant in Yemen, where the T genotype was more frequent among patients younger than 30 years than among older patients (55% vs. 48%). In Rwanda, (93%) *M. tuberculosis* isolates belonged to the T-family.

**Conclusions and recommendations:** The population structure of *M. tuberculosis* varied significantly in Nepal, Nigeria, Yemen and Rwanda. The distribution of genotypes among young patients differed from that in older patients in Nepal and Yemen, suggesting

a rapid change in the population structure of *M. tuberculosis* in these countries. In Rwanda strains of the T2 family with spoligotyping ST52 were strongly associated with MDR-TB.

### PC-241-16 Simple direct drug susceptibility testing: a simple, cost-effective solution for resource-poor high-burden countries

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**Background:** New techniques for rapid diagnosis MDR-TB have been endorsed by WHO, however, in resource poor countries health systems, infrastructure and supply management systems are not developed. Implementation of new and rapid techniques at intermediate level is a challenge.

**Objective:** To evaluate practical use of simple direct drug susceptibility testing (SDDST).

**Method:** We investigated an SDDST method for isoniazid (INH), rifampicin (RIF), in smear positive specimens from 93 pulmonary TB patients and compared it with standard indirect DST (IDST). Drug containing modified Ogawa medium was used for direct DST. All 1+ 2+ and 3+ smear positive specimens was decontaminated with equal volume of 4% NaOH vortexed for 20 sec and decontaminated for 15 min (Kudoh method). For 1+ and 2+ samples 0.1 ml and in case of 3+ sample, 0.1 ml of tenfold dilution of sample was inoculated into 2 drug free controls and one slope each of INH, RIF and Paranitrobenzoic acid (PNB, 500 µg/ml) containing media. Indirect DST was carried using the standard proportion method in L-J medium.

**Results:** SDDST was performed on 93 samples including 1+(30) 2+(30) and 3+(33), interpretable results by SDDST were obtained in 80 (86%) cases. Results were compared with Indirect DST. By standard technique MDR was reported in 17 cases (21%), mono resistant to INH in 5 (6%), and susceptible to both R and H in 58 (73%) cases. Over all agreement between two techniques was 95% (76) and discrepant result reported in 4 cases only. Sensitivity and specificity to RIF was 94% and 98% and for INH 91% and 100% respectively. Efficiency of simple

Table Simple direct DST results versus standard indirect DST results

Simple direct DST pattern	Indirect DST results			Total
	RIF and INH susceptible	INH resistance only	RIF and INH resistance (MDR)	
INH and RIF susceptible	57	0	0	57
INH resistance only	0	5	1	6
RIF resistance only	1	0	2	3
INH and RIF resistance	0	0	14	14
Total	58	5	17	80



and specificity for KM were 92% (12/13) and 98% (122/124). Sensitivity and specificity for OFX were 92% (34/37) and 100%. All of the false-susceptible results were found in samples with insufficient growth (<50 colonies) in control tube.

**Conclusions:** A simple direct DST showed good performance and was very easy to perform compared to conventional DST. Therefore, this method could be useful and affordable in resource-limited settings to detect multidrug-resistant and extensively drug-resistant TB.

### PC-244-16 Drug resistance patterns of hospitalised treatment failure tuberculosis patients in Bangladesh

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**Background:** This study was conducted with the hospitalized TB patients of Bangladesh. This study was planned with the aims of screening treatment failure hospitalized TB patients for multidrug-resistant (MDR) and extensively drug-resistant (XDR) and their genotypes.

**Design/methods:** *M. tuberculosis* was isolated on Löwenstein-Jensen slants from sputum samples of treatment failure hospitalized TB patients. Strains were tested for sensitivity to first line anti-TB drugs using proportion susceptibility testing (PST) method. MDR strains were tested for sensitivity to O-floxacin and amikacin using PST method. MDR strains resistant to these drugs were designated as XDR. Standard spoligotyping technique was practiced to genotype the MDR strains.

**Results:** During a period from February 2007 through December 2008, 270 sputum samples were cultured from hospitalized TB patients. *M. tuberculosis* grew from 73% sputum samples. All the strains were identified *M. tuberculosis*. Resistance to all first line anti-TB drugs was detected in 70% strains and 5.6% strains were sensitive to all these drugs. Five of 270 (2%) strains were XDR. Spoligo patterns of 80 strains were matched with SpolDB4 to ascertain phylogenetic clades. Of them, unique spoligo patterns were detected in 14 isolates. The remaining 64 patterns were grouped into East African Indian ( $n = 5$ ), Central Asian ( $n = 10$ ), Beijing ( $n = 23$ ) and principal genetic group 2 and 3.

**Conclusion and recommendations:** Prevalence of MDR is more among hospitalized treatment failure TB patients. MDR strains are heterogeneous in genotypes. XDR is an emerging threat to National TB Control Program.

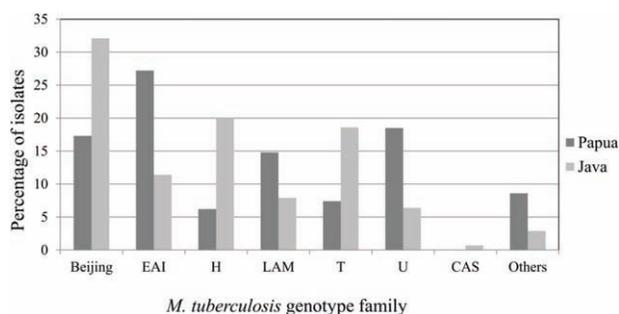
### PC-245-16 Large differences in *Mycobacterium tuberculosis* genotypes between Papua and Java Island in the Indonesian archipelago

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**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. We compared the distribution of *M. tuberculosis* genotypes in Papua and Java Island, two of the five largest islands in the Indonesian archipelago, which have marked differences in human population structure.

**Design/methods:** We randomly selected 81 *M. tuberculosis* isolates from pulmonary TB patients in Papua and 141 isolates from patients in Java. Spacer oligonucleotide typing (spoligotyping) was used to genotype all *M. tuberculosis* isolates. Spoligopatterns were analyzed and compared with patterns in the international Spoligotyping database (SPOLDB4).

**Results:** Both in Papua and Java, patients were mostly male (51.8% and 61.4%, respectively) with a first episode of TB (61% and 91%, respectively), and a mean age of 33 and 34 years, respectively. A high degree of genetic diversity was observed among the *M. tuberculosis* genotype. Sixty-five different patterns of spoligotyping was found in isolates from Java and 41 patterns in isolates from Papua. In Java, 32% of patients were infected with the successful Beijing genotype, compared with 17% in Papua ( $P < 0.05$ ). East African Indian (EAI) was more common in Papua (27.2%) compared to Java (11.3%, see Figure).



**Figure** Distribution of *M. tuberculosis* genotype families in Papua and Java.

**Conclusion and recommendations:** Our result showed a considerable degree of heterogeneity among *M. tuberculosis* isolates and a significant difference in

*M. tuberculosis* population structures between two different Indonesian islands. 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.

#### PC-246-16 Rapid testing of *Mycobacterium tuberculosis* resistance to second-line drugs by use of the XDR-test

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**Background:** The rapid spread of XDR-TB has exposed the dearth of new tools for tuberculosis control and prompt detection of drug resistance. In our Institute, XDR-test and technology of its production was developed. The XDR-test is a rapid semi-qualitative procedure for susceptibility testing of *M. tuberculosis* to isoniazid (INH), rifampicin (RMP), ofloxacin (OFX), kanamycin (KM), amikacin (AK) and capreomycin (CM) by the nitrate reductase assay in Löwenstein-Jensen (LJ) slants.

**Objective:** Evaluate the XDR-test for drug susceptibility testing (DST) of *M. tuberculosis* isolates to the second-line anti-TB drugs.

**Methods:** The BACTEC MGIT 960 system was used as reference technique. For BACTEC, testing concentrations used were OFX 2.0 µg/ml, KM 5.0 µg/ml, AK 1.0 µg/ml, CM 2.5 µg/ml. A total of 61 isolates (35 isolates were MDR, and 26 were susceptible) from patients were tested. Discordant results were repeated by both methods.

**Results:** We used the following critical concentrations for the drugs in the XDR-test: for OFX 2.0 and 3.0 µg/ml, KM 30 µg/ml, AK 30 µg/ml and CM 30 µg/ml. Results for KM, AK and CM were excellent, with 100% accuracy, and a result of 90.0% accuracy was achieved for OFX 2.0 µg/ml. The complete agreement was found for the detection of OFX resistance between both tools using concentration of 3.0 µg/ml of OFX for the XDR-test. The time required to obtain results was an average of 9.8 days by the XDR-test and 6.8 days by the BACTEC MGIT 960.

**Conclusion:** This study showed a good agreement of results obtained by the XDR-test and by the BACTEC method. The critical concentrations for KM and CM were the same as that recommended for the absolute concentration method in LJ slants used in RF. The critical concentration for OFX was used 3.0 µg/ml. The critical concentration for AK was chosen 30 µg/ml. Using these concentrations of the major second-line drugs no discordance was found between both the XDR-test and the BACTEC MGIT 960 system.

#### PC-247-16 Kanamycin resistance for common genetic families of *M. tuberculosis* in central regions of Russia

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**Background:** We estimated associated kanamycin (Kan) resistance among most frequently encountered in the central Russian regions of genetic families of *M. tuberculosis*.

**Design/methods:** 24 strains was isolated from new case patients (NC), 21 from patients after several courses of therapy by Kan. The degree of drug resistance was determined by means of minimal inhibitory concentrations (MIC) in Bactec-960 MGIT. For the *M. tuberculosis* spoligotyping DNA was amplified with DRa and DRb oligonucleotides. Mixtures of amplified DNA were hybridized to 43 oligonucleotides. Octal code determined according to the recommendations J. Daler.

**Results:** *M. tuberculosis* of the NC were distributed in the following families: Beijing (Bj) –16.6%, LAM4-4.2%, LAM9 –8.3%, Haarlem (H) –12.5%, Haarlem3 (H3) –4.2%, Haarlem4 (H4) –16.6%, X1 –4.2%, T-4.2%, T 1–12.5%, T1 Rus2 –4.2%, T4–8.3%. Most sensitive to Kan among this group were MTB of families Haarlem (H, H3, H4), in which 75% of MIC was 0.313 mg/l. The MIC was twice (0.63 mg/l) for families T 1–T4 and Beijing in 85% of the cases. For all strains of Lam9 MIC was 0.63 mg/l. Associated with resistance to Kan locus mutations in 16SrRNA (1288–1543 bp) were not detected. MTB from the treated Kan patients belonged to the following families: LAM9 –71.5%, LAM –9.5%, Beijing –9.5%, and U –9.5%. All Lam9 cultures had very high degree of resistance to Kan –5120 mg/l, while all of these cultures had mutations in the locus of 16SrRNA (1288–1543 bp). In 86% of cases the Kan resistance associated with mutations in a specific locus. One culture *M. tuberculosis* of families U, Lam, had MIC of 2.5 mg/l and one Bj MTB had MIC of 5.0 mg/l. All of these three cultures *M. tuberculosis* did not have mutations in the relevant locus.

**Conclusion and recommendations:** Among retreated TB patients *M. tuberculosis* were significantly less genetic diversity. Specific mutations in the locus 16SrRNA(1288–1543 bp) with a sensitivity of 85% and a specificity of 100% can serve as a marker for resistance of the *M. tuberculosis* to Kan.

## OCCUPATIONAL HEALTH AND INFECTION CONTROL

### PC-271-16 A photovoice intervention to promote infection control among Russian health care workers

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**Background:** Russian health care workers (HCWs) in TB facilities have a greater risk of nosocomial TB than do HCWs in other Russian healthcare settings. Reasons are multifactorial and include failure to use and fit-check respirators, even when knowledge of risk exists. Fear of infecting loved ones motivates Russian HCWs to remain infection-free. Our aim was to test a photovoice intervention, combining photographs of loved ones and narrative about desire to remain infection-free, to promote health behavior change among Russian TB HCWs.

**Design/methods:** This single-group experimental-design study was conducted with 20 HCWs at a TB hospital in Russia. Participants completed the Respirator Use Scale (RUS) then photographed a significant other and wrote a short narrative describing why that significant other motivated them to wear and fit-check respirators; these were developed into posters and displayed in the workplace. Subjects again completed the RUS after posters had been displayed for six months.

**Results:** Following the intervention, intention to wear ( $t(19) = -3.199, P = 0.005$ ) and fit-check ( $t(19) = -3.199, P = 0.005$ ) respirators increased significantly. Regression analysis showed only self-efficacy predicted intention to wear respirators, accounting for 72% of the variance. Important others ( $P < 0.001$ ) and self-efficacy ( $P = 0.022$ ) were both predictors of intention to fit-check respirators, accounting for 83% of the variance.

**Conclusions and recommendations:** Results suggest photovoice may be an efficacious intervention to promote respirator use and fit-checking in Russian HCWs in TB facilities. Larger scale testing is needed to determine the translational potential of the intervention.

### PC-272-16 High latent tuberculosis infection test conversion rates among health care workers in the country of Georgia

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**Background:** There are limited data on serial testing of healthcare workers (HCWs) with interferon-

gamma release assays (IGRAs) for latent tuberculosis infection (LTBI). The purpose of this study was to determine the rates and risk factors for LTBI conversion (positive test following documented negative test) among Georgian HCWs using the tuberculin skin test (TST) and QuantiFERON®-TB Gold In-Tube assay (QFT), in addition to determining prevalence and risk factors for LTBI.

**Methods:** A prospective longitudinal study was conducted among HCWs in the country of Georgia.

**Results:** Among 319 HCWs enrolled, 89% had BCG vaccination; 60% worked in healthcare facilities (HCFs) specializing in TB. HCWs from TB HCFs had higher prevalence of positive QFT and TST than those from non-TB HCFs: 107/194 (55%) vs. 30/125 (31%) QFT positive ( $P < 0.0001$ ) and 128/189 (69%) vs. 64/119 (54%) TST positive ( $P = 0.01$ ). There was fair agreement between TST and QFT (70%, kappa = 0.42, 95%CI 0.3 1–0.52). In multivariate analysis, frequent contact with TB patients was associated with increased risk of a positive QFT (OR 3.04, 95%CI 1.79–5.14) but not with positive TST (OR 1.29, 95%CI 0.76–2.18). Increasing age was associated with increased risk of a positive QFT (OR 1.05 per year, 95%CI 1.0 1–1.09) and TST (OR 1.05, 95%CI 1.0 1–1.10). High rates of HCW conversion were seen: the QFT conversion rate was 22.8/100 person-years, and TST conversion rate was 17.1/100 person-years. TST conversion was associated with working in a TB HCF ( $P = 0.04$ ), whereas QFT conversion was not. In multivariate analysis, females HCWs had a decreased risk of TST conversion (OR 0.05, 95%CI 0.0 1–0.43), and older HCWs had an increased risk of QFT conversion (1.07 per year, 95%CI 1.01–1.13).

**Conclusion:** A high prevalence of LTBI and a high rate of LTBI test conversion rates were seen among Georgian HCWs, especially among those working at TB facilities. These data highlight the need for effective TB infection control measures.

### PC-273-16 Improvement in infection control practices through provision of additional mobile clinics in 5 high-burden tuberculosis case load health facilities in Swaziland

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**Background:** Swaziland notifies the highest TB burden worldwide (WHO global TB report 2010). TB services are integrated within facilities but face challenges in adhering to essential IC measures due to lack of space. The USA Agency for International Development (USAID) through the Presidential Emergency Fund for AIDS Relief (PEPFAR)-funded University Research Co., LLC (URC), under the Health Care Improvement project to provide support to the

National TB control program. We evaluated the implementation of mobile TB clinics to improve adherence to IC measures by patients and staff.

**Methods:** URC set up prefabricated TB clinics (divided into 3 rooms with windows extractor fans and doors opening to outside waiting area) in 5 high TB caseload facilities in the country (2008–2010); the waiting areas are roofed and mid height walled to ensure maximum natural ventilation, patient comfort against weather conditions and confidentiality. Risk assessments conducted in the old TB sites were compared with baseline and follow up assessments in prefabricated clinics.

**Results:** TB prefabricated clinics availed consultation space at the health facilities for TB-HIV services, suspects of TB were now seen in a separate room; IC committees were formed, staff trained, plans developed, and implementation assessed regularly; facility staff conducted patients' education on triage and cough etiquette, implemented client flow, prioritization of infectious cases, and natural airflow.

**Conclusion:** In Swaziland provision of mobile clinics resulted in: 1) reduced risk for transmission of TB; 2) improved IC measures; 3) integrated TB-HIV services can be provided with limited risk of transmission of disease.

#### PC-274-16 Assessment of tuberculosis infection control practices in Inner Mongolia

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**Background:** Hospitals are an established risk factor for the emergence and transmission of respiratory infectious diseases, such as tuberculosis (TB). Providing TB infection control (IC) measures may help reduce transmission of TB in healthcare settings. There are very few systematical studies on TB IC status in different healthcare settings in China.

**Methods:** A cross-sectional study was conducted to assess the TB IC status among all 42 TB related HCF in Inner Mongolia using a standardized survey questionnaire in 2012. We collected demographic information, occupation, work location, and various exposures potentially associated with TB infection.

**Results:** The study covered 22 hospital, 16 disease control centers, 5 TB dispensaries and one prevention station in Inner Mongolia. All 42 HCF have implemented several but not all TB IC measures, including administrative control, personal protective equipments, monitoring and evaluation, and IC related training. At least one healthcare worker from surveyed facilities received training(s) on standard TB airborne IC and basic IC. Most HCF ( $n = 37$ ) supplied masks for the HCW who at risk of TB exposure, but only 15 facilities stated that they provide

N95 respirators. There is a lot of work need to be further strengthened. 6 out of 22 hospitals have a TB department, also few hospitals offers TST testing ( $n = 6$ ) and chest X-ray screening of TB ( $n = 11$ ). Only 9 facilities stated that TB IC is their priority, and 12 institutions monitored TB IC among staff members. TB IC related training was given at four facilities, education and advertising on IC were also inadequate.

**Conclusions:** TB IC is an important part of TB Prevention and Control. Efforts to strengthen IC in Inner Mongolia should focus on regular audits of actual practice, enforcement of existing rules, and provision of appropriate personal protective devices and training to healthcare workers.

#### PC-275-16 Tuberculosis among public health facility staff in Eastern Province, Kenya: a three-year observational study

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**Background:** Though Kenya is at initial stages of implementing TB infection control in hospitals, the burden of the disease among health facilities' staff remains largely unknown. The purpose of this study was to establish the burden, associated co-morbidities and outcomes of TB disease among public health facilities' staff in Eastern Province, Kenya.

**Setting:** 286 public health facilities in Eastern Province, Kenya, with 3321 staff members. These included dispensaries, health centre, district hospitals and regional referral hospitals.

**Design/methods:** From 1st January 2008 to 31st December 2010, District TB Coordinators retrospectively reviewed the facility TB registers at the end of every quarter recording relevant information on staff with TB disease.

**Results:** Total number of staff diagnosed with TB was 78. Median age of those affected was 35 (range 19–56), females constituted 54%. 25–44 years age-group accounted for 65% of all cases. Nurses were the most affected cadre at 38%. HIV-positive lay counselors accounted for 10% of all the cases. 76% of affected staff was from district and regional referral hospitals. Smear positive TB constituted of 51% of all cases; retreatment cases were 10%. No MDR diagnosed, DST only done for retreatment cases. 100% offered HIV test, 9% declined. HIV-TB was 30%, 3% had diabetes mellitus co-morbidity. The cumulative treatment success rate for the smear positive TB was 97%, while 5% of all affected staff died during treatment. Mean CNR for the three year period was 783 (not adjusted for age distribution).

**Conclusion and recommendations:** The data suggested a high incidence of TB disease among hospital staff with high volume facilities disproportionately affected. The significant HIV test decline rate among staff may suggest stigma of TB and HIV among health

workers. Use of HIV positive lay counselors in HIV care clinics exposed them to the risk of TB infection and needs to be evaluated. Need to provide routine DST to all staff diagnosed with TB.

### PC-276-16 Latent tuberculosis infection among village doctors in Inner Mongolia, China

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**Background:** No published data exists in China to document the burden of latent tuberculosis infection (LTBI) among village doctors. Village doctors are front-line healthcare providers in China. They potentially have a high risk of exposure to TB patients. In this study we report LTBI rate and analyze factors associated with infection among village doctors in western Inner Mongolia.

**Methods:** Between September and December 2011, we administered QuantiFERON<sup>®</sup> Gold In-Tube (QFT) tests, tuberculin skin tests (TST) and surveys to village doctors from two county-level areas, Linhe District and Hanggin Rear Banner in Bayan Nur Prefecture. The survey asked about demographic information, occupational history, social and medical history, and work practices. We evaluated risk factors for LTBI (defined as QFT  $\geq 0.35$  IU/ml or PPD diameter  $> 5$  mm) using a stepwise logistic regression model.

**Results:** Of 665 village doctors, 272 (40.9%) had a positive QFT. In multivariable analysis, positive QFT was associated with being male (adjusted OR 1.8, 95%CI 1.3–2.5),  $> 30$  years (adjusted OR 2.2, 95%CI 1.1–4.5), working  $> 20$  years (adjusted OR 2.7, 95%CI 1.5–4.7), and had TB (adjusted OR 3.6, 95%CI 1.1–11.6); 228 village doctors (34.3%) had a positive TST. Positive TST was associated with being male (adjusted OR 1.8, 95%CI 1.3–2.6), working in Linhe District (adjusted OR 3.5, 95%CI 2.5–4.9), and had TB (adjusted OR 3.7, 95%CI 1.3–10.4).

**Conclusions:** The prevalence of LTBI among village doctors in Inner Mongolia was high. The village doctors in this region of China need to strengthen their TB infection control measures.

### PC-277-16 Tuberculosis as the most common occupational infection among health care workers in the Limpopo Province of South Africa

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**Background:** Health care workers are exposed to infections in the course of their work. This study purported to investigate the prevalence of tuberculosis

and other occupational infections and their risk factors among healthcare workers from Limpopo Province of South Africa.

**Design/methods:** Cases about occupational infectious diseases of healthcare workers from Limpopo Province that were submitted to the Compensation Commissioner between January 2006 and December 2009, were reviewed. Demographic data of cases and details on reported infections were recorded per year. Descriptive statistics were calculated.

**Results:** The total number of cases of occupational infectious reported during the study period was 56; of these, 83.9% (47) of cases were for tuberculosis, 10.7% (6) for cholera, and 5.4% (3) for chickenpox. Nurses were the most affected. The majority of those infected were female (67.9%), aged over 40 years (57.1%), and who had worked for over 10 years (59.2%). With regard to length of time it took for one to be infected, overall it took  $13.6 \pm 9.7$  years, from the year of employment to being infected. Based on the geographical location, Mopani district, situated in a rural setting was the most affected as 24 of the 47 cases of tuberculosis occurred there.

**Conclusion and recommendations:** The most common occupational infection among healthcare workers in Limpopo province of South Africa was tuberculosis. It infected mainly nurses from the rural health district of Mopani. Younger age and being a nurse were significant risk factors associated with being infected early. Targeted educational and managerial interventions are needed.

### PC-279-16 Prevalence of positive tuberculin skin test and associated factors among Makerere medical students, Kampala, Uganda

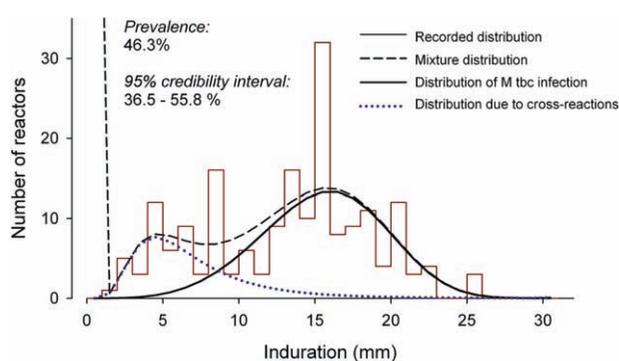
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**Background:** Tuberculosis infection among medical students is thought to be higher than that among comparable groups. In this study we determined the prevalence of positive tuberculin skin test (TST) as an estimate of infection with *M. tuberculosis* among medical students enrolled at Makerere University, Kampala, Uganda.

**Design/methods:** This was a cross-sectional study carried out among randomly selected medical students. TST was performed using intradermal technique, administering 0.1 ml of purified protein derivative [PPD RT-23, 2TU/0.1 ml, Statens Serum Institute (SSI)]. Readings were taken after 72 hours.

**Results:** Between April and June 2009, of 325 students selected to participate, 292 received TST and 288 analyzed. Of 288 students, 173 (60%) were pre-clinical (year 1 to 3) and 115 (40%) clinical (year 4

to 5). More male students 180 (62.5%) than female students 108 (37.5%) were enrolled. One hundred thirty students [45.1% (95%CI 39.3–51.1)] had positive TST using a cut of 10 mm to denote infection, this was not different from one derived from mixture analysis [46.3% (95% Bayesian credibility interval 36.5%–55.8%)]. Positive TST prevalence increase in a linear pattern with increasing years of study ( $P = 0.002$ , OR = 5.04); that is, an increase from 35.3% among year one students to 54.9% among year five students, although respective confidence intervals were overlapping across the years of study. Male sex, dental surgery course and positive contact were predictive of a positive TST.



**Figure** Tuberculosis skin test reaction sizes, observed, mixture, cross reaction and tuberculosis infection distribution, undergraduate Makerere University medical students, Kampala, Uganda, 2009 ( $N = 288$ ).

**Conclusion and recommendations:** We found this prevalence twice higher than that of adults living in the suburbs of the city the medical school is located. This and the observation of a steep increase in prevalence from year one to year five in a relatively short period suggests that exposure and infection might be related to clinical work. We recommend urgent institution of infection control measures in this institution.

### PC-280-16 Latent tuberculosis infection and tuberculosis infection control knowledge, attitudes, and practices survey of health care workers in the country of Georgia

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**Background:** There are no data available on knowledge, attitudes and practices (KAP) of healthcare workers (HCWs) for latent tuberculosis infection (LTBI). The aim of this study was to assess KAP of HCWs for LTBI and TB infection control (IC) in the country of Georgia.

**Design/methods:** Anonymous questionnaire survey was conducted in July–December 2011.

**Results:** Among 171 HCWs who completed the KAP survey, 159 (93%) were female; mean age was 46 years; 106 (62%) worked primarily with TB patients; mean employment length was 21 years. 100 (58.5%) HCWs believed they were at risk of acquiring LTBI; 124 (72.5%) and 100 (58.5%) agreed that ultraviolet lamps and N95 respirators were effective IC measures, respectively; 67 (39.2%) HCWs routinely used respirators. 93 (54.4%) desired annual screening and 88 (51.5%) treatment for LTBI. 114 (66.7%) knew the rationale for the treatment of LTBI. In multivariate analysis, HCWs working primarily with TB patients were more likely to know the rationale for the treatment of LTBI compared to non-TB HCWs (OR 3.1; 95%CI 1.34–6.92). HCWs were more likely to refuse LTBI treatment if they worked primarily with TB patients (OR 6.7; 95%CI 2.97–15.15), perceived their own risk of TB re-infection (OR 1.7; 95%CI 1.15–2.42), and were nurses vs. physician (OR 2.1; 95%CI 1.14–4.06). Routine use of respirators was associated with uninterrupted supply of respirators (OR 1.9; 95%CI 1.96–4.16), among HCWs who worked primarily with TB patients (OR 2.7; 95%CI 1.16–6.45), and being a nurse vs. physician (OR 3.1; 95%CI 1.47–6.38).

**Conclusion and recommendations:** Many HCWs in Georgia had incomplete knowledge about LTBI and TB IC measures. Intensive LTBI/TB IC trainings should complement IC implementation in the country.

### PC-281-16 Occupational health and safety issues among research staff working with and within a tuberculosis study in urban Lima, Peru

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An epidemiological study of tuberculosis requires a team of professionals with the research and social skills necessary to work with highly vulnerable populations. We are conducting a study among TB cases and their household contacts that will enroll 16 500 participants in some of the poorest neighborhoods in Lima, Peru. Our research team includes 120 data-collectors who interact with patients at urban health clinics and with their household contacts at the home. Many of the areas visited are crowded, have high crime rates, and are accessible only by foot. These work conditions may impose significant physical and emotional stresses on staff. Here, we describe some specific problems that we encountered and the steps taken to ensure staff health and safety.

Most study staff is female, aged 22 to 35, and a recent graduate from a nursing or nursing assistant program. Staff orientation and training focuses on

the knowledge and skills needed to interact with vulnerable patients and maintain biosafety. To ensure the team's health, a pulmonologist conducted initial medical evaluations and follow-up visits are provided as needed. Finally, the team completes an interim leadership and coaching workshop to ensure the continued high quality of work.

Significant events among staff since study initiation include nine new pregnancies and six TST conversions. All individuals with a TST conversion initiated INH therapy. Two nurses were diagnosed with active TB and started anti-TB treatment. Eighty-five staff members were robbed while conducting field work. Some of the incidences involved a weapon and resulted in hospital care and/or medical leave for the team member. Minor injuries due to falls on steep stairs and rough terrain were common.

Field workers involved in TB research often face significant physical and emotional challenges, requiring the implementation of preventive training and ongoing attention to their needs.

## IMMUNOLOGY: PATHOGENESIS AND VACCINES

### PC-309-16 Temporal changes of apoptosis-associated biomarkers in the development of tuberculosis

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**Background:** Predicting the development of tuberculosis (TB) from latent TB infection remains difficult. Among the candidate markers, apoptosis-associated serum biomarkers have been rarely studied.

**Design/methods:** From January 2009 to June 2011, TB patients and interferon-gamma release assay (IGRA)-positive and IGRA-negative family contacts were recruited to analyze changes in apoptosis-associated serum biomarkers, which include decoy receptor 3 (DcR3), prostaglandin 2 (PGE2), and lipoxin. The prognostic implications of clinical characters and serum biomarkers were also analyzed.

**Results:** A total of 100 TB patients and 92 IGRA-negative and 91 IGRA-positive family contacts were recruited. The DcR3 and PGE2 levels decreased from the IGRA-negative group to the IGRA-positive group, and then peaked in the active TB group. In contrast, lipoxin decreased to trough in the TB group. All of the three apoptosis serum markers and age were independent factors discriminating active TB from latent TB infection. In the TB group, older age, presence of co-morbidity, and higher serum DcR3 and monocyte chemotactic protein (MCP)-1 levels were

independently associated with poorer six-month survival.

**Conclusion and recommendations:** Apoptosis-associated serum biomarkers change along with the status of *Mycobacterium tuberculosis* infection. Aggressive mycobacteriologic study to detect active TB is necessary for IGRA-positive family contacts who are older and with high DcR3 and PGE2 levels, and low lipoxin. Older age, co-morbidity, and high DcR3 and MCP-1 levels are important outcome predictors.

### PC-310-16 The dynamics of cytokines in patients with newly diagnosed and recurrent pulmonary tuberculosis and before and after treatment with standard therapy

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**Background and objective:** To study the dynamics of cytokines in patients with NDTB and RPTB prior to and after 2-month treatment with standard anti-TB therapy (ATT).

**Methods:** Serum levels of cytokines (IL-2, IL-4, IL-8 and IL-10) in 100 RPTB patients (1st group), 150 NDTB patients (2nd group) and 30 healthy individuals (3rd group) were examined by ELISA method.

**Results:** At admission 1st group had (IL-2, 39.4 ± 0.7 pg/L; IL-4, 9.5 ± 0.2 pg/L; IL-8, 21.1 ± 0.3 pg/L; IL-10, 40.0 ± 0.7 pg/L), 2nd group (IL-2, 35.3 ± 0.7 pg/L; IL-4, 10.8 ± 0.3 pg/L; IL-8, 21.8 ± 0.3 pg/L; IL-10, 42.3 ± 0.5 pg/L), as opposed to control healthy group (IL-2, 21.6 ± 0.8 pg/L; IL-4, 29.9 ± 1.2 pg/L; IL-8, 9.9 ± 0.6 pg/L; and IL-10, 50.2 ± 1.2 pg/L) ( $P < 0.001$ ). With the exception of IL-8, cytokine levels were significantly different ( $P < 0.05$ ) between 1st and 2nd groups ( $P > 0.05$ ). After 2 months, there was a significant reduction in cytokine levels in 1st group (IL-2, 29.5 ± 0.5 pg/L; IL-8, 18.2 ± 0.2 pg/L) in 2nd group (IL-2, 27.0 ± 0.9 pg/L; IL-8, 17.2 ± 0.2 pg/L). However, IL-4 and IL-10 cytokines increased in 1st (IL-4, 16.6 ± 0.4 pg/L; IL-10, 48.5 ± 0.8 pg/L) and 2nd groups (IL-4, 21.0 ± 0.4 pg/L; IL-10, 51.8 ± 0.6 pg/L), when compared to entry levels and 2 month post-treatment ( $P < 0.001$ ).

**Conclusion:** Patients with pulmonary TB have higher IL-2, IL-8 and lower IL-4, IL-10 content than healthy controls. Chemotherapy resulted in a significant reduction in IL-2, IL-8 and increase in IL-4, IL-10 after 2 months of therapy. Patients with recurrent TB (RPTB) are more immunosuppressed than NDTB patients, both before treatment and after 2 months. This is perhaps due to higher incidence of MDR-TB in majority of such patients.

### PC-311-16 Characteristics of immunologic patterns in children with tuberculosis

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**Background:** Characteristics of the immunologic patterns in children with tuberculosis.

**Design/methods:** 135 patients 3–14 years old were examined during 2010–2012 in the children's department of the Saint-Petersburg Institute for Phthisiopulmonology. Two groups of patients were examined: I ( $n = 66$ ; 48.8%)—MBT infected without TB manifestation (control group); II ( $n = 69$ ; 51.2%)—with intrathoracic lymph nodes TB. TB diagnosis was decided basing on clinical and Rx symptoms. Examination included: assessment of leucocytes' subsets (CD3+, CD4+, CD8+, CD4+/CD3+, CD8+, CD16+, CD20+, CD25+, CD95+, HLAI), cytokines (TNF- $\alpha$ , IL-2, IL-4, INF- $\gamma$ ) by complex of serological tests (indirect hemagglutination, complement consumption (CCT), passive hemolysis (PHT) tests, ELISA IgA, IgG, IgM), QuantiFERON<sup>®</sup>-TB Gold IT (QFT-G).

**Results:** Levels of CD3+ ( $1.74 \pm 0.08$ ,  $P = 0.03$ ), CD25+ ( $0.57 \pm 0.03$ ,  $P = 0.04$ ), HLAI ( $0.82 \pm 0.05$ ,  $P = 0.04$ ) were significantly higher in II group compared to the control group (I). Specific antibodies titer was significantly higher in group II by CCT ( $P = 0.001$ ) and ELISA ( $P = 0.05$ ). The difference in levels of the IgA antibodies ( $63.10 \pm 7.1$  (II) vs.  $53.01 \pm 4.3$  (I), and IgG ( $97.49 \pm 10.7$  (II) vs.  $74.86 \pm 5.72$  (I)) was not statistically significant. Rate of QFT-G test positive results was significantly higher for children with TB (II) ( $P = 0.001$ ) (86.8% of cases (II) vs. 9.1% of cases (I)).

**Conclusion and recommendations:** Assays of the CD3+, CD25+, HLAI by CCT, ELISA and QFT-G are the most informative tests for TB disease diagnosis in children.

### PC-312-16 The polymorphisms of the detoxification gene in adverse drug reactions among patients with pulmonary tuberculosis

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**Background:** This study investigate the relationships between detoxification and repair protein gene polymorphisms and hepatitis adverse drug effects of anti-tuberculosis disease drugs.

**Design/methods:** 233 TB infected cases (83 cases with ATT induced hepatitis and 150 controls) are in-

cluded in analysis and some samples are excluded due to the incompetence of demography data.

**Results:** Genotypes of UGT 1A7\*1/\*3 may increase the risk and severity of anti-TB drug-induced hepatitis as the odds ratio (OR) are 2.52 (95%CI = 1.05–6.03). Genotypes of CYP2E1 C1 genetic may increase the risk and severity of anti-TB drug-induced hepatitis as the odds ratio (OR) are 1.87 (95%CI = 1.15–3.05) than C2 genotype. The synergistic effects were found between UGT1A7\*3, CYP2E1\*c1 in the study. The odds ratio of 5.61 (95%CI = 2.15–14.62) was found when patients with both UGT1A7\*3 and CYP2E1\*c1 genotype.

**Conclusion and recommendations:** This study indicated that the UGT1A7 polymorphism may correlate the drug-related hepatitis adverse drug effects among TB patients in Taiwan. Checking liver enzymes and detoxification genotype before treatment and regular monitoring liver enzymes during treatment are highly recommended. Application of pharmacogenetics or pharmacogenomics, such as assessing UGT genetic polymorphism, may help prevent ATT induced hepatotoxicity. The results from these investigations will prove to be helpful for understanding the adverse drug effects of TB and provide novel insights in controlling mycobacterial infection in our population.

### PC-313-16 *Mycobacterium tuberculosis* genotype influence upon morphological changes

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**Background:** We analyzed results of 17147 autopsies in 1980–2010, with 209 cases of tuberculosis (TB) among them. TB rate demonstrated more than 7 times increase during last ten years due to generalized forms.

**Design/methods:** 52 TB lethal cases were studied specially. Pathogens were identified as B (Beijing), T and LAM genotypes. Cases were divided in 2 groups: 1) 13 lung TB with classical clinical and morphologic features including numerous Langhans cells and positive Ziel-Nielsen staining. 2) 39—generalized TB with predominance of caseous necrosis, absence or low number of atypical giant cells, in 88% of cases acid firm rods were absent.

**Results:** In the first group MTB genotypes were 8 – T, 3 – LAM, and 2 – B type. In the group of generalized TB genotype B was in 32 cases, T – in 4 and LAM in 3.

**Conclusion and recommendations:** B genotype MTB are more frequent in generalized than in classic TB (82% and 61%,  $P < 0.05$ ). B genotype is important factor for development of generalized TB with poorly expressed proliferative changes. The absence of typical acid firm rods makes diagnostics difficult.

### PC-314-16 Studies on plasmid-based DNA vaccine to be used for providing protection against tuberculosis

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Tuberculosis in many parts of the world particularly in developing countries such as Pakistan, is a significant cause of morbidity and mortality in human and cattle. In this study, six genes of MTB namely ag85a, ag85b, ag85c, hsp<sub>x</sub>, esat6 and cfp10 were used as potential candidates for our DNA vaccine approach. Each gene was cloned separately in pcDNA3.1 Topo vector and later sub-cloned in pND mammalian expression vector to for optimal expression under both *in vitro* and *in vivo* conditions. Almost all of the constructs gave significantly high expression levels. Endotoxin-free pND-MTB gene constructs preparations were made and inoculated into eight week old female Balb/c mice in the quadriceps muscles and intradermally at rate of 50 µg DNA/leg and 25 µg intradermally at the base of tail. No booster injections were given. The animals were divided into six groups including positive and negative control groups. Eight animals were used for hsp<sub>x</sub>-pND vaccine, eight for cfp10-pND vaccine, two for esat6-pND vaccine and two for equally mixed ag85a, b and c pND vaccines. Four animals were used as positive control group and injected with Np-pND constructs; similarly four animals were used for negative control group by giving normal saline. The animals were bled after nine weeks post-vaccination through tail and finally with cardiac puncture technique. The antibodies were confirmed by Western blot (WB) analysis and their level was monitored by the multiplex microbead immunoassay (MMIA). The best humoral response was shown by hsp<sub>x</sub>-pND vaccinated animals both on WB and MMIA. Positive response was observed in animals vaccinated with esat6-pND14 and ag85a, b and c-pNDs, whereas, cfp10-pND vaccinated animals showed undetectable level of antibodies. We conclude that all of the MTB gene constructs in pND gave good expression under *in vitro* conditions except esat6 gene and under *in vivo* conditions except cfp10-pND constructs.

### PC-315-16 Relationship between calcium, oxidative stress and immune response in tuberculosis patients

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**Background:** *Mycobacterium tuberculosis*, the causative agent of tuberculosis can induce reactive oxygen species production which promotes tissue injury and inflammation leading to immunosuppression predisposing to infections. Calcium and micronutrients play an important role in maintaining oxidant-antioxidant balance and immune response in infections. The aim of this investigation was to assess the influence of calcium and micronutrients on oxidative stress and immunity status in tuberculosis patients.

**Design/methods:** Forty patients diagnosed with tuberculosis were recruited from The Institute of Thoracic Medicine and compared with age- and sex-matched healthy volunteers ( $n = 40$ ). Copper, iron, zinc, vitamins A, C, E, calcium, malondialdehyde, total antioxidant status, soluble immune complex, and immunoglobulins A, M, E, C-reactive protein, C3, C4, haptoglobin, ceruloplasmin levels in serum and myeloperoxidase in neutrophils were determined.

**Results:** Levels of calcium, copper, zinc, iron, vitamins A, C, E, and total antioxidant status were significantly low ( $P < 0.001$ ) and the concentration of malondialdehyde was significantly high ( $P < 0.001$ ) in tuberculosis patients. Serum soluble immune complex and myeloperoxidase in neutrophils were significantly low ( $P < 0.001$ ); C3 and C4 were slightly increased ( $P < 0.05$ ); IgA, IgM, IgE, CRP, haptoglobin and ceruloplasmin were increased significantly ( $P < 0.001$ ) compared to healthy volunteers.

**Conclusion and recommendations:** Our results showed high oxidant level accompanied with lower antioxidant potential, decreased calcium and micronutrient level; also there was a greater immune response but decreased elimination of pathogens. Our findings support the relationship between calcium, micronutrients, oxidative stress and immune response in tuberculosis. A novel approach to nutritional supplementation along with the regular treatment protocol may be recommended after proper pre-clinical trials.

### PC-316-16 Utility of simple laboratory tests for diagnosis of tuberculous meningitis in resource-constrained settings

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**Background:** Peruvian TB guidelines recommend the use of lymphocyte predominance as well as high protein and adenosine deaminase activity (ADA) levels in cerebrospinal fluid (CSF) as key elements in the diagnosis of tuberculous meningitis (TM), but this recommendation has not been formally assessed. Our objective was to evaluate the validity of these laboratory tests for the diagnosis of TM.

**Design/methods:** From November 2009 to November 2011, we included patients with clinical suspicion of TM (i.e., meningeal signs and/or alteration of consciousness) that were admitted to two reference hospitals in Lima and in which the treating physician decided to perform a lumbar puncture. We evaluated the presence of CSF white cell count > 5 with lymphocyte predominance, elevated proteins (>50 mg/dl) and high ADA (>5 U/L) levels as predictors. The reference standard for TM was a composite one including any of the following: positive liquid or solid culture or PCR from CSF; bacteriological or histological evidence from other body fluids or tissues; or expert opinion to treat and good evolution at one month.

**Results:** 106 patients were included. Median age was 34 years (IQR 23–64) and 75% were males. 42 patients had a final diagnosis of meningeal tuberculosis. Sensitivity and specificity of ADA, elevated proteins and mononuclear pleocytosis were 60% and 83%; 81 and 56%; and 67 and 70% respectively. 18 out of 19 (94%) patients that fulfilled these three diagnostic criteria had a final diagnosis of TM (LR+ of 27.4) while 6 out of 29 (21%) patients without any of the three criteria had a final diagnosis of TM (LR- of 0.4).

**Table** Number of criteria (mononuclear pleocytosis, high protein or high ADA levels in CSF) present in patients with and without tuberculous meningitis, Lima, Peru, 2009–2011

Number of criteria present	Tuberculous meningitis		Total
	Present	Absent	
All	18	1	19
1 or 2	18	40	58
None	6	23	29
Total	42	64	106

**Conclusion/recommendations:** The conjoint presence of mononuclear pleocytosis, high protein and

high ADA levels in CSF can be used as a reliable criterion to diagnose TM. This will lead to more timely treatment. However, its absence can not reliably rule out this diagnosis and culture remains necessary. The development of better diagnostic approaches is urgently needed.

### PC-317-16 In vitro and in vivo effects of HIV on cytotoxic lymphocyte activation by mycobacteria

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**Introduction:** Human immunodeficiency virus (HIV) infection is contributing to the re-emergence of opportunistic tuberculosis (TB) globally. Effects of HIV on the antiviral response by cytotoxic lymphocytes (CTL) have been extensively studied while effects on the antibacterial CTL response are poorly characterized.

**Objective:** To determine the effect of HIV-1 on the antigen specific and innate cytotoxic/antibacterial activity of lymphocytes in response to mycobacterial antigen.

**Study design:** Human TB patients and an in vitro model were used to investigate how HIV predisposes people to *Mycobacterium tuberculosis*.

**Study site:** The work was performed at the Centre for Respiratory Diseases Research, Kenya Medical Research Institute, Kenya, and the Department of Microbiology/Immunology, University of Texas Medical Branch, Galveston, Texas, USA.

**Methods:** We isolated human peripheral blood mononuclear cells (PBMC) from a healthy tuberculin-reactive donors and convalescent TB patients with or without HIV. We measured responses of peripheral blood CD8+T cells to mycobacteria and concanavalin A.

**Results:** Our results demonstrate that HIV infection may reduce the antimicrobial activity of cytotoxic lymphocytes through reductions in both granulysin expression and degranulation levels. HIV- and HIV+ human subjects that have recovered from *M. tuberculosis* disease still have strong constitutive expression of granulysin by the CD8+T cell population.

**Conclusion:** Understanding the effects of HIV on T cell activation is essential to understanding the physiological basis for inadequate antibacterial activity by CTLs in HIV patients. The knowledge gained is important for informed guidance of vaccines or immune modulation-based therapy to restore or augment cytotoxic lymphocyte function so as to boost host defense to MTB or other opportunistic pathogens.

### PC-318-16 Dextran against granulomatosis and fibrosis

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**Aim:** Granulomas prevent dissemination of mycobacteria (Mb) in tissues, but they also serve as a place of bacteria multiplication and as a shield from drugs action. Preventing granuloma formation might allow avoiding fibrogenesis and calcification of tissues. We focused our research on results shown in 1990-th for conjugate of dextran with isoniazid (INH) that had decreased number of granulomas twice and strongly decreased fibrosis in mice. Our aim was to develop the hypothesis of dextran-INH antigranulomatous action.

**Methods:** The long history of studies of dextran-INH conjugates originated in 1960-th was reviewed. Concept of lisosomotropic action of the dextran conjugate (that should have led to prolonged action, less toxicity and targeted delivery) was evaluated, but we consider it was not sufficient to explain antigranulomatous effect. Numerous probable effects and properties of dextrans were analysed and it allowed hypothesizing their specific immunomodulating action. **Results:** We hypothesize that dextrans alone may affect granuloma formation influencing the nature of Mb-macrophage and Mb-dendritic cell interactions. Known to date receptors for dextrans binding and uptake are mannose receptor (MR) and DC-SIGN family receptors (DFRs). Number of in vitro studies witness they promote intracellular and intercellular signals beneficial for Mb during tuberculosis. It allowed building a well-reasoned model of dextrans derivatives antigranulomatous and antifibrotic action.

**Conclusion:** In-depth examination of impressive results obtained for dextran-INH conjugate in 1990-th and analysis of newer data (2000-th) on dextran receptors were driven by interest in development of new antituberculosis drugs with antigranulomatous action. We suppose dextrans can partially inhibit MR and DFRs crucially changing results of interaction of mycobacteria with immune cells. We plan to test our hypothesis in vivo and in vitro. Being true it may open new approach to better tuberculosis treatment.

### PC-319-16 IL-6, IL8, GCSF, GMCSF, MCP1, MIP-1b as candidates for diagnosing pleural tuberculosis

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**Background:** The production of IFN $\gamma$  and TNF $\alpha$  are associated with effective cellular immune response against *Mycobacterium tuberculosis* infection, through cytokine-mediated macrophage activation. In extrapulmonary tuberculosis (TB), such as pleural TB, a wide array approach for cytokine responses has not been well studied in such patients.

**Design/methods:** *Ex vivo* non-stimulated cytokine responses in the pleural fluid from 43 patients with confirmed pleural TB, of whom 5 were HIV-infected, and 18 with other diseases were compared. A multiplex assay was performed using a commercial kit covering 17 cytokines and chemokines, and ELISAs were made to detect C-reactive protein (CRP in house) and matrix metalloproteinase (MMP)-9. Median values in three groups (TB-HIV+, TB-HIV other diseases) were compared using the Mann-Whitney test.

**Results:** Median IL6, IL8, GCSF, GMCSF, MCP1, MIP-1b were significantly higher in pleural fluid of TB than other disease patients as well as the already expected higher levels of IFN $\gamma$  and TNF $\alpha$  (Table). HIV-infected patients had a different cytokine profile: three-fold higher levels of IL-6, and the lowest production of CRP (<360 fold).

	TB-HIV-, median (IQR)	TB/HIV+, median (IQR)	P value*	Other diseases, median (IQR)	P value*
IL-1b	0.0 (0.0-1.5)	1.8 (0.6-8.7)	0.008	—	0.027
IL-2	0.0 (0.0-0.0)	19.5 (4.83-19.5)	0.047	0.0 (0.0-0.0)	0.010
IL-4	0.0 (0.0-2.0)	1.7 (0.85-11.77)	0.146	0.0 (0.0-0.0)	0.008
IL-6	69523.0 (27495-22754)	647770.2 (198584.3-283834.6)	0.061	5521.0 (4152.0-55759.0)	0.004
IL-8	842.0 (255.0-1866.0)	725.8 (399.72-2493.53)	0.906	465.0 (54.0-1455.5)	0.023
IL-10	0.0 (0.0-7.5)	0.1 (0.1-8.8)	0.485	0.0 (0.0-1.5)	0.441
IL-13	10.0 (10.0-10.0)	48.5 (10.6-88.3)	0.002	—	0.043
G-CSF	91 (2.5-294)	398.1 (36.8-726.85)	0.255	1.0 (1-32.5)	0.001
GM-CSF	17.0 (4.0-37.5)	24.1 (4.0-36.8)	0.891	4.0 (4.0-27.0)	0.315
INF-g	484 (211.5-894.0)	965.8 (305.8-2452.8)	0.172	57.0 (1.0-88.0)	0.000
MCP-1	1019.0 (606-1852.5)	1151.6 (520-3257.0)	0.448	702.0 (484-1907.1)	0.275
MIP-1b	134.0 (45.0-278)	128.5 (37-244.2)	0.933	35.0 (11.5-176.5)	0.147
TNF-a	40.0 (10.0-80.0)	43.7 (29.2-43.7)	0.647	1.0 (1.0-16.5)	0.000
CRP	24.0 (7.5-58.5)	19.2 (7.7-32.7)	0.553	19.0 (7.5-76.0)	0.907
MMP-9	3.0 (0.0-127.0)	365.1 (11.7-3462.4)	0.131	7.0 (0.5-3216.5)	0.392

\* P values were calculated using the Mann-Whitney test.

**Conclusion and recommendations:** The multiplex results points to possible strategies to identify *ex vivo* profiles of soluble factors that may help diagnosis, and together possibly provide insight into TB. The sample will be increased in order to build ROC curves to establish cut-off values for accurately distinguishing pleural TB from other diseases. The profile in HIV patients suggests abnormalities in adaptive and innate immune functions.

### PC-320-16 Relationship between the *Mycobacterium tuberculosis* properties and character of the inflammatory reaction of patients with pulmonary tuberculosis

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**Background:** Purpose was to study the relation of the properties of *Mycobacterium tuberculosis* (MTB) (cytotoxicity, C; viability, V; drug susceptibility, DS) with clinical disease state and levels of the acute phase's reactants (APR) in the blood.

**Design/methods:** We studied DS, V (ratio of colony forming units and time of MTB growth on Löwenstein-Jensen medium), C (induction of macrophages death, TNP-1 cell line) of MTB strains, levels of the APR (ceruloplasmin, haptoglobin, C-reactive protein, orosomucoid, albumin, neopterin, elastase,  $\alpha$ 1-protease inhibitor, adenoaminase activities) in the blood, bactericidal activity of circulating phagocytes (NBT test), time of abacillation and closure of cavity of 46 patients with infiltrative pulmonary tuberculosis.

**Results:** 1 group—patients with low level of C (45.7%), patients of 2 group excreted MTB with high level C. We didn't detect correlation between C and DS. We found out low level of correlation between C and V ( $r = 0.38$ ;  $P = 0.013$ ). 1 and 2 groups had not distinctions in mean values, frequency of pathological indices of APR and in NBT-test. In case of expressed C high level of response of phagocytes induced by zymozan was met in 2 times more often. To 87.5% patients a favorable clinical course (abacillation, closure of cavity) was coupled with low C,V and normal indices of APR. 77.0% of patients with adverse clinical course had combination of the high C,V and pathologic indices of APR. For rest of patients clinical course did not depend on MTB properties, but one depended upon initial APR level.

**Conclusion and recommendations:** According to results of multivariate analysis of the whole complex of the MTB properties, characteristics of inflammatory reaction intensity and clinical disease state, the outcome of the relation of pathogen-host is determined by adequacy of defensive reaction of the patient.

### MPOWER AND TOBACCO CONTROL POLICIES—1

#### PC-348-16 Levels of suspended particulate matter (PM<sub>2.5</sub>) as a marker of exposure to secondhand smoke in workplaces and hospitality settings in Egypt

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**Background:** Despite the existence of comprehensive smoke-free laws in Egypt since 2007, national data have revealed high levels of exposure to secondhand smoke (SHS) in hospitality settings and workplaces. Exposure to SHS has been associated with an increased risk of morbidity and mortality from variety illnesses, including lung cancer and CVD. We aimed to measure PM<sub>2.5</sub> levels as a marker of exposure to SHS in a sample of public and hospitality places (characterized by waterpipe smoking). Up to our knowledge, no previous published research in Egypt has assessed and compared PM<sub>2.5</sub> levels in hospitality settings and workplaces where cigarettes and waterpipe smoking are used.

**Intervention:** A convenience sample of 25 hospitality settings and 5 workplaces were selected in Cairo, Egypt, and PM<sub>2.5</sub> concentration levels were assessed using 'A TSI SidePak AM510 Personal Aerosol Monitor' for a minimum of 60 minutes at each selected venue. A mosque in which smoking was prohibited was taken as a baseline for PM<sub>2.5</sub> levels. The active cigarette and waterpipe smoker densities (ASD<sub>cig</sub> and ASD<sub>wp</sub> respectively) were calculated for each venue by dividing the mean number of cigarette or waterpipe smokers by venue volume (100 m<sup>3</sup>).

**Results:** The mean PM<sub>2.5</sub> concentration was 386.3  $\mu\text{g}/\text{m}^3$  and ranged from 41 to 1723  $\mu\text{g}/\text{m}^3$ . The highest levels were observed in cafes and governmental places (612.6  $\mu\text{g}/\text{m}^3$  and 478.4  $\mu\text{g}/\text{m}^3$ ). A significantly lower level was detected in the mosque (81  $\mu\text{g}/\text{m}^3$ ,  $P < 0.000$ ). The levels of PM<sub>2.5</sub> significantly correlated with ASD<sub>cig</sub> and ASD<sub>wp</sub>; with much stronger correlation observed with waterpipe smoking (Spearman's rho 0.33 for cigarettes and 0.54 for waterpipe,  $P = 0.000$ ).

**Conclusion:** Exposure to SHS remains a problem in many indoor public places, particularly in the hospitality industry. Visitors to these venues are exposed to much higher levels of PM<sub>2.5</sub>, which urges immediate and rigorous enforcement actions by the government to protect the health of its citizens.

### PC-349-16 Health care workers' exposure to tobacco smoke in Egypt: findings of the respiratory health survey

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**Background:** Exposure to secondhand smoke (SHS) has been associated with an increased risk of respiratory symptoms, upper and lower respiratory tract diseases and an increased risk of asthma, COPD and lung cancer. In Egypt, though comprehensive smoke-free laws exist, they are poorly enforced exposing workers to the detrimental health hazards of SHS. The purpose of this study was to assess exposure to SHS at hospitals in Port-said governorate in Egypt and to identify any association between respiratory and sensory irritation symptoms and SHS exposure.

**Intervention:** A cross sectional face to face survey was conducted with a standardized questionnaire of 415 adult hospital workers; representing 50% of all employees (81% response rate); recruited from 4 randomly selected general hospitals in Port-said governorate in Egypt.

**Results:** The mean age ( $38 \pm 11$  yrs), more than half of the respondents were females (64%). The majority were administrative employees and nearly one fifth was physicians (33% and 19% respectively). Smoking behavior was significantly associated with male gender (24% vs. 0.4%,  $P = 0.000$  for cigarette smoking, 8.2% vs. 0.4%,  $P = 0.000$  for waterpipe smoking). All respondents reported exposure to SHS at work and 58% ( $N = 242$ ) graded their exposure as being very frequent or frequent. The mean duration of exposure to SHS at work was 1.5 ( $\pm 2.6$ ) hours. After controlling for potential confounders, exposure to SHS at work was significantly associated with an increased risk of wheezes (OR 1.14), shortness of breath (OR 1.17), phlegm (OR 1.23), running and irritated nose (OR 1.14) and sore scratchy throat (OR 1.23).

**Conclusions:** These findings provide compelling evidence that workplace exposure to SHS is extensive in hospitals in Port-said governorate and that workers in health care settings are adversely affected by exposure to SHS at work. This underlines the importance of rigorous enforcement of smoke-free policies to protect the workers' health in Egypt.

### PC-350-16 Smoking prevention in Bangladesh: smoke-free homes

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**Background:** In Bangladesh, secondhand smoke (SHS) is recognised as a major public health problem and is a principal source of indoor air pollution. Despite this, there is a dearth of relevant data on smoking-related knowledge, behaviours and practices at home. We report the findings of the baseline survey, which was carried out as part of a cluster randomized control trial.

**Design/methods:** A total of 722 households were surveyed using semi-structured questionnaire. In addition, we used qualitative methods to examine the characteristics and attitudes of smokers, and on smoking practices inside home and exposure of children to SHS at home.

**Results:** Majority (55%) of the households surveyed had at least one smoker. It was common among the smokers in the study areas to smoke anywhere inside the house; only a fifth of the smokers smoked outside the house. Thirty percent of the households having at least one smoker smoked in front of children and 39% of the children were exposed to secondhand smoking. Moreover, there remained inadequate knowledge and misconception about SHS among respondents in the study areas.

**Conclusion and recommendations:** Exposure of children to SHS at home is significant posing a grave public health problem. In the absence of any desire to legislate against smoking in private places, an education intervention such as 'Smoke Free Homes' can be timely. However, a shift towards voluntary smoking restrictions at home would require behaviour change amongst smokers and other family members. It may be feasible to empower children to act as 'change agents', if appropriate training and support is provided.

### PC-351-16 Exposure of young people in rural Nigeria to secondhand smoke

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**Background:** Epidemiological data shows that non-smokers exposed to secondhand smoke are at risk of many of the health problems associated with direct smoking. Exposure to secondhand smoke (SHS) is significantly associated with low birth weight, tuberculosis infection in children and young people. Adults who are continuously exposed to SHS are at increased risk of developing lung diseases. There is an international consensus to reduce death by from respiratory diseases by 2015 (MDGs: Indicators 13, 14 & 23). Almost half the world's children are forced to breathe air polluted by tobacco. This study aims to contribute to the existing body of knowledge as there is scanty data on the exposure of young people to SHS in rural Nigeria.

**Method:** Cross-sectional study involving 72 (30 male,

42 female) respondents aged 13–19 years old, randomly selected and interviewed using a modified Global Youth Tobacco Survey (GYTS, 2007) questionnaire. Study location was Akpabu, a rural community in Rivers State, Nigeria.

**Results:** 51% (37) of the respondents were exposed to SHS daily. 45% (17) of this 37 are female and are exposed to SHS while indoors from cigarette smoking by their neighbors and siblings. Boys were exposed to SHS daily mostly from their friends as most (66%) of them admitted having a close friend who is an active smoker. In fact, 32% of the respondents have a close friend who is a regular cigarette smoker. Surprisingly, only 7% had parents who were regular smokers. The perceived risk of SHS was low. On all the days of the week, 25% was exposed to at least five minutes of SHS from basic goods stores within the community.

**Conclusion:** A great proportion of young people in rural Nigeria are constantly and ignorantly exposed to secondhand smoke daily. A comprehensive enlightenment campaign which incorporates best practices coupled with legislation is imperative to improve health, motivate smokers to quit and reduce exposure to secondhand smoke.

#### PC-352-16 Smoke-free Budgam

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**Background and/or objectives:** Budgam: central part of State Jammu and Kashmir population 7.35 lacs and is spread over 1371 sq. km of area. Smoking prevalence was high despite COTPA-2003 enactment. Thereafter, Voluntary Health Association of India (VHA) in collaboration with JKVHA (local NGO) and technical support from The Union–South East Asia carried strong advocacy and effective enforcement by Govt. of J&K; District Budgam earned the smoke-free status on 26th January, 2012.

##### Objectives:

- 1 To analyze process of making Budgam smoke free
- 2 To assess compliance level of smoke-free law in the public places

**Methods/description:** The process for making Budgam smoke free was assessed by the researchers by reviewing official documents of District Statistical & Evaluation Unit (Govt), observing compliance of smoke-free law.

**Results/outcomes:** The technical support, capacity building of international standard and compliance study by VHA and Union–South East Asia & strong advocacy movement through political consensus and technical trainings to law enforcers by JKVHA generated massive awareness among the general public and policy makers. The District Administration of

Budgam (Govt. of J&K) showed a strong commitment. District monitoring committees were notified, 8 Block level enforcement squads were formed with proper monitoring and reporting systems (monthly basis) at place hence Challenging process was made easy.

**Conclusions/lessons learnt:** Meeting the smoke-free criteria is just the beginning of institutionalization of a successful model of tobacco control in a particular jurisdiction. Increasing the level of compliance, sustaining the effort in long run and replicating the model in different settings are the guiding principles of smoke-free drive. The smoke-free initiatives can be made easy with commitment from different sections such as government, private agencies, civil society, police and media.

#### PC-353-16 Compliance monitoring survey of smoke-free law in a district of North India

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**Background:** Compliance survey of smoke-free law is an effective means of measuring progress towards a smoke-free society. They also aid policy makers to take action where breaches take place.

**Aims and objectives:** To ascertain the level of compliance with smoke-free law in a range of public places settings in a district of northern state of India.

**Methodology:** This cross-sectional study was conducted in month of December, 2011. A total 171 public places of district Mohali in State of Punjab, India including educational institutions, offices, health institutes, transit sites and hotels/restaurants were surveyed. The study tool was adapted from the guide on 'Assessing Compliance with Smoke-Free Law'.

**Results:** In 95.2% public places no active smoking was observed. 91.8% of places have displayed 'No-smoking' signage. Health and educational institutions had maximum compliance with the smoke-free law. More smoking activity was observed in rural area as compared to urban area. No designated smoking room and fire alarms were found in any public places in all the three areas.

**Conclusion:** There was high level of compliance of the smoke-free law. The government aim of protecting public from exposure to secondhand tobacco smoke at places is well in line.

### PC-354-16 The principles of primary health care are the key for tobacco control programmes and tobacco control legislation: a way forward

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**Background:** In response to the 39th World Health assembly resolution GOI enacted an Act under National Tobacco Control Programme to protect its citizens from the ill effects of tobacco known as COTPA 2003. Strict enforcement came from 2nd October 2008. Every country and state has its own law for the safety and security of its people. Most of them are specific to a particular department alone. Tobacco control law essentially needs the application of the core principles of primary health care for its success. This paper shares the experiences of application of the PHC principles in COTPA 2003 enforcement in Tamil Nadu, India.

#### Methodology:

*Intersectoral coordination:* Tobacco control cell was formed at Directorate of Public Health which brought all the government departments and NGOs under one umbrella of NTCP. To enforce COTPA 2003 three member flying squads from health, police and education departments were constituted. By effective intersectoral coordination the achievements are smoke-free educational institutions, police stations, postoffices, govt. offices, industries, transport vehicles, villages and districts. 18 000 smokers were fined.

*Community participation:* Traders banned selling tobacco products within 100 meter radius of educational institutions. Cancer Institute Adayar and more than 100 dentists started Cessation Clinic. AIRTEL. BSNL sent warning SMS. Panchayats have passed resolutions as tobacco-free villages.

*Appropriate technology:* Interpersonal communication, media campaign and air nicotine monitoring are appropriate scientific tools used.

**Results:** 90% educational institutions, all police stations, jails. Post offices, transport vehicles, public buildings declared smoke free. Rs2 million collected as fine.

**Conclusion and recommendation:** The core principles of primary health care intersectoral coordination, community participation and appropriate technology are the keys for the successes of the NTCP and implementation of tobacco control legislation in Tamil Nadu, India.

### PC-355-16 Egyptians in public places are exposed to dangerous levels of PM2.5 air pollution: urgent need for rigorous enforcement of smoke-free laws

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**Background:** Lung cancer and cardiovascular disease mortality risks increase with smoking, second-hand smoke (SHS), and exposure to fine particulate matter <2.5 µm in diameter (PM2.5) from ambient air pollution. Recent evidence confirms that only 100% smoke-free environments offer protection from increased risks of morbidity and mortality attributed to exposure to SHS; a major source of these air pollutants. We aimed to evaluate the baseline levels of PM2.5 air pollutants in a wide variety of public and workplaces prior to effective enforcement of smoke-free laws.

**Methods:** Air quality was measured in 43 randomly selected public and workplaces in Port-Said and Luxor Governorates in Egypt (19 health care facilities, 9 governmental offices, 4 schools, 9 restaurants and 2 methods of public transportation).

**Results:** The mean PM2.5 levels (microgram/cubic meter) were  $76.5 \pm 309$  and  $23.3 \pm 29.6$  in Port-Said and Luxor governorates respectively. In Port-Said City, the levels were lowest in schools ( $15.9 \pm 6.9$ ). Levels were  $18.4 \pm 8 \mu\text{g}/\text{m}^3$  in governmental offices,  $23.5 \pm 4.5 \mu\text{g}/\text{m}^3$  in health care facilities and were highest in restaurants  $374 \pm 712 \mu\text{g}/\text{m}^3$  ( $P = 0.000$ ). A similar pattern was observed in Luxor but with much lower levels of PM2.5 recorded in restaurants ( $32.9 \pm 53.7$ ,  $P = 0.000$ ). Smokers were observed in 5 out of 23 places in Luxor and 12 out of the 20 places in Port-Said. In Port-Said the mean levels of PM2.5 increased in a dose-response fashion with the increasing number of smokers observed in the place ( $P = 0.000$ ).

**Conclusions:** The levels of PM2.5 as well as smoking levels were higher in Port-Said governorate. The levels were highest in restaurants and cafes reaching to dangerous levels nearly 6 times higher than the threshold for air quality set by the US Environmental Protection Agency. This urges immediate and rigorous efforts by the Government of Egypt to protect the health of the workers and citizens exposed SHS particularly in hospitality venues.

### PC-356-16 Making educational institutions tobacco free: Tamil Nadu experience

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**Background:** India enacted tobacco control legislation in 2003, ratified the WHO FCTC in 2005 and issued guidelines to create Tobacco Free Educational Institutions (TFEI) based on section 6 of this act which bans sale of tobacco products around educational institutions and sale to and by minors.

**Objective:** To create TFEI in Chennai, India.

**Methods:** 2118 educational institutions including schools, colleges and professional institutions in Chennai City were identified and heads of these institutions were invited to participate in an orientation programme to implement TFEI. 1357 (64%) institutions responded to the invitation and orientation was conducted in 9 batches progressively. Participants were oriented on the importance of tobacco control and introduced to the TFEI guidelines. Institutions were urged to implement the TFEI guidelines through an administrative communication from the respective educational authority. Compliance to TFEI guidelines was conducted using four methodologies at different intervals, interview with heads of institutions (at 3 months), administrative communication from their respective educational authority (at 6 months), on-site survey by designated field investigators (at 1 year) and through questions addressed to heads of institutions through the Right to Information (RTI) act (at 1 year).

**Results:**

Follow-up method	Tobacco sale		Tobacco use		Signage board display <i>n</i> (%)	Sale around 100 meters <i>n</i> (%)
	Institutions covered <i>n</i>	inside the campus %	inside the campus <i>n</i> (%)	inside the campus <i>n</i> (%)		
Personal interview with principals (after 3 months)	80	0	0	32 (40)	52 (65)	
Survey (after 1 year)	316	0	85 (27.2)	66 (21.8)	230 (72.8)	
Communication at 6 months	73	2.7	—	63 (83)	10 (13.6)	
RTI response (after 1 year)	189	0	—	184 (97.3)	183 (96.8)	

Despite repeated reminders implementation of TFEI by educational institutions in Chennai City was only moderate. Most of the institutions did not prioritize tobacco control. Many 'women only' institutions stated that TFEI implementation was not applicable to them. Greater efforts are required to increase awareness of the harms of tobacco use and the legal provisions requiring educational institutions to be tobacco free, to remind educational institutions of their responsibility to protect children from easy access to tobacco and to empower educational institutions to implement and monitor TFEI systematically.

**PC-357-16 Community mobilisation in smoke-free policy implementation in Bangladesh**

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**Background and challenges to implementation:** Bangladesh ratified FCTC in 2004 and enacted tobacco control (TC) law 2005. Since then ministries and NGOs have been working together to implement and enforcement of TC law. Alliance for Cooperation and Legal Aid Bangladesh (ACLAB) an NGO has been collaborating with district and sub-district taskforces (coordinating body) for TC law enforcement with particular focus on smoke-free policies since 2009 in 74 out of 460 sub-districts in 11 districts in Bangladesh with the guidance of The Union. One of the objectives of this intervention is to make public places and public transports smoke free in the project areas.

**Intervention or response:** TC law implementation was intensified in Bangladesh since 2007 with the support of Bloomberg Initiative to Reduce Tobacco Use. Representatives from different stakeholders; authorities and owners of public places and public transports; and members of transport owners' and workers' associations were oriented on TC law and its implementation with particular focus on harmfulness of smoking and secondhand smoking. Encouraged them to make their workplaces and transports smoke free to keep environment healthy and protect people's health.

**Results and lessons learnt:** During October 2009 to March 2012, a total of 3401 authorities and owners of public places and public transports; 1400 members of transport owners' and workers' associations and 540 representatives of different stakeholders were oriented on TC law and implementation of smoke-free policies. About 7900 'No smoking' signage have been installed in public places and transports. As a result, a total of 3000 public places and 2700 public transports including water transports in project areas were made smoke free during this period.

**Conclusions and key recommendations:** Local level initiative and peoples participation are crucial in implementing smoke-free policies in Bangladesh.

**PC-358-16 Role of NGOs in facilitating tobacco control law enforcement in Bangladesh**

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**Background and challenges to implementation:** Bangladesh ratified FCTC in 2004 and enacted tobacco control (TC) law 2005. Since then Ministries and NGOs have been working together to implement and enforcement of TC law. One of the important elements of TC law is functioning of taskforces

(coordinating body) at different levels. Alliance for Cooperation and Legal Aid Bangladesh (ACLAB), an NGO has been collaborating with district and sub-district taskforces for TC law enforcement since 2009 in 74 out of 460 sub-districts in 11 districts in Bangladesh with the guidance of The Union. Objective of this intervention is to mobilize taskforces for implementing and enforcing tobacco control law.

**Intervention or response:** TC law implementation was intensified in Bangladesh since 2007 with the support of Bloomberg Initiative to Reduce Tobacco Use. ACLAB oriented taskforce members, civil society representatives and journalists on TC law. Taskforces were made functional and provided support for periodic meetings. Assisted taskforces to conduct mobile courts where law violations were found. Journalists reported violations of TC law and actions taken against the violations in the local and national level media.

**Results and lessons learnt:** Between October 2009 and March 2012, a total 675 taskforce members, civil society representatives and journalists were oriented on TC law. Total 275 taskforce meetings were organized by district and sub-district taskforces to review the progress of law enforcement and monitor the violations. These taskforces conducted 193 mobile courts in different strategic public places and public transports for strengthening the law enforcement.

**Conclusions and key recommendations:** Mobile court by taskforce is essential for strengthening TC law implementation. For effective use of taskforces, partnership between government and NGOs working for tobacco control is essential. Amendment of the TC law to address identified weaknesses to comply with FCTC is prerequisite to control tobacco in Bangladesh.

#### PC-359-16 Policy and legal advocacy for a ban on Gutka

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**Background and challenges to implementation:** Usage of smokeless tobacco has reached endemic proportion in India and it has made India 'oral cancer capital' with 90% cases in country. Yet, it is the most cheap and easily available tobacco product. Governments too shy away from imposing a higher tax burden on smokeless form, compared to smoking forms. There's a lacunae in India's tobacco control law to deal with smokeless forms.

**Intervention or response:** Health for Millions Trust filed an application before the Supreme Court to strengthen an on-going litigation (*Ankur Gutka and Others vs. Indian Asthma Care Society and Others*) where the challenge initially was on environmental grounds. Relying on reports submitted by Health

Ministry, it gave a ground to us to ask for a ban on gutka on health grounds. Subsequently in August 2011, Food Safety and Standards Authority of India, mandated prohibition and restriction on sale of food items, which have tobacco and nicotine as its ingredients. The Trust moved Court seeking its implementation as it will lead to a ban on gutka, which by way of an earlier Supreme Court ruling has been defined as a food product.

**Results and lessons learnt:** Madhya Pradesh became first State in India to ban manufacture/sale of gutka or any such product containing tobacco or nicotine with effect from April 1, 2012, under the same Notification—Food Security and Standard (Sales Ban and Restriction) Regulation, 2011. We realized that for a comprehensive ban, there has to be a commitment from the highest level of political leadership at the Union and State-level.

**Conclusions and recommendations:** The government must completely prohibit manufacture and sale across the country. It must not succumb to gutka lobby's tactics and pressures.

#### PC-360-16 Mouth freshener/pan masala: a proxy product for surrogate advertisements of tobacco products in India?

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**Background:** Article 13 of FCTC and section 5 of Indian anti-tobacco legislation (COTPA-2003) prohibits advertisement of tobacco products. Following this, tobacco industry is carrying out aggressive advertisement of the non-tobacco products (mouth freshener/pan masala) having same brand name and packaging design to tobacco products (*gutkha*). The present study is carried out to assess whether advertisements in Indian print media were for the intended products or serve as a surrogate for tobacco products.

**Design/methods:** Three most read Indian vernacular newspapers in Himachal Pradesh were observed from 1st January to 31st March 2012. Simultaneously, a cross sectional survey using pre-tested checklist was also done across 720 tobacco vending shops in 12 district headquarters.

**Results:** 27 coloured advertisements of seven brands of pan masala/mouth freshener were seen. Survey across tobacco vending shops revealed that on an average, there were 1.3 brands of pan masala/mouth freshener and 6 brands of *gutkha*. The advertised brand of pan masala/mouth freshener were not available for sale in any of tobacco vending shop whereas *Gutkha*, the tobacco containing product of same brand name and package design, was being sold in 446 shops.

**Conclusions and recommendations:** The pan masala/mouth fresheners advertisements serve surrogate for tobacco products through the print media in India. There is an immediate need for enforcement of complete ban on such advertisements.

### PC-361-16 Networking to monitor tobacco control law violation by tobacco company

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**Background and challenges to implementation:** Tobacco control law passed in 2005 to following some provisions of WHO Framework Convention on Tobacco Control (FCTC), which Bangladesh was first signatory in 2003 and ratified it in 2004. The law banned all kind of direct advertisement of tobacco products; including electronic media (TV channels, film, drama etc), newspaper ads, billboards, signboards, poster and leaflets. But Tobacco Company is violating the law. As the weakness of law, implementation failed on this ground. It is challenge for tobacco control activists to implement successfully this provision of law. Tobacco company print colorful poster, leaflet and display it in various shops. Also display colorful and big size cigarette packets. Organize events to promote smoking and provide gifts to the smokers. Tobacco company display various colorful ads in fast-food shops, restaurants, cyber café, where youth are target audience for the tobacco ads. **Intervention or response:** So, WBB Trust, the secretariat of Bangladesh Anti Tobacco Alliance (BATA) develops guideline for network associates how to monitor the tobacco control law violation. The network associates documented the law violation by Tobacco Company and collect all illegal ads. About 200 organizations (NGOs, CSOs, and Clubs) monitored this and send this entire document to us. They also sent this law violation information to the local administration.

**Results and lessons learnt:** As a result, local administration takes initiatives to remove these illegal ads. Local administration also runs mobile courts to remove illegal ads and give punishment to shop owner those who display the illegal ads. Also it's made strong recommendation to increase punishment of Tobacco Company for violation of existing law on the amendment of law, which is ongoing process.

**Conclusions and key recommendations:** Law monitoring is one of strong tools to implement it successfully.

### PC-362-16 Countering the tobacco industry interference/tactics in implementation of pictorial health warnings on all tobacco packs through media interventions

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**Background: Why pack 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.

### Tobacco industry tactics to derail the implementation of pictorial warnings

- 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
- Coercing the govt by announcing a closure of production and harping on loss of revenue incurred/day to exchequer

**Objectives:** To ensure implementation of stronger pictorial health warnings on all tobacco packs w.e.f the prescribed date of implementation.

### Methodology, time line

#### Media strategies used to counter tobacco industry

- Releasing 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
- Using Right to Information Act to expose govt-industry nexus
- Period: Year 2009 to 2012

#### Outcomes/achievements

- 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 and state level media. About 20 press meets held on pack warning at national level and 15 states of India continuous pressure on govt
- RTI responses proved crucial evidences

### PC-363-16 The necessity of continuous public actions to maintain behaviour changes in health: an analysis of the implementation of the Recife tobacco control policy's implementation

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**Background:** Smoking is considered by the World Health Organization (WHO), the biggest single cause of avoidable death. It is addictive and needs integrative, decentralized and continuous health education

actions to improve results. The Tobacco Control Policy of Recife was implanted in 2001 and until 2008 had developed a Tobacco Control Comprehensive Policy focused in the objectives of the Framework Convention on Tobacco Control (FCTC), directed to a healthy city creation. Were used health education, inter and intrasectorial partnerships, social participation, spread of the Basic Smoke Cessation Approach, Smoke Cessation Centers and Smoke-Free Environments (SFE).

**Objective:** To analyze the evolution of a tobacco control policy in a city of Brazil.

**Methodology:** Participant-research and bibliographical revision.

**Results:** 100% of the municipal public offices, day-care centers, health units, leisure and hospitality establishments, shopping centers, among others, in a total of 7.873 as SFE, benefiting more than 1 000 000 people/month; more than 5 000 workers qualified for Basic Smokers' Approach, with more than 2600 acting as multipliers in workplaces' Tobacco Control Executive Commissions; qualification of the Municipal Health Council to enhance advocacy; qualification of the Health Surveillance; public events, seminars, ample media repercussion. Smokers' prevalence fell from 18% (2001) for 10.4% (2008), 34.6% in one year (2009). Brazil's 4th smaller and the smallest men's prevalence of the country: 9.2% that year. Recife was chosen to integrate a case study of WHO Kolbe Center Smoke-Free Cities Project representing Brazil. In 2009 the government has changed, all the actions were decreased or had stopped and the rates went to 13.2%, 14% and 12% (2012).

**Conclusions:** The educational actions and health communication interventions have to have sufficient reach, frequency and duration. Only a comprehensive tobacco control policy can manage the smokers' prevalence reduction.

## ADVOCACY AND PUBLIC EDUCATION

### PC-392-16 Impact evaluation of smoke-free mass media campaign on knowledge, attitude and behavior of the target audience in India

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**Background:** Tobacco use in India leads to around 1 million deaths annually. Govt. of India passed the 'comprehensive smoke-free' law in 2008. State Tobacco Control Cell, Government of Gujarat launched a mass media campaign on 'smoke-free' awareness in April–May 2010 through television, radio and bill-

boards in two intervention districts to: raise awareness, build knowledge and create positive attitudes towards the smoke-free policy among public and policymakers, bolster support for enforcement of the smoke-free law, and change behavior of smokers to not smoke in public places and protect people from exposure to secondhand smoke (SHS).

**Evaluation methods and results:** A post-campaign impact evaluation survey was conducted in July–August 2010 in Ahmedabad and Gandhinagar districts. The survey utilized a rigorous household survey methodology with a multi-stage sampling plan. Information about the impact of the campaign was obtained from the eligible male and female respondents in the age bracket of 15–60 years. A total of 3298 respondents were recruited across the two districts with a response rate of over 98 percent.

**Results:** Among the various media channels (television, radio and billboards), reach of television has been the most effective. Seven out of ten persons are exposed to television in a typical week. Majority of respondents who recalled the campaign advertisement said that it provided them new information, was relevant to them, and made them stop and think. Significantly more aware smokers compared to unaware smokers 'discussed smoking and health at home' (OR = 2.0); 'thought about its harm to self' (OR = 2.5); 'thought about its harm to non-smokers' (OR = 2.3); and 'considered seriously quitting' (OR = 4.1) in the last three months, after controlling for confounding factors.

**Conclusions:** The campaign was effective in raising awareness about secondhand smoke and had positive impact on smoker's behavior.

### PC-393-16 Case study: implementation of the ban on surrogate advertisements

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**Background and challenges to implementation:** While direct and surrogate advertisement of all tobacco products has been banned since 2004 in India, the advertisements of various pan masala continue, suggesting their apparent nontobacco nature. In recent times, buses advertised plain pan masala (areca nut with lime) with name similar to tobacco products had been observed in and around Mumbai. Salaam Bombay Foundation (SBF) conducted a study with an objective to understand how the advertisements of pan masala with names similar to tobacco products were understood by the public and to obtain context-relevant evidence to persuade policy makers to implement the tobacco control law.

**Intervention or response:** The study was carried out in Mumbai in May 2011. The sample size was 3000 respondents from across the Mumbai including 1500 children aged 12 to 18 and 1500 adults aged 19 to

50. On the basis of the study results, a demand charter was submitted to the appropriate government authorities for immediate action by the children of SBF's tobacco control school program.

**Results and lessons learnt:** The study revealed that all three brands—Goa 1000, RMD and Rajshree—were highly associated as guthka instead of pan masala by the respondents. SBF kids conducted an advocacy meeting with the Superintendent, Bombay Municipal Corporation (BMC) License and Advertisement Department. As a result, on July 8, 2011, BMC issued an official letter to all the vendors strictly restricting the display of any surrogate advertisements for tobacco products and within a month, all the advertisements of pan masala, promoting corresponding tobacco products, were removed from buses.

**Conclusions and key recommendations:** This case study illustrates the power of studies to provide context-relevant evidence alongside targeted advocacy results in compelling decision-makers to enforce strong tobacco control.

#### **PC-394-16 Using community festivals to strengthen implementation of the ban on surrogate advertising**

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**Background:** Ganpati is a ten day festival celebrated in Maharashtra. An idol of lord Ganesha is put up by different groups across Mumbai City called pandals (a specially created temporary structure). These pandals attract a lot of devotees as well as tobacco product advertisement. Salaam Bombay Foundation (SBF) thus decided to effectively use this popular festival to carry the message of tobacco control to the community at large. In 2008, for the first time, SBF began to conduct tobacco control activities during the Ganpati festival.

**Intervention:** Letter was submitted to all pandals requesting them not to take any form of direct or indirect advertisement from tobacco companies. SBF children then visited and performed in these pandals, thus creating awareness on ill effects of tobacco usage and the law through street plays and songs.

**Results:** The program has been running for three years now. The fight has now been joined by the Municipal Corporation of Mumbai and managing committees of multiple pandals. Starting with 81 pandals in 2008, the program has now been extended to more than 200 pandals with almost 1000 young advocates carrying the tobacco control message across. There has been increase in the number of pandals opting to refuse tobacco surrogate advertisements. In July 2011, the Mumbai Municipal Corporation issued an official circular to ban tobacco surrogate advertising in all the Ganpati pandals and a suspension of their license if they fail to follow the law.

**Conclusions:** Advocacy during festivals provides another opportunity to reach large segments of the population with key tobacco control messages. Subsequently, taking organizers of public events, stakeholders and policy makers into confidence can lead to effective implementation of the COTPA, here the ban on all tobacco direct and indirect advertising.

#### **PC-395-16 Enforcing the law on ban of sale of tobacco products within 100 yards of educational institutions**

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**Background and challenges to implementation:** Mumbai is the most populous city in India (20.5 million). Here most schools are located within the densely populated city and children in these schools are regularly exposed to the tobacco products thereby increasing the likelihood of children buying and consuming tobacco. Despite the law 'ban on sell of tobacco products within 100 yards of any educational institute' (sec 6 for COTPA 2003), large number of vendors sell cigarettes and other tobacco products within the restricted zone outside schools across Mumbai.

**Intervention or response:** An observational study was conducted by SBF in 91 schools with the help of the SBF trained children and reports revealed that 82% of schools have 219 vendors selling tobacco products within 100 yards of the institution. The objective of this project was to first, assess enforcement of section 6 of COTPA that bans the sale of tobacco products in and around 100 yards of school premises, and second, advocate with government authorities for the effective enforcement of the law.

**Results and lessons learnt:** Following these findings, SBF kids did advocacy meeting with Food and Drug Administration, Mumbai Municipal Corporation and Ministers to ensure effective enforcement the law and also launched 'Tobacco Free Educational Institute Campaign'. The youth advocacy efforts persuaded the Municipal Corporation of Mumbai to circulate a rule to all the Education Officers for strict implementation of sec 6 of COTPA and also to monitor the compliance of the law. In addition, FDA also raided those shops who sold tobacco products within 100 yards of school premises.

**Conclusions and key recommendations:** These activities not only support the children to exercise their knowledge and skills in spreading awareness but also support broad civil society advocacy efforts to strengthen the enforcement of India's tobacco control law.

**PC-396-16 A study: smoking is uncool**

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**Background:** In Indian context, peer pressure is often found as one of the major reasons to take up smoking. They avoid raising their voice as they fear giving up their social connections with coworkers. Similarly, a spouse smoking was also acceptable and one had to live with it. Therefore, a survey was conducted by Salaam Bombay Foundation (SBF) with an objective to find out if an individual would raise his/her voice if they found someone smoking around them especially their bosses, hence avoiding exposure to SHS and to assess the attitude of Mumbai youth towards a smoking partner/spouse.

**Intervention:** A survey was done at the Kalaghoda Festival in Mumbai. It is a seven days literary and art festival, which is organized every year in Mumbai and visited by people all around India. 2 questionnaires were developed and were filled through personal interviews. The survey was undertaken for all the seven days of the festival in February 2009. 1358 males and 554 females were interviewed to understand people's attitude to exposure to SHS at workplace and 524 males and 267 females expressed their views on a smoking partner. People between 18 and 45 years were interviewed.

**Result:** The result of the survey revealed that 85% of the respondents were aware of ill effects of SHS but only 43% were willing to raise their voice against their exposure to SHS. 42% were confident enough to ask even their boss or senior to go and smoke elsewhere. In the other survey, 80% of the total respondents said that they do not find a smoker attractive. 67% of the respondents said that they would never date a smoker and 75% said that they would not marry a smoker. 47% of both males and females said that they are not comfortable being around smokers.

**Conclusion:** Focused public awareness campaigns highlighting ill effects of secondhand smoke at home and in public places need to be undertaken.

**PC-397-16 Well-orchestrated mass media campaign makes a big difference!**

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**Background and challenges to implementation:** The Global Adult Tobacco Survey 2009 reveals that 43.3% of people aged 15 years and above in Bangladesh are using tobacco in one or other form. Tobacco-attributable diseases are rampant, malnourished children in smoking household are increasing, health care costs associated with tobacco-related illness are increasing and deforestation is widening.

**Intervention or response:** At the backdrop of the situation, Bangladesh Center for Communication Programs (BCCP) was commissioned by World Lung Foundation to manage first-ever national tobacco control mass media campaign titled 'Sponge' campaign in Bangladesh around the World No Tobacco Day 2011. The campaign disseminated hard-hitting messages on the harmful effect of smoking on television and radio channels; posted 30 000 posters in the strategic locations of all 64 districts in Bangladesh by involving the government and NGOs; arranged press conference to urge the journalists to generate increased coverage on anti-tobacco message; and organized rallies with colorful placards. All happened in a synchronized and sequential manner and continued for a month.

**Results and lessons learnt:** Evaluation survey conducted among 7000 adult tobacco users revealed that 33% of the smokers and 27% of smokeless users reported making a quit attempt during the 'Sponge' campaign, with about a third (32%) reporting they would definitely or very likely quit (GATS reported smokers quit attempt in the past 12 months 47.3%). Seventy percent reported that the message made them concerned about their smoking habit.

**Conclusions and key recommendations:** A multimedia campaign could make a big difference when it is thoughtfully designed and implemented. The campaign has created demand to run the similar campaign in Bangladesh.

**PC-398-16 Evaluation of a low-cost social marketing campaign in the province of Nueva Vizcaya, Philippines**

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**Background:** The study aimed to assess the effectiveness of the 'Cigarettes Are Eating You Alive' campaign, an international campaign adapted to the Philippine setting with the help of the World Lung Foundation. The campaign, which depicts how smoking damages smokers' bodies, was endorsed by the provincial government of Nueva Vizcaya to the local media. The local media responded by giving discounted rates for airing the campaign.

**Design/methods:** A household survey was conducted to assess the public's exposure to the campaign and analyze their attitudes towards tobacco use after campaign exposure.

**Results:** The survey showed that 54% saw the ad on television, while 44% heard the same on radio. Among those who saw or heard the ad 63% discussed it with others while 65% tried to persuade others to quit. Among smokers who saw the ad, 95% agreed that the ad made them concerned about the effect of smoking to their health, 89% became concerned about the effects of smoking to their family's health while 61% of smokers said the ad made them more likely to quit.

**Conclusion and recommendations:** The 'Alive' campaign proved that exposure to a hard-hitting ad can lead to changes in public knowledge and attitudes towards tobacco use. The implementation of the campaign which involved international and local organizations, the local government and local media also showed how different institutions can work together to run a cost-effective and successful campaign.

#### PC-399-16 Who do people know: a study in 14 high-burden low- and middle-income countries regarding people's knowledge of harm caused by smoking

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**Background:** Understanding the harms associated with smoking is an important factor in people's decision to not or quit smoking. It is also a key contributor for effective tobacco control efforts. Knowledge of harm caused by smoking among the population was investigated in 14 high-burden low- and middle-income countries (including Bangladesh, China, Egypt, India, Mexico, Russia, and Viet Nam) where the Global Adult Tobacco Survey (GATS) was conducted from 2008 to 2010.

**Methods:** GATS adopted standard protocol and questionnaires for systematically monitoring tobacco smoking, allowing direct comparison across GATS countries. GATS applied a multi-stage clustered sample design to obtain nationally representative data among adults. A total of 248452 respondents completed the survey, representing 58% of the world population. Respondents were asked whether they believe smoking causes lung cancer, strokes or heart attacks.

**Results:** The percentage of respondents believing smoking causes lung cancer ranged from 77.5% in China to 97.5% in Thailand. The percentage believing smoking causes strokes ranged from 27.2% in China to 82.1% in Turkey. The percentage believing smoking causes heart attacks ranged from 38.7% in China to 95.0% in Egypt. Compared to males, females had similar level of knowledge; however females in

Bangladesh reported less knowledge and females in Russia and Ukraine reported more knowledge.

**Conclusions:** Respondents from the 14 countries consistently reported better knowledge of smoking causing lung cancer than knowledge of smoking causing strokes or heart attacks. People's knowledge about the health hazards of smoking has not improved as much despite the rapid economic development in many countries, as demonstrated by the results from China. It is time for the advocates and policy makers of tobacco control to reconstruct their efforts on the 'warn' element of MPOWER, especially in low- and mid-income countries.

#### PC-400-16 Do clinicals students have better perception towards smoking habits than pre-clinical students?

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**Background:** It is presumed that, as medical students progress through medical student learning timeline, a greater knowledge and perception in all aspects of disease control and prevention would be equipped. Tobacco, being the most preventable cause of premature morbidity and mortality is to no exception. This study objective is to identify the differences in smoking perception among the preclinical and clinical students in a public medical university in Malaysia.

**Design/methods:** We conducted a cross-sectional study in a public medical university in Malaysia. All medical students (year 1 to 2 = preclinical; year 3 to 5 = clinical) were recruited and filled up a questionnaire on socio demographic characteristics and smoking perception.

**Results:** A total of 522 students responded. This comprised of 207 preclinical and 315 clinical respondent. The majority of students had good baseline knowledge on tobacco related effects. However, some notable differences existed. As for example, many clinical students (16.5%) disagreed that quitting cigarette can release stress compared to preclinical students. A greater number of clinical students ( $N = 11$ ), compared to preclinical students ( $N = 0$ ) also thought male smokers were more attractive, although majority disagreed. Preclinical students unanimously (100%) was not planning to smoke in 5 years time, as compared to 2.5% of clinical students who had plans. However, 7.2% preclinical students claimed they will accept free cigarettes from tobacco companies when being offered, compared to clinical student (2.9%). There was no significant differences found between preclinical and clinical students in terms of cigarette exposure, knowledge on the detrimental effects of tobacco on health.

**Conclusion and recommendations:** Medical students, both preclinical and clinical have good understanding

on the ill effects of tobacco but lacking in the area of smoking cessation and its effects. Years in medical school does not affect the perception and consumption.

### PC-401-16 A stitch in time: anti-tobacco youth advocacy strategy in Western Kenya

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**Background and challenges to implementation:** Tobacco usage is the single most preventable cause of cancer and other serious health problems in the society today. By the year 2010, 70% of the deaths were estimated to occur in the developing countries. Kenya like other developing countries is included. Kenya implemented comprehensive tobacco control law in 2007 as regulatory measure to reduce tobacco usage. There exists good infrastructure and opportunities for tobacco control in Kenya both within the government and civil society. However, its impact in the community is yet to be realized due to the perception or inadequate information. For its success the role of media, ICT and community based strategies is vital in delivering health messages and influencing health policy.

**Intervention or response:** Promote public health through community based interventions.

**Methods:** Letters are sent to randomly selected schools, and community youth groups. Several institutions responded positively and talk days are arranged in the form of:

- Video presentations in schools, churches and youth groups
- Radio talks and community sports tournament with a rotating annual 'Smoke-Free' trophy
- Training community leaders on 'Training-of-Trainers' skills

**Results and lessons learnt:** Positive attitude change in youth, community and religious leaders has been observed. In 2009 directly sensitized 2555, in 2010—2185 and in 2011—2028 participants were sensitized in schools and others gatherings. In 2012 the program demand is overwhelming.

**Conclusions and key recommendations:** Youth and community based programs is a very effective way of implementing the tobacco control, cost effective and culturally acceptable. However challenges of the potential and impact of ICT exist.

### PC-402-16 Communication in tobacco control: the health care provider's perspective

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**Introduction:** The role of communication within comprehensive tobacco control programmes is recognized at a number of levels. National Tobacco Control Program accords priority to communication. However, limited primary data on the felt needs of health care providers (HCPs) regarding tobacco control communication is available in Indian context.

**Methods:** A two phase sequential technique using formative research and quantitative research was conducted. Semi-structured questionnaire was administered to capture perception of HCPs on tobacco control communication in the state of Gujarat and Andhra Pradesh.

**Results:** Health care providers are exposed both to the messages related to tobacco promotion (53%) and harmful health effects of tobacco. However, majority of HCPs encountered information related only to the harmful health effects (59%) followed by legislation (32%). About two-third of HCPs regarded audio-visual methods as the best method for educating patients. Only a minority (32%) felt that inter-personal communication were also required in tobacco control. Although 70% HCPs mentioned that raising awareness is sufficient to control tobacco usage yet a few expressed the need of a comprehensive communication package.

**Conclusions and recommendations:** Majority of health care providers noticed information on tobacco control however, messages were limited only to the health effects of tobacco. Inter-personal communication which is the back bone for tobacco control did not seem to be the preferred choice of HCPs. Behavior change and communication program with an emphasis on inter personal communication should be targeted towards HCPs for enhancing their skills and awareness on tobacco control.

### PC-403-16 Influence of health education on tobacco control

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**Background and challenges to implementation:** Bangladesh is overburdened with tobacco-related illnesses. Current tobacco use among all adults is 43.3%. Among them 97.4% of adults believe that smoking causes serious illnesses. Anthropologically village is the functional unit of lifestyle and social constitution in Bangladesh.

**Objective:** To execute the effect of health education program on tobacco control.

**Intervention or response:** A study was conducted in January–March 2012 in selected villages of Comilla District to explore consciousness and behavioral change to control tobacco use. The view of villagers on the use of tobacco was collected using a questionnaire to take a personal interview. The survey was

conducted in the Pushkanirpar village on 30 families. The participants' included both male and female of ages 30–50 years. We conducted baseline and end line survey. After conducting the baseline survey, we gave an intervention to control tobacco use by health education program and then conducted the end line survey. Yard meeting started on January 2012. More than ten yard meeting was organized in the village. In these meeting presence of participants were 30. During meeting IEC materials were distributed among the participants and doing advocacy about healthy lifestyle. Different posters and flip charts were used during intervention. After two months, end line survey was conducted in the same village on same families to assess the post interventional situation of the village.

**Results and lessons learnt:** By the pattern of use of smoking tobacco 90% regular, 10% occasional in baseline and 73.3.% regular, 16.7% occasional, 10% past in end line. By the pattern of use of smokeless 86.7% regular, 6.7% occasional, 6.7% past in baseline and regular 70.0%, 13.3% occasional, 16.7% past in end line.

**Conclusions and key recommendations:** Health education has a great role to control tobacco consumption.

#### **PC-404-16 Coordinated campaign and advocacy effort against tobacco cultivation: an example from Bangladesh**

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**Background and challenges to implementation:** Tobacco cultivation is not only major public health concern, it is also an important issue perspective from deforestation and environment, soil fertility and agriculture, nutrition and food security, air and water pollution. Tobacco cultivation cause to continue economic crisis for poor farmers and also create mental pressure to them, its very hard labor oriented work. Farmers were treated as labor by the tobacco company. Involving tobacco cultivation means farmer's health costs increase, as well as government health costs. Tobacco Company is desperately increasing tobacco cultivations in Bangladesh using propaganda that, poor farmers would be reach; when Tobacco Company avoids the truth of tobacco cultivations. Although tobaccos control movement focused the consumption issues and cultivation not focused strongly.

**Intervention or response:** Last 5 years in Bangladesh, anti-tobacco organizations have run social movement against tobacco cultivations. Demonstration and advocacy meetings were organized with different government departments, ministries, banks to take action to reduce tobacco cultivations.

**Results and lessons learnt:** Though the tobacco culti-

vations are not reduced, but policy makers are sensitized about bad impact of tobacco cultivations. As a result, some of good initiatives made by different government bodies.

- BCIC (Bangladesh Chemical Industries Corporation) under the Ministry of Industries stopped to provide free fertilizer and chemicals to Tobacco Company, which they were disseminated to farmers for tobacco cultivations.
- Bangladesh Bank (controlling Bank of Banking sector) made an order to all Banks to stopped loan to Tobacco Company or any of tobacco related purposes.

**Conclusions and key recommendations:** Campaign and advocacy, combined effort to reduce tobacco cultivation would be successful.

#### **PC-405-16 Media advocacy for implementation of stronger pictorial health warnings on all tobacco packs**

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**Background:** Even though tobacco is a preventable cause of the death among adults in India, one way of creating more awareness and information on the extreme health hazards of tobacco consumption is to place more information on tobacco products in the form of pictorial warnings. Strong pictorial warnings were mandated by the Indian government and as ratified under the FCTC.

**Objectives:** To ensure implementation of stronger pictorial health warnings on all tobacco packs w.e.f the prescribed date of implementation.

- To sensitise the media about the importance of implementing stronger pictorial warnings and showcasing other countries best practices in this regard to act as a motivator to the policy and decision makers.

#### **Methodology, time line:**

- Media interactions (both on a one to one basis and through press meets and media sensitization workshops)
- Exclusive stories to leading national dailies/TV channels
- Period: year 2009 to 2011

#### **Outcomes/achievements:**

- Pro-active media advocacy resulted in nearly 650 stories on pictorial health warnings from the national and state level
- Extensive media coverage pan India (spanning national, regional and local media). About 23–30 press releases were shared with the national and state level media. About 20 press meets held on pack warning at national level and 15 states of India
- Exclusive stories by the leading English news channel of India that exposed the alleged government–tobacco nexus.

**Challenges faced:**

- Shifting priorities of media houses which receive huge amounts of revenue through tobacco company advertisements
- New and innovative industry strategies—traditional methods of direct advertising, brand stretching, internet marketing through social networking sites, music, fashion, sports events, sms marketing

**Way forward:**

- Continuous advocacy with media—new evidences and story angles to be presented
- Huge potential of regional media waiting to be tapped

**PC-406-16 Using the right to information act as a tool for pro-active advocacy on tobacco control**

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**Context and background:** Right to Information is part of the fundamental rights under Article 19(1) of the Constitution of India. Under the RTI Act, Indian citizens can access information under the control of public authorities, question the government, take copies of government documents and also monitor government functioning. In the area of tobacco control, Right to Information can be used by the public health fraternity to track policy decisions related to the implementation of smoke-free rules and pack warnings and tax-related information.

**Methodology and time line:** Applications containing specific and carefully worded questions seeking information in the prescribed format are filed with the concerned Public Information Officers of Government Departments to seek information. The department is obliged to get back with a response within 30 days. VHAI have been using this medium to seek information on important policy related decisions.

**Period:** Years 2009–2012.

**Target audience:** Policymakers, public health experts, civil society, general public and media.

**Specific outcomes/achievements:** The RTI initiative has helped civil society to effectively strategize and mount a stringent campaign on tobacco control across the country, sensitize the media and seek general public support for compliance, implementation and enforcement of the smoke-free laws.

- No. of RTIs Filed: 790 RTI's were filed from national and state level
- Media stories through right to information act: exclusive stories in the leading print/TV channels of India that exposed the government–tobacco nexus. A total of 80–90 stories generated as an outcome of the RTI
- Advocacy with policymakers on tax: RTIs were filed to get information on taxation on revenue

generated in different states from cigarettes, bidis and smokeless tobacco

- Smoke-free law compliance RTIs were filed to assess the implementation status of smoke-free rules created pressure on the government for various policy decisions especially the Smoke-Free Law in India.

**PC-407-16 Expenditure on tobacco product: using economy for advocacy**

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**Background:** Tobacco use is associated direct loss of resources for purchasing the product. In India, average monthly expenditure of the current smoker on cigarette is 399 INR and on bidi is 93 INR. Spending on tobacco products in low income households constitute 11% of their home expenditure which crowds out expenditures on education, clothing and food. Apart from health concerns saving money have been cited as a motivator to convince people not to smoke. This study quantified the savings owing to abstinence from tobacco use for advocacy purpose.

**Methods:** Using economic principles, the monthly expenditure on tobacco was modeled as savings. Formula  $FV = IV * (1 + RI/100 * n)^{nt}$  {FV = Final Value, IV = Initial Value, RI = Rate of Interest, t = No of year, n = Number of times compounded in a year} was used to estimate the wealth generated from tobacco savings. The recent tobacco inflation rate of 4% and RI of 8.5% have been fixed for calculation purpose. The result of the economic model was compared with most trusted and high yielding public savings schemes in India.

**Results:** The wealth that could be generated from 300 rupees monthly savings on tobacco products at 5, 10 and 15 years time are rupees 31 594; 79 879 and 160 291 respectively. The equal monthly savings in provident fund would yield 28 813; 67 206 and 125 672 rupees at 5, 10 and 15 years respectively. The popular profitable life insurance scheme also would yield 14 178; 63 872 and 133 319 at similar time period with insurance coverage.

**Conclusion:** Abstinence pays as the monetary value of savings on tobacco products is higher than other popular profitable investments in India. Health benefits serve as bonus. The money thus saved can be channelized for education of child, eating nutritious food and other important household expenses. The public advocacy message should include money saved on expenses of tobacco which can appeal the community.

## EPIDEMIOLOGY: TUBERCULOSIS IN HIGH- AND LOW-BURDEN COUNTRIES – 2

### PC-439-16 Time to adjust national tuberculosis guidelines in Belarus: insights from a nationwide drug resistance survey

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**Background:** Alarming levels of multidrug-resistant tuberculosis (MDR-TB) were documented in Minsk City in 2010. A large nationwide survey was subsequently conducted to assess the extent of the problem across the country and to help evaluate whether the national TB programme's measures to address the challenge are adequate.

**Design/methods:** Drug susceptibility testing (DST) for first and second-line drugs was performed in 1420 TB patients between mid-2010 and mid-2011; 934 of them were new, and 410 were previously treated cases. DST results were complemented with demographic, socio-behavioural and clinical information for each patient.

**Results:** MDR-TB was found in 32.3% (95%CI 29.7–35.0) and 75.6% (95%CI 72.1–78.9) of new and previously treated patients, respectively. Of the 612 patients with MDR-TB, 11.9% (95%CI 9.7–14.6) had extensively drug-resistant (XDR) TB.

**Conclusion and recommendations:** The current standard regimen for re-treatment cases that uses only first-line drugs (i.e., category II) is in fact ineffective in the vast majority of previously treated cases, and therefore deserves serious reconsideration. The current standard treatment regimen for new cases (i.e., category I) is effective in only two thirds of new cases, and may also warrant future change. As a priority, establishment of high-quality and routine DST incorporating rapid diagnostics is vitally important in the country to ensure all patients are started on effective treatment regimens as soon as possible.

### PC-440-16 A validation study of the Malay version of Minnesota Nicotine Withdrawal Scale for adults with medical illness

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**Background:** The Minnesota Nicotine Withdrawal Scale (MNWS) is considered as the briefest scale among the self-report measures of nicotine withdrawal symptoms currently available. The present study aimed to translate and validate the scale for practical and academic purposes among Malay speaking people.

**Design/methods:** A cross sectional design was used to elaborate the study data. Adult smokers who attend the Quit Smoking Clinic in Penang General Hospital at Penang State, Malaysia were included in the study. The translation was done according to standard guidelines: forward translation, back translation, pretesting and cognitive interviewing, and preparing the final version of the Malay scale for the reliability and validity study. Eligible subjects were interviewed by expert counsellor with the use of structured questionnaire to overcome any non-response by those who had reading difficulties. The interview was performed after subject's quit date. Internal consistency and homogeneity was used to test reliability of the Malay version of MNWS. Furthermore factor analysis and concurrent validity was employed to validate the psychometric properties of the scale.

**Results:** The Malay version of MNWS scale has excellent reliability with Cronbach's alpha of 0.91. The test-retest reliability for the scale were presented and an excellent reliability and stability of the translated scale with Spearman's Rank Correlation Coefficient,  $r = 0.876$  ( $P < 0.001$ ). In addition, There was a significant positive correlation between carbon monoxide level, FTND total score and number of cigarettes smoked per day with MNWS total score ( $r = 0.72$ ,  $r = 0.68$  and  $r = 0.68$ ,  $P < 0.001$ ; respectively). A principal components analysis with orthogonal rotation yielded a uni-dimensional model which includes all the items of MNWS.

**Conclusion:** The Malay version of MNWS is reliable and a valid measure for nicotine withdrawal symptoms and it is applicable for clinical practice and research study.

### PC-441-16 Epidemiological impact of mass tuberculosis screening: a two-year follow-up after a national tuberculosis prevalence survey

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**Background:** Much attention has been paid to detecting smear-positive TB from the viewpoint of public health. However, the anticipated decline in TB incidence of more than 5% annually from improved

case detection of smear-positive TB has not been observed in any high-TB-burden countries. The objective of the study is to assess the epidemiological impact of detecting and treating all bacteriologically positive TB cases in the community.

**Methods:** A follow-up survey was conducted 2 years after a nationwide TB prevalence survey in Cambodia to capture incident cases: 22160 subjects who participated in the prevalence survey were followed up and 1753 subjects who had abnormal findings on chest radiography (CXR) were examined by CXR, smear-microscopy and mycobacterial culture.

**Results:** A total of 34 cases with new smear-positive TB were detected by registry check, which amounted to 0.38 (95% confidence interval (95%CI 0.27–0.53) of the age-adjusted expected number of cases notified in the study areas, showing a two-thirds reduction in notification. Seven smear-positive TB cases and 93 smear-negative, culture-positive TB cases were newly detected through medical examination; incidence rates of bacteriologically positive TB were 8.5%/year (95%CI 6.3–11.2%/year) in those with CXR suggestive of active TB and 2.9%/year (95%CI 2.2–3.7%/year) in those with CXR suggestive of suspected TB, healed TB, other lung diseases or minimal abnormality.

**Conclusion:** Detecting and treating smear-negative, culture-positive TB as well as smear-positive TB cases leads to a rapid reduction in incidence of smear-positive TB. Sputum culture-negative individuals with abnormal CXR findings are at a high risk of disease progression in a short period of time and require follow up and potentially preventive treatment in settings where a significant proportion of disease may occur by reactivation.

#### PC-442-16 Tuberculosis prevalence rate declines in Cambodia, but still remains the top in Asia: the 2nd National Prevalence Survey 2011

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**Background:** The 2nd national prevalence survey (NPS), Cambodia was conducted in 2010–2011, 9 years after the 1st NPS which revealed the prevalence rate of 269/100 000 (95%CI 211–343) in all ages in smear-positive pulmonary (S+) TB. The DOTS began to be decentralized to health center in 1999 and expanded nationwide in 2004.

**Methods:** 42 clusters were selected by the population proportionate multistage cluster sampling method. A total of 37413 (93%) subjects of 40373 eligible

persons were screened with chest radiography (CXR) and symptoms for collecting two sputum specimens. A direct smear of every sputum specimen was screened with fluorescent microscopy, followed by Ziehl-Neelsen method if positive. Culture examination with solid medium and identification test of *Mycobacterium tuberculosis* were performed. A panel of experts decided the final radiological findings.

**Results:** Out of the 37413 subjects, 95 TB survey cases were identified as S+TB and 218 as S-C+TB, which showed the S+ prevalence rate of 171/100 000 in all ages (a 36% reduction compared with that in the 1st NPS). The number of S-C+TB identified was 2.3 times larger than that of S+TB. The male to female ratio in S+TB was 1.4 and the age groups of 35 years or older accounted for 91%. In the smear-negative, culture-positive (S-C+) TB, the male to female ratio was 1.53 and the age groups of 35 years or older accounted for 80%. Out of the 313 Bac+TB cases, 27 (9%) had past history of TB and 6 (2%) were on treatment. The TB cases who met the criteria of 'cough more than 2 weeks' and/or hemoptysis accounted for 47% in S+TB and only 22% in S-C+TB.

**Conclusion:** Around 4% annual decline rate in S+TB prevalence rate was observed. However, Cambodia remains the top in Asia and all the current effort made by the NTP and other organizations should be continued.

#### PC-443-16 Tuberculosis in less symptomatic cases and tuberculosis in the elderly are big challenges to the National Tuberculosis Program, Cambodia

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**Background:** The 1st national TB prevalence survey (NPS), Cambodia was carried out in 2002 when the DOTS was being decentralized. The NTP conducted a 2nd NPS in 62 clusters selected by the population proportionate multistage cluster sampling in 2010–2011, 6 years after a nationwide DOTS expansion, to evaluate the effect of the DOTS program on TB epidemiology.

**Methods:** Survey subjects in the two surveys were screened with chest radiography (CXR) and symptoms for selecting 'eligible for sputum'. Two sputum specimens collected from the selected subjects were examined with fluorescent microscopy, followed by Ziehl-Neelsen stain. Culture examination with solid media and identification test of *Mycobacterium tuberculosis* were performed. We compared the results

among the cases aged 15 or older between the two surveys to evaluate the effect of TB control program.

**Results:** The 2nd NPS showed a 43% reduction in the S+ prevalence rate from 437 in 2002 to 251/100 000 (aged 15 years or over). The S+ prevalence rate reduced by 58% among the symptomatic (cough more than 2 weeks and/or hemoptysis), but only 17% among the asymptomatic or less symptomatic. Although the reduced prevalence rates were observed at any age group, the patient detection rates (PDR), being defined as a ratio of a prevalence rate to a notification rate, became worse in the elderly, while they were improved in the younger age groups of both males and females.

**Conclusion:** Although the DOTS is effective in reducing symptomatic TB, its effect is limited in less symptomatic TB. The NTP has succeeded in cutting the chain of transmission to children, but faces difficulty in TB control in the elderly where many incident cases may occur by reactivation. To further decrease TB burden, not only symptomatic patients but also less symptomatic patients at higher risk should be targeted though active case detection.

#### PC-444-16 Mortality rate and cause of death by time on tuberculosis treatment

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**Background:** Despite integration of TB and HIV/ART programmes across sub-Saharan Africa, TB mortality remains high in many settings, even after diagnosis. Detailed understanding of mortality within TB programmes will enable focussed interventions. This retrospective study quantifies mortality rates and autopsy-verified causes of death by HIV and ART status, and by time on treatment.

**Methods:** Routine TB-programme data, from 1995 to 2008, were obtained for male platinum miners in North West Province, South Africa. We obtained cardiorespiratory autopsy data, conducted for compensation purposes regardless of the cause of death, for a subset of men. Records were expanded into person years (py) at risk by days on TB treatment. Age- and calendar year-adjusted incidence rate ratios (IRR) and 95% confidence intervals were determined using Poisson regression.

**Results:** 3335 men had a first TB episode (mortality = 18.3/100 py); 2146 (64%) were HIV positive. There were 835 retreatment episodes (mortality = 31.4/100 py). Mortality was highest in the first month of TB treatment (Table): compared to the first month

of treatment, IRR at 3–6 months was 0.13 [95%CI 0.05–0.36] in HIV negative men, 0.26 [0.11–0.63] in HIV positive men on ART and 0.66 [0.47–0.92] in HIV positive men not on ART. Overall mortality during TB treatment was higher in HIV positive men than HIV negative (IRR 5.8 [3.84–8.78]), but for HIV positive men, ART was not associated with reduced overall mortality (IRR 0.90 [0.57–1.44]). TB caused death in half of HIV negative and 31% of HIV positive men undergoing autopsy, with the proportion attributable to other causes increasing by time on TB treatment.

**Table** Rate of death by time on TB treatment, HIV status and antiretroviral therapy for first episode of TB treatment

HIV/ART status, time on treatment	People <i>n</i>	Deaths <i>n</i>	Case fatality rate %	Person years	Rate per 100 py	IRR (95%CI)
HIV negative or unknown						
1st month	1189	11	0.9	97.1	11.3	1.00
2nd month	1178	8	0.7	99.5	8.0	0.71 (0.28–1.76)
3rd–6th month	1170	6	0.5	389.6	1.5	0.13 (0.05–0.36)
Total	1189	25	2.1	586.2	4.3	
HIV positive (all)						
1st month	2146	64	3.0	173.5	36.9	1.00
2nd month	2082	43	2.1	174.8	24.6	0.67 (0.45–0.98)
3rd–6th month	2039	145	7.1	657.3	22.1	0.60 (0.44–0.80)
Total	2146	252	11.7	1005.7	25.1	
HIV positive on ART*						
1st month	180	10	5.6	14.3	69.8	1.00
2nd month	170	1	0.6	14.4	7.0	0.10 (0.01–0.78)
3rd–6th month	169	10	5.9	54.6	18.3	0.26 (0.11–0.63)
Total	180	21	11.7	83.3	25.2	
HIV positive not on ART						
1st month	1750	48	2.7	141.7	33.9	1.00
2nd month	1702	39	2.3	142.8	27.3	0.81 (0.53–1.23)
3rd–6th month	1663	120	7.2	537.6	22.3	0.66 (0.47–0.92)
Total	1750	207	11.8	822.1	25.2	

Rates per 100 person years, \*already on ART for at least 30 days prior to commencing TB treatment (216 men who started ART during TB treatment or less than one month prior to commencing TB treatment, and 24 deaths in this group, are excluded from both ART categories to avoid contamination of groups).

**Conclusions:** Mortality was substantially higher in the first month of TB treatment for all patient groups, and we found many men died from causes other than TB. These findings highlight the importance of targeted resource allocation to improve diagnostic accuracy and ensure effective clinical care in the early stages of TB treatment.

### PC-445-16 Incidence of smear-positive tuberculosis at Dabat Health and Demographic Surveillance System in Ethiopia: a longitudinal study

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**Background:** The incidence of tuberculosis (TB) is an important measure to monitor the progression of the disease and the impacts of TB control strategy. However, epidemiological information from population based studies on the incidence TB was poorly documented in Africa.

**Design/methods:** Longitudinal study was undertaken to determine incidence of smear-positive TB at Dabat Health and Demographic Surveillance System in Ethiopia. All individuals aged  $\geq 14$  years were followed prospectively from January to December 2011. Interviews using a uniform questionnaire were done to detect individuals with chronic cough ( $\geq 15$  days) and two sputum (spot and morning) samples were gathered for standard smear microscopy. Poisson regression model was used to calculate incidence rate ratios.

**Results:** A total of 281 820.3 person-months were observed in one year, in which 74 had smear-positive results. The incidence of smear-positive TB was 311 per 100 000 person-years [95%CI 240–382]. Higher rate ratios were observed with increasing age [ARR: 1.83, 95%CI 1.10–2.99], no formal schooling [ARR: 3.55, 95%CI 1.03–12.29], urban residence [ARR: 2.90, 95%CI 1.53–5.53], and dry season of the year [ARR: 1.35, 95%CI 1.14–1.59].

**Conclusion and recommendations:** The incidence of smear-positive TB is higher in this study setting, suggesting that a significant number of patients with active TB remain undiagnosed. The higher incidence rate of TB with increased age people, no formal schooling and urban residence warrants appropriate TB control strategies. Factors responsible for the higher incidence of TB in dry season need further investigation.

### PC-446-16 How long is the journey to tuberculosis diagnosis and treatment in India?

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**Background:** Early diagnosis of tuberculosis (TB) has important patient and public health implications. Although India has more than 25% of the world's TB burden, data on delays in the diagnosis and treatment of TB patients has come from non-representative,

small surveys with few participants, and frequently excluded patients treated by private providers. We analyzed data from a large community-based survey involving 395 districts of India (population 750 million) to assess the length of time from onset of TB symptoms to diagnosis and treatment from both NTP and private providers.

**Methods:** The selection of districts and households within the districts was done by multistage cluster random sampling methodology and door to door survey. TB patients identified during this community survey were interviewed by trained field investigators using a semi-structured questionnaire.

**Results:** The survey sample consisted of 30 of 374 GF project districts, and included household visits to ~73 000 households with ~374 000 household members, and identified 609 TB patients. Overall median delay from onset of symptom to initiation of treatment was 29 days with interquartile range of 16 to 47 days. Median delay for diagnosis was 21 days (IQ 10–35) and patient delay was 12 days (IQ 10–35). 307 (50%) of the 609 TB patients had delay in diagnosis of more than 20 days, delay of more than 20 days for presenting to any health facility was the reason in 279 patients (46%).

**Conclusion and recommendations:** From this household survey covering half of India, about one quarter of persons taking TB treatment experienced  $>47$  days from symptom onset till initiation of TB treatment. Large-scale national interventions are underway to raise community awareness about TB, engage all health care providers, and improve TB diagnosis through better tools and delivery systems. This baseline data, can be used to assess the effectiveness and impact of efforts for early detection of TB cases.

### PC-447-16 Drug resistance survey among Tibetan refugees in India

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**Background:** Tuberculosis is one of the major health problems among Tibetans-in-exile in India. Drug resistant TB was perceived as a common finding in the clinical practice, but precise data on its incidence were lacking.

**Methods:** We conducted a drug resistance survey in 5 Tibetan settlements, covering approximately 70% of the Tibetan population in India. Culture and drug susceptibility testing (DST) for streptomycin, isoniazid (H), rifampicin, and ethambutol were

performed using MGIT-960 at Hinduja Hospital (Mumbai, India) on all consecutive new and previously treated smear-positive and smear-negative cases diagnosed from April 2010 to September 2011. DST for kanamycin, ethionamide, PAS, and ofloxacin was performed on MDR isolates. The variables recorded at the time of enrollment were: age, sex, previous TB treatment, HIV status, risk factors, living setting, country of birth, and city of residence.

**Results:** 301 patients were enrolled. 260 had positive culture and available DST. 192 were new cases (74%) and 68 were previously treated cases (26%). All patients tested for HIV (total 245) were negative. Among new TB cases, 28 were MDR (14%) and 11 were H-monoresistant (6%). Among previously treated cases, 20 were MDR (29%) and 11 were H-monoresistant (16%). Of the MDR isolates, 78% were resistant to ethambutol, 70% to ethionamide, 29% to ofloxacin, and 14% to kanamycin (6% were XDR). MDR-TB was associated with history of previous treatment (RR 2.02;  $P = 0.0115$ ) and with female sex (RR 1.85,  $P = 0.0306$ ). No other relevant association was found.

**Table** MDR prevalence in different subgroups and additional resistances in MDR patients

Variable	n	MDR		P value	In the MDR subgroup, %		
		n	%		Oflo-R	Kana-R	XDR
Type of patient				0.0115			
New	192	14			36	14	7
Previously treated	68	29			20	15	5
Sex				0.0306			
Male	192	15			28	7	0
Female	68	28			32	26	16
Country of birth				0.1251			
Tibet	104	13			28	0	0
Other	156	22			29	21	9
Living setting				0.6359			
Congregate	154	16			32	8	0
Private house	106	23			23	22	13

**Conclusions:** MDR-TB is common in new and previously treated cases among Tibetans in India. Tibetan MDR-TB patients show additional complex resistance patterns. Of particular concern is the high percentage of MDR strains resistant to ofloxacin, kanamycin, or both. Early detection of MDR-TB is essential in Tibetan patients to guide therapy and further DST. The use of an empirical MDR regimen might not be adequate in Tibetan TB patients.

### PC-448-16 Adherence to national treatment guidelines and impact on treatment outcome among tuberculosis patients in three provinces of South Africa

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**Background:** In South Africa (SA) standardized therapy for TB through directly observed treatment (DOT) is available, however the extent of its utilization is not known. Our objectives were to describe and evaluate the impact of adherence to standardized treatment and DOT on TB treatment outcomes in three provinces of SA.

**Design/methods:** We conducted a secondary analysis of data collected for a national surveillance evaluation in three provinces of SA, including only patients with data on treatment regimen, DOT and treatment outcome available. Treatment outcomes were classified as poor (death, default, treatment failure) or favorable (cure, treatment completion). Treatment regimens were considered as appropriate or inappropriate based on national guidelines. DOT adherence was categorized as full, partial (intensive or continuation phase only) and no DOT. A multivariate regression model was developed to estimate risk ratios and 95% confidence intervals.

**Results:** Of 741 cases, 124 (17%) had a poor and 617 (83%) had a favorable outcome. Patients receiving DOT during the intensive phase only (76/268, 30%) had a higher proportion of poor outcomes versus patients with DOT during the entire course (43/443, 10%). Retreated after default (8/16, 50%) had a higher proportion of poor outcomes versus new patients (102/635, 16%). The proportion of patients with a poor outcome was similar among patients receiving inappropriate and appropriate treatment (5/35, 14.3% vs. 118/679, 16.9%). Independent predictors of a poor outcome were receiving DOT during the intensive phase only (aRR = 2.9, 95%CI 1.6–5.0) and treatment default during previous TB episode (aRR = 3.0, 95%CI 2.1–4.2).

**Conclusion:** Insufficient DOT compliance and default during previous TB treatment were independently associated with a poor treatment outcome in three SA provinces. Providers should recognize the importance of adherence to treatment standards, including DOT throughout the course of TB treatment.

### PC-449-16 Integrity of smear results used for tuberculosis patient management and determining treatment outcomes, KwaZulu-Natal, South Africa

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**Background:** In South Africa, sputum smear is used for diagnosis of tuberculosis (TB) disease and monitoring TB treatment. Smear results are sent from the laboratory (lab) to health facilities then captured on the Electronic TB Register (ETR); however the lab register and ETR are not directly linked. This study was conducted to validate smear results on the ETR against those in the lab register in KwaZulu-Natal.

**Methods:** A retrospective evaluation was conducted among all AFB smear positive TB patients recorded in the ETR during quarter 4, 2009. Patient level data from the ETR were compared to the lab register.

**Results:** Of 1036 smear positive patients in the ETR, 683 (65.9%) had positive smear results in the lab register (Figure). Of these, 364 (53.2%) had smear results recorded in the ETR at the end of the intensive phase of treatment: 326 (89.6%) were recorded

as converted to smear negative (sm-) in the ETR, with 220 (67.5%) confirmed as sm- in the lab; and 38 (10.4%) were documented as positive in the ETR of which 25 (65.8%) were verified positive in the lab. End of treatment smear results were documented in the ETR for 331 patients. In the ETR, 302 (85.8%) patients were recorded as cured, but only 105 (34.8%) were bacteriologically confirmed in the lab. Two hundred patients were missing end of treatment lab results.

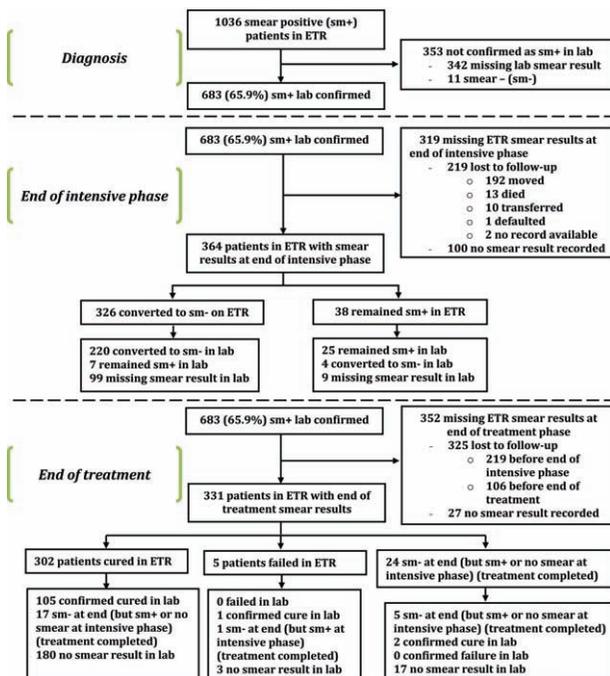
**Conclusions:** Over one-third of TB patients registered as smear positive in the ETR were not able to be confirmed based on laboratory results. While the ETR reported high cure rates among this cohort of smear positive TB patients, less than half were able to be verified in the laboratory database. Many patients were missing laboratory results at the time of conversion and at the end of treatment, leading to uncertainty as to the validity of smear results and final outcomes recorded in the ETR. Complete recording and direct linkage between the lab and ETR would eliminate missing data and discrepancies, and more accurately inform the NTCP.

### PC-450-16 Lack of patient registration in ETR.Net for sputum smear-positive patients in KwaZulu-Natal, South Africa

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**Background:** In South Africa, tuberculosis (TB) diagnosis is confirmed by microscopic evidence of acid-fast bacilli from a sputum smear. Testing is performed by the National Health Laboratory Service (NHLS) and sent to facilities where it is manually recorded in the electronic TB register (ETR.Net), utilized by the National TB Control Program (NTCP). However, these systems are not directly linked, and accuracy of data in ETR.Net for documenting TB case burden based on laboratory diagnosis is unknown. The objective of this study was to identify diagnostic smear positive cases at the NHLS level and compare patient registration in the ETR.Net.

**Methods:** A retrospective evaluation of laboratory TB sputum smear records from Quarter 4 of 2009 was conducted. The facility, name, gender, hospital numbers and dates from each positive smear result obtained from the NHLS laboratories were matched with records in ETR.Net. Patient records of cases not recorded in ETR were located at the health facility,



**Figure** Flow charts of patients identified as having smear positive (sm+) tuberculosis (TB) in the Electronic TB Registry (ETR) and availability and concordance of smear results in the ETR and laboratory register from diagnosis through treatment completion.

and categorized as having started treatment, moved, died, or not found.

**Results:** Of 794 smear positive TB patients, 158 (19.9%) patients from 24 health facilities (range 0–36 per facility) were not registered in ETR.Net. Of the 158, patient records for 110 could be located in the health facility: 65 (59.1%) had been started on treatment, 8 (7.3%) had moved, 4 (3.6%) died, and 33 (30.0%) did not have any follow-up information.

**Conclusions:** Analysis of diagnostic smear positive records from NHLS shows that not all patients are being registered. However, review of paper patient records suggests that the majority of non-registered TB patients are being treated at health facilities. Improved communication and coordination between the laboratory and clinics and registration of all TB cases are critical for effective TB control and management. Directly linking laboratory and clinical records would greatly enhance recording and reporting of TB cases.

#### PC-451-16 Challenges for recruiting and retaining participants in a large, population-based tuberculosis study in Lima, Peru

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**Background:** Conducting large, population-based, epidemiological studies have important challenges for recruiting and retaining participants. In urban area of Lima, Peru including 20 districts, from September 2009 we carried out a prospective cohort study of TB in the community.

**Methods:** Through March 2012, we enrolled 16 730 participants (4032 TB patients and their household members). Follow-up is 12 months for contacts and 24 months for TB patients. Study visits are being conducted in 120 health centers or participants' homes by 120 field workers. Study procedures include clinical evaluations, interviews, chest X-rays, sampling of blood and sputum, HIV testing, TST application and reading, and recording of the geographic coordinates of participants' homes. Innovative strategies include activities with study staff (ongoing training, diverse communication approaches via phones, e-mails, mass SMS alerts, an electronic 'billboard' in the study site with important updates real-time mobile phone data collection, and the use of highly skilled mobile teams to resolve operational problems in the field), with health center staff (study information dissemination—video, monthly newsletters, delivery of laboratory results and regular meetings— and continual training), and participants (study information—use

of flip charts and explanatory leaflets—and additional time for guidance and counseling on TB care).

**Results:** Currently we are enrolling between 850 and 1000 participants per month, with an overall enrollment rate of 86.59% in TB patients and 94.33% in household members. Overall attrition rates are 6.0% for contacts and 8.1% for TB patients.

**Conclusions:** Most strategies are low cost, reliable and easy to implement, however, the large scale of the study demands constant vigilance, highly coordinated communication and the ability to adapt to new challenges rapidly and efficiently.

#### PC-452-16 Factors associated with the implementation of the RHZE-DFC scheme for the treatment of tuberculosis in Brazilian municipalities

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**Background:** Since late 2009, Brazil adopted the regimen RHZE fixed dose combination (FDC) for the treatment of tuberculosis. Knowing the process of implementation of health policies and factors that favor its process could allow to predict their effectiveness.

**Objectives:** This study aims to identify socio-demographic, epidemiological and operational that influence the implementing the new FDC regimen in Brazilian municipalities (BM).

**Methods:** It is an ecological study with analytical unit, the municipalities. We studied: (i) population size, (ii) population density and (iii) incidence of tuberculosis. The operational factors studied were: (i) adoption of directly observed treatment (DOT), (ii) diagnosis and (iii) bacteriological monitoring of treated cases. The outcome (implementation process) consisted of: (i) the early implementation of the new regimen and (ii) rapid deployment on the time until reaching the maximum coverage in BM. Were eligible, all municipalities with reported cases in (SINAN, the Morbidity Information System) during the period from December 1, 2009, to March 31, 2011.

**Results:** Both demographic and epidemiological factors were associated to the fast implementation ( $\leq 3$  months) of the new regimen, but the demographic factors had the greatest strength of association. BM with smaller populations, lower population density and a lower tuberculosis incidence rates were most likely to quickly deploy the new regimen. Likewise, those with better performance of the NTP, as judged by the use of DOT and microbiological confirmation, also were more likely to deploy quickly.

**Conclusion:** Demographic and operational characteristics of the municipalities influenced this implementation. Possible limitations to this study include the analysis of variables of SINAN database and the

possible overestimation of the use of FDC inferred from the use of RHZE after the implementation date of the regimen.

Supported by the Bill & Melinda Gates Foundation, grant OPGH 5254.

## MEDICAL MANAGEMENT OF TB–2

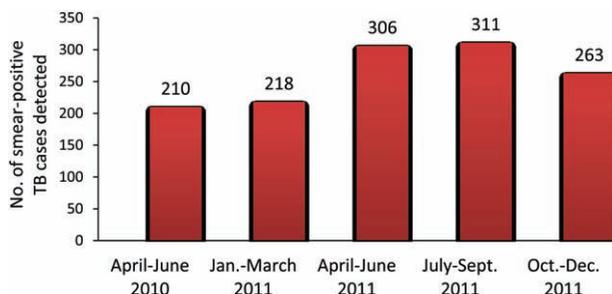
### PC-471-16 Improving tuberculosis case detection by implementing standard operating procedures in selected health facilities of Ethiopia

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**Background:** Ethiopia is ranked eighth among the 22 high burden countries for TB. MSH/TB CARE I has been working with Regional Health Bureau (RHB) in Oromia to implement an innovative four-pronged approach to improve TB case detection using SOPs: 1) improving TB organization within health facilities, 2) improving staff's knowledge and skills of TB, 3) provision of SOPs and job aides to improve TB case detection, and 4) improving recording and reporting including on job training, mentoring and referral of patients.

**Methods:** MSH/TB CARE I did a needs-assessment, and findings were communicated to the FMOH, RHBs, and partners. The local team developed SOPs based on the gaps identified. RHBs sensitized on the SOPs showed interest on implementing them. A pilot zone (West Arsi) was selected and an action plan of implementation was agreed upon. SOPs were implemented in 28 HF: 3 hospitals and 25 health centers.

**Results:** The TB suspect identification rate was 2.8% (775/26800) in April–June 2010 and increased to 7.3% (2644/36044) during July–September 2011 and 7% (2774/39556) during October–December 2011. The TB SS+ case notification was 210 in April–June 2010 and increased to 306 in April–June 2011. Similarly, it increased to 311 during July–September



**Figure** TB case notification in SOP sites before and after intervention.

2011. The TB SS+ case notification rate progress after the intervention is also shown in the Figure. The lab. smear positivity rate also improved from 8.4% baseline to 10.5% during April–June 2011 and 9.1% July–September 2011.

### PC-472-16 Addressing the challenges to isoniazid preventive therapy uptake among PLWHA in Nigeria: the Anambra State TB-HIV TWG experience

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**Background:** Poor patient adherence leading to INH mono-resistance and diagnostic challenges of ruling out active TB remains a major hindrance to IPT acceptance in developing countries. IPT implementation started in Nnamdi Azikiwe University Teaching Hospital (NAUTH) Anambra State, as a pilot in 4th quarter 2010.

**Intervention:** TB-HIV Technical working group (TWG) was set up in the state in 2009 to drive the process. Advocacy and situation assessment to the selected pilot site were done by the TWG team. IPT implementation at take-off was guided by the National Tuberculosis and Leprosy Control Program (NTBLCP) guideline for implementation of TB-HIV collaborative services. The Institute of Human Virology Nigeria (IHVN) provided pre-financing support for the cost of chest X-ray to all HIV patients with probable pulmonary TB symptoms to rule out active TB. The revised TB-HIV tools were used in data collection and integrated TB-HIV supportive supervision were carried out by both the TB and HIV teams in the site.

**Results:** Within the implementation period of 4th quarter 2010 to 4th quarter 2011, 2143 PLWHA were screened for TB. Four hundred and seventy two of them (215 males and 257 females) were found to have active TB and 1003 out the 1671 PLWHA without active TB have already been commenced on IPT.

**Conclusions:** Despite the initial challenges to IPT acceptance, considerable targets were met within the period of implementation and the lessons learnt have informed ongoing IPT scale up in the country with the issue of limited access to INH being addressed by the NTBLCP.

### PC-473-16 Early and improved tuberculosis case detection through the use of GeneXpert® in Nepal

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**Background:** Case detection is one of the major challenges of the National TB Program (NTP) Nepal. The

International Organization for Migration in collaboration with the NTP aims to improve case detection in the Eastern Development Region and selected districts of the Central Development Region of Nepal through the use of GeneXpert® MTB/RIF technology. The project is funded under the second wave by the TB REACH initiative.

**Designs/methods:** GeneXpert instruments were deployed in nine microscopy diagnostic centres. Sputum smear negative individuals with chest X-ray suggestive TB were tested with MTB/RIF assay. Additionally, the testing was extended to individuals with high risk of MDR-TB regardless of smear results.

**Results:** From January 2012 to March 15, 2012, 701 tests were performed and 171 MTB/RIF positive cases were detected. Overall MTB/RIF positivity was 24% (95%CI 21–28). Among 590 smear-negative cases, MTB/RIF positivity was 20% (95%CI 17–24). Among 49 smear-positive cases, 46 were MTB/RIF-positive and 3 were MTB/RIF and culture-negative. In 62 cases results of sputum smears were unknown. 27 cases (4%, 95%CI 3–6) were RIF-resistant. RIF resistance was 22% (95%CI 15–32) among patients at risk of MDR-TB and 0.9% (95%CI 0.3–2.1) among other patients. There were 67 test failures, 37 of which were due to power interruption. Underutilization of the GeneXpert testing was found to be due to insufficient referrals, short working hours in the laboratories and power supply interruptions.

**Conclusions and recommendations:** The preliminary project results show that MTB/RIF assay can be effectively used to increase TB case detection and detect RIF resistance in resource-limited settings. Power back up, referral mechanisms and staff motivation are among the main issues to be considered while planning roll out of this technology in Nepal.

#### PC-474-16 Evaluation of the impact of an electronic information system for tuberculosis monitoring in the Archangelsk region of Russia

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**Background:** InIT-TB is an information system for tuberculosis (TB) monitoring and management developed in Archangelsk region of Russia and installed in December 2009 in Archangelsk regional antituberculosis dispensary (ARAD). More than 40 client computers are running the system through local area network of the dispensary, including automated workplaces in registry, in-patient and out-patient departments, laboratory and X-ray department. Doctors in all 24 district hospitals in the region and

prison hospital use a web-based module to access the system.

**Objectives:** To assess the impact of InIT-TB system on ARAD routine procedures, quality of data and statistical reports, to detect current system and business process bottlenecks for further development.

**Methods:** Business process modeling was used to detect changes in workflow, routine registry procedures and reporting. Models were created for processes used before and after introduction of the system. Changes of dispensary staff work load were assessed using questionnaires.

**Results:** InIT-TB system was found to speed up data entry, analysis, submission of quarterly reports (saves 3–5 days of work per quarter) and detection of errors in clinical records. For 28 of 32 (88%) of respondents the InIT-TB system reduces number of errors in clinical data and rises quality of reports. For head doctors of departments and specialists responsible for data analysis the InIT-TB system simplified their work. For specialists responsible mostly for data input (laboratory and registry staff, nurses) there was no clear reduction of work load.

**Conclusions and recommendations:** The new electronic system speeded up entry of data from districts, and reduced delays in analysis and submitting reports. While all head doctors of departments reported decrease of their work load, TB-doctors, nurses and laboratory staff did not feel significant improvement related to InIT-TB system use. Further development is required to address this issue.

#### PC-475-16 Multidrug-resistant tuberculosis in Pskov region, northwestern Russia: critical impact of the *Mycobacterium tuberculosis* Beijing genotype

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**Background:** Pskov Oblast (670 000 population, 55 400 sq. km) is located in northwestern Russia on Russian-Latvian (European Union) border. In 2011, the tuberculosis (TB) incidence here was reported 70.8/100 000, rate of multidrug resistant TB (MDR-TB) is 16.7% among newly diagnosed patients with pulmonary TB.

**Design/methods:** Ninety *M. tuberculosis* strains from epidemiologically unlinked TB patients, permanent residents in Pskov Oblast, Russia were studied by spoligotyping, VNTR typing, *rpoB*, *katG315*, *inhA*, *ahpC* drug resistance mutations detection. Phylogenetic and statistical analyses were done using PAUP and EpiCalc programs.

**Results:** Beijing genotype ( $n = 40$ ) was most prevalent followed by LAM ( $n = 18$ ), T ( $n = 12$ ), Haarlem

( $n = 10$ ), and Ural ( $n = 5$ ) families. Beijing strains were subtyped by 15-loci VNTR typing. The 'classical' 12-MIRU-VNTR (Supply et al., 2001) differentiated 40 Beijing strains into 14 types; major types were M2 (223325153533) prevalent throughout former USSR and M11 (223325173533) prevalent in Russia and East Asia according to database (Mokrousov, 2008, 2012). 12-MIRU identified 14 profiles (HGI = 0.82); additional use of 3 hypervariable loci resulted in 18 profiles (HGI = 0.89). A high rate of MDR among Beijing strains from new TB cases (79.3% vs. 44.4% in LAM) was noted. The *rpoB531* mutations were more frequently found in Beijing and *rpoB516* and *inhA-15* mutations in LAM strains. Beijing strains were in similar rate in both newly- and previously-diagnosed patients (44.6 and 44.0%, respectively). In contrast, LAM strains were more prevalent among chronic patients (36.0 vs. 13.8%,  $P = 0.04$ ).

**Conclusions:** The high rate of Beijing genotype and prevalence of LAM is similar to the other Russian settings. A feature specific for *M. tuberculosis* population in Pskov is a relatively higher rate of Haarlem and T types. The ongoing transmission of MDR-TB in the Pskov region in northwestern Russia is critically influenced by dissemination of the MDR Beijing genotype strains.

#### PC-476-16 Active case finding among Nepalese seasonal labour migrants to India in selected districts of Nepal

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**Background:** Case detection is one of the major challenges of National TB Program (NTP) Nepal. Under the guidance of Nepal's NTP and funding from TB REACH initiative, FHI Nepal implemented a project to increase case finding in Nepal through active case finding among hard to reach populations including seasonal labour migrants in Nepal.

**Designs/methods:** The project was implemented from October 2010 to September 2011. Screening and sputum collection sites were established at the Indo-Nepal Borders. Migrants were clinically screened at the borders and sputum was collected from the symptomatic. Existing microscopic centres were used for the sputum tests. Sputum smear positive (ss+ve) migrants were enrolled for treatment at the existing DOTS centres.

**Results:** A total of 66 573 migrants were screened for TB and 5728 were identified as TB symptomatic. Three sputum samples were prepared from 5226 persons and 296 positive cases were detected. Of them, 286 cases were enrolled in TB treatment in DOTS centres. The project achieved over 95% of its screening target. However, there was substantial gap between the expected and actual percentage of symp-

tomatic and ss+ve case (expected 20% and 10% respectively). Only 8.6% migrants were identified as TB symptomatic and ss+ve yield was only 5.7%. Moreover, the project outcome did not show expected additionality in case finding and did not receive rollover to year two. Ambitious target, overload and staff motivation at microscopy centres were major reasons of project failure.

**Conclusions and recommendations:** Substantial number of migrants can be screened for TB through border screening sites. Cross border activities, community mobilization, microscopic centre strengthening and migrant friendly services are the major issues to be considered while planning roll out TB case finding activity among seasonal migrants in Nepal.

#### PC-477-16 Factors associated with default and treatment failure among pulmonary tuberculosis patients in Plateau State, Nigeria, 2011

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**Introduction:** Tuberculosis burden in Nigeria is one of the highest in the world with estimated incidence of 133/100 000 populations. Multi-drug resistant TB (MDR-TB) is an emerging threat of the TB control in Nigeria. Recent study showed MDR-TB is 9.4% among retreatment cases arising mainly from incomplete treatment. We explored factors that determine outcomes of treatment among pulmonary TB patients undergoing direct observation of TB treatment in Plateau state, Nigeria.

**Method:** We reviewed medical records of pulmonary TB patients in their eighth month of treatment using checklist to extract data on their demographic and clinical characteristics. We interviewed them including the health care workers on factors associated with outcome of treatment using structured questionnaires. We conducted focus group discussions (FGD) with patients and health care workers about factors responsible for poor treatment outcomes. Data were analyzed with epiInfo software.

**Results:** Of the 378 (males: 61%, mean age 37.6 ± 13.5 years) 16 (4.2%) either failed or defaulted from treatment (unfavorable outcomes). Independent factors that remained significantly associated with unfavorable outcomes were living > 5 km from treatment sites adjusted odds ratio (AOR) 18.27, PV 0.008, cigarette smoking (AOR 23, PV 0.007) and lack of knowledge of duration of treatment (AOR 18.48, PV 0.014). FGD revealed unfriendly attitude of health towards patients and poor knowledge of TB control services from the patients and health workers perspective respectively.

**Conclusion:** Decentralization of TB treatment sites, training of health workers on TB control services, patients' education including smoking cessation will prevent defaults and failures of TB treatment in the state.

#### PC-478-16 Serum microRNAs as biomarker for active and latent tuberculosis infection

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**Background:** Expression patterns of microRNAs in body fluids underscored their potential as noninvasive biomarkers for various diseases including TB. The aim of this study is to identify a pattern of microRNAs to be used as biomarker for diagnosis and follow up in active and latent TB infection in immunocompetent and immunodeficient hosts.

**Methods:** The study enrolled consented participants, 50 from European region and 136 from African region. Two pools of 10 participants for each category and geographical region were measured using qRT-PCR. Circulating miRNAs were compared between patients belonging to pulmonary aTB, healthy control (HC), and LTB. A Student's *t*-test was used to compare mean concentrations of miRNAs with STATA 11.

**Results:** Results from HC were used as reference controls. Among 119 miRNAs detected in European individuals, 33 and 48 miRNAs were up/down regulated respectively in the aTB compared to their levels in the HC ( $P < 0.05$ ). 56 miRNAs were detected from African subjects. A statistically significant difference was found for nine miRNAs which were downregulated, and 43 which were unregulated. In LTB, 114 miRNAs were up/down-regulated and could be used as discriminatory markers between aTB and LTB from HC respectively.

**Conclusions and recommendation:** A significant change in serum miRNAs levels occurred in patients with aTB providing useful information which may lead to the improvement of TB diagnosis and detection of LTB. Further validation of findings will allow defining specific miRNAs patterns to be used for TB diagnosis.

#### PC-479-16 Risk factors for treatment default in adult tuberculosis patients in urban Indonesia

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**Background:** Patient default from treatment is a major barrier to successful tuberculosis control programs. Defaulting patients are more likely to fail treatment, remain infectious, and develop MDR-TB. Indonesia is one of the high burden countries that has achieved the WHO recommended treatment success rate (85%) however in some settings default rates remain unacceptably high, exceeding 14% at the study lung clinic.

**Methods:** We recruited adult pulmonary TB patients who were diagnosed and received medication in a lung clinic in Bandung Indonesia. Information regarding possible pre and during treatment risk factors for defaulting was gathered using structured interviews at baseline and at two months. Treatment default was defined as a pre-commencement default (not starting treatment after diagnosis), and permanent default (stopping treatment for more than 2 months after one month of treatment). Patients were contacted to determine reasons for default. Risk factors were analysed by logistic regression.

**Result:** Over 14 months 262 patients were recruited. Overall 12% defaulted treatment of which, 20% were pre-commencement, and 80% were permanent default. The majority of permanent default occurred in month 2 (32%). The most common reasons for default were a lack of time to collect medication and problems with the medication itself. Baseline and during treatment predictors of treatment default were male sex of the patients, if the patient was a smoker, poor accessibility, poor knowledge of medication requirements, work commitments, the financial burden of TB and poor financial autonomy.

**Conclusions:** In this setting default rates remain high, occur early in treatment and are driven by poor accessibility, time constraints and a lack of TB treatment knowledge. By increasing clinic accessibility and by providing TB related education programs defaulting rates may be reduced in this and similar settings.

### PC-480-16 Case fatality among HIV-infected tuberculosis patients with CD4 count > 350 cells/mm<sup>3</sup>

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**Background:** In 2010, WHO recommended that all HIV-infected TB patients should be initiated on ART irrespective of CD4 count, while acknowledging that there is limited data on the case fatality of HIV-infected TB patients with CD4 count more than 350 and if initiating ART is really useful. Here, we assess the case fatality among HIV-infected TB patients with CD4 count more than 350/mm<sup>3</sup>.

**Methods:** We evaluated all TB patients recorded in treatment registers of the Revised National TB Control Programme in June 2010 in the high HIV prevalence state of Karnataka, and cross-matched HIV-infected TB patients with ART programme records.

**Results:** Of 6182 TB patients registered, HIV status was ascertained for 5761 (93%) and 710 (12%) were HIV-infected. 146 (21%) HIV-infected TB patients were on ART prior to TB diagnosis. Of the remaining 564, 477 (85%) had their CD4 count assessed; of these, 86 (18%) had a CD4 count of more than 350 and 73 (85%) were not initiated on ART. Of 86, 9 (10%) died during TB treatment (Table). Overall, ART was associated with reduction in case fatality.

**Table** Case fatality rates among HIV-infected TB patients (not on ART at the time of TB diagnosis) registered under RNTCP, by ART initiation status, Karnataka, India, June 2010

CD4 count	Number of deaths/total number of HIVTB (%)			P value	RR (95% CI)
	Total n	Not initiated on ART	Initiated on ART		
<50/cc	54	3/7 (42.9)	10/47 (21.3)	0.21	2.01 (0.73–5.57)
50–200	226	14/33 (42.4)	24/193 (12.4)	<0.001	3.41 (1.98–5.89)
201–350	111	1/24 (4.2)	9/87 (10.3)	0.35	0.40 (0.05–3.02)
>350	86	6/73 (8.2)	3/13 (23)	0.12	0.36 (0.10–1.25)
Unknown	87	29/86 (33.7)	0/1 (0)	0.48	Not applicable
Total	564	53/170 (23.8)	46/341 (13.5)	0.002	1.76 (1.23–2.52)

**Conclusion:** Since India followed WHO 2006 ART guidelines at the time, most of the HIV-infected TB patients with CD4 count more than 350 were not started on ART and had a case fatality of about 10% which is twice higher than that reported among HIV-negative TB patients (4%). In HIV-TB patients with CD4 counts more than 350, ART initiation also depended on clinical status of the patient, with clinically more severe preferentially started on ART; this partly explains the paradoxical association of ART with increased case fatality. Whether ART was asso-

ciated with reduction of case fatality in this group could not be conclusively studied due to small sample size and requires further research.

### PC-481-16 Village health workers, horse riders and text messaging contribute to improved tuberculosis case detection in Lesotho

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Lesotho has the second highest incidence of tuberculosis (TB) cases in the world. TB diagnosis has relied on passive case finding, and community level screening was largely absent. Four highly mountainous districts, comprising 48 health centres, and 5 district laboratories were targeted for intervention. Three village health workers (VHWs) per health centre were trained to perform TB screening according to national TB guidelines and were deployed. Two VHWs carried out community awareness campaigns and undertook community-wide and door to door screening. Patients were referred to the nearest health centre for sputum collection. A horse rider sputum transport service was introduced, in selected communities with poor access to the nearest health centre, to collect sputum specimens from the community. A VHW based at the health centre screened all patients attending the health centre irrespective of their presenting complaint using a standard screening tool. Specimens were transported from the health centres to the district hospital laboratories for AFB smear microscopy. An SMS-based system was developed and implemented to decrease the turn-around time for reporting results and treatment initiation. A 17% increase in total TB cases and a 23% increase in smear positive cases were detected in the target districts compared with baseline prior to the project period. These increases compared with a 10% and 11% decrease respectively where no interventions were introduced. Microscopy results sent by SMS were available at the health centre within 1 day of testing. Additional features of the SMS system, including patient reminders were not well utilised during early implementation and are being prioritised during refresher training. Community outreach activities and integration of TB screening into routine services offered at health centres increases TB case detection. Results may be rapidly reported by SMS for rapid TB treatment initiation in remote settings.

### PC-482-16 Impact of Xpert® MTB/RIF on multidrug-resistant tuberculosis case detection in one South African district one year after implementation

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**Background:** Xpert® MTB/RIF was implemented in South Africa in a phased manner since March 2011, in selected districts across the nine provinces of the country. In one of these districts, Gert Sibande, preliminary analysis of data from one of the seven sub-districts revealed a remarkable increase in the number of MDR-TB cases, approximately 58% (34) newly detected cases over a period of nine months since implementation of Xpert MTB/RIF, compared to the number of cases previously detected over a period of more than two years (58). This observation underscored the need for further investigation on contribution of Xpert MTB/RIF to this increased number of MDR-TB cases in this sub-district as well as the entire district. The impact on other program indicators was also investigated.

**Design/methods:** A retrospective review of the paper-based and electronic TB registers was conducted for the entire district for a period of six months pre- and one year post-implementation of Xpert MTB/RIF. The following key indicators were analyzed: total number of TB cases, number of smear-positive and smear-negative cases, and proportion of rifampicin (RIF) resistant cases detected. As a secondary objective, a comparative analysis was done to determine the proportion of Xpert MTB/RIF detected RIF-resistant cases that were RIF mono-resistant, MDR-TB or XDR-TB according to conventional drug susceptibility testing (DST) results.

**Results and conclusion:** Sudden increase in the number of MDR-TB cases detected as a result of Xpert MTB/RIF implementation requires scaling up of capacity for the TB program to be able to initiate and sustain patients on treatment.

### PC-483-16 Combined treatment for patients with HIV-HCV-TB co-infection

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**Background and challenges to implementation:** Standard treatment of HCV can cause severe immunodeficiency, which can lead to development of tuberculosis (TB). Little is known about treatment of active TB in hepatitis C virus (HCV) co-infected patients on HCV treatment.

**Intervention or response:** After 4 months of the standard treatment of HCV with the diagnosis of HCV, genotype 3a, a 36-year-old man was diagnosed with new active pulmonary TB (smear, culture positive,

sensitive case). At the beginning of the HCV treatment routine screening tests for TB and HIV were performed according to the Infection Disease and Gastroenterology Society Guideline on HCV treatment. Result of X-ray for TB was negative, HIV positive (CD4 cells 550). TB therapy was started under DOT. HIV treatment was not started and further HCV treatment was under discussion. There were several consultations between infection disease doctors infectionists and pulmonologists, which resulted in the decision to continue HCV treatment because of good response on the treatment (HCV-RNA decreased from 1 000 000 to 12 IU/ml after 4 months of the treatment). During the therapy liver function tests were all the time within reference meanings. Sputum conversion was in the 10th treatment week. CD4 and HIV-RNA were performed every 3 months (decreased from 550 cells to 256 after 3 months of TB treatment and to 196 after 6 months of TB treatment).

**Results and lessons learnt:** After completion on 8 month TB treatment, HIV treatment was started. HCV treatment was completed after 12 months. At the end of the treatment HCV-RNA was negative.

**Conclusions and key recommendations:** The absence of the clinical trials and only few articles in this field is a big concern for the medical doctors to manage treatment for patients with HIV-HCV-TB co-infection. Taking into account good results obtained for this particular case, should we continue HCV treatment among HIV-HCV-TB patients from the very beginning of treatment.

### PC-484-16 Positioning of the Xpert® MTB/RIF diagnostic system in rural KwaZulu-Natal, South Africa: preliminary findings from a cluster randomised trial

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**Background:** The Xpert® MTB/RIF system is a molecular diagnostic for the detection of *Mycobacterium tuberculosis* and rifampicin resistance. Data on diagnostic performance and clinical outcomes at different levels of the health system are required to inform scale-up within high burden countries.

**Methods:** A cluster randomised trial comparing two Xpert® MTB/RIF positioning strategies for adult pulmonary TB suspects: point-of-care [POC] strategy (system positioned at primary health care clinic) vs. hospital laboratory [HL] strategy (system positioned at district hospital laboratory). Unit of randomisation

is two-week time block; participants recruited from single clinic if: age  $\geq 18$  yrs, current cough, HIV infection  $\pm$  high risk of MDR-TB. This preliminary analysis incorporates first twelve randomisation blocks (7 POC, 5 HL) and focuses on diagnostic performance and retention in diagnostic pathway. Sensitivity and specificity for detection of *M. tuberculosis* were calculated with reference to a single MGIT culture.

**Results:** 486 individuals enrolled; 446 submitted specimens (266 POC, 180 HL). Xpert positivity was similar in both strategies (17.7% POC vs. 13.9% HL,  $P = 0.29$ ). Sensitivity for detection of *M. tuberculosis* was 80.0% (95%CI 63.9–90.4) at POC and 71.4% (95%CI 42.0–90.4) at HL. Specificity was 96.1% (95%CI 91.3–98.4) at POC and 91.4% (95%CI 84.3–95.6) at HL. The proportion of tests with invalid/error results was similar (3.4% POC vs. 4.4% HL,  $P = 0.62$ ). The proportion of participants who received their result within 30 days was 96.6% POC vs. 79.4% HL ( $P < 0.001$ ).

**Conclusions and recommendations:** These preliminary results suggest that implementation of the Xpert<sup>®</sup> MTB/RIF system at primary health care clinic level produces comparable diagnostic performance to implementation within the normal laboratory system but reduces loss to follow-up within the diagnostic process. The ongoing trial will explore the impact on individual clinical outcomes.

#### PC-485-16 The potential utility of Xpert<sup>®</sup> MTB/RIF for real-time surveillance of drug resistance in rural KwaZulu-Natal, South Africa

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**Background:** The Xpert<sup>®</sup> MTB/RIF system is a molecular diagnostic for the detection of *Mycobacterium tuberculosis* and rifampicin resistance. Linkage of basic clinical information to the laboratory system could enhance real-time surveillance of drug resistance at a population level.

**Methods:** A cluster randomised trial comparing two Xpert<sup>®</sup> MTB/RIF positioning strategies for adult pulmonary TB suspects. This preliminary analysis uses individual-level data across the trial arms combined from the first 30 weeks of enrolment and focuses on prevalence of rifampicin resistance in specific groups of suspects (current TB/previous TB/no previous TB). Current TB group includes participants suspected of MDR-TB (smear non-conversion or treatment failure on a standard TB treatment regimen).

**Results:** 558 submitted sputum specimens; 546 (98%) with valid Xpert<sup>®</sup> MTB/RIF result. Sensitivity and specificity for detection of multidrug resistance (against reference of line probe assay on culture isolate) were respectively 83.3% (95%CI 36.5–99.1) and 100% (95%CI 88.3–100). The Xpert<sup>®</sup> MTB/RIF results for the three groups are displayed in the table. Rifampicin resistance was defined most commonly by probes E (58%) and B (33%).

	Current TB	Previous TB	No previous TB
MTB detected	17/21 (81.0%)	30/228 (13.2%)	47/297 (15.8%)
Rifampicin resistance detected	5/17 (29.4%)	5/30 (16.7%)	2/47 (4.3%)

**Conclusions and recommendations:** The detection of rifampicin resistance by the Xpert<sup>®</sup> MTB/RIF assay is a reliable indicator of multidrug resistance in this high burden setting. As expected, the prevalence of rifampicin resistance is higher among previously treated cases than among those not previously treated. As implementation is scaled up, incorporation of basic clinical data into Xpert<sup>®</sup> MTB/RIF laboratory systems could enhance the utility of this molecular diagnostic tool for real-time surveillance of drug resistance at a population level.

#### STOP TB STRATEGY PUBLIC-PRIVATE MIX – 1

##### PC-511-16 Initiative to engage private providers in the Revised National Tuberculosis Control Programme to improve case finding and holding in Karnataka urban slums

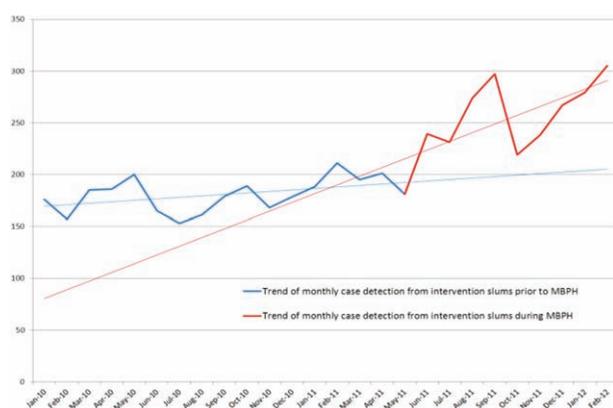
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**Background:** Most chest symptomatics (CS) in India visit private healthcare providers (pHCP) in the first instance but few pHCP comply with international standards of TB care when managing clients. Market-based Partnerships for Health (MBPH) aimed to demonstrate effective means to improve RNTCP case finding and holding through pHCP engagement in an urban slum population of 794 049 in 13 districts of Karnataka.

**Methods:** MBPH engaged and built the capacity of allopaths, ISMH (practitioner of Indian systems of

medicine and homeopathy) LTFQ (less-than-fully-qualified provider) and chemists, conducted outreach activities to increase demand for DOTS and established an interface to bridge gaps between public sector and pHCP and between pHCP and patients. On-ground implementation was supported by research and a web-based client-specific MIS.

**Results:** 1491 pHCP (616 allopaths; 258 ISMH; 57 LTFQ; 560 chemists) were trained on RNTCP and 489 of them networked. Knowledge of DOTS increased among pHCP. Communication activities reached 538 599 people and health-seeking behavior improved among CS. 7030 CS were referred by MBPH and underwent sputum microscopy with a positivity rate of 16%. Referrals led to notification of 1087 TB cases (542 NSP). Data from DMCs covering MBPH slums showed overall increase in sputum microscopy of 14% in the period May–Dec 2011, over the same months of 2010. The corresponding increase in testing of CS from MBPH slums was 79%. TB units covering program slums reported an overall 9% increase in notification of all types of TB in the period May 2011 to Feb 2012, over the same months a year before. Increase in case notification from MBPH slums was 41% during this period. For NSP cases, these increases were 3% and 73% respectively.



**Figure** Number of TB cases (of all type) detected each month from MBPH slums (pop. 794,049). Data source: RNTCP TB registers of 56 TU covering MBPH intervention slums in Karnataka.

**Conclusions:** MBPH demonstrated increase in case finding. The comprehensive nature of the model, including a collaborative and synergistic relationship with the public sector in the state appears to have been the key influencing factors.

### PC-512-16 Public-private partnerships for tuberculosis control in Bangladesh: a framework for sustainable partnerships with private sector health care providers

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**Background:** We conducted research in Dhaka between 2004 and 2008 to develop and evaluate a public-private partnership (PPP) model to involve private medical practitioners (PMPs) within the NTP's TB control activities. Since 2008, this PPP model has been scaled up in two other big cities—Chittagong and Sylhet.

**Design/methods:** We used NTP service statistics to compare the TB control outcomes between the intervention and control areas. To capture detailed insights of PMPs and TB managers about the process and outcomes of the study, we conducted in-depth interviews, focus group discussions (FGDs), and workshops.

**Results:** The systematic involvement of PMPs had a significant impact on the key TB control outcome by increasing case finding of smear sputum positive TB cases—since the inception of the PPP in 2004, 703 participating PMPs referred almost 19 000 TB suspects and 3959 SS+ TB cases—contributing about 36% of all TB cases registered in the project areas. The framework guided the public, NGO and private sector providers to work together for achieving the common goal for TB control, although PMPs were initially sceptical about the motive of the public sector regarding this partnership. Our participatory approach to planning and designing the partnership, including involvement of all stakeholders in the process of selecting service components, selecting partners, and monitoring of the PPP, played a crucial part in securing commitment and ownership for sustainable scale up.

**Conclusion and recommendations:** The PPP model is simple, effective, and sufficiently robust to provide guidance in developing strategies and actions for long-term sustainability. This framework suggests eight steps and four principles for involving private sector providers in a health programme. These steps and principles aim to provide guidance for people working for sustainable health programmes with the emerging strategies.

### PC-513-16 Quality of tuberculosis services from patients' perspective: a cross-sectional study at public and private hospitals in North Jakarta, Indonesia

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**Background:** To measure the quality of TB services in a public hospital and a private hospital in North Jakarta from the patients' perspective.

**Design/methods:** A descriptive cross-sectional research was conducted from January 2011 to February 2012. We selected 156 patients from a public hospital by systematic sampling and all 68 patients at a private hospital. Data were taken using Quality of Care as seen through the Eyes of the Patient (QUOTE-TB) instrument and analyzed descriptively.

**Results:** There were eight aspects of services that needs to be improved both in the public and private hospital, i.e., waiting time, discrimination in services, safe drinking water, cost of TB services, transport support, food aid, the relationship of HIV-TB and HIV prevention. In addition to these eight services, there were aspects that also need to be addressed in the private hospital, i.e., consistency of service, convenient opening hours, TB service opening hours, and surcharges. More patients valued TB services in the private hospital (63.5%) compared to the private hospital (53.0%). 77.6% and 47.1% of TB patients in the public hospital and the private hospital respectively would recommend TB care facilities to their friend or relatives.

**Conclusion and recommendations:** Patients perceived aspects of TB services needs to be improved. The patient's perspective may relate their recommendation of TB care facilities to their friend/relatives. Adaptation of QUOTE-TB instrument in different health facility types should be explored.

### PC-514-16 Novel methodology to assess sputum smear microscopy quality in private laboratories

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**Background:** In South Asia, an estimated 80% of patients choose to attend a private facility for their healthcare needs. Although patients believe the private sector provides high quality services, private diagnostic laboratories (PLs) are largely unregulated and little is known about the accuracy of results provided. This study assesses the accuracy of sputum

smear microscopy for pulmonary tuberculosis diagnosis in PLs operating in Karachi, Pakistan. A novel evaluation methodology was designed in which patient-actors submitted sputum specimens spiked with cultured *Mycobacterium tuberculosis* (MTB) for testing such that PLs were not aware that they were being assessed.

**Methods:** Smear-negative sputum specimens were collected Indus Hospital TB patients and combined with an attenuated, cultured MTB strain to create MTB-spiked samples; for negative standards, no MTB was added to the smear-negative specimens. Seven of the largest PLs across Karachi were chosen for evaluation and were sent six MTB-spiked and one MTB-negative sputum specimens. Patient-actors pretending to be laboratory customers submitted these specimens to each PL for testing over a three day period. Specimens were also blindly submitted to Indus Hospital, which serves as a reference lab for the province.

**Results:** Only three PLs accurately classified all the MTB-spiked specimens which were submitted. A further three misclassified all the MTB-spiked specimens as smear-negative, thus providing the 'patients' with false negative results. Result accuracy was not correlated with the cost of sputum smear microscopy testing at each PL.

Laboratory ID	Laboratory type	Correct Diagnosis		
		All specimens n (%)	Smear-positive specimens n (%)	Smear-negative specimens n (%)
1	Network	3 (42.9)	2 (33.3)	1 (100)
2	Network	7 (100)	6 (100)	1 (100)
3	Standalone	1 (14.3)	0	1 (100)
4	Standalone	1 (14.3)	0	1 (100)
5	Network	1 (14.3)	0	1 (100)
6	Standalone	6 (85.7)	6 (100)	0
7	Network	7 (100)	6 (100)	1 (100)
Indus Hospital	N/A	7 (100)	6 (100)	1 (100)

**Conclusions:** TB sputum smear microscopy services are highly variable across PLs and are often of extremely poor quality. Engagement, capacity building and rigorous monitoring of standards at PLs are of vital importance for the control of TB. Our findings, while specific for TB diagnostic tests, could be symptomatic of other tests performed in PLs and warrant further investigation.

### PC-515-16 Tuberculosis management practices by private practitioners in Visakhapatnam, South India

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**Background:** Worldwide, about 1 in 8 TB cases are managed by a private provider in India. Anecdotally, poor TB diagnostic and treatment practices are rampant in the Indian private healthcare sector, but very

**Table** Private practitioners adhering to International Standards of TB Care diagnostic and treatment practices in Visakhapatnam, Andhra Pradesh

Standard Practice	Respondents (N = 201)	Reported adherence n (%)
DX1: Cough of 2–3 weeks to suspect TB	201	137 (68)
DX2: Two sample sputum smear examination for diagnosis of pulmonary TB	198	87 (44)
DX3: extrapulmonary TB diagnosis based on appropriate investigations	176	93 (53)
DX4: Sputum microbiological examination in those with radiological findings suggestive of TB	182	85 (47)
DX5a: Diagnose sputum smear-negative pulmonary TB based on both sputum microscopy and X-ray	155	75 (48)
DX5b: Use of the right trial antibiotic*	161	85 (53)
DX6: Diagnose pediatric TB based on at least 3 of 5 recommended approaches†	188	144 (77)
RX7: Adopt methods to ensure adherence to treatment	188	159 (85)
RX8: Prescribe standard TB treatment regimen 2HRZE and 4RH (daily and thrice weekly) in FDC	177	61 (35)
RX9: Practice DOT or foster adherence with treatment supporter or other enablers	195	40 (21)
RX10: Follow up cases with sputum microscopy	187	160 (85)
RX11: Prescribe culture and drug susceptibility testing for previously treated TB cases	151	59 (39)
RX12: For diagnosed DR TB, prescribe standardized regimen, or individualized TB treatment regimen based on availability of drug susceptibility testing	97	37 (38)
Core diagnostic and treatment standards (DX1, DX2, and RX8)	181	28 (14)

\* Response to what antibiotic was used as trial antibiotic. 85 (53%) used non-fluoroquinolones.

† 5 approaches included history, clinical examination, tuberculin skin testing, bacteriological evaluation or relevant investigations to diagnose cervical lymph node TB.

TB = tuberculosis; DX = diagnostic standard; RX = treatment standard; DR TB = drug-resistant TB; DOT = directly observed treatment; FDC = fixed-dose combinations = tab INH; R = tab rifampicin; Z = pyrazinamide; E = ethambutol.

little representative information is available to understand the extent of inadequate TB diagnostic and treatment practices.

**Methods:** We conducted a cross-sectional survey in a random sample of all private medical practitioners (PMP) formally qualified in allopathic, homeopathic, or ayurvedic medicine in Visakhapatnam District in South India. Using a semi-structured questionnaire, we assessed self-reported TB diagnostic and treatment practices, relative to benchmark practices articulated in the International Standards of Tuberculosis Care (ISTC), and assessed risk factors for non-adherence.

**Results:** Among the 3956 PMP enlisted in the study area during December 2010–July 2011, 296 private practitioners were randomly selected, and 201 (68%) were successfully interviewed. There were 28 (14%) PMP who complied with a combination of three core ISTC recommendations, i.e., using cough to identify tuberculosis suspects, sputum smear examination to evaluate TB suspects, and internationally-approved standardized treatment regimens. Self-reported adherence to these three core ISTC recommendations was higher among PMP not practicing modern medicine (risk ratio [RR] 2.4, 95% confidence limit [CL] 1.2–4.9), PMP who cared for >20 TB patients annually (RR 2.1, 95%CI 1.1–4.1), and those sensitized to TB control guidelines (RR 3.2, 95%CI 1.5–7.0). Only 11 (6%) PMPs reported following all 6 ISTC diagnostic standards, and only 1 reported following all seven treatment standards.

**Conclusion:** Most PMP in Visakhapatnam District, India, reported TB diagnostic and treatment practices that were inadequate relative to international standards. Interventions are urgently required to accountably improve TB care in the private healthcare sector.

### PC-516-16 Experience of the new model of integrating tuberculosis services with general hospitals in Zhejiang, China

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**Background:** Traditionally TB service are provided by TB dispensaries located in the Centres of Disease Control (CDC) in China. The new integrated model moves TB clinics to a general hospital, called the TB designated hospital. Patients can be diagnosed and treated there without referrals. The study aims to report the experience from the health providers and patients regarding the integration of TB service in the general hospital in Zhejiang, China, and provide relevant policy recommendations.

**Method:** Six counties in Zhejiang were selected according to their economic development levels. In each county, we randomly selected 50 uncomplicated TB patients registered in 2008. Patient questionnaire were conducted and their medical charts were collected. 83 in-depth interviews were conducted with health staff.

**Results:** CDC has faced the challenges of poor clinical and technological capacity. Though TB clinics were removed to the designated hospitals, less government funding was provided for the initial setup and the daily operation. TB clinic doctors complained about low income. 79% patients visited  $\leq 2$  health providers, with the total median delay of 21 days. 15% patients were hospitalized, incurring an average medical cost of RMB 8001. The average total medical cost was RMB 4145, or 36% of the household income. 70% of the medical cost was spent in the designated hospital, while 61% was spent in the TB clinic. In TB clinic, the costs of liver protect drugs account for 43% of total medical cost.

**Conclusion:** We found the new integrated model reduced patient burden, but unnecessary hospitalization outside the designated hospitals were still a problem and need to be addressed. Auxiliary drugs and tests accounted for the majority of TB patient expenditure during treatment in the designated hospitals. There was a lack of government input and regulation.

#### PC-517-16 Contribution of private-public mix DOTS programme to the tuberculosis programme in Ethiopia and its performance: a five year retrospective analysis

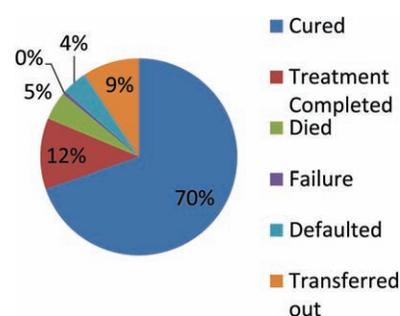
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**Background:** With the support of USAID/Private Health Sector Program (PHSP) led by Abt Associates Inc., the Ethiopian Ministry of Health had initiated Public-Private Mix-Directly Observed TB Treatment Short course (PPM-DOTS) service in 2006. At present the program is implemented in 295 PPM-DOTS private facilities all over the country. Including these PPM-DOTS facilities, currently there are over 3000 TB DOTS providing facilities (both public and private) in the country.

**Design/methods:** A quantitative study was conducted using quarterly reported data from both public and private health facilities between August 2006 and July 2011. Simple descriptive and comparative statistical analyses were performed using EPI-Info 3.3.2.

**Results:** The national contribution of PPM-DOTS in detecting all forms of TB cases progressively increased from 1% (1354/126 806) in 2006 to 9.5% (15 052/159 017) in 2011. Of 15 052 all forms of TB

patients diagnosed in 197 PPM-DOTS facilities in 2011, 3960 were retained and treated in the facilities while the majority 11 092 (73.7%) were referred to other public facilities. Treatment success rate progressively increased from 77% in 2006 to 81.5% in 2011. There was no statistically significant difference between private and public facilities in terms of major TB treatment outcome indicators.



**Figure** Treatment outcomes of patients treated in 197 PPM-DOTS facilities in 2011.

**Conclusion and recommendations:** PPM-DOTS program in Ethiopia is contributing significantly to the national all forms of TB detection. It is also effective and efficient way of improving case detection if it is scaled up, integrated and owned by the national TB program. High referral rate calls for establishing strong referral linkages between the public and private health facilities.

#### PC-518-16 Improving tuberculosis control through public-private collaboration in Viet Nam

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**Background and challenges to implementation:** Viet Nam ranks 12 among the 22 high-burden countries for TB. In 2010 TB incidence and prevalence were 199 and 334 per 100 000 population, respectively. With a 54% case detection rate (all forms), almost half of estimated TB cases remain undetected and a significant portion of the population first seeks health care in the private sector.

**Intervention or response:** In collaboration with the National TB Program (NTP) PATH implements a public-private mix (PPM) referral model in 22 out of 68 districts in four provinces of Hai Phong, Can Tho, Nghe An and Ho Chi Minh City to increase identification of TB suspects in private and public non-TB facilities and refer them to public TB facilities for diagnosis and treatment. The project trained 815 PPM providers on TB symptoms, and provided recording and reporting tools to track referrals and monitor case finding.

**Results and lessons learnt:** From July 2011 to March

2012, 7502 TB suspects were referred by PPM facilities to TB facilities. Of these suspects, 4467 (59.5%) were received at public TB facilities for diagnosis and 840 (18.8%) of those were diagnosed with active TB. This represents 6.2% of the total number of TB cases reported by the four provinces. Routine monitoring of key outcomes is challenging due to lack of necessary data in the current NTP reporting system. PATH and partners are working with the NTP to build consensus on the minimum data needed and integrate these variables with routine NTP reporting.

**Table** PPM referral model results by province, July 2011 through March 2012

Indicator	Hai Phong (9/15 districts)	Can Tho (5/9 districts)	Nghe An (6/20 districts)	Ho Chi Minh City (2/24 districts)
Collaborating PPM facilities, <i>n</i>	115	108	211	224
TB suspects referred from PPM facilities, <i>n</i>	1707	3083	1350	1362
Referred TB suspects received at public TB facilities for diagnosis, <i>n</i> (%)	1256 (73.6)	2161 (70.1)	795 (58.9)	255 (18.7)
TB cases (all forms) diagnosed, <i>n</i> (%)	404 (27.8)	213 (9.9)	169 (19.0)	54 (21.2)
Total new TB cases (all forms) (as reported by provincial NTP), <i>n</i>	1687	1441	1618	8714
TB cases (all forms) contributed by PPM to overall case notification, %	23.9	14.8	10.4	0.8

**Conclusions and key recommendations:** Participation by private and public non-TB facilities in TB control is essential for improving case detection rate, and reducing delays in TB diagnosis and treatment in Viet Nam.

### PC-519-16 Factors associated with patient and health systems delays in the diagnosis and initiation of treatment of tuberculosis in Karnataka, India, 2011

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**Background:** A single person with infectious TB could infect 10–15 others in a year; therefore, early detection of cases, followed by effective treatment, is

imperative for the successful control of TB. Delay in diagnosis of TB causes spread of infection in the community, increases patient expenditure and is associated with a higher risk of mortality. Therefore, there is a need to study the patient and health system delay and the factors affecting delays among new smear positive TB patients.

**Methods:** A study was conducted among new smear-positive TB patients who started treatment between July and October 2011 in RNTCP facilities and reported to have taken medication less than 2 months prior to date of interview. The patients were randomly selected and interviewed using a semi-structured interview schedule.

**Results:** Among 227 patients, the median patient, health system and total delay was 15, 19, and 42 days respectively. A private provider was contacted first by 55% of patients, a government provider by 41% and an indigenous medicine practitioner by 4%. In multivariate analysis, the patient delay was 15 days or less if the patient was literate (adjusted odds ratio [AOR] 0.5,  $P \leq 0.05$ ) and knew that TB is curable (AOR 0.4,  $P \leq 0.05$ ). Health system delay was >14 days among 63% of patients. Factors associated with reducing health system delay were: knowledge that TB is curable (AOR 0.3,  $P \leq 0.05$ ) and belief that ‘people who are important will not look down upon me if I visit a doctor immediately after TB diagnoses’ (AOR 0.6,  $P \leq 0.05$ ).

**Conclusion:** There is a need to motivate people to visit a qualified provider immediately after noticing persistent cough. The key communication message should emphasize that ‘TB is curable’. It is equally essential that both private and public qualified providers are enabled to carry out early evidence-based diagnosis and treatment of TB.

### PC-520-16 Dramatic increase in childhood tuberculosis case detection with private sector engagement

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**Background:** Children with tuberculosis (TB) remain largely undetected and unreported in Pakistan due to a lack of awareness and training and a focus on sputum smear-positive cases. A majority of patients seek treatment in the private sector in high TB burden countries. We conducted a multi-faceted intervention targeting the private sector in Karachi, and assessed its impact on childhood TB case detection.

**Intervention:** A communications campaign advised persons with two or more weeks of productive cough

to seek care at 54 general practitioner (GP) clinics and at the Indus Hospital out-patient department (OPD). Community laypersons used forms on mobile phones to evaluate patients and attendants in GP clinics and at the OPD, and received cash incentives for finding cases. All suspects <15 years of age were encouraged to seek evaluation at the pediatric TB clinic at Indus Hospital. The primary outcome was the change in childhood tuberculosis notifications to the National Tuberculosis Program (NTP) following the intervention.

**Results and lessons learnt:** We identified 342 pediatric TB cases through this intervention, including 59 cases through GP clinics, and 73 through the OPD. An additional 123 children with TB were brought by parents directly to the Indus Hospital TB Clinic, and 117 were referred there from other clinics and wards within Indus Hospital. Pulmonary tuberculosis notifications in children increased by 7.32 times (4.93–10.87) in 2011 relative to 2010.

**Conclusion:** Engaging the private sector using a multi-faceted intervention strategy resulted in a dramatic 7-fold increase in childhood TB case detection. Childhood TB is underreported in urban Karachi, and likely to be underreported in similar settings where most patients seek care in private facilities.

### PC-521-16 Success of GeneXpert® MTB/RIF use as a case-finding strategy in private laboratories in Pakistan and Bangladesh

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**Background:** In South Asia, the lack of fast and accurate diagnostic tests and limited engagement with the private healthcare sector by NTPs hinders TB control efforts. The Xpert® MTB/RIF (GXP) test has proved successful at increasing case-detection and identifying rifampicin resistance, yet no studies have described its implementation and effectiveness in private-sector, low-HIV settings.

**Methods:** 6 GXP systems were placed in private laboratories in Karachi, Pakistan, and Dhaka, Bangladesh. All individuals visiting the labs were screened for symptoms of TB. Suspects that produced a sputum specimen received a smear-microcopy test and a chest X-ray. GXP testing was indicated based on two criteria: previous TB treatment for ≥1 months, regardless of smear and chest X-ray results (*History of ATT*) or as a follow-on test for smear-negative suspects whose chest X-ray was suggestive of TB (*SSCXR*

*Suggestive*). GXP tests were performed by field workers who had no previous laboratory experience.

**Findings:** 4894 sputum specimens were submitted between September 2011 and March 2012 across both sites. 1561 GXP tests were indicated and 1466 (94%) were performed. GXP positivity was significantly higher among *SSCXR Suggestive* suspects compared with *History of ATT* [23% vs. 11%, adjusted Rel Risk: 1.9 (1.5, 2.4)]. However, among GXP positive cases, rifampicin resistance was significantly higher in the *History of ATT* gateway [16% vs. 3%, aRR: 4.6 (1.9, 12.5)]. 2.8% of tests performed produced an Error or Invalid result. GXP testing significantly increased bacteriological positivity compared with smear microscopy alone (11% vs. 6%,  $P < 0.0001$ ).

**Table** GeneXpert results by testing site and gateway with age- and sex-adjusted relative risk and 95% confidence intervals

	Karachi			Dhaka			Both Sites		
	n	(%)	aRR (95% CI)	n	(%)	aRR (95% CI)	n	(%)	aRR (95% CI)
TB Suspects Submitting Sputum	3,676			1,218			4,894		
GXP Tests Indicated	1,218			343			1,561		
History of ATT	516			209			725		
SS-, CXR Suggestive	702			134			836		
GXP Tests Performed	1,148 (94.3)			318 (92.7)			1,466 (93.9)		
History of ATT	478 (92.6)			189 (90.4)			667 (92)		
SS-, CXR Suggestive	670 (95.4)			129 (96.3)			799 (95.6)		
GXP Positivity	202 (17.6)			56 (17.6)			258 (17.6)		
History of ATT	58 (12.1)	-	-	18 (9.5)	-	-	76 (11.4)	-	-
SS-, CXR Suggestive	144 (21.5)	1.63 (1.2, 2.2)		38 (29.5)	2.98 (1.8, 5.0)		182 (22.8)	1.87 (1.5, 2.4)	
RIF Resistance	13 (6.4)			5 (8.9)			18 (7)		
History of ATT	8 (13.8)	4.14 (1.4, 12.2)		4 (22.2)	8.44 (1.0, 70.2)		12 (15.8)	4.85 (1.9, 12.5)	
SS-, CXR Suggestive	5 (3.5)	-	-	1 (2.6)	-	-	6 (3.3)	-	-
Error Results	9 (0.8)			13 (4.1)			22 (1.5)		
Invalid Results	13 (1.1)			6 (1.9)			19 (1.3)		
Smear Positivity	250 (6.8)			43 (3.5)			293 (6)		
Bacteriological (Smear & GXP) Positivity	430 (11.7)	$p < 0.0001$		95 (7.8)	$p < 0.0001$		525 (10.7)	$p < 0.0001$	

**Interpretation:** The GXP system was easily integrated into the study's diagnostic algorithm, despite the absence of experienced lab technicians, and significantly improved case-finding over smear-microscopy alone. While the positivity yield was higher on *SSCXR Suggestive* suspects, testing of *History of ATT* suspects was important in identifying rifampicin resistance.

### PC-522-16 Findings from a simulated patient study among non-allopathic health care providers in 30 districts of India

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**Background:** Population Services International/India sub recipient to The Union is implementing Project Axshya in thirty districts of six states. Under the project 944 non allopathic providers were trained on basics of TB diagnosis and treatment. A simulated patient (SP) study was conducted with the objectives to see if the trained providers were able to identify suspect TB cases correctly and whether these providers

referred suspect TB cases for sputum examination to the nearest designated microscopy center (DMC).

**Methodology:** Simulated patients were recruited and exit interviews were conducted using structured questionnaires. Lot quality assurance sampling methodology was used for the study and 152 provider clinics were included in the sample size. Data collected was analysed using SPSS software.

**Results:** The key findings on data analysis were: Overall 29 percent of the providers referred TB suspects to DMC or private lab for sputum test; 27 percent of the providers gave information on sputum examination and informed the client that it was free of cost; 16 percent provided information on TB.

**Conclusions and recommendations:** The simulated patient study has revealed that intended behaviour change in some of the trained providers has been found to happen only after one modular training. However the proportion of such ideal behaviour change post-training has been seen to be low. It is hereby recommended to conduct refresher courses and establish a continuous engagement process with the providers to deliver better results. The SP study using mystery clients has its own limitations, as it gives outcomes based on recall of unreal patients.

#### PC-523-16 Performance-based cash incentives for tuberculosis screeners in the private sector in Karachi, Pakistan

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**Background:** Performance-based incentives are proving effective in TB control programs to expand access to treatment. We evaluated a performance-based cash incentive system for community laypersons using a multifaceted case-detection strategy in the private sector in Karachi, Pakistan.

**Intervention:** We trained 55 community laypersons to use a mobile phone-based screening and incentive system and positioned them as TB screeners at 54 general practitioner clinics. A flexible yet closely monitored incentive scheme encouraged workers to use innovative case detection strategies tailored to their catchment area. Incentives for case detection included US\$11.80 for smear-positive cases, and US\$5.88 for smear negative or extra-pulmonary cases. With less than 0.5% of persons screened expected to result in a TB case, we provided process incentives for daily reports and a monthly stipend of US\$23.50 for travel support and to encourage retention.

**Results:** Screeners evaluated 372 941 individuals at GP clinics detecting 6472 suspects and 574 tuberculosis cases from January to December 2011. We had

retention rate of 70% and a median monthly disbursement of US\$50 (range US\$25–279) for a screener. A one-way analysis of covariance (ANCOVA) was conducted to determine the mean differences in number of persons screened, TB suspects identified and cases detected for the income quartiles controlling for the covariate of months in the incentive scheme. Pairwise comparisons indicated that statistically significant differences existed between screeners in the highest incentive quartile versus all the others.

**Table** Mean number of persons screened, TB suspects identified and TB cases confirmed by cumulative income quartile of TB screener

Cumulative incentive quartiles USD	No. of persons screened* mean ± SE	No. of TB suspects* mean ± SE	No. of cases detected* mean ± SE	No. of months mean ± SD
Q1 ≤35.7	6 619.9 ± 1363.7	85.8 ± 21.4	6.9 ± 3.3	6.7 ± 3.2
Q2 35.8–51.9	6 126.9 ± 1288.7	78.3 ± 20.2	6.3 ± 3.1	8.9 ± 2.6
Q3 52–68.1	9 515.2 ± 1295.8	130.5 ± 20.3	12.9 ± 3.2	7.9 ± 3.0
Q4 ≥68.2	12 805.8 ± 1469.5	323.2 ± 23.1	28.8 ± 3.6	10.9 ± 1.9

\* Controlling for number of months worked under incentive scheme.

**Conclusions:** Screeners in the highest incentive quartile performed significantly better in process and outcome measures than others signifying flexible performance-based cash incentive models that employ a mix of process and outcome measures are likely to be effective in motivating and retaining TB screeners to increase case detection in low-income, urban settings.

#### PC-524-16 Effectiveness of enhanced case-finding strategies in private-sector settings in Karachi, Pakistan

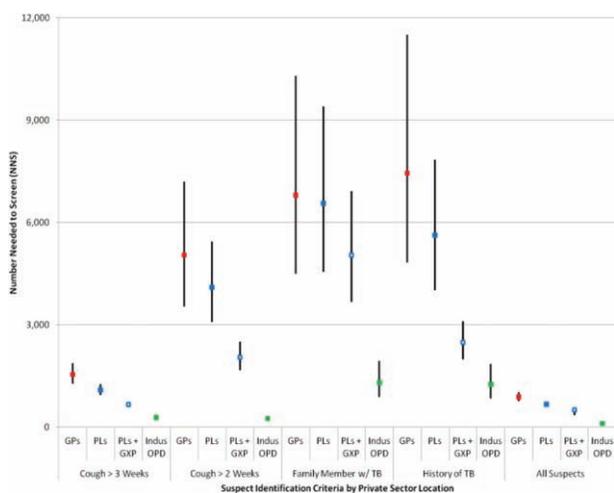
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**Introduction:** Up to 80% of TB patients in South Asia attend private-sector healthcare facilities. Currently we have few estimations of the number of persons needed to screen (NNS) to identify a TB case using public-private mix (PPM) efforts, targeting general practitioner clinics (GPs), laboratories (PLs) and hospital outpatient departments (OPDs).

**Methods:** Enhanced case-finding (ECF) interventions were set up across Karachi with 54 GPs, 7 PLs and a tertiary hospital OPD. At all sites, all persons presenting at the facility were screened for TB symptoms. All TB suspects able to provide a sputum specimen received a smear microscopy test. In PLs, TB suspects also received a chest X-ray (CXR) and, based on self-reported history of TB treatment or their smear and

CXR results, a subset also received a Xpert MTB/RIF test (GXP). The NNS to find a smear-positive or bacteriologically-positive case was calculated by suspect identification criteria (symptoms/exposure), category of site and diagnostic algorithm. The cost per case detected was also calculated across category of site and diagnostic algorithm.

**Results:** From October 2011 to March 2012, 3080 suspects were identified out of 385 676 screened across all three site categories. The NNS to detect a smear-positive case through any suspect identification method was lowest at the OPD [112 (95%CI 100–125)]. Suspects reporting a cough >3 weeks had the lowest NNS across all three intervention types. In PLs, GXP testing lowered the NNS to find a bacteriologically-positive case by 42% compared with smear-microscopy. The cost per case detected was \$180 with GPs, \$127 at PLs, \$160 at PLs + GXP, and \$80 at the Indus OPD.



**Figure** NNS and 95% confidence intervals by suspect identification criteria, intervention site and diagnostic algorithm.

**Conclusion:** Targeting PPM ECF strategies at hospital OPDs was shown to be the most efficient, both in terms of cost and yield in cases. Though initial investments are high, GXP testing can significantly increase case-detection with small increases to the cost per case detected.

## PUBLIC POLICY – 2

### PC-547-16 Costs faced by (multidrug-resistant) tuberculosis patients during diagnosis and treatment

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**Background:** Recently, a tool to measure tuberculosis (TB) patient costs has been developed under TBCAP and implemented in several countries. This tool does not specifically include multidrug-resistant (MDR) TB patients. Patients with MDR-TB face higher costs than patients with susceptible TB, mainly due to longer pre-diagnosis and treatment periods involving more visits and procedures and to relocation costs. With programmatic management of drug-resistant TB (PMDT) programs rolling out, it is important to make available a tool that also generates patients' costs data to support National TB Control Programs (NTPs) in developing policies to tackle bottlenecks in access to and continuation of MDR-TB treatment.

**Design/methods:** We adapted the existing patient cost tool to include MDR-TB patient costs. The modified tool is used to collect data on direct costs, out-of-pocket costs and indirect costs to patients and their families and financial barriers before and during diagnosis, during the intensive phase, and during the continuation phase of treatment in Ethiopia, Indonesia and Kazakhstan.

**Results:** Findings on the magnitude and key components of costs associated with TB and MDR-TB and potential policy options will be presented.

**Conclusion and recommendations:** The development and launch of the tool is one of the critical steps in policy formulation. Building on evidence and understanding of TB and MDR-TB burden on patients and households, a set of recommendations and an action plan for the future to decrease the economic burden of (MDR) TB among patients will be developed.

### PC-548-16 Setting a National Framework for the engagement of tuberculosis treatment supporters: the Nigeria tuberculosis programme experience

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**Background:** The National Tuberculosis and Leprosy Control Program (NTBLCP) co-ordinates TB

control program activities across the 36 states and the Capital City TB control programs in Nigeria. In order to improve adherence to DOTS, the NTBLCP in 2011 developed a national framework for TS engagement.

**Intervention:** A 16-item standard operating procedures (SOP) for TB TS engagement that is patient entered was developed. Steps in the SOP are categorized into; selection of TS by patients, patient and TS education on TB and roles of TS and health care workers (HCWs). Following production of the SOP, the NTBLCP used her quarterly zonal review meetings to introduce the SOP and train the state teams on the use for subsequent step down of the training during various states TB program quarterly review meetings. Copies of the SOP were laminated and distributed. With these copies the various tuberculosis and leprosy supervisors (TBLS) provided on the job training on TS engagement to health care workers (HCWs) at the DOTS centers as they distribute the SOPs to the centers.

**Results and lessons learnt:** The SOP presently is widely used in all the 3931 DOTS centers in the country. In these centers the SOP use has ensured standardized procedure in TS engagement and also has contributed to increased use of TS by TB patients.

**Conclusions:** A program wide standardized engagement of TS that is patient entered is in operation in all the DOTS centers in the country and it is hoped that this practice will ensure improved TB treatment success rate in the NTBLCP.

#### PC-549-16 Expansion with Inclusion: to achieve the target of 90/90 in India

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**Background and challenges to implementation:** India has set a target of 90% case detection and 90% cure rate in the next phase of RNTCP. However, without a paradigm shift in government policies related to private sector involvement, this seems to be over-ambitious, going by the fact that government spend miniscule proportion (around 2%) of its program budget in PPM activities even now and that government still lacks vision in engaging modern medicine doctors in the private sector with the flexibility that the profession demands.

**Intervention or response:** Government has to address the professional concerns of MBBS doctors if it has to bring in real results. Modern medicine (MBBS) doctors' run institutions in private sector should get

the status of peripheral health institutions (PHI) just like any government institution. It is an injustice if we equate such a centre with a DOT centre run by a non-medical volunteer like Anganawadi worker or ASHA worker. Kerala has started to pilot this initiative.

**Results and lessons learnt:** Previously a MBBS doctor has to depend on government centre for each and everything to manage a TB patient if he wants to manage the patient under DOTS. Considering the complexity involved in the public-private sector relationship they were reluctant to do so. But once they are recognised as PHIs, they will have freedom to diagnose, categorise, treat and follow-up their TB patients within the ambit of the program guidelines-supported and supervised by RNTCP program managers, will have RNTCP drugs stocked, can avoid their apprehension of losing private patients; and for the program it will aid in getting all cases reported from private sector, reduce non-DOTS, reduce resistance and improve the reach and quality.

**Conclusions and key recommendations:** This policy change should pave the way for the development of an Indian standard of TB Care, where the government will lay down standards of TB care with due consultation but services will be provided by both public and private sector.

#### PC-550-16 Using a customised 'case finding cohort tool' in the Nigeria tuberculosis programme: a critical initiative in the year 2011 to improve data quality

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**Background:** Data, a major health asset, with quality remains the cornerstone for decision making. The data reporting system within the National TB Program (NTP) starts from the community and peripheral health facility units to the central unit of the NTP. During routine national summary reviews, key data quality challenges observed included discrepancies in disaggregated case finding data; inconsistencies in cohort reports and incompleteness. Moreso, response by state programs to correct noted data errors were usually delayed. In 2010, the NTP customized the existing reporting tools, which was officially introduced in 2011.

**Objective:** To show how the 'case finding cohort' tool helped in reducing data discrepancies and provide quick analysis in the NTP.

**Method:** This is a comparative study of data quality across states in Nigeria pre- and post-development of the tool. The paper based forms were transmitted

into electronic versions and formatted to alert errors, with pop ups of colour coded prompts when erroneous entries were made both for case finding and cohort reports. Automated data analysis was also generated in the tool. Standard operating procedures on the use of tool were developed. Central and zonal officers were trained on the tool which was scaled down to state levels. State programs were further empowered through provision of laptops for electronic transmission.

**Results:** Overall adherence to the use of the tool was 57% (21 out of the 37 states). Using discrepancy as a measure of quality, error rate reduced by 53% (19 states each with at least 2 observed errors in 2010, while 9 states had errors by end of 2011 for at least 2 quarters). All 9 were noted not to have commenced the use of the tool, while 7 other states did not adhere to its use.

**Conclusions:** A key challenge to use of the tool was phobia for info technology by some state programs. All 37 states should be supported to commence and adhere to using the tool in order to reduce discrepancies to the barest minimum.

#### **PC-551-16 The modelised analysis of patient pathway: a systemic approach to improve the quality of tuberculosis control programmes**

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**Background:** Despite the long-standing existence of available and effective drugs, TB still dramatically affects human health and well-being. Instead of investing only in expensive drugs and new techniques that are unaffordable for most countries, there is a crucial need to improve the quality of each step of TB programs.

**Method:** In order to know at what stage and how to improve quality, programs can be assessed easily with the 'Modelized Analysis of Patient Pathway' tool. The MAPP allows following a patient through the different steps encountered from getting TB until being cured. The pathway can be broken down in multiple stages, according to the context, but the basic model is:

Target population\*Incidence\*Perception\*Utilization\*Diagnosis\*Treatment = Number of patients cured

By using this method, problems can be identified at each step, discussed and solved with the program staff, in order to facilitate the passage of patients to the next step. If no simple consensual solution is found, research may be undertaken, especially action research which combines research with sustainable changes. For instance, used in Burkina Faso within the FORESA project, this approach allowed identify-

ing huge direct and indirect costs for TB patients. As a response, actions were taken to decrease the costs. This model involves technical aspects such as diagnostic techniques and behavioral factors (e.g., patient perception) but most importantly it involves operational factors that are directly related to every aspect of quality (e.g., technical, organizational and relational).

**Conclusion:** Breaking down patients' pathways drives health professionals to adopt a new insight, more patient centered into the difficulties faced by TB patients. Throughout the whole analysis, emphasis should be given to the crucial role of health workers, who need to be appreciated and valued for their work. Patients should receive comprehensive care and useful information to be empowered as real actors of their own health.

#### **PC-552-16 The burden of tuberculosis and other lung disease in a large urban hospital in a high HIV prevalence country: the case of South Africa**

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**Background:** South Africa (SA) had 490 000 incident TB cases registered in 2010, of which  $\approx$  50% were smear negative and 15% were extra-pulmonary TB (EPTB). It also has a high TB-HIV co-infection rate estimated at 60%. These epidemics place a huge strain on public health care, including inpatient facilities. We analyzed inpatient records at a large secondary hospital in central Johannesburg to evaluate the burden of TB and lung disease.

**Design/methods:** We selected a random sample ( $n = 1000$ ) of all medical patients admitted to the hospital from January to June 2010 ( $n = 8272$ ). 80% ( $n = 803$ ) of the files were accessible, from which we collected age, sex, HIV status, discharge diagnosis, and length of stay. Mortuary and laboratory records indicated that patients with inaccessible files had similar HIV status and mortality as those included.

**Results:** Of the sample 54% were female; the mean age was 45 yrs; and 45% were confirmed HIV+, 21% confirmed HIV and 34% unknown. TB was the most common diagnosis, accounting for 19% of admissions, with 40% of this attributed to EPTB. The next most common diagnosis was pneumonia (7%). 26% of all admissions involved lung conditions. Inpatient stays averaged 7.4 days, with 23% of bed days related to TB. TB related admissions had a median stay of 7 days, compared to 5 days for non-TB related admissions ( $P = 0.00$ ). Most (87%) TB patients were confirmed HIV+ compared to only 36%

for those without a TB diagnosis. Only 31% of the HIV+ TB patients reported being on antiretrovirals at admission.

**Conclusions/recommendations:** TB-HIV co-infected patients utilized nearly a quarter of all bed days at this general hospital. Improvements in active TB case finding, early diagnosis, and treatment completion would have a significant impact on reducing the burden on inpatient facilities in South Africa. Earlier initiation of antiretroviral therapy for TB-HIV co-infected patients is likely to prevent large numbers of hospitalizations.

### PC-553-16 Tuberculosis infection control measures in health care facilities in Mukono and Wakiso Districts, Uganda

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**Background:** To assess tuberculosis infection control (TB IC) practices in two districts in Uganda.

**Design/methods:** We conducted a cross-section study in 52 health facilities in the districts of Mukono and Wakiso. The survey included; individual interviews with health workers, a facility survey, observations of practices and in-depth interviews with facility managers and TB focal persons concerning barriers to implement TB IC.

**Results:** 34% of the respondents knew that surgical masks do not protect the wearer from getting TB. 56% were aware that TB is more likely to be transmitted in the waiting area than in the TB wards. 12 facilities (23%) had a written TB IC plan. Direct observations indicated that 5 (10%) facilities were screening patients for cough and, though not consistently. Patients, including TB suspects, mingled freely in with other patients in the waiting areas. Only two facilities reported providing masks to coughing patients, with only one giving them only to confirmed TB patients. Less than half (20/52) the facilities had well ventilated waiting rooms. None of the facility had air cleaners, except in one facility. No facility possessed N95 masks. Perceived barriers included: under-staffing, lack of space for patient separation, not all health workers being knowledgeable in TB IC and lack of funds to purchase masks.

**Conclusion and recommendations:** Even simple TB IC measures are not implemented in the health facilities in the two Ugandan districts where the survey was done. Health system factors like, staffing and funds are critical in TB IC.

### PC-554-16 Alarming high failure among polyresistant tuberculosis cases treated with first-line anti-tuberculosis drugs under the National Tuberculosis Programme in Kerala, India

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**Background:** TB patients affected with MTB having in vitro resistance to two or more of the first line anti-TB drugs except rifampicin (non-rifampicin polyresistant TB cases) are currently being treated under the Revised National Tuberculosis Control Program (RNTCP) in India with the standard first line regime for the previously treated which consist of isoniazid, rifampicin, ethambutol, pyrazinamide and streptomycin. The regime which contains most of the same drugs to which the bacilli are resistant could not only fail, but also could favor development of resistance against rifampicin during treatment. We studied various outcomes of treatment of these patients and the sensitivity to rifampicin among patients who failed this regime.

**Methods:** Retrospective cohort study by interviewing the non-rifampicin polyresistant cases treated with standard regime for previously treated. The non-rifampicin polyresistant cases treated with any second line drugs were excluded from the study.

**Results:** Of 128 patients, 30 did not qualify since they were treated with additional second line drugs. Among the 88 patients studied, 50 (57%) failed the regime for previously treated. The failure rates did not differ among the male and the female patients. Of the 23 failed patients subjected for repeated drug sensitivity test, 14 (61%) had developed additional resistance to rifampicin.

**Conclusion:** Standard first line regime for the previously treated is highly inefficient for the patients with proven in vitro resistance to streptomycin, INH and/or ethambutol. The treatment of the polyresistant cases with an inefficient regime leads to the emergence of multidrug resistance. This fact alone necessitates the treatment of these patients with a better regime, which needs to be formulated and efficacy established through controlled trials.

### PC-555-16 Use of smart phones for supportive supervision in Nigeria: a need to collaborate with partners for rapid scale-up

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**Background:** Based on in-country consultations, capacity to provide high-quality TB/TBHIV services is sub-optimal and not unrelated to weak supervision. Within the National TB Program (NTP) in Nigeria, supervision is entirely paper based, time consuming and structured in a way that rapid review of results is not available nor timely resolution of problems.

**Objective:** Describe the value of smart phones in improving quality of supervision.

**Methods:** This is a descriptive study. With the NTP open to exploring innovative ways of strengthening supervision, Health Systems 20/20 in collaboration with the NTP commenced a pilot study on use of smart phones for supervision at health facilities, with focus on 4 states. A stakeholders meeting was convened to fully engage all key TB partners. Situation analysis was conducted in Abia State, a south-east state selected for the pilot, out of which 4 facilities were identified. National and state supervisory checklists were reviewed, programmed and uploaded onto the smart phones. The state TB teams were trained on the use of the smart phone and 6 supervisory visits were conducted within 4 consecutive quarters in Abia State for each facility.

**Results:** Within the pilot sites, the smart phones were noted to be user friendly with rapid review of results done at each visit. Immediate feedback and corrective action for identified challenges were made. A record of previous findings and recommendations could be retrieved on the spot during subsequent visits. The time spent on supervision was reduced to 2 hrs per facility using the smart phones compared to 4 hrs when using the paper based at other sites. With scale up from 4 to 45 DOT centers, the treatment success rate in the state TB program increased from 76% in Q2 of 2011 to 85% in Q1 of 2012 reporting year, for cases registered in the corresponding quarters of the previous year(s).

**Conclusions:** NTP through support of other partners should adopt and scale up the use of smart phones for supervision nationwide.

### PC-556-16 Approaches to reducing financial barriers to tuberculosis diagnostic and treatment tools

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**Background and challenges to implementation:** The increasing number of TB cases, low cure rate and longer treatment period remain a critical stumbling block to progress towards TB control. An improvement in the care of TB patients requires not only new tools but also an expansion of existing tools, while strengthening TB programs overall. TB programs in most countries are heavily dependent on international donor funding, which is expected to decrease greatly over the next few years. Successful uptake of TB tools will require viable strategies and activities to establish financing mechanisms. Intervention or response the approach was developed to assess financing of TB diagnostic and treatment tools and identify financing barriers to maintaining existing TB tools and introducing additional TB tools. Financing options to eliminate access barriers, approaches to optimize a mix of various sources of financing, and strategies to reduce costs including TB drug management were examined.

**Results and lessons learnt:** Addressing TB financing is important to make TB control sustainable in the longer term. The approach was applied to a low income country in Africa to assist country in developing financing strategies and findings will be presented.

**Conclusions and key recommendations:** Developing financing strategies for TB tools will be a recurring challenge, as governments are increasingly expected to contribute financially to health care in an environment of competing needs and scarce resources. The approach will be a critical tool in assisting countries to develop financing mechanisms for TB diagnostic and treatment tools.

### PC-557-16 Intensive tuberculosis screening in HIV-infected persons not yet on antiretroviral treatment, in Macha, rural Zambia

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**Background:** TB is the most common cause of morbidity and mortality in HIV infected individuals in sub-Saharan Africa. WHO estimates that only 50% of TB cases are detected, creating a need to intensify active case finding.

**Design/methods:** All new HIV-infected pre-ART adult patients seeking care at Macha Hospital in rural southern Zambia between April 2010 and March 2012 were screened. Those presenting with a cough, were invited to enroll in the study and asked to produce 3 sputum samples. Information on TB history and exposure was collected from medical records. Per sputum sample a smear was made for Ziehl-Neelsen (ZN) and fluorescent microscopy (FM) staining. Subsequently samples were decontaminated and inoculated onto MGIT culture media. In case of MGIT positivity, a direct smear (ZN) and inoculation of blood agars was performed to confirm mycobacterial growth and to exclude bacterial contamination. Results of ZN and FM staining were compared to the outcomes of the MGIT cultures. Species identification was done using HAIN genotyping.

**Results:** 173 patients producing 493 sputum samples were enrolled. Median age was 39 (range 18–66), 100 (58%) were female, 9 (5%) had a history of TB, and 25 (15%) reported current TB exposure by a household member; 73 (42%) had a CD4 count of  $<200$  cells/mm<sup>3</sup> at enrolment, with 21 (29%)  $<50$  cells/mm<sup>3</sup>; 110 (64%) patients started on ARV drugs between enrollment and April 2012. In 41 (8%) samples of 28 (16%) patients mycobacteria were cultured; in only 28 (6%) samples of 10 (6%) patients these were shown to be *M. tuberculosis* complex (TB). Sensitivity to detect TB was 50% for ZN and 70% for FM, with a specificity of 99% and 83% for ZN and FM respectively. 18 (10%) patients died, of whom 7 (39%) were confirmed TB patients, 3 of them were on TB treatment.

**Conclusion and recommendations:** The prevalence of TB in this cohort of HIV-infected pre-ART patients was lower than anticipated and reported earlier. This could be related to the strict definition of TB (positive culture with *M. tuberculosis* complex), but could also be associated with the extensive roll-out of ART since 2005 in this area. Using ZN only, 50% of TB cases would have been missed. Although FM has a much higher sensitivity than ZN to detect mycobacteria, it also overestimates the number of 'TB' cases, potentially leading to unnecessary TB treatment.

**PC-558-16 Advocacy, communication and social mobilization as a convergence and sustainable tool for universal access in India: Satara, a model Axshya District**

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**Background:** The vision of the Government of India is for a 'TB-free India' until it is no longer a major

public health problem. To achieve this vision, the Revised National Tuberculosis Programme (RNTCP) has now adopted the objective of universal access for quality diagnosis and treatment for all TB patients in the community. 'Project Axshya' is being implemented in 300 districts in India led by The Union under Global Fund Round 9. Satara is one of the Project Axshya Districts in Maharashtra and it has been chosen as Model Axshya District to implement ACSM activities since April 2011.

**Intervention:** Satara–Model Axshya District aimed to reach 2.8 million people with its key stakeholders through ACSM activities. Departments in the District like Health, AYUSH, Education, Agriculture, Panchayatraj, Revenue, Rural, Women and Child and Youth have been advocated to integrate TB care in their activities. Sensitization programmes were organized for schools, colleges, selected private industries, self-help groups (SHGs) and private pharmacists. Innovative mass media communication strategies were used. Satara District RTNCP believed and adopted ACSM as a convergence model to bring in other players for TB care.

**Results:** Now, Satara is a Model Axshya District in India implementing ACSM activities on its own under RNTCP for scaling-up quality improvements focused on health systems management, health worker performance, effective delivery of intervention mix and health technologies towards improved RNTCP outcomes since April 2012. The community representing 'TB Forum' is facilitating District ACSM Project Implementation Plan (PIP) for the period 2012–2013.

**Conclusion:** ACSM entails sustaining the achievements of the programme to date, extending the reach and quality of services to all. Further, ACSM addresses the issue of health in the context of sector-wise approach addressing basic determinants of good health in order to have greater convergence among related sectors.

**PC-559-16 Effectiveness of patient referral and linkage to care from community active tuberculosis case-finding efforts in Kampala, Uganda**

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**Background:** Community active case finding efforts are valuable in identifying additional undiagnosed TB cases. For these efforts to accrue benefit, patients must be linked to appropriate care. However, it is quite unclear how effective patients follow-up referrals after diagnosis.

**Objective:** To evaluate the effectiveness of patient referrals in community active TB case finding efforts.

**Methods:** A cross-sectional study was conducted in Rubaga division Kampala. Residents aged 15 years or older with cough for two weeks were screened for active TB using smear microscopy and/culture. Smear positives were referred to Mulago National Referral hospital TB clinic or a local public health center and smear negative were referred to local public health centers for treatment. Follow-up visits at points of referral and participants' homes was made.

**Results:** Out of 5103 residents screened, 56 (1.1%) had active TB. Of these, 41 (73.2%) were treated and 9/56 (16.1%) failed to go while 6/56 (10.7%) were lost to follow-up. Among those treated, 13/41 (31%) reported the day referral was due and 12/41 (30%) went within 2–7 days whereas 16/41 (39%) reported after a week. The most common reasons for failure or delay was lack of transportation money, the fear of family members to know about their TB status and feeling much better after using antibiotics whereas that for going on time was the fear of worsening the condition.

**Conclusion:** Referral and linkage to care for new TB patients from community active TB case finding is effective but, innovative and sustainable strategies that ensure timeliness are needed.

#### PC-560-16 Perspectives of community-based approaches for tuberculosis case finding in southern Ethiopia: qualitative research to support sustainability

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**Background:** Since 2010 an innovative community-based TB intervention project has been implemented in Sidama, southern Ethiopia, with female community based health extension workers (HEWs) and their supervisors. The project has doubled the number of TB cases identified and improved treatment outcome among rural populations with limited access to health services. Qualitative research was used to understand the experiences and perspectives of key constituents; support the ongoing intervention and assess its sustainability.

**Methods:** Qualitative interviews were undertaken with purposively sampled participants: TB suspects/patients who had undergone screening by HEWs ( $n = 21$ ), HEWs and promoters ( $n = 20$ ) supervisors ( $n = 5$ ) and laboratory technicians ( $n = 14$ ). Focus group discussions were conducted with HEWs, supervisors and laboratory technicians ( $n = 5$ ). A framework analysis approach was undertaken.

**Results:** TB suspects/patients had learnt about TB

from HEW mobilization activities, they found free community-based TB services acceptable and convenient. Poverty was a major barrier to diagnosis in the past, especially for women, and the elderly. Smear negative cases were anxious about next steps. HEWs/supervisors were motivated by involvement in preventive and curative work, supporting communities, and prospects of career development. Ongoing commitment at higher levels was considered a potential challenge. Laboratory technicians recognized that the intervention increased smear-positive TB diagnosis. They benefitted from the intervention but were initially challenged by the quality of slides prepared by HEWs in the community which is improving after giving feedback.

**Conclusion:** Service users and providers found the intervention highly acceptable and most challenges were overcome with training and regular feedback. Assessing the perspectives of patients and stakeholders using a community based approach is vital to gauge the both the suitability and sustainability of interventions.

#### PC-561-16 Voices from the diagnostic window for tuberculosis in Ethiopia

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**Background:** Not all adults with chronic cough complete the submission of sputum specimens required for diagnosis of TB. Much has been reported about the barriers faced by TB suspects to reach diagnostic services and by patients to adhere to treatment, but few studies have explored patient experiences during the diagnostic process—a crucial window for accessing treatment. Here we report the patient experience during their diagnosis as part of a larger study to identify factors inhibiting and facilitating completion of diagnosis.

**Methods:** The study, based in 2 health centres in Southern Ethiopia, included in depth interviews and focus group discussions with patients that completed the diagnostic process (51; 6) or registered for treatment (20; 3). A thematic analysis was conducted within a 'contextualist' research paradigm.

**Results:** Key factors influencing completion of diagnosis and treatment registration included physical and geographical, economic, socio-cultural, support and knowledge of the diagnostic process and disease. Patients were constrained variously by distance and travel, clinic fees, loss of earnings, the attitude of health professionals, a perception that private health-care was superior, lack of understanding about the need for repeated tests and clinic appointments and receipt of a clinical diagnosis based on negative

smears and X-ray results. Enabling factors included a supportive home and work environment, a realistic expectation of the length and routine of the process, knowing someone with TB and attendance following personal recommendation.

**Conclusion:** Patient experiences were mediated by socio economic status, education, gender and residence. Sensitising health systems to the factors shaping patients' experience of the diagnostic pathway may improve both diagnostic completion and treatment adherence. The barriers faced by symptomatic adults in the community are likely to be greater and warrant further exploration.

### PC-562-16 Active tuberculosis and labour force participation in low- and middle-income countries: results from the World Health Survey

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**Background:** TB presents a significant economic burden to affected individuals and their families as well as the society, disproportionately so in low- and middle-income countries (LMICs). Aside from the direct medical costs, patients with TB may also bear the indirect costs of the disease in the form of lost productivity. This study examined the association of active TB and labour force participation in LMICs.

**Design/methods:** This study used data from a sample of 153 805 adults aged <60 in 50 LMICs in the World Health Survey. Country-level random-effects logistic regression was estimated to examine the associations of active TB symptoms with 1) labour force participation and 2) illness as the main reason for not working for pay among individuals who were not working. Covariates included age, level of education, marital status, and urban-rural setting. Both models were estimated separately by gender.

**Results:** Males with active TB symptoms were less likely to be in the labour force (odds ratio (OR) 0.87 [95% confidence interval (CI) 0.80–0.93]), while females exhibited a small and statistically insignificant association (OR 0.98 [95%CI 0.92–1.03]). Among individuals who were not working, those with active TB symptoms were more likely to cite illness as the main reason for not working for pay for both males and females (OR 2.03 [95%CI 1.70–2.42] and OR 2.1 [95%CI 1.83–2.46], respectively).

**Conclusion and recommendations:** Having active TB symptoms is associated with a lower likelihood of labour force participation in LMICs. These results highlight the importance of addressing the TB problem for both population health and economic development in LMICs.

## SURVEILLANCE, TUBERCULOSIS SCREENING AND HIV TESTING

### PC-580-16 Integrating tuberculosis case detection information in medical clinical records improves tuberculosis screening and detection among HIV and AIDS patients: a case TASO Uganda

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**Background and challenges to implementation:** Globally 9.2 million new TB cases and 1.6 million deaths occur annually, 16% of new TB patients are HIV positive (WHO, 2009), Uganda estimated 70% of TB cases are HIV positive (NTLP, 2007). In 2010 out of 82 114 (94%) of TASO registered clients screened for TB, 1960 (2.4%) were diagnosed with TB and treated (TASO MIS). Globally case target detection target is 70% of infectious TB and successfully treat 85%. Uganda detection rate is 60.1%, cure rate 62.2% (HSSP II), integrating TB screening tool reminded clinicians to screen for active TB in TASO.

**Intervention:** This involves completing clinical record forms by assessing if the patient enrolled for TASO care is symptomatic for TB using a screening tool. Patients who screened positive for one or more signs/symptoms were further investigated to confirm active TB by sputum analysis, chest X-ray, lymph node aspirates and pleural tap for analysis. Cases with confirmed TB received respective treatment as they continue to attend the usual medical review on appointment.

**Results and lessons learnt:** Overall percentage of patients screened for TB improved from 78% to 98% between fourth quarter 2011 and first quarter 2011. Of those screened the percentage of patients with at least one or more positive signs/symptoms increased from 23.3% to 42.5% within the same period TASO Tororo MIS, out of those with a positive screen who took a test, the percentage of patients diagnosed with TB increased from (26/126) 15.9% to (38/141) 27% within the same period.

**Conclusions and key recommendations:** Integrating screening tool in clinical record will; prompt clinicians to screen for active TB at each clinic visit, allow continuity and quality of TB care, prevent unmasking of TB through immune reconstitution syndrome in patients with lower CD4 cell count initiating ART and monitors TB investigation results, treatment, progress and outcomes.

**PC-581-16 Active tuberculosis surveillance could improve the linkages between tuberculosis and HIV care: an impact assessment of a self-developed system in a rural district of Zambia**

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**Background:** Early identification of HIV infection among TB patients and timely initiation of HIV care for TB-HIV co-infected patients has remained as big challenges in countries with high prevalence of HIV infection. Our operational research aimed to evaluate whether active TB surveillance system developed by ourselves improved the linkages between TB and HIV services in a resource-limited district, Zambia.

**Methods:** Active TB surveillance system was developed by Chongwe district medical officers in 2011. Health facility staffs in the district are given special designed forms including some essential variables related to TB and HIV care. The filled forms are sent to the district medical office where the information is entered into the electronic surveillance system made with CDC-Epi Info ver. 3.5.3. The indicators associated with TB-HIV collaborative activities between 2009 and 2010 were compared with those after the introduction of the system in 2011 to evaluate the effectiveness of our system.

**Results:** Median age (33.0 vs. 32.0 years) and gender balance (female 42.4% vs. 44.4%) between before and after the surveillance system started did not show any differences. HIV testing rates among TB patients also showed no statistical differences (88.0% vs. 82.0%). Although the percentage of those who were enrolled into HIV care among TB-HIV co-infected patients was poor in 2009 and 2010 (43.1%), that was dramatically improved after the system was introduced in 2011 (72.1%,  $P < 0.01$ ). The percentage of ART initiation within 2 months after anti-TB treatment starts was also significantly improved from 32.3% to 52.1% ( $P = 0.02$ ).

**Conclusion:** Remarkable improvement in the linkages between TB and HIV services were observed in our research. Active TB surveillance system might contribute to not only improving the linkages but also improving the outcomes of co-infected patients. More efforts to achieve the goals in which all TB-HIV co-infected patients were enrolled into HIV care require to be made.

**PC-582-16 Monitoring the trend of the desire for HIV counselling and testing in Nigeria: reference for policy measures and appropriate strategies for procurement**

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**Background:** HIV counseling and testing (HCT), is the gateway for the prevention, and impact mitigation of HIV.

**Methods:** Data used was from the National HIV/AIDS and Reproductive Health Survey (NARHS) conducted across the 36 states and the Federal Capital Territory (FCT) in Nigeria in 2003, 2005, and 2007 by the Federal Ministry of Health. A total of 28 956 men and women who have ever heard of AIDS or HIV, aged 15 to 64, male: 15 612, and females: 13 344, were included in the data used for this paper.

**Results:** At the bivariate level, analysis shows significant increase in the trend for desire for HCT among respondents; 2003:41.7%, 2005:43.5%, and 2007: 72.4% ( $P < 0.0001$ ). At the multivariate level, respondents in 2007 were 200% more likely to be tested for HIV than those interviewed in 2003 (OR = 3.657, 95%CI 3.431–3.899,  $P < 0.0001$ ). Findings showed significant association with knowledge of HIV transmission and prevention. Respondents who had complete and correct knowledge of HIV prevention were 80% more likely to desire HCT compared with those who have no such knowledge (OR = 1.804, 95%CI 1.715–1.897,  $P < 0.0001$ ).

**Conclusions:** Access to HCT should be enhanced. Uninterrupted supply of HIV kits should be top priority for policy makers and implementers. The proportion of those who have missed opportunities for HCT should be estimated for improved planning and procurement of HIV test kits.

**PC-583-16 Scale-up of provider-initiated HIV testing and counselling for tuberculosis patients in Viet Nam**

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**Background:** The World Health Organization recommends provider-initiated HIV testing and counselling (PITC) for all TB patients. In Viet Nam PITC has been implemented since 2008 and was expanded to 26 provinces in 2011, with counselling and testing offered by TB program staff.

**Methods:** HIV testing and referral data were analyzed from routine quarterly reports of 114 TB sites in 26 provinces from 2008 to 2011.

**Results:** Among 99 763 registered TB patients who

were offered PITC, 3791 (4%) were already known to be HIV-infected. Of 95 972 TB patients with unknown HIV status, 86 225 (90%) received HIV counseling and 83 391 (97%) of these agreed to testing. A total of 2046 patients were newly diagnosed with HIV infection for an overall HIV prevalence in TB patients of 6%. Of the 5837 known HIV-infected TB patients, 61% were successfully referred to HIV care facilities (59% in 2008, 51% in 2009, 63% in 2010, 66% in 2011), 36% had a documented CD4 cell count, 80% received co-trimoxazole preventive therapy (CPT), and 32% received antiretroviral therapy (ART) during TB treatment (27% in 2008, 17% in 2009, 33% in 2010, 43% in 2011). There were significant trends ( $P < 0.001$ ) for HIV-infected TB patients in proportions of successful referral and ART.

**Conclusions:** 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 ART indicate that barriers remain and greater efforts are needed to provide standard HIV care and treatment.

#### PC-584-16 HIV surveillance in India: an overview and implications for the future

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**Introduction:** Surveillance of risky behaviors of HIV infection and its manifest diseases has provided a better understanding of the complex nature of the HIV epidemic in India. However, little attempt is made to analyse progress of these surveillance activities.

**Methods:** A review and analysis of surveillance activities undertaken in India was done. Pub-med, cochrane library and peer-reviewed journals were referred for relevant literature.

**Results:** Initially, medical officers from multiple types of government hospitals in India were expected to report AIDS cases, including deaths. However, this reporting mechanism was inadequate, complicated by many disparate types of reporting units with incomplete and delayed reports. Therefore AIDS case reporting has been replaced by HIV case reporting from the 4532 integrated counseling and testing centers. Newer surveillance strategies like behavior sentinel surveillance measure behaviors that affect risk for acquiring HIV. However, behavioral and biological data are resource-intensive and time-consuming. Starting with 55 urban sentinel sites HIV sentinel surveillance expanded to 1215 in 1994. Most of these pre-selected sites are antenatal clinics but also include sexually transmitted infections clinics and special facilities.

**Conclusions/lesson learned:** While acknowledging the vastness and diversity of India, the key limitations

remain suboptimal coverage and lack of representativeness surveillance data. Moreover, due to selection bias, the populations selected for HSS at targeted intervention sites may not represent everyone in that community. There is lack of national information system to collect HIV testing information from the private sector. Further efforts are needed to improve HIV surveillance data and usage of this data to predict the epidemic.

#### PC-585-16 Assessing the microbiological effectiveness of HIV care using dried blood spots in DR Congo

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**Context and rationale:** The national TB and AIDS programmes of DR Congo, and The Union IHC program on TB-HIV coinfection in the province of North Kivu, East DR Congo implemented ART in HIV-TB for the past 5 years. We previously showed that dried blood spots (DBS) allow viral load measure and HIV genotyping.

**Objective:** Assess the feasibility of assessing microbiological antiretroviral treatment (ART) outcomes using DBS in the context of national programmes routine operations.

**Methods:** After ethics clearance, 95 HIV-TB cases with 12 months ART and 23 ART-naïve HIV-TB cases were recruited from the HIV register of 13 health facilities and sampled whole blood on DBS further thoroughly packed with desiccant and stored at  $-12^{\circ}\text{C}$  in health facility freezer. They were collected through TB program regular supervision before being shipped to 2000 km distant national AIDS reference lab, and further to WHO reference lab in France

**Table** Viral load in patients on and without ART, and gene amplification success rate

Group	ART M12	ART naïve	
N	95	23	
VL $\geq$ 1000 copies/ml (positive)	38 (40%)	18 (78%)	
300 < VL < 1000 copies/ml (test threshold)	23 (24%)	3 (13%)	
VL < 300 copies/ml	54 (57%)	2 (9%)	
Gene amplification in the 56 patients with VL $\geq$ 1000 copies/ml:			
	VL $\geq$ 1000	1000 <VL < 5000	VL $\geq$ 5000
Reverse transcriptase	40/56 (71%)	16/28 (57%)	24/28 (86%)
Protease	47/56 (84%)	19/28 (68%)	28/28 (100%)

No resistance mutation was observed in ART naïve patients. Mutation profiles will be presented.

for viral load (VL) measure and HIV genotyping. VL was measured with Biocentric assay, and genotyping followed the ANRS protocol, modified for DBS.

**Results:** Mean time between sampling and storage at  $-80^{\circ}\text{C}$  is 3.5 months. Viral load results and amplification success are presented in the Table.

**Conclusions:** Our data show that DBS sampling for viral load and genotyping make feasible the use of microbiological indicators to assess the success of ART programs in low-income countries, including in the most difficult operational conditions. The observed level of virological failure after 12 months ART calls for urgent solutions to improve adherence to ART before any further ART scale-up, in order to protect HIV sensitivity. Although possible from a 1000 copies/ml VL, genotyping success is high from 5000 copies/ml. Test cost remains high for use on an individual patient basis, but virological outcome and HIV sensitivity assessment can be done through regular surveys.

#### PC-586-16 Evaluation of screening for HIV-associated tuberculosis in Indonesia

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**Background:** HIV-associated tuberculosis remains a major public health problem and a diagnostic challenge. Screening algorithms have been developed and adopted by the WHO. We examined daily practice regarding tuberculosis screening among HIV-infected patients in Indonesia, which has a rapidly growing HIV-epidemic and a high burden of tuberculosis.

**Methods:** We selected ART-naïve patients with information on tuberculosis from an open cohort of HIV-infected patients in a referral hospital in West-Java. Hospital guidelines have introduced universal symptom screening, chest X-ray and sputum examination at time of enrollment in HIV-care. We compared screening practice before and after introduction of a screening algorithm, and evaluated the predictive value of symptoms.

**Results:** 754 patients were enrolled before introduction of screening, 594 afterwards. A similar proportion of patients had symptoms suggesting TB in both periods, with weight loss being the most common symptom. More sputum examination and chest X-rays were done after implementation of screening, and bacteriological confirmation of TB was more common (Table). Overall, 229 patients (16.9%) were started on TB treatment, of whom 9% had bacteriologically proven TB. At the same time, 47 patients with culture-proven TB did not receive TB treatment.

	Before implementation of screening ( <i>n</i> = 754) <i>n/N</i> (%)	Afterwards ( <i>n</i> = 594) <i>n/N</i> (%)
CD4 cell count, median [IQR]	71 [17–296]	62 [14–257]
TB suggestive symptoms		
Fever	283/754 (37.5)	180/594 (30.3)
Weight loss	265/754 (35.1)	239/594 (40.2)
Cough	156/754 (20.7)	141/594 (24.5)
Sputum examination		
Microscopy-positive	21/27	37/93
MTB culture positive	9/27	24/92
Chest X-ray performed		
Suggestive for TB	60/115	98/150
TB treatment		
Microscopy/culture-positive	6/143	14/86
Culture-positive, no treatment	18/143	29/86

**Conclusion:** HIV-associated tuberculosis is often suspected but rarely confirmed in this setting in Indonesia. Efforts should be made to improve implementation and accuracy of the WHO-proposed screening algorithms for HIV-associated tuberculosis. Better use should be made of radiological and microbiological examination, and point of care testing should be implemented in HIV-clinics in Indonesia.

#### PC-587-16 Contribution of CBOs to active case finding among contact people living with HIV/AIDS in Burkina Faso

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**Background and challenges to implementation:** According to WHO detection rate of the country is 55/100 000 smear-positive pulmonary tuberculosis. HIV prevalence is around 1.2%. PLWHA is a high risk group because of the high risk linked to tuberculosis. NTP and civil society actors established a partnership to reinforce collaborative TB-HIV activities.

**Intervention or response:** The intervention aim to detect earlier TB cases among PLWHA by reducing the two delays and barriers. The strategy included chronic cough screening during outreach awareness activities on TB (educational talks, support groups discussion) made by 30 CBO's involved in HIV community based care. Chronic cough identified received a reference (card) to the DTC.

#### Results and lessons learnt:

Around 30 outreach activities conducted by the CBO's during period. The detection rate of 79.55/100 000 is more than 2 times higher than general population and greater than the notification in the total group PLWHA (51.09/100 000). The contribution of the active cases finding among PLWHA of the country is around 1% of total TB cases detected smear positive in 2011 (35/3934).

PLWHA touch in 2011	Number of PLWHA chronic cough receiving card (%)	Number of PLWHA received at DTC	Number of PLWHA tested by smear exam	Number of PLWHA detected smear positive	Number of PLWHA smear exam positive by 100 000 habitant
12257	243 1.98%	203 83.54%	193 95.07%	35 18.13%	79.55

**Conclusions and key recommendations:** Some cases referred by association missing to count because of difficulty to measure the other form of TB detected after reference and probability that some people referred came without their card. The result achieved used to establish new TB-HIV indicators taking in account all TB form detected by referral for global funds round implementation and to increase earlier cases detection. A study also planned to measure this cases finding strategy.

## EXPANSION OF THE STOP TB STRATEGY – 2

### PC-605-16 Reducing tuberculosis patient delays: frequency and causes

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**Background:** TB active case finding approaches requires better information than currently exists regarding the causes of patient delays in approaching TB services. Reducing TB patient delay in receiving TB diagnosis and treatment will reduce transmission in the community and improve patient's quality of life. We analyzed causes contributing to TB patient delay in two high burden countries: Bangladesh and Swaziland.

**Design/methods:** Under the USAID TB CARE II Project we developed structured questionnaires that were administered to TB patients, public and private providers, community/NGO leaders and NTP managers. Total sample size in Swaziland 441 and 120 in Bangladesh. Data was collected to measure time delays and causes contributing to patient delay in each country. Data was analyzed using SPSS and level of significance was obtained.

**Results:** TB patient delay was higher (double) than TB health system delay in both countries, 57 vs. 20 days for Bangladesh and 67 vs. 36 days for Swaziland. Main factors: Patients were unaware of the severity of the symptoms; mostly in patients with TB-

HIV coinfection in Swaziland (40% did not have cough), long distance and transportation costs to facilities (Swaziland), fear of stigma mostly associated to HIV (Swaziland); and fear of job loss (Swaziland and Bangladesh). Women in Bangladesh presented a 32% longer delay in seeking initial care compared to males (41 days vs. 31 days). 60% women said they need permission from husband/relatives to access health care. 20% of women sought initial care from untrained village healers compared to 4% of males. 50% TB patients in Bangladesh sought care from public providers vs. 87% in Swaziland.

**Conclusion and recommendations:** Strategies to reduce TB patient's delay should be targeted to the different causes found to play a major role in each country. An initial assessment of those causes should be conducted to guide program implementers in expanding the TB DOTs Strategy.

### PC-606-16 Beyond collaboration: exploring partnership with the corporate sector for sustainable tuberculosis control activities in Bangladesh

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**Background:** The Bangladesh National TB Control Programme (NTP)'s five-year Strategic Plan 2006–2010 emphasised the involvement of the corporate sector to provide TB services at workplaces, in line with WHO recommendations for TB control expansion. However, key questions remained about how to operationalise and sustain standardised TB services at workplaces. Therefore, we conducted an operational research to develop a sustainable workplace TB intervention, focusing on garment factories of Dhaka City.

**Design/methods:** The study was carried out jointly by the NTP, four NGOs and the Bangladesh Garment Manufacturers and Exporters Association. The project had four phases: collection and analysis of data to inform development of a TB workplace model that could feasibly be scaled up; development and implementation of the model; collection and analysis of post-implementation data for evaluation; and dissemination of results and discussion of implications with stakeholders. Strategies, protocols, guides and tools were developed with stakeholders. We assessed the impact of the project using quantitative and qualitative measures.

**Results:** The project brought positive changes in knowledge, attitudes and practices of managers, workers and health care providers on TB care and

control. During 2008–2010, a total of 3372 workers from a workforce of 69 000 were referred for sputum microscopy and 598 were diagnosed with smear positive TB, 145 of which received care at their workplace. Workers who previously would have hidden their disease, resigned from their work or been dismissed because of their TB are now able to continue to work normally.

**Conclusion and recommendations:** It is feasible to engage corporate sector in TB control activities in Bangladesh, and thereby increase case notifications, improve treatment outcomes and improve patients' quality of life. This approach is now being scaled up across other garment factories in Bangladesh.

### PC-607-16 High yield of community-based TB-HIV intensive case finding in rural South Africa

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**Background:** WHO-recommended Intensive Case Finding (ICF) has been used primarily in health care settings; there is limited data regarding its utility at the community level. We present data on the yield of community-based ICF in rural South Africa.

**Methods:** Nurses, health educators, and HIV counselors visit rural congregate settings, including taxi ranks, secondary schools, social grant pay points, and municipality and home-based care events. They offer health education and voluntary integrated screening for TB and HIV. Those with TB symptoms are asked to submit sputum for microbiological examination; TB therapy is managed by the local DOTS office. Those eligible for ART initiation are referred according to national guidelines.

**Results:** From March 2010 to October 2011, 186 community visits were conducted; 4204 people accepted screening. Median age was 42 years (IQR 21–57); 2991 (71.1%) were women. Cough of any duration was reported by 1014 (24.1%). Sputum specimens were collected from 812 (19.3%) TB suspects. Ten (1.4%) had AFB+ sputum; 24 (2.9%) were culture positive, representing 26 total cases. Nine (37.5%) were MDR/XDR-TB; all were found alive and referred for treatment. The number needed to screen was 350 to find one AFB+ case and 175 to find one culture positive TB case. HIV testing was accepted by 3875 (92.2%) screeners; 297 (7.7%) were HIV positive, with median CD4 cell count of 358 (IQR 236–536). Of 20 TB cases tested, only 2 (10%) were HIV coinfecting. The microbiologically confirmed TB notification rate was 619/100 000 overall, and 214/100 000 for drug resistant TB.

**Conclusion:** Rural, community-based TB-HIV inte-

grated ICF identified a large number of TB suspects and high rates of TB and MDR/XDR-TB, but a low proportion of TB-HIV coinfection. Community-based ICF for TB-HIV is a feasible, acceptable and high-yield strategy in high prevalence settings. Early community-based TB-HIV diagnosis may reduce transmission, improve outcomes, and decrease community TB burden.

### PC-608-16 Strengthening facility and community structures increases access to TB-HIV services: lessons from East Central Uganda

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**Background and challenges to implementation:** In Oct 2009, the nine districts of east central Uganda had poor TB-HIV indicators due to poor service delivery at facility and community level. HCT uptake was 61%, CPT and ART enrollment was 66% and 17% respectively. 52% of HIV patients were screened for TB in HIV care settings. This was mainly attributed to, knowledge gaps in TB-HIV co-management and gaps in TB-HIV care linkages.

**Intervention or response:** JSI with funding from USAID is implementing the STAR-EC program that supports the National TB and Leprosy program to strengthen TB activities in the districts. STAR-EC supported the training and mentorship of healthcare providers in 80 facilities using district based teams of trainers on TB-HIV co-management, synchronization of TB and HIV care appointments and physical referral of clients to either TB or HIV clinics: trained people living with HIV infection and village health team members to sensitize the communities on the relationship between TB and HIV and referral of suspects to facilities.

**Results and lessons learnt:** Over a period of 21/2 years, there has been progressive improvement in the TB-HIV indicators. 99% of TB patients tested for HIV, 99% and 72% of co-infected patients started on CPT and ART respectively. 97% of HIV patients are screened for TB. Using district teams of trainers for quick scale up of the trainings to lower level facilities and synchronization of patients' appointments leads to realization of results.

**Conclusions and key recommendations:** In order to increase TB-HIV integrated services, there is need to train providers at facility level, synchronize appointments and involve community level workers.

### PC-609-16 A 'Blitz' approach to active tuberculosis case finding in the community, Eastern Province, Zambia

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**Background:** Zambia has TB notification rate; of 375/100 000 with an estimated case detection rate of 58% while Eastern Province has a notification rate of 166/100 000. Despite many achievements, TB case detection remains a challenge in the Province due to long distances, few diagnostic centers, and shortage of qualified staff. In February 2011, Eastern Province staff planned an intensified ('blitz') approach to active TB case finding.

**Objectives:** To determine whether an intensified approach to TB case finding using community sputum collection points will increase detection of TB cases.

**Intervention:** Provincial Health Office with Districts came up with an intervention to intensify TB cases. A plan was mooted to establish temporary posts where sputum was collected. Posts were located in areas with high numbers of TB patients, people living with HIV and in prisons. Health centre staff and community-based volunteers sensitized and encouraged persons with a cough for sputum collection. District Health Offices provided training and supervision. Volunteers that participated were provided with a small stipend. Provincial Health Office coordinated and supervised implementation that took two weeks. Additional laboratory staff were allocated to examine the sputum specimens.

**Results:** Through active TB case finding intervention, 1897 TB suspects presented to posts; 1740 (92%) had sputum examined and 35 (2%) had positive smears and were put on TB treatment. This represented 15% (35/227) of smear positive cases notified for 1st quarter 2011. Six cases detected were from the prisons. The response from the community was overwhelming. The cost of the activity was US\$7875 for reagents and logistics.

**Conclusions:** Our 'blitz' approach to active TB case finding in the community showed that many additional cases can be identified with relatively inexpensive, focused approaches. These cases can be treated earlier and thus reduce transmission of TB in the community.

#### PC-610-16 Exploring the effectiveness of incentivising health staff for increased case detection in 47 health facilities of five provinces in Afghanistan

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**Background:** Despite great contribution of Afghanistan's integrated health care system in TB control, TB cases are missed in many health facilities (HFs) due to high workload and low interest in TB work. As part of strategy to improve case detection, under TB REACH wave 1 grant, ATA-AP/ACREOD provided an incentive of US\$10/additional SS+ case detected which was distributed among doctor, nurse and lab

technician. This aimed to explore effectiveness of health staff incentivizing in increased case detection.

**Design/methods:** The intervention targeted 47 HFs with low case notification as compared to estimated prevalence and catchment population. Additional supports as training, frequent supervision/monitoring visits and incentives were provided. Achievements towards quarterly set targets were monitored through visits and review meetings. This project compared the NTP Q4, 2009–Q3, 2010 data (baseline) with the Q4, 2010–Q3, 2011 (project's lifetime) data in 47 target and 12 control HFs to find additionality.

**Results:** In 47 target HFs, the SS+ case notification increased overtly from 1378 (baseline) to 1986 (project's lifetime) while slightly from 135 in baseline to 157 in 12 control HFs. The project tested an additional 9820 suspects and achieved 93% of its target SS+ cases. The total cost of the incentives was US\$6080.

**Conclusion and recommendations:** Small monetary incentives greatly affected underpaid health staff, encouraged them to spend time on TB screening and timely diagnose and treat TB patients. In addition, the volume of cases detected has convinced skeptical health care workers of the real magnitude of TB problem in their respective areas going forward.

#### PC-611-16 Successful integration of TB-HIV care: case of a rural setting

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**Introduction:** Tuberculosis (TB) is the leading cause of morbidity and mortality among people living with HIV (PLHIV) while human immunodeficiency virus (HIV) is the greatest risk factor for TB. Control of the dual epidemic in resource limited settings calls for integrating of service delivery despite challenges faced.

**Settings:** A rural hospital in Western Kenya where TB care is provided by National TB Program (NTP) under the Ministry of Health (MoH) while HIV care is run by USAID-Academic Model Providing Access To Health Care (AMPATH) partnership. Poor tracking systems, lack of harmonization of both treatment progresses, increased default to care and staff shortages were among setbacks to successful treatment. In the NTP 4th quarter report 2009, 54% of the TB-HIV co-infected had no evidence of being on HAART.

**Intervention:** Situation analysis was done by stakeholders and a team formed to oversee integration. MoH and AMPATH staff capacity built to be able to work in both TB and HIV clinics addressing shortages. The TB clinic was moved into the HIV care clinic, files for TB-HIV co-infected patients tagged for easy identification and prompt updating of HIV care

indicators in TB recording and reporting documents. Routine monitoring addresses arising challenges.

**Results:** Improved treatment outcome: 1st quarter NTP report 2012 shows 90% patient retention rate with 87% cure rate, 75% clinic attendance up from 67% in the 4th quarter NTP 2009 report. There was improved working relationship among both clinics' staff.

**Conclusion:** Successful integration of HIV and TB care is viable in resource limited rural settings. One-stop shop kind of care is convenient. There is need for a National TB-HIV Integration Committee for harmonization and creation of a national treatment/appointment card for TB-HIV co-infected patients.

### PC-612-16 Humanising tuberculosis case detection and treatment through implementation of Rural DOTS in 3 provinces of Afghanistan: Wardak, Samangan, Sar-e-Pul

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**Background:** 2 million people are living in Samangan, Sar-e-Pul and Wardak provinces in rural areas with high social stigma, overcrowding, population density, poor sanitary facilities, limited access to health services (66%) and TB indicators and, thus TB has become one of the major causes of death in these provinces. SCA aimed to assess the impact of Rural DOTS implementation in these provinces.

**Methods:** SCA Health Management Teams visited 78 health centers from January to March 2012. They conducted 78 supervisory visits and collected data from January 2010 to December 2011 through National TB recording/reporting checklist, structured questioners, review of TB treatment cards, TB medical records and TB register book in health centers.

**Results:** In 2010, 59 health facilities were involved as DOTS diagnosis and treatment centers that covered 42% of population, while it increased to 78 centers and covered 64% of population with free access to DOTS services. In 2010, 16 196 TB suspects were examined for AFB, 505 were SS+, 78 were relapsed, 573 start DOTS treatment and NSS+ conversion rate

**Table** SCA performance in TB control services (Rural DOTS), 2010–2011

Explanation	Year	
	2010	2011
Total number of HFs covered by SCA	132	132
HFs covered by DOTS (diagnosis and treatment)	59	78
New pulmonary TB (SS+) cases notified	505	558
TB cases treatment completed/cured	408	432
NSS+ conversion rate, %	54	63
Pulmonary TB suspected examined (AFB slides examined)	16 196	17 222
Relapse cases	78	57

was 54%. In 2011, 17 222 TB suspects were examined for AFB, 558 were SS+, 57 were relapsed, 612 started DOTS treatment and NSS+ conversion rate was 63%.

**Conclusion:** This is evident that rural DOTS contributed significantly on TB services. It improved case notification, increased treatment success rate and decreased relapse. Moreover, TB reporting-recording system is improved; staffs are motivated, TB drugs and lab reagents supply regularly, and hospitals are engaged in TB control program. The success rate rose to 73%, and the relapse decreased from 15% to 10%, thus, we would recommend the scale-up rural-DOTS to other rural areas.

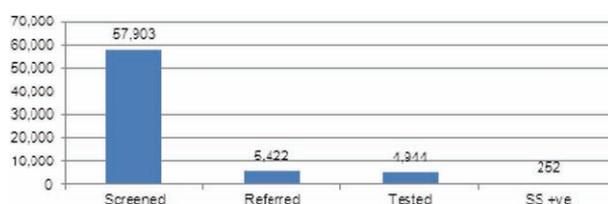
### PC-613-16 Reaching seasonal labour migrants with active tuberculosis case finding in Nepal

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**Background and challenges to implementation:** Migrant-focused TB activities are needed in Nepal where annual internal and external migration is estimated to be between 1.5 and 2 million, made up mostly of economically poor laborers with little social support and access to health care. The Nepal TB REACH Project aims to address needs between Nepali-Indian border where >1 million laborers migrate.

**Interventions or response:** Using inclusion criteria, outreach and clinical staff performed a standard clinical screening and sputum microscopy examinations among migrants returning from India in six districts. Border entry points and major bus parks drop-in-centers had rest areas, clean drinking water access and IEC materials which attracted migrants for screening. Outreach workers collected addresses for home-based sputum collection or referred migrants to sites for testing. Maps with a list of government-run sites facilitated access for referred migrants. Formal agreements were made with sites to test referred migrants.

**Results and lessons learnt:** Out of 57 930 migrants screened for TB symptoms 5 422 suspects were detected and 252 SS+ cases were found (91% referred were tested). 5% of migrants were SS+ with one district recording >9% SS+. Altogether 97% SS+ migrants were enrolled for treatment. These cases identified through active case finding would have been identified only at a later stage, if at all.



**Conclusions and key recommendations:** This first ever active case finding in Nepal shows it can be successful among migrants, who, due to their large population size, are important population for TB screening/treatment. Their mobility poses treatment follow-up challenges requiring more effective inter-governmental collaboration.

**PC-614-16 Evaluating the impact of decentralising tuberculosis microscopy services to rural township hospitals in Shandong and Gansu Province, China**

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**Background:** In 2004, the Ministry of Health issued the policy of decentralising microscopy services (MCs) to one third of all township hospitals in China. MCs were required to check TB suspects and refer them for confirmation in the county TB dispensary. The study evaluated the performance of the MC policy in Shandong, a relatively rich eastern province and Gansu Province, a poor western one in China.

**Methods:** All 497 MCs in 113 counties of Shandong, and 523 MCs in 87 counties of Gansu completed an institutional survey regarding their performance. Informant interviews were conducted with health staff at township and county levels.

**Results:** 8% and 14% MCs did not examine any TB suspects in 2006/07.66% (Shandong) and 54% (Gansu) MCs did not find any smear-positive cases. In Shandong, MCs contributed to identifying 3% of all smear-positive patients in the province, a bit higher in Gansu (9%). MC performance was positively correlated with the population, individual income, trained laboratory technicians in the township hospital. Barriers policy implementation included inadequate financing, low laboratory capacity, poor treatment and management capacities.

**Conclusion:** Microscopy centre performance was low in the two provinces, and the contribution of MCs to TB case detection was insignificant considering the number of MCs established. The national policy of MC only decentralised limited functions. Poor western provinces should be given a high priority for TB service decentralisation.

**PC-615-16 Improvement of tuberculosis treatment outcome under TB-HIV intensified case finding and community DOTS project in Zambia**

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**Background and challenges to implementation:** Between 2009 and 2011, Japan Anti-Tuberculosis Association Zambia (JATA Zambia) has implemented TB-HIV case finding and care project in an urban community, Lusaka, Zambia, in collaboration with national TB control program. Before the project, a treatment defaulter rate of new smear positive TB cases in the targeted area was as high as 26.8%. The number of TB treatment supporters was quite low and the quality of care provided for TB patients was limited.

**Interventions:** We have trained 33 TB treatment supporters. They worked at TB treatment unit of the government clinic under the supervision of nurses. They have provided regular health educational talk to patients, TB case finding through community sensitization activities (e.g., drama performances or door-to-door visitations), contact tracing, and directly observed treatment (DOT) every day in intensive phase and once per month in continuation phase. They also tried to trace some patients who had missed clinic appointment more than two times.

**Results:** The treatment outcome has remarkably improved after the project. The success rate rose from 57.0% to 77.0%, and the defaulter rate decreased from 26.8% to 9.9%. The total of 439 tracing trials have been done during the project for 254 patients at risk of defaulting, however, 33.0% of all tracing trials were unsuccessful. TB treatment supporters could not see the targeted patients at their homes because of incorrect addresses reported by patients (31.7% of unsuccessful trials) or moving out without any information (20.0%). The treatment success rate and defaulter rate among the patients, who may have defaulted but have been traced successfully, was 66.6% and 19.6% respectively.

**Conclusions and key recommendations:** TB treatment supporters have played important roles for improvement of TB treatment outcome. Patient tracing activity is still big challenge while we find some positive impact on TB treatment outcome.

### PC-616-16 Awareness about NTP services among tuberculosis patients identified in a community-based survey in India

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**Background:** The Revised National TB Control Programme (RNTCP) of the Government of India provides free TB diagnostic and treatment services. A large community based survey involving ~73 000 households (with ~374 000 household members) had identified 609 TB patients. Nearly 46% of these TB patients were taking treatment from non-RNTCP sources by paying for their medication.

**Objectives:** As a part of this survey, patient's awareness about the free diagnostic and treatment services provided by RNTCP was assessed.

**Methodology:** TB patients identified during this community survey were interviewed by trained field investigators using a semi-structured questionnaire. These patients were from 30 out of the 374 Global Fund Round 9 project districts. The selection of districts and patients within the districts was done by multistage cluster random sampling methodology and door to door survey.

**Results:** Overall, 426 (70%) of the 609 TB patients knew about the free treatment services. 36% of the patients who knew about the free treatment services were not availing treatment from RNTCP. 45% of the 278 patients who were on non-RNTCP treatment did not know about the free treatment services.

**Conclusions:** This survey shows that nearly a third of TB patients did not know of free treatment services provided by RNTCP. Nearly a third who knew about free treatment services were not availing the services hinting that there may be challenges in accessing the programme services or treatment provided by the programme is not being prescribed by their treating health care providers. This study highlights that in India, in addition to raising awareness about free treatment services there appears to be a great need to make the services accessible.

### PC-617-16 Improving outreach of diagnostic services through a sputum collection and transportation system under programmatic conditions

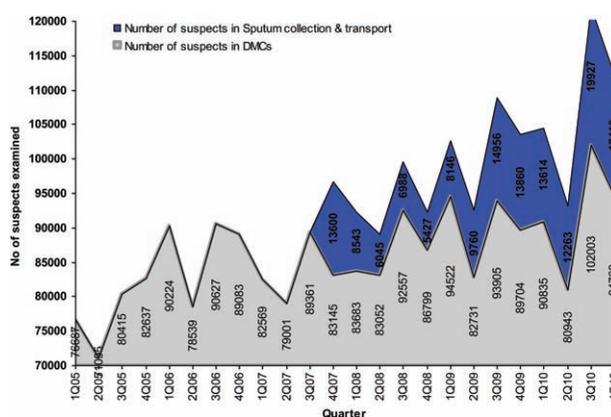
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**Background and challenges to implementation:** After complete geographical coverage of Revised National

Tuberculosis Control Programme in the state of Gujarat in early 2004, more than half of the tuberculosis units had very low suspect examination rates mostly due to inadequate decentralization of the diagnostic services. Almost 2/3rd of the peripheral health centers had no diagnostic services (sputum smear microscopy) and referral of symptomatic patients to nearest microscopy centers did not yield much results. This was also reflected in low case detection rates in these Units. Thus it was a major hurdle in achieving global targets for TB control.

**Intervention:** Sputum collection system and transport system was developed with standard operating procedures and the same was piloted and found to be feasible and economic. The same was then expanded to cover complete state with more than 900 sputum collection centers. Training of the human resources for sputum collection and transportation was supported with minimal financial incentives. Implementation of intervention also included logistics management (sputum collection boxes and cups etc), supportive supervision, optimal recording and reporting. Data was routinely collected from all sputum collection centers and microscopy centers.

**Results:** TB suspect examination rate increased by 25–30% maintaining quality. Decentralized diagnostic services at PHCs as sputum collection centers contributing to more than 20% of sputum examinations and smear positive cases diagnosed in the state over five years since the pilot in 2006 indicating increased access to TB care, a step towards universal access. This system also created a strong foundation for decentralized sputum collection for drug resistance TB diagnostic services.



**Figure** Number of TB suspects examined in Gujarat (1Q05–4Q10).

**Conclusion:** It is feasible to effectively decentralize TB diagnostic services by establishing sputum collection and transport system in peripheral health centers and programmes should invest in creating such network.

### PC-618-16 Measuring the impact of technical assistance with the aim to improve Global Fund tuberculosis grant performance

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**Background:** The TB TA mechanism database records and coordinates external TA missions to countries in support of TB programmes including Global Fund (GF) grant implementation. The GF historical grant performance database records regular grant performance scores. The authors linked and examined these two routine databases to investigate if TA has an impact on GF grant performance.

**Design/methods:** The databases were linked by creating two key variables, time and domain of support. Initial analyses were carried out on impact of TAs on achievement score of SDAs, study of dose-response by number of TAs, and length of TAs, and temporal association by SDA (planning support only). SPSS was used for descriptive and conformational statistical analysis.

**Results:** In those countries where specific TAs took place, the achievement score of most related performance indicator of GF grants is higher than in those countries without specific TA support. This effect is statistically significant at 7.6% and is seen in almost all SDAs (Table). A time limited association with better grant scores is also shown at the time of TA and within the following 6 months. Increased duration of TA though not number of TAs are associated with improved grant ratings.

**Table** Achievement score difference per SDA determined in the same quarter of the TA

SDA	No TA support	TA support	Score differ.	P value
Planning and M&E	80.8 %	89.9 %	9.1 %	< 0.0001
Community support	84.2 %	99.7 %	15.5 %	0.031
ACSM	81.0 %	105.0 %	24 %	0.027
TB-HIV	83.0 %	103.8 %	20.8 %	0.0004
PPM	81.7 %	78.6 %	- 3.1 %	0.640
MDR	72.1 %	76.6 %	4.5 %	0.356
HSS	75.0 %	86.2 %	11.2 %	0.310
ALL	80.8 %	88.4 %	7.6 %	0.035

**Conclusion and recommendations:** The small size of the TA effect demonstrated could be real, due to systematic deficiencies in the databases or uncontrolled confounders. It is proposed to improve the harmonization of coding of both databases, to link missions with indicators up front, and to gather confounder information and conduct further analyses.

### IMPROVING DIAGNOSIS AND TREATMENT OF CHILDHOOD TUBERCULOSIS

#### PC-647-16 Helminth infections and cytokine profiles are strongly associated with risk of infection in Warao Amerindian childhood tuberculosis contacts

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**Background:** Understanding of the immune regulatory mechanisms in asymptomatic but tuberculosis (TB)-infected children could provide insight in their increased susceptibility to developing disease compared to adults. Little is known about the immunological mechanisms underlying the development of latent TB infections (LTBI) in populations where parasitic infections and malnutrition are highly prevalent. We performed a cross-sectional observational study to determine the influence of parasitic infections and associated plasma cytokine profiles on the acquisition of LTBI in Warao Amerindians in Venezuela.

**Methods:** One hundred and forty-three household contacts of active TB cases aged 1 to 15 years were enrolled for tuberculin skin testing (TST) and QuantiFERON®-TB Gold In-Tube assay (QFT-GIT) performance. Plasma samples for cytokine analyses and stool samples for parasitic examinations were collected. Factors associated with LTBI were studied using generalized estimation equations (GEE) logistic regression models.

**Results:** The prevalence of LTBI as determined by TST was 38.5%. The risk of developing LTBI was significantly associated with low plasma levels of T helper 1 (Th1) cytokines and a high prevalence of *Trichuris trichiura* infections. Furthermore, *Ascaris lumbricoides* infections and both a Th2-dominated and an interleukin (IL)10-dominated cytokine profile were significantly positively associated with LTBI. QFT-GIT indeterminate results were significantly more often observed compared to negative results in children with helminth infections ( $P = 0.02$ ). Finally, we observed a significant negative correlation of QFT-GIT mitogen response with the magnitude of both Th1 and Th2 cytokine responses (correlation coefficients varying from  $-0.23$  to  $-0.39$ ), age ( $-0.40$ ) and total white blood cell count ( $-0.28$ ).

**Table** Odds ratios (OR) and 95% confidence intervals (CI) from the final GEE multivariable logistic regression model predicting LTBI in Warao Amerindian childhood TB contacts

	LTBI vs. no TB OR (95% CI)*
Helminth infection	
<i>Trichuris trichiura</i>	3.2 (1.04–10.0)
<i>Ascaris lumbricoides</i>	1.1 (0.45–2.9)
Immune response	
Th1-dominated response (IL2, IL12p70, IFN $\gamma$ , TNF $\alpha$ )	0.46 (0.29–0.71)
Th2-dominated response (IL4, IL5, IL13)	0.86 (0.51–1.4)
IL-10-dominated response	0.56 (0.29–1.1)
Interaction between immune response and helminth infection	
Th2-dominated response $\times$ <i>Ascaris lumbricoides</i>	3.4 (1.1–10.2)
IL10-dominated response $\times$ <i>Ascaris lumbricoides</i>	2.4 (1.1–5.2)

\*Adjusted for age, gender and nutritional status.

**Conclusions:** Helminth infections and low Th1 cytokine levels are strongly associated with the development of LTBI in indigenous Venezuelan pediatric TB contacts.

#### PC-648-16 Linezolid-containing regimens for the treatment of drug-resistant tuberculosis in South African children

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**Background:** Treatment options for drug-resistant (DR) tuberculosis (TB) are limited. Linezolid has been used successfully to treat DR-TB in adults but there are few case reports of use in children for TB. The reported rate of adverse events in adults is high.

**Methods:** We conducted a retrospective review of children with DR-TB treated with linezolid-containing regimens from February 2007 through March 2012 at two South African hospitals.

**Results:** Seven children (four HIV-uninfected) received a linezolid-containing regimen. All had culture-confirmed DR-TB; five had previously failed second-line anti-tuberculous treatment. Four children were cured and three were still receiving TB treatment, but had culture converted. None of the HIV-uninfected children experienced adverse events while receiving linezolid. Three HIV-infected children had adverse events, one of which was life threatening and linezolid was permanently discontinued. Adverse events included lactic acidosis (1), pancreatitis (2), peripheral neuropathy (1) and asymptomatic bone marrow hypoplasia(1).

**Conclusion:** Linezolid-containing regimens can be effective in treating children with DR-TB even after failing second-line treatment. Adverse events must be monitored for, especially in combination with medications that have similar adverse effects. Linezolid remains costly and a reduced dosage and duration may result in fewer adverse events and lower cost.

#### PC-649-16 Effect of *Ascaris lumbricoides* specific IgE on tuberculin skin test responses in children

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**Background:** Immune responses to *M. tuberculosis* are associated with Th1 cell mediated responses; these may be downregulated by Th2 immune responses, typically associated with helminth infection, often prevalent in high-burden tuberculosis settings.

**Design/methods:** We completed a community-based household contact tracing study with matched enrolment of children with and without household MTB exposure in an urban community, Cape Town, South Africa. We documented demographic, clinical, MTB exposure (contact score), HIV, MTB infection status (tuberculin skin test; TST). *Ascaris lumbricoides* specific serum IgE (*Ascaris* IgE) was used as proxy for *Ascaris* infection/exposure.

**Results:** Of 271 children enrolled (median age 4.4 years), 65 (24%) were *Ascaris* IgE positive while 168 (62%) had a documented household tuberculosis contact; 107 (40%) were TST positive. Increasing age (Odds Ratio (OR) = 1.17,  $P < 0.001$ ), MTB contact score (OR = 1.17,  $P < 0.001$ ), previous TB treatment (OR = 4.8,  $P = 0.06$ ) and previous preventive TB therapy (OR = 3.16,  $P = 0.01$ ) were associated with a positive TST. BCG scar (OR = 0.42,  $P = 0.01$ ) was protective. Positive *Ascaris* IgE status was not associated with TST positivity in univariate analysis (OR = 0.9,  $P = 0.6$ ), but multivariable logistic regression modelling adjusted for *Ascaris* status, age and MTB score, suggested an inverse association between *Ascaris* IgE positivity and TST positivity (OR = 0.6,  $P = 0.08$ ). Adding an age interaction term to this model indicated that the effect of age was stronger among children with a positive *Ascaris* IgE result with the most prominent effect amongst younger children.

**Conclusion and recommendations:** Our preliminary findings indicate a high prevalence of helminth and

MTB co-infection in children. Helminth infection may alter the immune responses following MTB exposure in children. Our data are relevant to the interpretation of immunological tests of MTB infection in high-burden tuberculosis settings.

### PC-650-16 Pharmacokinetics of anti-tuberculosis drugs in Venezuelan children: supportive evidence for revised World Health Organization recommendations

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**Background:** The World Health Organization (WHO) has recently issued revised first-line antituberculosis (anti-TB) drug dose recommendations for children, with dose increases on a mg/kg base proposed for each anti-TB drug. It is important to examine the need for implementation of these revised guidelines in different pediatric populations. No pharmacokinetic data are available from children from the South American region.

**Methods:** Thirty Venezuelan HIV-negative TB patients aged 1 to 15 years old were included during the intensive phase of daily anti-TB treatment. Anti-TB intensive phase treatment regimens in Venezuela at the time of research followed the old WHO guidelines. Plasma isoniazid, rifampicin, pyrazinamide and ethambutol concentrations were assessed prior to and at 2, 4 and 8 h after intake of anti-TB drugs to describe pharmacokinetic parameters using noncompartmental analysis. Pharmacokinetic parameters were log transformed before statistical analysis. The effects of dose in mg/kg, age, sex, body weight, malnutrition and acetylator phenotype on maximum plasma drug concentrations (C<sub>max</sub>) and exposure (AUC<sub>0-24</sub>) were determined using independent sample *t*-tests and Pearson correlation coefficients on the log-transformed parameters.

**Results:** Twenty-five patients (83%) had peak plasma isoniazid levels below 3 mg/L and 23 patients (77%) had peak plasma rifampicin levels below 8 mg/L. One patient (3%) had a peak plasma pyrazinamide concentration below 20 mg/L. The number of patients on ethambutol (*n* = 5) precluded firm conclusions. C<sub>max</sub> and AUC<sub>0-24</sub> of all four drugs were significantly and positively correlated with age, body weight and dose. Patients aged 1–4 years had significantly

lower C<sub>max</sub> and AUC<sub>0-24</sub> values for isoniazid and rifampicin and a trend to lower values for pyrazinamide. The geometric mean AUC<sub>0-24</sub> for isoniazid was much lower in fast acetylators than in slow acetylators (5.9 vs. 12.5, *P* < 0.01).

**Table** Summary of pharmacokinetic parameters of anti-TB drugs

Drugs and PK parameters*	Isoniazid (n = 30)	Rifampicin (n = 30)	Pyrazinamide (n = 30)	Ethambutol (n = 5)
AUC <sub>0-24</sub> (h*mg/L)	8.8 (2.2–34.9) 2.6–31.0	20.6 (6.1–70.4) 7.4–94.2	318.5 (145.5–697.5) 108.0–1389.5	12.0 (2.7–53.6) 5.4–28.2
C <sub>max</sub> (mg/L)	1.9 (0.7–5.1) 0.7–5.2	5.1 (1.7–15.6) 1.5–13.6	31.5 (17.3–57.5) 10.3–71.7	1.8 (0.5–6.3) 0.9–3.7
% within reference range†	17	23	94	60
t <sub>max</sub> (h)	2.0 (2.0–2.0) 2.0–4.0	3.0 (2.0–4.0) 2.0–8.0	2.0 (2.0–2.0) 2.0–8.0	4.0 (2.0–4.0) 2.0–4.0
CL/F (mg/L)	10.3 (2.6–40.3) 2.7–45.6	8.1 (2.8–23.0) 2.5–17.1	1.4 (0.5–4.0) 0.7–6.0	45.5 (28.6–72.2) 36.1–61.2
Vd/F (L)	31.6 (11.6–86.4) 13.9–85.3	16.0 (4.3–59.3) 5.8–57.4	14.1 (4.8–41.8) 5.5–50.2	216.2 (89.0–525.0) 137.2–452.3
t <sub>1/2</sub> (h)	2.1 (1.0–4.3) 1.3–5.7	1.4 (0.4–5.2) 0.4–4.6	6.8 (3.2–14.3) 2.3–24.2	3.3 (1.3–8.1) 2.5–7.4

\* Apart from t<sub>max</sub>, for which median (IQR) and range was displayed, geometric means, 95% CI and range were shown for all pharmacokinetic parameters.

† Reference ranges in mg/kg are 3–6, 8–24, 20–50 and 2–6 for isoniazid, rifampicin, pyrazinamide and ethambutol, respectively.<sup>1–3</sup>

**Conclusion:** Our data provide supportive evidence for the implementation of the revised WHO anti-TB drug dose recommendations for children in Venezuela. Follow-up studies are needed to describe the exposures that are achieved when children take the recommended increased doses of anti-TB drugs.

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### PC-651-16 Modifiable risk factors for tuberculosis disease in children in Lima, Peru: a case control study

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**Background:** We aimed to identify modifiable risk factors for tuberculosis disease (TB) in children.

**Design/methods:** We conducted a matched case-control study among children less than 15 years of

age living in one of two health districts in Lima, Peru. Cases were children diagnosed with TB for the first time at the Peruvian National Institute of Child Health. Friend controls were matched to cases by age, neighborhood and gender. Children and/or guardians completed interviews, and children submitted stool specimens for parasite testing. Data were analyzed using conditional logistic regression analyses.

**Results:** Mean age among the 194 cases and 194 controls was 6.8 years (standard deviation: 4.4), and 50% of participants were female. In multivariable analysis, a known TB contact was the strongest TB risk factor (RR 9.1; 95%CI 4.6–17.4;  $P < 0.0001$ ). Infection with *Blastocystis hominis* or *Giardia lamblia* was found in 32% and 14% of controls respectively. Both infections were associated with a reduced rate of TB (*Giardia lamblia* RR: 0.18; 95%CI 0.05–0.67;  $P = 0.01$ ); *Blastocystis hominis* RR 0.16; 95%CI 0.07–0.41;  $P = 0.0001$ ). Consuming fruits and vegetables daily or near daily was also associated with a lower rate of TB (RR 0.43; 95%CI 0.19–0.96;  $P = 0.04$ ). Only 14% of 162 children with a known TB contact had received prophylaxis with isoniazid.

**Conclusions:** The observed association between fruit and vegetable intake and TB suggests that the role of diet could be further evaluated in a prospective study in order to determine whether a tailored dietary intervention could curtail TB risk. The finding that *Blastocystis hominis* and *Giardia lamblia* infection were associated with a reduced risk of TB was unexpected and should be interpreted with caution and explored in future research. Last, the benefit of isoniazid prophylaxis for TB prevention is well-established, and efforts should be made to promote isoniazid uptake in children with a TB contact.

#### PC-652-16 A prospective cohort study to evaluate the incidence of tuberculosis in infants, Western Kenya

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**Introduction:** Diagnosing tuberculosis (TB) in infants is challenging in areas with high HIV co-infection and malnutrition rates, where clinical score charts can be unreliable. Under these circumstances, cohort studies that include comprehensive TB diagnostic methods can provide reliable estimates of TB incidence. We sought to determine TB incidence in infants in such an area in preparation for TB vaccine trials.

**Methods:** Infants aged 0–6 weeks were enrolled in Western Kenya. Through follow up and sick visits, TB suspects were identified based on contact history,

TB symptoms, and/or history of hospitalisation for lower respiratory tract illness, meningitis, malnutrition or other symptoms. Suspects were investigated through collection of induced sputum and gastric aspirate specimens, chest radiographs, Mantoux, and DNA PCR/rapid HIV tests. Definite TB cases were culture confirmed after speciation, while probable cases had Keith Edward Scores of  $\geq 7$  and/or suggestive chest radiographs.

**Results:** Of 2900 enrolled infants, 1488 (51.3%) were male and 406 (14%) were HIV seroexposed. Of 753 TB suspects investigated, 285 (37.8%) had contact history, and/or TB symptoms while 392 (52.1%) had relevant hospitalisation history, 76 (10.1%) had other reasons. Ten (10) definite and 38 probable cases were identified, resulting in a TB incidence rate of 1.44 per 100 person years [95%CI (1.09, 1.91)]. Predictors of definite TB were malnutrition [OR 9.4 (95%CI 4.0, 22.0)], HIV infection or exposure [OR 8.0 (95%CI 3.6, 18.0)], abnormal chest X-ray [OR 6.0 (95%CI 2.6, 13.5)], positive TST [OR 3.0 (95%CI 1.6, 5.5)].

**Discussion:** We found high TB incidence (1.44%) compared to Kenya's estimated incidence (0.3% WHO 2010). Identified predictors of TB disease can guide endpoint discussions for TB vaccine trials and help clinicians in similar settings suspect and diagnose TB appropriately.

#### PC-653-16 Tuberculous meningitis in children: a prospective observational study

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**Background:** Childhood TBM remains a difficult clinical entity and there have been few contemporary prospective systematic studies in Asia and none from Viet Nam. Thus, we conducted a observational study to define the clinical phenotype and outcome of children with TBM in Viet Nam.

**Design/methods:** Prospective descriptive study. Sample size: 100 children with suspected TBM.

**Study site:** Pham Ngoc Thach Hospital, Viet Nam.

**Outcome measures:** Clinical features, mortality, disability, HIV prevalence, and imaging results. R software was used.

**Results:** 100 patients were enrolled (October 2009 and March 2011). Median age was 4 years and male was 64%. Patients over 5 (33/100) were graded with UK MRC TBM grading system and others were graded using BCS. HIV infection was 4%. Clinical features were fever (99%), vomiting (76%), headache (49%), confusion (25%), unconsciousness (35%) and fits (40%). 20% had hemiparesis. Cranial nerve

palsy was 26%. Grade I: 15, Grade II: 12, Grade III: 6. 43/67 scored 4–5, 12/67 scored 2–3 and 12/67 scored 0–1. CSF results: mean protein was 1.74 g/L, glucose was 1.76 mmol/L, glucose in blood and was 5.67 mmol/L. Mean lymphocytes were 174/mm<sup>3</sup>. Brain MRI and CT scans: hydrocephalus occurred in 27/61, meningeal enhancement in 9/61, ganglia infarction in 4/61.

**Outcome:** The overall mortality was 15%, one is HIV-infected. Severe and mild complications were 7% and 28% among survivors.



**Conclusion and recommendations:** Childhood TBM is associated with significant mortality and morbidity. Convulsion is much more frequent than is seen in adults. An important finding given the potential drug interactions of anticonvulsants with anti-tuberculous therapy. HIV infection occurs in 4%. MRI and CT scans make TBM diagnosis around 57%.

#### PC-654-16 Sputum induction for paediatric tuberculosis in Botswana: programme description and findings

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**Background:** To aid paediatric TB diagnosis in Botswana, since 2008 we have been training health care workers to perform sputum induction (SI) in children. To optimize ongoing training and inform future versions of Botswana's diagnostic algorithm for paediatric TB, we aimed to determine the predictive value of individual signs/symptoms in diagnosing microbiologic pulmonary TB.

**Design/methods:** This project operated from 2008 to 2010 in four Botswana referral hospitals, including all children ( $\leq 18$  years) referred by clinicians for SI

due to suspected pulmonary TB. In our analysis, data was excluded if subjects were on anti-TB treatment (ATT) at time of SI; if all culture results were not available; or if only mycobacteria other than *Mycobacterium tuberculosis* (MTB) were isolated. Microbiologic TB was defined as AFB present on sputum microscopy or MTB cultured. Presenting signs/symptoms evaluated were: cough, low energy, night sweats, low appetite, chest pain—all  $>14$  days—weight loss, hemoptysis and TB contact. Sensitivity, specificity and negative predictive value (NPV) of each sign/symptom for microbiologic TB was calculated for 3 risk groups: HIV-positive, HIV-negative  $<3$  years, HIV-negative  $\geq 3$  years.

**Results:** Data from 1394 subjects were analyzed. 743 (53%) male, median age 3.8 years (IQR: 1.3–8.4), 373 (27%) HIV-positive, 419 (30%) HIV-negative, 602 (43%) unknown HIV status, 114 (8.2%) had microbiologic TB. Between cohorts with and without microbiologic TB there were significant differences in subjects with weight loss ( $P = 0.03$ ), chest pains ( $P = 0.003$ ), and TB household contacts ( $P = 0.003$ ). The presence of  $\geq 2$  symptoms was 100% sensitive with 100% NPV in HIV-negative  $\leq 3$  yrs; 87% sensitive/94% NPV in HIV-positive. Sensitivities and NPV were low in HIV-negative  $>3$  yrs.

**Conclusions/recommendations:** The presence of 2 or more symptoms predicts microbiologic TB in HIV-positive children and HIV-negative children less than age 3.

#### PC-655-16 Assessing symptoms of pulmonary tuberculosis diagnosed by gastric aspirates in Botswanan children, 2008–2010

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**Background:** Since September 2008, we have trained nurses in Botswana to do gastric aspirates (GAs) to enhance the diagnosis of pediatric tuberculosis (TB). To inform future versions of Botswana's pediatric TB diagnostic algorithm, we determined the value of individual symptoms to diagnose microbiologic pulmonary TB.

**Design/methods:** An operational research project in 3 health districts of southern Botswana included all children ( $\leq 13$  years) referred for a GA due to suspicion of pulmonary TB. Subjects were excluded if on anti-TB treatment (ATT); culture results were

unavailable, or a Mycobacterium other than TB was isolated. *Microbiologic TB* was defined as the presence of AFB on sputum microscopy or *Mycobacterium tuberculosis* cultured. Events assessed were: cough, low energy, night sweats, low appetite, chest pain (all >14 days), weight loss, hemoptysis and TB contact. The sensitivity, specificity and negative predictive value (NPV) of each was calculated for 3 risk groups: HIV negative <3 years or ≥3 years, and HIV positive. Radiologic and immunologic data were not collected. We used Wilcoxon rank-sum or Pearson  $\chi^2$  for comparisons.

**Results:** Of 502 subjects referred for GA's, 415 were eligible for analysis. Of these, 217 (52%) were male, median age 3.3 years (IQR: 1.4–5.3), HIV status was 24 (6%) positive, 126 (31%) negative and 264 (64%) unknown; and 94 (23%) had *microbiologic TB*. There were no significant differences in gender, age, HIV status, TB contact or symptoms between subjects by microbiologic TB status. The value of different events varied by risk group—cough was most useful with 88% sensitivity (95%CI 62–98) and 90% NPV (68–99) in HIV negative ≥3 years; and 100% sensitivity (48–100) and NPV (29–100) in HIV positives. Hemoptysis was 98% specific (89–100) in HIV negative ≥3 years; all events performed poorly in HIV negative <3 years.

**Conclusion and recommendations:** Although most events performed poorly, some were valuable in certain risk groups.

#### PC-656-16 Yield of multiple sampling methods to diagnose children with tuberculosis in Yemen

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**Background:** The latest NTP report returned no cases of TB in children from Yemen. Paediatric TB diagnosis is technically difficult. Symptomatic children are hospitalized and investigated by collecting gastric aspirates for at least three consecutive days. Many children fail to complete the process due to parental withdrawal. This project aims to accelerate the diagnosis of TB in children by collecting multi-site (anatomical) specimens in a single day. It also aims to improve treatment adherence in children with TB.

**Methods:** Children attending Al-Sabeen and Al-Thawara hospitals in Sana'a with symptoms suggestive of TB (according to the WHO guidelines) were invited to participate. After obtaining informed parental consent, children were hospitalised to obtain specimens for diagnosis. These comprised one expectorated sputum or induced sputum (S) (if the child

cannot produce sputum), one nasopharyngeal aspirate (NPA), one gastric aspirate (GA) and one chest X-ray. Anti-TB therapy was initiated, as soon as TB diagnosis was confirmed or clinically and radiologically suspected. A text message reminder was used to increase the rate of adherence.

**Results:** 58 out of 60 invited (97%) children were enrolled and gave specimens and 2/58 (3%), 4/58 (7%) and 4/58 (7%) were positive by smear, culture and LN biopsy, respectively. In total, 10/58 (17%) were confirmed to have TB. Of those 42/58 (72%) children received anti TB treatment. 38/42 (88%) adhered to treatment which is significantly higher than before (>50% were found to be non-compliant).

**Conclusion:** This strategy is effective in increasing the detection rate. The positivity rate was more than 8 times than previous reports. Two to three samples from different anatomical sites in a single day is an efficient approach to detect TB cases among children. Sending alerting messages to the parents/legal guardian is a novel technology in increasing adherence to anti TB treatment.

#### PC-657-16 Drug-resistant tuberculosis in Pakistani children: clinical characteristics, treatment and outcome

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**Background:** Drug-resistant tuberculosis (DR-TB) is under-diagnosed in children. There is limited experience with the management of children with DR-TB in Pakistan. The objective of our study was to assess the clinical characteristics and response to treatment of children with DR-TB at the Indus Hospital Pediatric DR-TB program.

**Methods:** All children <15 years who were diagnosed with DR-TB (confirmed or presumed), and treated at the Indus Hospital Pediatric DR-TB program, Karachi, from January 2008 till March 2012, were included in this study. We measured 2-month culture conversion in children that were culture positive at baseline, and determined cure clinically in culture-negative children.

**Results:** Twenty-five children (median age: 14 years, IQR: 2–14 years) were enrolled in the program. 38.4% (10/25) children were diagnosed by active contact tracing. 86% (19/22) were culture confirmed cases. 58% (11/19) culture converted at or before 2 months. 60% (15/25) were undernourished (Z score = <-2 SD). The most frequently reported adverse events were nausea and vomiting (18% of patients). Twenty (80%) children were either cured or

are still on treatment and doing well. Two children died (8%) and no one defaulted.

**Conclusion:** Most children in our program were over 10 years of age, which accounted for the large proportion that were culture confirmed. More aggressive screening of younger child suspects, including sputum induction, broncho-alveolar lavage and genexpert testing may be of value. Most patients tolerated treatment well and culture-converted at 2 months.

### PC-658-16 Hearing and renal impairment in children treated for drug-resistant tuberculosis

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**Background:** The aminoglycosides and polypeptides are vital drugs for the management of drug-resistant (DR) tuberculosis (TB). Both classes of drug are associated with renal and hearing impairment. The frequency and severity of hearing loss and renal dysfunction is unknown in children treated for DR-TB.

**Methods:** In this retrospective study, all children (<15 years) admitted to Brooklyn Chest Hospital, Cape Town, South Africa, from January 2009 until December 2010, were included if they had been a) diagnosed with probable or confirmed DR-TB, b) treated with an injectable TB drug for >1 month and c) had received  $\geq 1$  audiological assessment. Children were routinely assessed using otoscopy, tympanometry, pure tone audiometry and distortion product otoacoustic emissions. The American Speech and Hearing Association criteria were used to classify hearing loss. Serum creatinine concentration was routinely assessed. Ethical approval was obtained.

**Results:** 94 children were included (median age: 43 months). 45 (48%) were boys, 30 (32%) had extrapulmonary involvement and 28/93 (30%) tested were HIV-infected. 23 (24%) children had certain hearing loss, 27 (29%) had no hearing loss and the remainder were unclassifiable using study criteria. Confirmed, as opposed to probable, diagnosis of DR-TB was a risk factor for hearing loss (OR: 4.12; 95% CI 1.13–15.0;  $P = 0.02$ ). 7 of 11 (64%) children classified as having hearing loss using audiometry had progression of hearing loss after finishing the injectable. Only five (of 183) creatinine assessments were above the upper limit of normal for age; all minor and all resolved spontaneously.

**Discussion:** Hearing loss is common in children treated for DR-TB. No children developed renal dysfunction evident on available testing. Prospective studies are needed to determine optimal dosages for the injectable agents in children, in order that they

may be effective but cause minimal toxicity. New drugs are required for the treatment of DR-TB in children.

### PC-659-16 Stool analysis by GeneXpert® MTB/RIF for the diagnosis of paediatric tuberculosis: a pilot study

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**Background:** Early and rapid confirmation of tuberculosis (TB) in young children can prevent disease progression and death. Stool sampling for the diagnosis of paediatric TB has undergone minimal investigation to date. There are no published data on the performance of GeneXpert® MTB/RIF (Xpert; Cepheid, Sunnydale, CA) on paediatric stool samples. Mycobacterial DNA from swallowed sputum is detectable in stool by nucleic acid amplification techniques, making stool an attractive sample in children as it is non-invasive and easily obtained.

**Design/methods:** A cross-sectional pilot study was conducted in children admitted to hospital with suspected TB. In addition to routine investigations, one gastric aspirate and one stool sample were obtained from each participant. After decontamination and neutralization, samples were centrifuged in 2 steps of 20 minutes each at 3000 g. The resuspended pellet was used for 1) smear microscopy, 2) mycobacterial liquid culture, and 3) Xpert analysis.

**Results:** Four of 23 (17%) children with suspected intrathoracic tuberculosis had culture confirmation, of whom 3 (75%) were positive by GeneXpert from stool and respiratory samples. Xpert had 100% specificity compared to mycobacterial liquid culture. Time to result was <48 hours with Xpert vs. 5–22 days for respiratory culture. No indeterminate Xpert tests or contaminated cultures were recorded.

**Conclusion and recommendations:** These preliminary data demonstrate that stool can yield clinically relevant results with Xpert for the diagnosis of childhood TB. Improved concentration techniques may further increase diagnostic yield. The incremental benefit of stool investigation through Xpert, and its potential use within diagnostic algorithms should be systematically investigated.

## MULTIDRUG-RESISTANT TUBERCULOSIS: FOCUS ON LABORATORIES

### PC-681-16 Evaluation of the MTBDRs/® line probe assay from direct sputum in a high-volume diagnostic laboratory

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**Background:** Rapid detection of multi-drug resistant tuberculosis (MDR-TB) has dramatically improved the process turn-around time (TAT) in some public health laboratories since the implementation of the MTBDRplus line probe assay (LPA). However, the TAT for conventional drug susceptibility testing (DST) for the second-line drugs still lingers on due to the DST incubation protocol. The objective of this study was to assess the performance of the MTBDRs/® LPA (Hain Lifescience, Nehren, Germany) for the rapid detection of resistance to ofloxacin (associated with the *gyrA* gene) and amikacin (associated with the *rrs* gene), against conventional DST on solid media, to rapidly identify XDR patients.

**Design/methods:** A total of 736 direct patient specimens were screened for resistance using the MTBDRplus LPA, and the same DNA extract was tested on the MTBDRs/ LPA. The proportion method on Middlebrook 7H11 agar slants was used as the 'gold standard' for ofloxacin and amikacin. A total of 508 single patient specimens, both pulmonary and extrapulmonary, were used for analysis.

**Results:** The sensitivity for detection of ofloxacin amikacin- and extreme drug-resistance was 84.2%, 100% and 92.3%, respectively. Specificity for detection of ofloxacin, amikacin and extreme drug resistance was 98.9%, 99.4% and 99.6% respectively.

**Conclusion and recommendations:** The genotypic results obtained in this assessment of the MTBDRs/ showed favourable correlation with conventional DST results in our high MDR and XDR burden setting. This assay can be a rapid additional tool to screen for XDR-TB in high at risk patients or in those where initial conventional DST or MTBDRplus® LPA identified MDR-TB or other drug resistant TB. If the MTBDRplus LPA is already implemented in the diagnostic algorithm, an XDR strain can be identified within one day of the first line results, thereby drastically improving on the current diagnostic delay.

### PC-682-16 Mutations in genes of *M. tuberculosis*, are coding for drug resistance to isoniazid and rifampicin in patients without detection of pathogen

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**Aim:** Study prevalence of mutations in genes *rpoB*, *katG*, *inhA* and *ahpC*, coding for resistance to rifampicin and isoniazid in TB patients without detection of pathogen method of biological microchips.

**Materials and methods:** The study involved 108 patients newly diagnosed with active pulmonary tuberculosis at age of 18 to 72 years. The patients were divided into 2 groups depending on the presence or absence of detection in sputum *M. tuberculosis* with traditional microbiological methods (sputum smear microscopy for acid-fast bacilli, fluorescent microscopy, inoculation on solid nutrient medium). In group 1 included 53 patients in whom study with repeated sputum were not detected *M. tuberculosis* (MBT-), group 2 included 55 patients with positive results sputum at MBT (MBT+). In all patients, the definition of drug resistance (DR) MBT to isoniazid and rifampicin, and analysis of DNA mutations *M. tuberculosis* was carried with biological microchips. Technology research, sets of reagents and equipment developed of Institute Molecular Biology, Moscow.

**Results:** DNA of *M. tuberculosis* was detected in 24 (45.3%) patients in group 1 and 47 (85.5%) in Group 2. Mutations in genes *rpoB*, *katG*, *inhA* and *ahpC* coding for resistant to rifampicin and isoniazid were detected in 9 (17%) patients with MBT (-) and 8 (14.5%) with MBT (+). In 6 (11.3%) patients group 1 revealed multiple (2 to 6) mutations in gene *rpoB*. The combination of most adverse of mutations, namely, *ser531 rpoB* gene, encoding the DR to rifampicin and *ser315 katG*, encoding the DR to isoniazid, conjugate with high levels of MDR, were found in 18 (33.9%) patients in group 1 and 18 (32.7%) in Group 2.

#### Conclusions:

- 1 Not identified differences in the number and in spectrum of mutations in genes encoding MDR in groups of patients with MBT (+) and MBT (-).
- 2 Patients without detecting *Mycobacterium tuberculosis* in sputum represent a hidden, but no less dangerous reservoir of multidrug resistance.

### PC-683-16 Pyrazinamide resistance in *Mycobacterium tuberculosis* complex is associated with phylogenetic lineages

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**Introduction:** *M. bovis*, a member of the MTBc, is naturally resistant to PZA and often suspected based

on monoresistance to PZA. However, PZA monoresistance has also been identified in *M. tuberculosis* (MTB). We sought to determine if different phylogenetic lineages of MTB are associated with specific patterns of PZA resistance.

**Methods:** Data on culture-positive TB cases reported by 38 U.S. jurisdictions in the U.S. National TB Surveillance System were linked to National TB Genotyping Service data for 2004–2009 to distinguish MTB from *M. bovis* and determine phylogenetic lineage.

**Results:** A total of 28 080 cases had reported drug susceptibility testing for PZA and genotyping data; 925 (3.3%) had PZA-resistance. *M. bovis* accounted for 50.3% (500/925) of cases with any PZA-resistance, and 68.3% (427/625) of PZA-monoresistant cases. *M. bovis* cases were excluded from further analysis. The prevalence of any PZA resistance differed by MTB lineage: 2.9% of East Asian (110/3857), 2.4% of Indo-Oceanic (121/5037), 1.8% of East African Indian (25/1367), and 1.2% of Euro-American (206/17 314). Among MDR cases, PZA-resistance was lower in the Indo-Oceanic (22.0%) vs. East Asian (43.4%) lineage (adjusted prevalence ratio [aPR] = 0.54, 0.32–0.90), while in non-MDR cases, PZA-resistance was higher in the Indo-Oceanic (2.2%) vs. East Asian (0.9%) lineage (aPR = 2.26, 95%CI 1.53–3.36), controlling for age, race, foreign birth, HIV status, previous TB diagnosis and site of TB disease.

**Conclusions:** PZA monoresistance is not a reliable marker of *M. bovis* species. Further research is needed to determine if the association between phylogenetic lineage and PZA resistance is due to local drug prescription practices or genetic differences between lineages. The phylogenetic diversity of MTB may have important clinical consequences and implications for development of molecular assays for PZA resistance.

#### PC-684-16 Performance of the Xpert® MTB/RIF test for detection of *M. tuberculosis* and rifampicin resistance in sputum specimens in two regions of Russia

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**Background:** Rapid detection of multidrug-resistant tuberculosis (MDR-TB) is essential for optimal patient care. Our objectives were to compare results of testing unconcentrated and concentrated portions of the same sputum specimen with Xpert® MTB/RIF assay (Cepheid, Inc.), and with conventional smear, culture and drug susceptibility tests (DST).

**Methods:** From 07/2011 to 10/2011, initial sputum specimen from TB suspects at Central TB Research

Institute and Vladimir TB Laboratories was homogenized and split for: (1) direct Xpert (D/Xpert) and smear, and (2) concentration for Xpert, smear, culture (Löwenstein-Jensen [LJ] and MGIT) and DST.

**Results:** A total of 109/238 (45.8%) specimens were culture-positive for MTBc (65-direct smear-positive, 93-concentrated smear-positive), 4 grew non-TB mycobacteria; 67 MTBc had rifampicin resistance [RIF-R]. A single D/Xpert was more sensitive (95.3%, 102/107) than direct (59.6%, 65/109) or concentrated smear (85.3%, 93/109) or LJ culture (80.8%, 84/104), but slightly less sensitive than MGIT (98.2%, 107/109). D/Xpert detected 50.9% (27/53) direct smear-negative specimens. D/Xpert specificity was 86.0% (104/121) compared to culture and 89.3% (50/56) compared to a combined reference standard of culture and clinical criteria. D/Xpert indeterminate rate (3.4%) was lower than the MGIT contamination rate (4.2%). Centrifugation did not improve the sensitivity of Xpert but decreased the indeterminate rate to zero. Concordance of Xpert with phenotypic reference tests was 91.9% (57/62) for RIF-R and 97.4% (38/39) for RIF-S. Of 12 isolates in which Xpert and phenotypic results differed, 6 were tested by Biochip and all results supported the Xpert result. In 93.9% (62/66) RIF-R specimens, INH-R was also detected by DST.

**Conclusion:** In a high MDR-TB prevalence setting, the direct Xpert test reliably detected 95% of TB cases including 51% direct smear-negative cases and identified 94% of MDR-TB cases within hours of specimen collection.

#### PC-685-16 Comparison of Xpert® MTB/RIF with TB-Biochip MDR assay for rapid detection of drug-resistant *Mycobacterium tuberculosis* in Russia

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**Background:** Several molecular methods are available for rapid detection of MTBc and drug resistance in clinical specimens. We compared results of the automated Xpert® MTB/RIF test (Cepheid, Inc.) and TB-Biochip MDR system (Biochip, Biochip-IMB Ltd, Moscow, Russia), with culture and phenotypic drug susceptibility tests (DST) from the same sputum specimen.

**Methods:** From 07/2011 to 10/2011, sputa from 104 TB suspects at the Central TB Research Institute Laboratory, were homogenized and split for direct Xpert (D/Xpert) and concentrated by centrifugation for Xpert (C/Xpert), Biochip, culture and DST.

**Results:** A total of 71/104 (68.9%) specimens were MTBc culture-positive (64 smear-positive; 55-rifampicin-resistant [RIF-R] and isoniazid-resistant

[INH-R], 2 were mono-RIF-R, 4 were mono-INH-R); 3 grew non-tuberculosis mycobacteria. The sensitivity of D/Xpert, C/Xpert and Biochip for MTB detection compared to culture was 97.1% (67/69), 98.6% (70/71) and 97.3% (69/71), respectively; specificity was 77.4% (24/31), 81.3% (26/32) and 78.1% (25/32). Sensitivity of Xpert and Biochip for detection of RIF-R were 92.5% (49/53) and 92.7% (51/55), respectively, compared to phenotypic DST. Xpert and Biochip specificity for exclusion of RIF-R was 100%. Isolates with discordant results comparing Xpert with phenotypic DST were tested by Biochip and all results supported the Xpert result. The most frequent mutation in *rpoB* gene detected by Biochip was *rpoB531Ser\*ARLeu* (94.4%, 51/54). Concordance of Biochip with phenotypic DST for INH-R was 98.3% (56/57) and 91.7% (11/12) for INH-S. The indeterminate rate for D/Xpert test was 2.9% and 0% for C/Xpert and Biochip.

**Conclusion:** Both assays were similar in accuracy for detecting MTBc and RIF-R compared to conventional methods. Biochip offers simultaneous detection of INH-R, but its use is limited to reference laboratories with appropriate infrastructure and molecular expertise. D/Xpert was faster and suitable for smaller laboratories.

#### PC-686-16 Comparison of drug susceptibility testing using solid and liquid media yield to identify patients with MDR-TB in Nigeria

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**Background:** The aim of the study was to compare *Mycobacterium tuberculosis* culture and drug sensitivity testing (DST) patterns obtained with solid (LJ) and liquid (BACTEC-MGIT-960) culture media in a high burden TB country.

**Design/methods:** Cross sectional survey of adults with pulmonary TB and patients failing first-line TB treatment in Nigeria. Sputum specimens were cultured on LJ and BACTEC-MGIT-960. Positive specimens underwent DST for streptomycin, isoniazid, rifampicin and ethambutol.

**Results:** 527 specimens were cultured. 428 (81%) were positive with BACTEC-MGIT-960, 59 (11%) negative, 36 (7%) contaminated and 4 (1%) had non-tuberculosis mycobacteria (NTM). 411 (78%) LJ cultures were positive, 89 (17%) negative, 22 (4%) contaminated and 5 (1%) had NTM. The mean (SD) detection time was 11 (6) and 30 (11) days for BACTEC-MGIT-960 and LJ. 449 cultures had concordant results. Both cultures were positive in 389,

negative in 49, contaminated in 7 and 4 had NTM. Concordant positive results had similar DST results. 29 patients had MDR-TB by one method. Of these, 27 were detected by LJ and 25 by BACTEC MGIT 960 with good agreement (kappa 0.876).

**Conclusion:** A substantial degree of agreement was observed between the two systems. Usage of either culture method should depend on their availability, costs and test performance characteristics.

#### PC-687-16 Reporting Xpert® MTB/RIF resistance data from South Africa's national programme

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**Background and challenges to implementation:** South Africa (SA) has a high burden of HIV and TB co-infection and high MDR rates. Based on strong WHO recommendations the NDoH in SA began a phased implementation of the GeneXpert technology in March 2011. To date, 311 117 Xpert MTB RIF tests have been conducted in 55 centres using 77 instruments of varying throughputs. National averages revealed high MTB detection rates ~17%, with rifampicin (RIF) resistance rates of ~7%. Xpert RIF resistance was compared to phenotypic DST and/or MTBDR<sub>plus</sub> line-probe assay.

**Intervention or response:** One Xpert assay replaces two smear microscopies for early MTB diagnosis. RIF resistant patients are initiated on MDR treatment. A second sample is submitted for LPA or DST for confirmation and to determine INH status. All GeneXpert analysers are interfaced to the LIS and data transferred to the Central Data Warehouse (CDW) daily. Matching software at CDW links Xpert RIF to corresponding LPA and DST results with a high degree of certainty.

**Results and lessons learnt:** 864 Xpert RIF resistant cases had matched results. Currently, only ~40% cases submit the second sample. The national concordance for Xpert with LPA RIF resistance is 89.6% and with DST is 85.4% (combined rates: 83%). Combined INH resistance is 79% in these cases. RIF mono-resistance shows geographic variation with a national average of 20% (range of 5–40%).

**Conclusions and key recommendations:** RIF resistance detected by Xpert showed good concordance with LPA and/or DST. RIF mono-resistance was high in certain sites and requires further investigation. Ongoing clinical training is important to ensure adherence to the testing algorithm. A repository of all discordant strains is essential for future sequencing and monitoring of assay performance.

### PC-688-16 Consequences of acquired resistance to anti-tuberculosis second-line drugs: time to culture conversion in the US, 1993–2008

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**Background:** Acquired resistance (AR) to second-line drugs (SLD) is a problem in treating patients with drug-resistant tuberculosis (TB) worldwide. Conversion of sputum cultures from positive to negative is an important indicator of the effectiveness of treatment. Our objectives were to evaluate the impact of AR to injectable second-line drugs (ISLD) and fluoroquinolones (FQ) on time to sputum culture conversion among culture positive TB cases in the USA, 1993–2008.

**Design/methods:** We defined AR as drug resistance at the final drug susceptibility test (DST) but susceptibility to the same drug at the initial DST. We analyzed the impact of AR on time to culture conversion using Kaplan-Meier plots and multivariate Cox proportional hazards regression models.

**Results:** Of 2268 cases with both initial and final DST for ISLD, 49 (2.1%) acquired resistance. Of 1138 cases with both initial and final DST for FQ, 32

(2.7%) acquired resistance. Sputum cultures converted to negative in 71% (35/49) of cases with AR to ISLD and 81% (1837/2268) without AR to ISLD. Sputum cultures converted in 72% (23/32) individuals with AR to FQ compared to 81% (918/1138) without AR to FQ. Median time to culture conversion was significantly longer among cases with AR to ISLD (6 vs. 3 months,  $P < 0.001$ ) and AR to FQ (7 vs. 3 months,  $P < 0.001$ ) compared to persons without AR. AR to FQ (aHR = 0.54 [0.35–0.82]), positive HIV status (aHR = 0.68 [0.54–0.83]), and MDR-TB at treatment initiation (aHR = 0.76 [0.65–0.89]) were independently associated with culture conversion, while positive HIV status (aHR = 0.64 [0.55–0.74]) and MDR-TB at treatment initiation (aHR = 0.74 [0.66–0.83]) were independently associated with AR to ISLD.

**Conclusion and recommendations:** Sputum culture conversion was significantly delayed among MDR-TB cases with AR to ISLD or FQ. Providers should consider emergence of AR to SLD among MDR-TB patients with longer time to culture conversion.

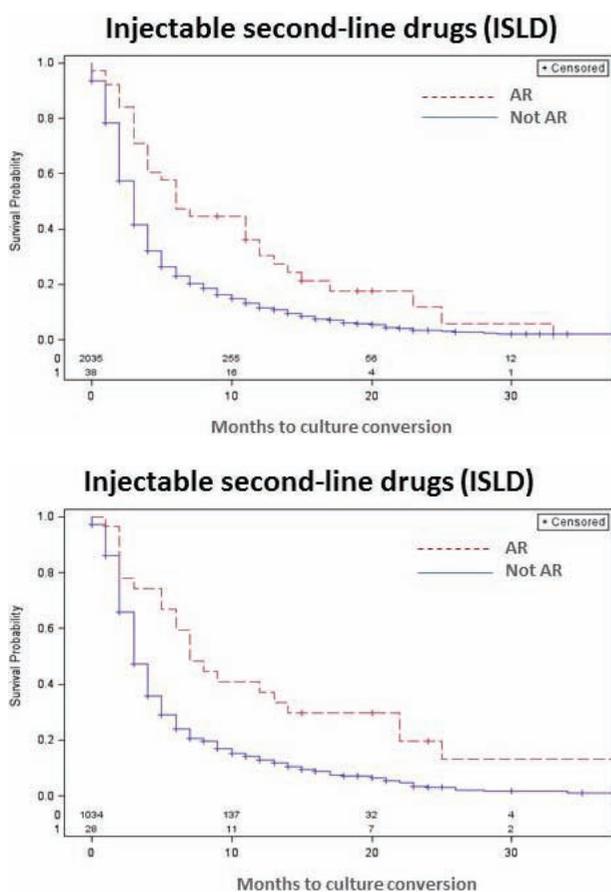
### PC-689-16 Detecting XDR-TB phenotypes with single nucleotide polymorphisms

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**Background:** Molecular diagnostics, based on the detection of specific mutations associated with drug-resistance, are currently the most promising technologies for rapidly detecting extensively drug-resistant tuberculosis (XDR-TB) isolates. For molecular diagnostics to be effective globally, we need a comprehensive understanding of these mutations as markers of resistance. For this study, the Global Consortium for Drug-resistant TB Diagnostics (GCDD) conducted a detailed analysis of the sensitivity and specificity of mutations found in genes associated with drug-resistance in XDR-TB isolates from India, Moldova, Philippines and South Africa.

**Design/methods:** Each isolate underwent drug susceptibility testing for resistance to isoniazid (INH), rifampin (RIF), moxifloxacin (MOX), ofloxacin (OFX), amikacin (AMK), capreomycin (CAP) and kanamycin (KAN) using MGIT 960 and WHO cut-off concentrations. The genes: *katG*, *inhA*, *rpoB*, *gyrA*, *gyrB*, *rrs*, *eis* and *tlyA* were sequenced and mutations were analyzed.

**Results:** We collected 416 highly-resistant *M. tuberculosis* isolates. 370 were INH<sup>R</sup>, 356 RIF<sup>R</sup>, 292 MOX<sup>R</sup>/



**Figure** Kaplan-Meier survival curves of time to initial sputum culture conversion.

OFX<sup>R</sup>, 230 AMK<sup>R</sup>, 219 CAP<sup>R</sup> and 286 KAN<sup>R</sup>. Mutations in *katG* and *inhA* had a combined sensitivity of 95% for the detection of INH<sup>R</sup>. *rpoB* mutations had a combined sensitivity of 97% for detection of RIF<sup>R</sup>. *gyrA* mutations had 88% and 97% sensitivity and specificity respectively for detection of MOX<sup>R</sup>. The A1401G *rrs* mutation had high sensitivity/specificity for detection of AMK<sup>R</sup>/CAP<sup>R</sup> but not KAN<sup>R</sup>, which was best detected with a combination of mutations in the *rrs* and *eis* genes.

**Conclusion and recommendations:** Approximately 45 different mutations in 6 genes were needed to 'detect' most of the DR-TB isolates we examined. Understanding the sensitivity and specificity of individual mutations and combinations of mutations will enable us to maximize the diagnostic and clinical utility of molecular diagnostics.

#### PC-690-16 Genotypic analysis of drug-resistant *Mycobacterium tuberculosis* strains isolated from pulmonary tuberculosis Sudanese patients

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**Background:** Tuberculosis is an infectious disease caused by the bacillus *Mycobacterium tuberculosis*. It typically affects the lungs (pulmonary TB) but can affect other sites as well (extra-pulmonary TB). It is an ancient disease and remains the number one global killer among infectious diseases today due to the emergence of drug-resistant *Mycobacterium tuberculosis* strains.

**Objectives:** The study aimed to compare PCR-based molecular techniques to the conventional culture methods for detecting anti-tuberculosis drug resistance.

**Methods:** This a comparative study, following informed consent, data was collected for consecutively registered sputum smear positive patients from selected NTP diagnostic centers in Khartoum state. Species were identified with biochemical tests and DNA based method. Drug resistance was determined using conventional culture technique as standard technique compared to PCR-based molecular techniques. All parameter indicators calculated to evaluate PCR-based molecular methods against conventional DST.

**Results:** Four hundred and six cultures were carried out for drug susceptibility testing. Strains were typed as *M. tuberculosis* using IS6110 primer in addition to conventional identification tests. The positive and negative predictive values, sensitivity and specificity of PCR-based molecular techniques compared to the

conventional drug susceptibility testing method for detecting anti-tuberculosis drug resistance were found to be 96%, 87%, 77% and 98% for rifampicin, 96%, 79%, 88%, 92% for isoniazid, 76%, 81%, 65% and 88% for ethambutol and 90%, 97%, 90% and 97% for streptomycin respectively. Overall accuracy of MDR stains was found to be 85%.

**Conclusion:** Molecular techniques are simple, rapid as accurate as conventional DST methods for detecting drug resistance and can be implemented in our setting.

#### PC-691-16 Mutation analysis using PCR-RFLP in the genes associated with isoniazid and streptomycin-resistant *Mycobacterium tuberculosis* strains

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**Background:** The emergence of drug-resistant strains of *Mycobacterium tuberculosis* complex is an increasing problem for populations and tuberculosis control programs in developed and developing countries alike.

**Objectives:** This study aimed to confirm the presence of mutant genes associated with isoniazid and streptomycin resistance using PCR-RFLP molecular method. **Methods:** Following informed consent, data was collected for consecutively registered sputum smear positive patients from selected national TB control program (NTP) diagnostic centers in Khartoum state. Drug resistance was determined using conventional culture technique as standard technique compared to PCR-based molecular techniques. Confirmation of mutation analysis was done by PCR-RFLP for *rpsL*<sub>43</sub> and *KatG*<sub>315</sub> mutant genes associated with streptomycin and isoniazid resistance respectively.

**Results:** The prevalence of the *rpsL*<sub>43</sub> and *KatG*<sub>315</sub> mutant allele among the STM and INH resistant *M. tuberculosis* was found to be 60% and 63% respectively. In the absence of mutation in *rpsL*<sub>43</sub> region, *MboII* restriction enzyme digests *rpsL*<sub>43</sub> and results in a 212-bp and 58-bp fragments which appeared in all SM sensitive strains and only four of the SM resistant isolates (33 out of 39 = 85%). Wild-type isolates generated only a single band at 209 bp and this characteristic was shown in 31/49 (63%) of the INH resistant strains with a single band and no enzyme digestion occurred. PCR-RFLP test is not 100% sensitive for the detection of isoniazid resistance but it is 100% specific.

**Conclusion:** The use of the PCR-RFLP technique in detecting nucleotide mutations provides a rapid,

accurate and relatively inexpensive method for predicting the resistance profile of the isolated organism. The methods used in detecting these genes could be adapted to assist in monitoring the spread of drug resistance in our setting.

**PC-692-16 Evaluation of GenoType® MTBDR for molecular detection *Mycobacterium tuberculosis* multidrug-resistant strains at the tuberculosis central reference laboratory**

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**Background:** The rapid emergence of multidrug-resistant *Mycobacterium tuberculosis* (MDR-TB), defined as resistance to rifampicin and isoniazid, poses a serious threat to the treatment of tuberculosis worldwide. A delay in the diagnosis of MDR-TB associated with standard drug susceptibility testing methods is likely to contribute to the transmission of resistant strains. The GenoType® MTBDR<sup>plus</sup> enables a rapid result from pulmonary patient specimen and from culture material. The identification of rifampicin resistance is enabled by the detection of the most significant mutations of the *rpoB* gene. For testing the high level isoniazid resistance, the *katG* gene is examined and for testing the low level isoniazid resistance, the promoter region of the *inhA* gene is analyzed.

**Objective:** The purpose of this study was to evaluate the GenoType MTBDR assay on its ability to detect resistance to INH and RIF among retreatment cases at the central reference laboratory (CRL) in Kenya.

**Methods:** Data from CRL on confirmed MDR cases was abstracted for the year 2010. The GenoType® MTBDR<sup>plus</sup> assay was evaluated using this data for the detection of rifampicin and isoniazid resistance.

**Results:** A total of 87 retreatment cases had complete data and were declared MDR-TB. Of these only 37.9% (33) had HIV results and 33.3% (11) were HIV positive. Out of the 87 cases 73.5% (64) were direct smear positive. All the 87 specimens showed growth on LJ. The resistance to RIF was indicated in all the 87 cases. Both *KatG* and *inhA* mutations were detected in 5.7% (5) of 87 MDR isolates. The overall rates of concordance of the MTBDR<sup>plus</sup> and the MGIT 960 TB for the detection of isoniazid and rifampicin resistance was 100% for *rpoB* and *katG*.

**Conclusion:** These results show that the MTBDR<sup>plus</sup> assay is useful in the detection and management of tuberculosis especially when MDR-TB is suspected, thus representing a reliable and upgraded tool for the detection of MDR-TB.

**PC-693-16 The biological fitness of MDR and XDR clinical strains of the F15/LAM4/KZN and Beijing families**

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**Background:** This study aims to explore differences in growth kinetics between drug-susceptible and multi- and extensively drug resistant (MDR and XDR) strains, some of which were associated with the rapid spread and high mortality rates in KwaZulu Natal in 2005.

**Methods:** The biological fitness was ascertained for 11 clinical isolates belonging to the F15/LAM4/KZN family (6), the Beijing family (4) and H37Rv. Optical density (OD) measurements, colony forming units (CFU) counts and the Alamar Blue viability assay were used to measure growth rate at 4-day intervals for 24 days. The competitiveness of DR and susceptible pairs of isolates was assessed by means of a competition assay using 4 antibiotics. OD measurements and CFU counts were performed for the competitive pairs at 6-day intervals for 30 days.

**Results:** No significant differences in growth were found between strains of the KZN family. Significant differences in growth rate were found between B910 (DS) and R283 (MDR) in the OD ( $P < 0.022$ ) and Alamar Blue assay ( $P < 0.026$ ). OD and CFU results for the competition assay showed a higher growth capacity for KZN DS strains, V9124 and V4207 than V2475 (MDR) and KZN 605 (XDR). Similarly, B910 (DS) and B1528 (DS) presented as more fit than R35 (MDR) in competition.

**Conclusions:** The preliminary results suggest that some drug resistant strains incur a fitness cost compared to susceptible strains. Genotypic analysis still needs to be performed on these isolates to determine the association of strain genetic background and drug-resistance conferring mutations with growth phenotype.

**PC-694-16 Culture conversion among multidrug-resistant tuberculosis patients on second-line anti-tuberculosis drugs in Nigeria**

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**Background/objective:** Conversion of sputum mycobacterial cultures from positive to negative growth of *Mycobacterium tuberculosis* is considered the most important interim indicator of the efficacy of anti-TB treatment. The aim of this study was to evaluate the initial sputum culture conversion at the third month of therapy.

**Methods:** A cross-sectional study involved 61 MDR-TB patients admitted into the University College Hospital, Ibadan, Nigeria between 2010 and 2011. The patients were placed on second line intensive

phase of 6 months standardized treatment regimen using amikacin/kanamycin (Am/Km), cycloserine (Cs), prothionamide (Pto), pyrazinamide (Z) and levofloxacin (Lfx). Two sputa samples of each patient were cultured for tuberculosis monthly using Löwenstein-Jensen medium.

**Results:** A total of 61 patients were studied who were sputum culture-positive at baseline. The ages ranged between 15 and 75 with mean  $33.12 \pm 8.1$  yr. There were 43 males and 18 females. After initiation of second-line therapy, 48 (78.6%) first converted by 2nd month, 9 (14.8%) by 3rd month, 1 (1.6%) by months 4 and 5, but 2 patients died before the end of intensive phase.

**Conclusion:** A good proportion of patients achieved sputum culture conversion within 2 to 3 months of starting treatment. Sputum conversion is a useful and appropriate interim indicator of treatment outcome in patients with multidrug resistant TB. A good laboratory support is mandatory for management of MDR-TB to monitor the progress of treatment and early identification of failure of the regimen.

#### PC-695-16 Evaluation of tuberculosis drug resistance using the Genotype MTBDR<sub>plus</sub> test: the experience IHVN ACTION PEPFAR Nigeria

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**Introduction:** Resistance to both isoniazid and rifampicin is termed multidrug-resistant tuberculosis (MDR-TB) which is classically diagnosed with slow solid culture methods. This study was carried out to assess the molecular characterization of drug resistant *Mycobacterium tuberculosis* complex (MTBC) by determining the presence of MTBC from smear positive sputum samples and the resistance pattern of the MTBC strains.

**Methodology:** It was a prospective study, on 188 confirmed TB patients, to examine TB drug resistance using a recently WHO endorsed PCR based test: MTBDR<sub>plus</sub> assay from Hain Lifesciences. This test examines 3 genes, one conferring RIF and two conferring INH resistance. Statistical analyses using SPSS Ver 17.0 was employed using a 95% confidence interval, a significance level of  $P < 0.05$  and  $\chi^2$  test of independence was carried used.

**Result:** A total of 188 smear positive samples were analyzed between January and August 2010 for RIF or INH resistance. *Mycobacterium tuberculosis* complex was found in 181 (96.3%) and non-tuberculous *Mycobacterium* was found to be 7 (3.7%). Only 2 cases of MDR-TB were detected (1%), 17 mono resistance to RIF (9%) and 1 mono resistance to INH (0.5%). Out of 181 MTBC strains, 31.6%, and 100% had S531L mutation (MUT 3) in RIF-mono resistant

strains and MDR strains, respectively. In addition, mutations in the *rpoB* gene at the 530–533 regions (WT8) combined with S531L mutation (MUT3) were responsible for 8 (42.1%) of RIF-resistant out of the 19 RIF-resistant MTBC while mutation at the 530–533 regions (WT8) only were found to be responsible for 3 (15.8%) of the RIF-resistant MTBC. Of all INH-resistant strains found in this study, 100.0% had a mutation in the *katG* gene mediated by codon 315 while 33.3% had mutation in the *inhA* gene (codon S3C15T). Moreover, *katG* mutation in 100.0% of INH-resistant MTBC strains while *inhA* mutation was found in 33.3% of INH-resistant strains. All the MDR strains had mutations at the *katG* gene, accounting for 66.7% of mutations at the *katG* while only 1 (33.3%) MDR strain was found with mutation at the *inhA* gene.

**Conclusion:** The study found the common mutation for RIF and MDR-TB as *rpoB* gene at the 530–533 regions (WT8).

#### MULTIDRUG-RESISTANT TUBERCULOSIS: CLINICAL ASPECTS

##### PC-725-16 Study of very infectious (super-spreader) multidrug-resistant tuberculosis in Japan and Asia

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**Background:** Multidrug-resistant (MDR), *Mycobacterium tuberculosis* (MTB) is a big problem in Japan as well as in the world. Recently, we found very infectious MDR-TB (super spreader MDR-TB) in Osaka Japan using VNTR and RFLP analysis. On the other hand, foreigner (immigrant) patients from China with MDR-TB are recently increasing in Japan. Furthermore, genetic analysis of MDR-TB in China (Harbin City) was studied to elucidate the presence and immigration of super-spreader MDR-TB in Asia. **Design/methods:** Genetic analysis of foreigner MTB was studied using RFLP, VNTR and MST analysis. Genetic analysis of super-spreader MDR-TB was studied using VNTR and RFLP.

**Results:** By using genetic analysis of foreigner MTB, Cluster 1 (Beijing type, modern type) and Cluster 2 (non-Beijing type) of MTB were demonstrated. It is suggested that TB infection between foreigner patients with Cluster 1 MTB and 2 is spreading in Japan. On the other hand, we found first the super-spreader MDR-TB from 7 patients with MDR-TB in Osaka.

They showed same VNTR and RFLP patterns. Furthermore, super-spreader MDR-TB were found in Harbin City, China. We analysed MDR-TB DNAs of 50 patients in Harbin. MDR-TB from 6 patients out of 50 (12%) showed same VNTR pattern of super-spreader MDR-TB in Osaka. Using in vivo murine model, it was demonstrated that super-spreader MDR-TB exerted higher toxicity and shorten (make worsen) the survival than those of conventional MDR-TB or drug sensitive TB.

**Conclusion and recommendations:** These data first indicate the presence of very infectious and toxic (super-spreader) MDR-TB in China as well as Japan. Some patients with super-spreader MDR-TB might immigrate to Japan from Asia. It is also indicated that TB infection between foreigner patients with TB showing cluster of same DNA patterns is spreading in Japan.

(Co-worker : Shimouchi A, Suzuki K).

#### PC-726-16 Resistance to anti-tuberculosis treatment: study conducted on 960 smear-positive patients under first-line anti-tuberculosis care in Burundi

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**Background:** Improve the management of TB in Burundi. Highlight the factors responsible of the anti-TB multidrug resistance. Evaluate the results of the national third-line treatment protocol. Establish rules to prevent anti-TB multidrug resistance.

**Design/methods:** We conducted a direct interview of patients receiving anti-TB first line care with data collection on a questionnaire; we analyzed the sputum (only positive sputum was considered). We carried out the culture, isolation of the organism and antibiotic susceptibility. Finally, we put our patients on treatment of multi-resistant protocol (third line) to assess the results. Close monitoring yielded outcomes of our study.

**Results:** Of 960 followed patients under anti-TB first-line care (2RHZE 4R3H3), 7 have developed multidrug resistance and 953 responded to the treatment. The extremes of ages were 17 and 60 years with an average age of 33.71. The sex ratio M/F was 4/3. 7 of 7 patients were from poor settings with a precarious level of education. 4 patients had a history of multi-resistant smear-positive TB whose primary treatment had been misbehaved. The notion of multi-

resistant TB contagion was noted for 2 patients living together in close contact. 5 of 7 patients were put on the third line of treatment (3KCOPHZE 12OPHZE): remission of symptoms was achieved to 3/5 patients while 2/5 patients discontinued the treatment all in the second phase. All 3/5 of patients have relapsed and died  $\leq 2$  years.

**Table** Clinical and bacteriological features of our 7 multi-resistant patients

Patient	Sex	Age	Isolated germ	Resistance to anti-TB			History of tuberculosis	Type of resistance
				H	R	E Z		
K <sup>1</sup>	M	17	<i>M. tub</i>	R	R	S R	<ul style="list-style-type: none"> <li>No concept of TB previous contagion</li> <li>Previous treatment misbehaved</li> </ul>	Acquired
ND <sup>2</sup>	M	30	<i>M. tub</i>	R	R	R R	<ul style="list-style-type: none"> <li>Concept of TB previous contagion</li> <li>No previous treatment</li> </ul>	Primary
NJP <sup>3</sup>	M	31	<i>M. tub</i>	R	R	S R	<ul style="list-style-type: none"> <li>No concept of TB previous contagion</li> <li>Previous treatment misbehaved</li> </ul>	Acquired
BD <sup>4</sup>	M	40	<i>M. tub</i>	R	R	S R	<ul style="list-style-type: none"> <li>No concept of TB previous contagion</li> <li>Previous treatment misbehaved</li> </ul>	Acquired
NR <sup>5</sup>	F	24	<i>M. tub</i>	R	R	R R	<ul style="list-style-type: none"> <li>Concept of TB previous contagion</li> <li>No previous treatment</li> </ul>	Primary
K <sup>6</sup>	F	60	<i>M. tub</i>	R	R	R R	<ul style="list-style-type: none"> <li>Concept of TB previous contagion</li> <li>No previous treatment</li> </ul>	Primary
NG <sup>7</sup>	F	34	<i>M. tub</i>	R	R	R R	<ul style="list-style-type: none"> <li>No concept of TB previous contagion</li> <li>Previous treatment misbehaved</li> </ul>	Acquired

TB = tuberculosis; *M. tub* = *Mycobacterium tuberculosis*; S = sensitive; R = resistant; M = male; F = female; H = isoniazid; E = ethambutol; R = rifampicin; Z = pyrazinamide.

**Conclusion and recommendations:** The causes of multidrug resistance are attributable to both patients (non adherence, side effects, etc.) and medical staff (poor clarifications of the disease). The third line of treatment is ineffective, expensive, of long-term and has side effects that the patients have to bear since it is the last resort support. Physicians must ensure close monitoring and rigorous surveillance. The prognosis is poor and is even worse if multidrug-resistant TB is associated with HIV.

### PC-727-16 Quantifying the burden of second-line drugs resistance in previously treated patients in Niger

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**Background:** To evaluate second line drug susceptibility of *Mycobacterium tuberculosis* strains isolated from first-line retreatment patients in Niger. Second-line treatment for multidrug-resistant (MDR) tuberculosis was not programmatically organised before 2008.

**Methods:** From January 2008 to December 2011, 209 sputum specimens after retreatment with regimen 2RHZES/1RHZE/5RHE were analysed. Forty originated from patients previously treated with second-line drugs (SLD) and 37 of them with no standardized regimen (3 followed standardized treatments in 2008). Culture, identification and proportion method drug susceptibility testing (DST) were undertaken at the Institute of Tropical Medicine, Antwerp, Belgium.

**Results:** From 137 failures and 72 relapse cases, 142 strains of *M. tuberculosis* were isolated. Fifteen strains were susceptible to all drugs, two were resistant to isoniazide, three were poly resistant not MDR and 122 (85.9%) were MDR. SLD resistance was present in 22 of the MDR strains (18%): 14 were resistant to one drug, 7 to two and 1 to three drugs. From these SLD resistant strains, 4 were resistant to kanamycin (3.3%), 10 to ofloxacin (8.2%) and 17 to ethionamide (13.9%). Six strains were resistant to ofloxacin and ethionamide. Two strains had extensively drug resistant (XDR) profile (1.6%): Km/Ofx and Km/Ofx/Eto. Ten of 22 patients took SLD in the past: two with kanamycin resistance profile took amikacine and six with ofloxacin resistance took quinolones in no standardized regimen. Two patients with XDR strains had poor compliance with 18-months standardized treatment.

**Conclusion:** The majority of patients after tuberculosis retreatment in Niger carry MDR strains and some of them previously untreated with these drugs are also SLD resistant. XDR strains were detected in two cases. Standardised, programmatic, short course second line regimen is in place since 2008, overcoming this resistance and preventing its increase.

### PC-728-16 Successful 12-month treatment for multidrug-resistant tuberculosis patients in Benin

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**Background:** Treatment results of MDR-TB patients in Cotonou, Benin, according to a standardised short-course regimen.

**Design/methods:** Since 2007, all TB-MDR patients identified and residing in Benin are treated with a 12-month regimen: 12 months of gatifloxacin, prothionamide, clofazimine, ethambutol, and pyrazinamid supplemented the 4 first months by kanamycin and isoniazid. Patients are usually hospitalised/hosted for all the duration of their treatment. The intake of all the drugs is systematically daily supervised by a nurse. Bacteriological controls (smear and culture) are made at months 1, 2, 3, 4, 6, 8, 10, 12 and then 18 and 24 for the follow-up.

**Results:** From 2007 to 2010, 23 MDR-TB patients were treated: 15 patients were registered as failure cases (14 failures after retreatment regimen), and 8 as relapses (7 with more than one relapse). 22 patients (96%) were declared cured (5 negative cultures) and 1 died at month 4 with negative bacteriological results at months 1 to 3. The only 2 HIV positive patients were cured; both were women who got pregnant after being cured and both delivered a healthy baby. Most of the cultures were negative at month 2 and all of them at month 3. Zero relapse at 18 months, zero relapse at 24 months for the 15 patients which can be analysed.

**Conclusion:** The efficacy of this regimen is excellent. At national level, it has been decided since 2011 to reduce the length of the MDR-TB treatment to 9 months, with moxifloxacin replacing gatifloxacin (no more available on the market).

### PC-729-16 Experiences on using second-line anti-tuberculosis drugs in patients with a previous treatment history in a Chinese setting

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**Background:** Second-line anti-TB drugs are available in most of TB clinics in China. This study aims to describe the experiences on using 2nd-line anti-TB drugs in patients with multiple treatment history, and to find evidences for the prevention of XDR-TB in China.

**Design/methods:** A cross-sectional study was carried out in 10 county/district TB clinics from 5 provinces of China. The study participants were TB patients with a history of at least two treatment courses ( $\geq 4$  weeks). Face-to-face interviews were given by

trained investigators to the consented participants who were also provided with drug susceptibility tests (DST).

**Results:** Of the 328 eligible TB patients, 289 were bacteriologically confirmed, with a mean age of 48 years. Of them, 23.8% had a history of taking 2nd-line drugs, with 5.5% and 14.6% in their 1st and 2nd treatment episode respectively. Of those who received 2nd-line drugs, 77.8% were treated in county TB clinics where only sputum microscopy was applied in diagnosis. The proportions to use of 2nd-line drugs in susceptible, MDR and other drug-resistant patients were 14.9%, 19.5% and 13.3%, respectively ( $P = 0.511$ ). Multivariate analysis found that frequency of previous treatment was significantly associated with the use of 2nd-line drugs ( $P < 0.01$ ), whereas no statistically significant associations were found between MDR status, age, gender, medical insurance and the use of 2nd-line drugs.

**Conclusion and recommendations:** The use of 2nd-line anti-TB drugs has not been well regulated in China. The behavior of prescription of the 2nd-line drugs mainly depends on the treatment history of patients, rather than drug-resistance profile. Accessibility in DST should be assured for the high risk TB patients in order to prevent the epidemics of XDR-TB.

### PC-730-16 Diagnosis and treatment of multidrug-resistant tuberculosis in three Chinese cities

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**Background:** Although China has a quarter of the world's MDR-TB cases, little is known about the current diagnosis, treatment and management of MDRTB patients in China's hospital system.

**Method:** In the main hospital providing TB care in three Chinese cities, we reviewed the medical records of all patients diagnosed with MDR-TB cases between January 1, 2006, and April 30, 2009. We contacted these patients and administered a structured questionnaire to those available for interview.

**Results:** Of the 93 patients with laboratory-confirmed MDR-TB, 83 had medical records available for review and 44 patients were interviewed. During the hospitalization when sputum specimens were sent for mycobacterial culture and drug susceptibility testing (DST), patients were hospitalized a median of 31 days (range 29–32). The median hospital expense for the initial hospitalization was 6950 RMB. It took a median of 64 days (range 44–75) for the laboratory to confirm MDRTB. All patients had been discharged by the time DST results became available. The hospital tried to contact these

patients and 24 patients came back for treatment; however, only 32% of these patients were treated in accordance with global standard. These patients were hospitalized a median of 20 days (range 8–42). The median expense for this hospitalization for treatment was 5458 RMB. Nearly 70% of all hospital expenses were paid by patients.

**Conclusion:** The delay in MDR-TB diagnosis results in lost to follow-up for a large number of MDR-TB patients. But the majority of patients received inappropriate treatment with second-line TB drugs after the diagnosis of MDR-TB. Economic burden of MDR-TB diagnosis and treatment is high.

### PC-731-16 Pulmonary tuberculosis treatment based on drug susceptibility test results in Arkhangelsk region

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**Introduction:** The problem of drug-resistant TB is an urgent problem in Arkhangelsk region of Russia.

**Aim:** To evaluate the efficiency of chemotherapy regimens based on DST results for pulmonary TB patients registered in 2010.

**Material and methods:** In 2010 in Arkhangelsk region 584 TB patients started treatment (495 new cases, 81 relapses, 4 after default, 4 after failure). Before treatment start drug susceptibility tests to H, R, E, Ofx, Km, Cm were carried out by the GenoType method for all patients. Patients with TB susceptible to the first line drugs, resistance to S, with unidentified resistance (smear and culture negative) were prescribed 2HRZE/4HR; with resistance to H, 3RZEKm (Cm)Ofx/6RZEOfx; MDR-TB patients, 6-9ZEEKm (Cm)OfxPtoPASCs/18 ZEOfxPtoPASCs.

**Results:** In the group of patients with susceptible TB (131) and monoresistance to S (50) 85.1% (154) were cured; in the group of 212 with unidentified drug resistance (8) and smear and culture negative (204), 73.6% (156) were cured and completed treatment; out of 39 patients with monoresistance to H, 64.1% (25) were cured. There was no statistically significant difference between cure rate of different treatment regimens ( $P > 0.05$ ). 176 patients were detected with MDR (151 before treatment, 18 clinical cases of MDR, 7 MDR were detected after more than 1 month of treatment), 165 patients started treatment, out of them 11 were cured, 5 failure, 20 defaulted from treatment, 12 died from TB, 11 died from other reasons, 3 transferred out, 103 still on treatment. Out of 584 patients 348 reported as successful treatment, 10 failure, 38 default, 39 died from TB, 29 died from other reasons, 11 transferred out, 6 TB was not confirmed, 103 patients are still on

treatment. By March 2012 only 6 MDR-TB patients (3.6%) out 2010 cohort are still smear positive.

**Conclusion:** Treatment regimens based on DST results have led to a high cure rate among patients registered in Arkhangelsk in 2010.

### PC-732-16 The impact of Genotype MTBDR<sub>plus</sub> line probe assay in reducing MDR-TB treatment commencement time

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**Background:** A Technology, Research, Education and Technical Assistance for Tuberculosis (TREAT TB) Project has been implemented in Cape Town, South Africa to assess the impact of new molecular diagnostics on the diagnosis and treatment of multi-drug resistant tuberculosis (MDR-TB). The aim of this study is to assess the impact of MTBDR<sub>plus</sub> line probe assay (LPA) in reducing the time from specimen collection to treatment commencement (TCT).

**Design/methods:** MDR-TB patients diagnosed through culture and conventional drug sensitivity tests (MGIT-960) in 2005–2007 were compared with patients diagnosed through LPA in 2008–2011. The study was undertaken in a routine operational setting in 10 high TB burden facilities. All new MDR-TB cases diagnosed through sputum evaluation were included. Pre- or XDR-TB cases were excluded. Patients diagnosed with MDR-TB were identified from laboratory electronic records and clinical folder reviews undertaken. Demographic, laboratory and clinical data was recorded on case-report forms, entered into a database and descriptive data analysis done using STATA 10.

**Results:** Preliminary results are presented in the Table for 52 MDR-TB patients diagnosed through conventional drug sensitivity tests (DST) and 295 patients diagnosed through LPA. Treatment commencement time for patients diagnosed through LPA (mean 53 days; 95%CI 49–57 days) was significantly shorter compared to conventional DST (mean 83 days; 95%CI 63–104 days) ( $P < 0.000$ ). Age, gender, MDR risk profile and HIV status had no effect on TCT for either LPA or conventional DST groups.

**Conclusion and recommendations:** LPA has significantly reduced TCT when compared to conventional DST in this setting. A limitation to the study is that TCT results also reflect temporal changes. A mean TCT of 53 days with LPA is cause for concern. A better understanding of the health system factors that may contribute to delays in TCT within an operational setting is required.

**Table** Comparison of MDR-TB patients diagnosed with conventional DST and LPA

	Diagnosed with conventional DST ( $n = 52$ )	Diagnosed with LPA ( $n = 295$ )
Age		
Range	18.9–57.8	7.7–81.0
Mean	34.5	35.4
95% confidence interval	31.4–37.6	34.1–36.7
Sex		
Male	25 (48%)	173 (52%)
Female	27 (59%)	122 (41%)
	$\chi^2: P = 0.59$	
MDR risk profile		
Unknown	0 (0%)	7 (2%)
Low	14 (27%)	120 (41%)
High	38 (73%)	168 (57%)
	$\chi^2: P = 0.069$	
HIV status		
Unknown	3 (6%)	4 (1%)
Negative	30 (58%)	116 (39%)
Positive	19 (37%)	175 (59%)
	$\chi^2: P = 0.003$	
Time from sputum taken to MDR-TB treatment commencement (TCT)		
Mean	83 days	53 days
95% confidence interval	63–104 days	49–57 days
	$\chi^2: P < 0.000$	
<b>Assessment of cofactors in each group</b>		
TCT for low MDR-risk group		
Mean	77	48
95% confidence interval	56–98	43–54
TCT for high MDR-risk group		
Mean	86	57
95% confidence interval	57–115	51–63
<i>P</i> value comparing means for low and high MDR-risk	$P = 0.663$	$P = 0.053$
TCT for HIV-negative		
Mean	74	52
95% confidence interval	62–86	48–57
TCT for HIV-positive		
Mean	104	54
95% confidence interval	44.4–162.6	48.2–59.6
<i>P</i> value comparing means for HIV-negative and HIV-positive	$P = 0.181$	$P = 0.671$
TCT for males		
Mean	92	56
95% confidence interval	47–138	50–62
TCT for females		
Mean	76	50
95% confidence interval	62.5–90.1	43–56
<i>P</i> value comparing means for males and females	$P = 0.436$	$P = 0.170$
TCT for age <35 years		
Mean	90.1	50.4
95% confidence interval	57–123	45–57
TCT for age ≥35 years		
Mean	73	56
95% confidence interval	58–87	49–63
<i>P</i> value comparing means for age <35 years and ≥35 years	$P = 0.409$	$P = 0.176$

### PC-733-16 Initial XDR-TB resistance and treatment outcomes in Tomsk, Russia

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**Background:** There is a limited data describing factors for treatment success and failure among XDR-TB patients.

**Objectives:** To examine factors influencing the proportion achieving treatment success among XDR-TB patients.

**Methods:** We conducted a retrospective cohort analysis of all XDR-TB patients enrolled on individualized MDR-TB treatment with quality assured second-line drugs between September 12, 2000, and February 2, 2009. The data was extracted from Tomsk TB civilian and penitentiary databases.

**Results:** Out of 64 patients with XDR-TB, not all had drug susceptibility testing (DST) against all first- and second-line drugs. We found that 40/62 (65%) were resistant to ethambutol, 64/64 (100%) to kanamycin, 31/63 (49%) to capreomycin, 29/54 (54%) to ethionamide, 10/63 (16%) to cycloserine, and 22/53 (42%) to PAS. The results of treatment were the following: 25/64 patients (39%) were cured, 32 patients (50%) failed, 2 patients (3%) defaulted and 5 (8%) died. The resistance to PAS had statistically significant protective effect (only 26% of patients without resistance to PAS were cured as compared to 55% of patients with resistance to PAS,  $P = 0.04$ ). Resistance to other drugs did not have significant effect on treatment outcome. Treatment results were significantly influenced by radiologic extent of the disease: patients with localized TB had 13/21 (62%) treatment success, those with extensive disease and old cavities had 5/27 (17%) treatment success,  $P$  value = 0.0028.

**Conclusions:** Due to limited second-line drug options for treating XDR-TB, factors other rather than resistance to other second-line medications might play an important role in determining cure rates. Further research should be conducted to explore the role of adherence and previous exposure to second-line medications on XDR-TB cure rates.

### PC-734-16 Prevalence and incidence of hearing loss in a cohort of patients treated for drug-resistant tuberculosis in South Africa

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**Background:** South Africa had over 6000 cases reported of DR TB in 2010. DR TB treatment in-

volves ototoxic drugs, including aminoglycosides for 6 months.

**Materials and methods:** Prospective study of patients admitted to Sizwe Hospital, the DR-TB treatment referral site for Gauteng, South Africa. Using the Hughstone Westlake Audiometry method, adults were screened monthly for 6 months, at 9 and 12 months. Hearing loss was graded according to the Brock Criteria.

**Results:** From Sept 2009 to Feb 2011, 129 participants were enrolled. Median age was 37.7 years (IQR 31, 41), 72 (55.7%) were female, 104 (80.1%) were HIV infected. Median follow up time was 279 days (IQR 203, 365). Participants had  $\geq 4$  hearing tests, the first within 30 days of therapy initiation. The treatment regimen contained kanamycin in 96.9% and amikacin in 3.1%. On admission, hearing was normal in 106 (82.7%) participants, bilateral Grade 3 or 4 hearing loss was present in four, and bilateral Grade 1 or 2 in seven. Participants with bilateral loss were older (35.9 vs. 40.0 years  $P = 0.049$ ) but not more likely to have received streptomycin (OR 0.55, 95%CI 0.23–1.32) or a history of working in mines (OR 1.63, 95%CI 0.6 1–4.34). Of the 106 participants with normal hearing at baseline, 73 (68.9%) never developed hearing loss. Thirteen developed unilateral loss after a median of 79 days (IQR 58, 113.0) followed by bilateral loss at a median of 160 days (IQR 115, 196) after therapy initiation. Eleven patients developed bilateral loss after a median of 71 days (IQR 56, 91). In those with hearing loss present at baseline, 6 had progressive bilateral loss after a median of 123 days (IQR 75, 137). Patients with incident hearing loss were associated with older age. (39.5 vs. 34.2,  $P = 0.002$ ). The overall rate of bilateral loss was 35.5 per 100 py, the rate of grade 3 or 4 hearing loss was 16.5 per 100 py.

**Conclusions:** The high rate of incident severe hearing loss underpins the need for new drugs for the treatment of DR TB.

### PC-735-16 Risk factors for MDR-TB among new tuberculosis cases in Lima, Peru

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**Background:** Selection criteria to screen new tuberculosis (TB) patients for multi drug resistant TB (MDR-TB) should be based on the local epidemiology. We studied the risk factors (RF) for MDR-TB in an urban district in Lima with high rates of TB and MDR-TB.

**Methods:** From March 2010 to December 2011 we enrolled new smear-positive TB subjects in the health

centers in a district in North Lima. An additional sputum sample was obtained and cultured in Löwenstein-Jensen (LJ); drug susceptibility test (DST) was performed using the LJ proportion method. A structured questionnaire was applied to obtain data on the presence of RF for MDR-TB, which included local criteria used to decide on routine screening for MDR-TB, as well as other factors reported in the literature.

**Results:** Among 892 patients with full data, 65 (7.3%, 95% confidence interval (CI) 5.6–9.0) had MDR-TB. The HIV rate among those tested (69.4%, 619/892) was 3.1% (95%CI 1.7–4.4) (19/619). HIV status was not associated with MDR-TB, aOR 2.5 (95%CI 0.8–8.3). Of the RF used for routine screening of MDR, MDR-TB contact (adjusted odds ratio (aOR) 2.7; 95%CI 1.11–6.55) and diabetes (aOR 3.2; 95%CI 1.08–9.71) were significantly associated to MDR-TB, while having been in contact with a TB patient that died, ex-prisoner, health care workers and substance addiction were not significantly associated. Additional significant factors were male sex (aOR 2.0; 95%CI 1.0–3.7) and TB contact (aOR 0.51; 95%CI 0.28–0.93). Patients reporting no risk factors for MDR-TB had a significantly lower MDR rate, 5.5% (95%CI 3.67–7.24), than that of those who reported at least one RF, 11.5% (95%CI 7.71–15.34).

**Conclusions:** Overall, MDR rates were high among new TB patients. MDR rates were higher among patients routinely selected for MDR screening, but the RF set to make this selection should be optimized.

#### PC-736-16 Genotype MTBDRplus effect on multidrug-resistant tuberculosis therapy initiation in a rural tuberculosis hospital, South Africa

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**Background:** Recognition of drug resistance and timely initiation of effective MDR-TB therapy are essential to reduce transmission and improve TB patient outcomes. In May 2008 the WHO endorsed the use of the MTBDRplus line probe assay to rapidly screen patients for MDR-TB; shortly thereafter the assay was implemented in the Western Cape Province, South Africa. Evaluation of whether the test has had the effect on shortening time to MDR-TB treatment start and identification of patients at higher risk for diagnostic delay is essential for implementation success.

**Methods/results:** We conducted a retrospective cohort analysis of 197 MDR-TB patients treated at

Brewelskloof, a rural TB hospital in the Western Cape, between 2007 and 2011. 89 patients (45%) received conventional liquid culture and DST on solid medium and 108 (55%) the MTBDRplus assay after positive AFB or culture. Mean age was 37.1 years (SD 12.2), 55% were men, 30% were known to be HIV infected. 171 (88%) had only pulmonary disease, 69 (38%) were smear positive, and mean BMI was 18.9 (SD 4). Median time from sputum taken to MDR therapy initiation was reduced from 80 days (IQ 62–100) for conventional DST to 55 days (IQ 37.5–78) with MTBDRplus. Reduction in laboratory processing time decreased significantly ( $P < 0.0001$ ) while time in transit to the laboratory and time from reporting resistance to when the patient started therapy stayed constant. Laboratory processing time was still 27 days (IQ 20–24) for patients who received MDRTBplus, with smear positive cases a median 22 days (IQ 20–34) and smear negatives with a median 29.5 days (IQ 24–38.5). In multivariate analysis, patients with a MTBDRplus test had a reduced risk of starting treatment 60 days or more after sputum collection of 0.53 ( $P < 0.0001$ ) compared to patients with culture based DST, after adjustment for smear status and site of disease.

**Conclusion:** The introduction of a rapid diagnostic for DST significantly reduced the time to MDR-TB treatment initiation. No patient characteristics other than site of disease and smear positivity predicted delayed time to start in multivariate regression. However, treatment delays often still exceeded the expected one week, perhaps in part due to dependence on smear or culture positivity prior to MTBDRplus performance.

#### PC-737-16 Prevalence of serum electrolyte and renal disturbance in patients being treated for drug-resistant tuberculosis in Windhoek, Namibia

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**Background:** Namibia is a country in southern Africa with a population of 2.1 million, and a TB incidence rate of 603/100 000. Since the implementation of PMDT in 2008, 1305 patients have been treated for DR TB under a government funded programme. Although guidelines recommend monthly electrolyte and renal monitoring of patients at least during the initial phase of treatment, this is often poorly implemented due to reduced staff capacity and distances from laboratory. In the event that the tests are done, there is often suboptimal documentation and follow-up. We present the prevalence of life-threatening electrolyte disturbances in patients being treated with 2nd line anti-TB drugs as well as the prevalence of renal and hepatic impairment while on treatment. It is

hoped that the final results will inform the NTP on the value of frequent monitoring, and alert clinicians to the magnitude of frequently missed adverse events.

**Methods:** This is a retrospective review of patient records for adults enrolled for DR TB treatment and receiving 2nd line injectable at Katutura TB Unit in 2010 and 2011. 70 records were included, with serum potassium, sodium, urea, creatinine clearance, age, sex, HIV status, TB resistance profile, comorbidities, current medications and regimen being analysed.

**Results:** 70 records were analysed, of which 40 (57%) were males. Mean baseline weight of 46.5 kg  $\pm$  SD 1.9.30 (43%) had at least one episode of hypokalemia (defined as a K  $<$  3.6 mmol/L) during 8 months of intensive phase. Hyponatremia occurred in 40/68 (59%) patients, while uremia occurred in 17/70 (24%) of patients. 46 patients (66%) had renal insufficiency (CrCl  $<$  97 ml/min for males or 88 ml/min females). 17 (19%) patients had hyperbilirubinemia and 5 (7%) patients had elevated ALT ( $>$ 45). 26/70 (37%) patients had elevated TSH, suggesting hypothyroidism.

**Conclusion:** Electrolyte and renal impairment are common in patients on treatment for DR TB. While this study needs further validation with a larger patient sample, clinicians should strengthen monitoring for subclinical adverse events. The NTP should encourage the practice of expectant management of adverse events in patients with DR TB, as they may be responsible for significant mortality.

### PC-738-16 Adverse reactions among hospitalised MDR-TB patients on intensive phase: experience from Nigeria

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**Background/objectives:** Second line drugs (SLD) used for treating multidrug resistant tuberculosis (MDR-TB) is frequently associated with high rates of unacceptable adverse reactions needing frequent interruption and change of regimen. The aim of this study was to describe the prevalence of adverse drug reactions in patients with MDR-TB hospitalized during the intensive phase in a treatment centre in Ibadan, Nigeria.

**Methods:** A cross sectional study of MDR-TB patients admitted between July 2010 and December 2011 at the Treatment Centre of the University College Hospital, Ibadan, Nigeria. They were on standardized six months intensive phase regimen (weight based dosing) consisting of amikacin, levofloxacin, cycloserine, prothionamide, and pyrazinamide. The adverse drug reactions were clinically evaluated.

**Results:** A total of 61 MDR-TB patients were studied. Their ages ranged between 15 and 70 yrs with mean age of 33.12  $\pm$  8.1 yr. The most commonly re-

ported adverse event was pain at the injection site 58 (95%). Others were; peripheral neuropathy 40 (66%), nausea 42 (68.8%), vomiting 18 (29.5%), diarrhoea 9 (14.8%) and arthragia 8 (13%). Rashes were recorded in only 5 (8.1%) patients. The gastrointestinal reactions and rashes were observed within the first two months of therapy while the others persisted throughout their treatment. The most alarming adverse effects were recorded among 9 patients, 5 (8.1%) of whom had hearing loss (ototoxicity), 3 (4.9%) had psychosis and the last had renal impairment (1.6%). All patients were treated symptomatically and no drug has been stopped or differed. Two of the patients died from the complications of the MDR-TB.

**Conclusion:** Adverse reactions are common with the use of SLD in MDR-TB patients. Therefore, anticipation and close monitoring for these reactions are necessary to ensure timely recognition and adequate management.

## TUBERCULOSIS MANAGEMENT: COSTS, SMOKING AND MORE

### PC-768-16 Assessment of patient costs and patient perspectives of tuberculosis treatment in Tanzania

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**Background:** Clinical trials of new anti-TB drugs with shortened four-month regimens are underway (Phase II and III). Health systems would benefit from treatment shortening but the perspectives of patients are rarely considered. This mixed-method study assesses the costs and impact of current TB treatment on patients both early and late in treatment, and considers whether patients might value shorter regimens. The initial results presented here from Mwanza, Tanzania, are part of a multi-country comparative study. **Design/methods:** A questionnaire to measure TB patient expenditure and opportunity costs ( $n = 94$ ) was complemented with focus group discussions ( $n = 12$ ) with patients to understand the broader impact of TB treatment. The study population included urban and rural participants from a range of economic backgrounds and variable access to health centres.

**Results: Quantitative:** Borrowing money (35.1%), selling property (43.6%) and hospital admissions (18.1%) typically occurred during the intensive phase (first 2 months of treatment). 84% of patients stopped working due to TB, 50% were unable to work for at least 4–5 months. The difference in the mean direct

cost incurred by patients from different poverty subgroups was not statistically significant ( $P = 0.6$ ), suggesting that the poorer subgroups bear a disproportionately high financial burden of TB treatment. **Qualitative:** Patients described greater hardship during the intensive phase: loss of earnings coupled with higher medical, transport and food costs; substantial side-effects; fear and some discrimination. They were well-informed about treatment duration and adherence and were therefore motivated to complete treatment. **Conclusion and recommendations:** Initial analyses show the intensive phase is physically, financially and emotionally difficult for many patients. Further analyses on patients' regimen preferences, costs proportionate to income level and patients' perceptions at different stages of treatment are forthcoming.

#### PC-769-16 Missed opportunities for preventive therapy for contacts screened in Singapore's national tuberculosis programme

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**Background:** Since 1998, Singapore's national TB programme has performed targeted tuberculin skin testing of close contacts to identify candidates for preventive therapy (PT). In view of universal BCG vaccination at birth and a BCG re-vaccination policy for school leavers from the 1950s to 2001, a threshold of TST  $\geq 15$  mm was taken to recommend PT while those with TST readings 10–14 mm were recommended on a case-by-case basis at the physician's discretion.

**Methods:** To determine if using these TST thresholds resulted in missed opportunities for PT among household/family contacts, we cross-matched contacts screened from 2005 to 2010 with the national TB notification registry as at April 2012.

**Results:** During this period, 20669 household/family contacts were screened around 5041 bacteriologically positive index cases of whom 3017 (59.8%) were sputum acid-fast bacilli (AFB) smear-positive. 4824 (23.3%) and 8154 (39.4%) contacts had TST readings  $\geq 15$  mm and 10–14 mm respectively. Of the latter group, 2527 (31%) were recommended and commenced PT. Of the 5627 contacts with TST 10–14 mm who were not recommended PT, 25 developed active TB. These comprised 2/2224 (0.09%), 9/1896 (0.47%) and 14/1507 (0.93%) contacts of sputum AFB smear-negative, AFB smear 1+/2+ and AFB smear 3+/4+ index cases respectively ( $\chi^2 P = 0.001$ ).

**Conclusion:** Degree of index case sputum AFB smear positivity was significantly associated with likelihood of developing active TB among household/family contacts with TST 10–14 mm. We recommend a uniform threshold of TST  $\geq 10$  mm for PT in household/family contacts of sputum AFB 3+/4+ cases.

#### PC-770-16 Is tuberculosis control financially sustainable in the absence of major donor funding? Reflections from Indonesia

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**Background:** Indonesia has greatly improved TB services over the last few years but needs to continue to scale up, which will require significant increases in funding. Donor assistance, especially from the Global Fund, has been a major factor in the program's success but much of that assistance is expected to end in 2015 and the government needs to replace that from domestic sources.

**Response:** The Ministry of Health (MOH) has prepared an initial analysis of the future program costs and the funding sources based largely on government data. These sources include government budgets, insurance reimbursements and corporate social responsibility.

**Results:** The preliminary projections of the scaled-up program costs indicate an increase from just under US\$100 million in 2011 to almost US\$130 million in 2015. The preliminary targets are for the government to increase its funding from 31% of costs in 2011 to 80% in 2016, with the balance to come from insurance schemes and other sources.

**Conclusions:** The impact of the increased TB costs and the strain that these may place on government and insurance financing systems are a concern, especially since the HIV/AIDS and malaria programs are in a similar situation. Cost-effectiveness of service delivery is likely to become critical and service prioritization may also be needed.

#### PC-771-16 Pulmonary tuberculosis and bronchial asthma: possible inverse relationship

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**Background:** In clinical practice, it was observed that TB patients rarely developed bronchial asthma and vice versa. Also as TB has started to disappear from the world, asthma prevalence has started to rise.

**Objectives:** To compare asthma prevalence in TB and non-TB subjects. To compare severity and frequency of asthma attacks before and after TB.

**Design/methods:** The study was performed in Kosti City (Sudan) on 123 TB patients (69 males and 54 females) at TB centers. TB patients were asked to complete a questionnaire about bronchial asthma. Prevalence of asthma in TB and non-TB subjects were

compared. In TB asthmatics, severity and frequency of attacks before and after TB infection were compared. Parallel study on BCG vaccinated asthma mouse model was going on, but the results are not yet ready.

**Results:** Prevalence of asthma in TB patients was found to be 4.87% (4.3% in males and 5.4% in females) compared to 8.6% (according to wheeze plus other symptom) in non-TB subjects (8.4% in males and 8.8% in females), although 14.6% of TB patients had reported that they had family history of bronchial asthma. 70% of asthmatics in TB group had reported that they developed asthma before TB and that severity and frequency of attacks were more before TB infection.

**Conclusion and recommendations:** Prevalence of asthma in TB patients was found to be less than that in non-TB subjects. Severity and attacks of asthma decreased with TB infection. All this indicated the reverse relationship. Asthma prevalence in female TB patients was found to be more than in male TB patients. Experimental study on mouse asthma model is needed to understand the theory behind this inverse relationship. Fortunately this study is going on now, but more time is needed for the results.

#### PC-772-16 Treatment outcomes of pulmonary tuberculosis in Istanbul, Turkey

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We conducted a historical cohort study using the Turkish National Tuberculosis Register to examine treatment outcomes for pulmonary tuberculosis among 11 186 smear-positive and/or culture-positive subjects aged  $\geq 18$  y and receiving treatment between 1 January 2006 and 31 December 2009 in Istanbul, Turkey. Adverse treatment outcome was defined as the occurrence of death (occurring in 205 (1.8%) subjects) or default (occurring in 679 (6.1%) subjects) or treatment failure (occurring in 126 (1.1%) subjects), yielding a combined total of 1010 (9.0%) subjects with adverse treatment outcome. Factors associated with adverse treatment outcome included birth outside of Turkey (OR 5.38, 95%CI 3.67–7.91); previous history of tuberculosis treatment (OR 3.77, 95%CI 3.26–4.36); age  $\geq 65$  y (OR 2.79, 95%CI

2.21–3.53); and male sex (OR 1.91, 95%CI 1.59–2.27). Death was most strongly associated with age  $\geq 65$  y (OR 45.1, 95%CI 27.0–75.6); default with history of interrupted treatment (OR 11.6, 95%CI 8.94–15.1); and treatment failure with prior history of treatment failure (OR 17.1, 95%CI 6.97–41.6). Multidrug resistance (MDR-TB) was strongly associated with adverse treatment outcome (OR 10.8, 95%CI 8.02–14.6), especially due to treatment failure (OR 92.8, 95%CI 56.1–153.2). Age  $\geq 65$  y, male sex, birth outside of Turkey, and prior history of treatment failure identify patients at increased risk for adverse treatment outcome. Patients with any of these characteristics should be carefully monitored and aggressively treated.

#### PC-773-16 Effect of financial incentives for community-based organisations for tuberculosis patient support

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**Background:** Swaziland has the highest rate of TB in the world with treatment success of only 70%. MDR-TB is an increasing challenge, although drug resistance is not routinely tested.<sup>1</sup> The aim of this study was to evaluate the effect on outcome of providing incentives to community-based organizations to facilitate TB treatment support.

**Design:** A before and after study with control group comparison was conducted. Community-based organisations were provided financial incentives for providing treatment support to TB patients around Swaziland. Financial incentives were spread over the 6 month treatment period, with a bonus given on treatment completion. The primary outcome was treatment success, and comparison of death and default rates were used as secondary outcomes. Confidence intervals were calculated around the rates to detect significance in the findings.

**Results:** 1077 patients were initiated on TB treatment between 1 January 2010 and 30 September 2011 at Good Shepherd Hospital, with 161 receiving treatment support. There was no significant difference in baseline characteristics between the intervention and control groups. There is a significant increase in treatment success (completion + cure) from 67.1% (95%CI 64.0–70.3) without treatment support to 80.7% (74.3–87.1) with treatment support. Rates of death were lower in the intervention group compared with the control group 11.7 (6.5–17.0) vs. 26.1 (23.1–29.1). No significant difference in default rates was detected.

**Conclusions:** Incentives to community-based organizations to provide TB treatment support appears to be effective in improving treatment success and reducing rates of death. A wider analysis across 12 community-based organizations in Swaziland is currently being undertaken.

<sup>1</sup> World Health Organisation. Global Tuberculosis Control 2011 [online]. Available from [http://whqlibdoc.who.int/publications/2011/9789241564380\\_eng.pdf](http://whqlibdoc.who.int/publications/2011/9789241564380_eng.pdf)

### PC-774-16 Self-reporting of symptoms in tuberculosis cases: influence of smoking, HIV and hyperglycaemia

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**Introduction:** TB is more common among people who smoke, have diabetes mellitus and who are HIV positive. Guidelines for community TB screening through symptoms have been developed for HIV positive individuals but as yet no such evidence-based guidelines exist for the high TB risk groups such as those who smoke or have diabetes. This study aims to determine the differences in TB symptom reporting among TB cases who smoke, have diabetes, or are HIV positive, compared to TB cases without these influences.

**Methods:** Culture-confirmed TB cases (confirmed through 16S DNA sequencing) from a TB prevalence survey conducted in 2010 in 24 high TB and HIV burden communities in South Africa and Zambia were analysed. Odds ratios and 95% confidence intervals were calculated for self-reported TB symptoms and smoking, HIV (Abbot Determine HIV test), and/or hyperglycaemia (fingerprick glucose test) or self-reported diabetes mellitus. The association between symptoms, smear grade and previous TB were also investigated.

**Results:** 64463 participants were enrolled. 884 culture-confirmed TB cases were identified. Of the TB cases, 59% reported symptoms and 56% smoked, were HIV positive or had hyperglycaemia. Cases who were HIV positive, smoked or had hyperglycaemia were 1.99 times (95% CI 1.50–2.64,  $P < 0.001$ ) more likely to report symptoms. Previous TB was reported in 18.6% of all TB cases. 20.68% of cases who smoked, had hyperglycaemia or were HIV positive had previous TB, compared to 16.9% of cases without these influences. 23% of HIV positive, 22% of smokers, and 12% of hyperglycaemic TB cases reported previous TB.

**Conclusions:** TB cases who smoke, who are HIV positive and those with hyperglycaemia, are (1) more likely to report TB symptoms and (2) more often have had previous TB than TB cases without these additional influences. Further research is thus warranted to investigate the best predictive community symptom-screening algorithm for hyperglycaemics, and smokers, as have been developed for those with HIV.

### PC-775-16 Influence of contact with tuberculosis patients on drug resistance pattern of new tuberculosis patients

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**Objective:** Study influence of contact with TB patients on drug resistance pattern of new TB patients.

**Materials and methods:** 773 new TB patients from Orel Oblast registered in 2007 and 2010 were included. In Orel Oblast drugs sensitivity of *M. tuberculosis* is testing for all TB culture positive patients and concordance of results for isoniazid and rifampicin obtain 95% according to results of federal system of quality external evaluation. New TB patients who had close contact with TB patients before their illness were selected, DST results of new TB patients and their most probable sources of infection were compared on isoniazid and rifampicin and four first line drugs (isoniazid, rifampicin, streptomycin, etambutol).

**Results:** Close contacts with TB patients before illness were determined at 77 (10.0%) new TB patients, DST results were known at 48 (6.2%) pairs. It was established that DST results of new TB patients coincided with DST results of most probable sources of infection at 42 (87.5%) patients on isoniazid and rifampicin and at 39 (81.3%) patients on first line drugs.

**Conclusion:** DST results of new TB patients coincide with DST results of most probable sources of infection at 80% of cases. Consequently, regimen of chemotherapy for a new TB patient with known DST result of most probable source of infection should be based on DST result of most probable source of infection and after that it should be corrected in accordance with an own DST result.

### PC-776-16 Impact of cigarette smoking on rates and clinical prognosis of pulmonary tuberculosis in southern Mexico

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**Background objective:** To examine the relationship between cigarette smoking and development of pulmonary tuberculosis (TB) and treatment outcomes.

**Design/methods:** From 1995 to 2010, individuals with cough for >2 weeks in southern Mexico were screened. Clinical and mycobacteriological information (isolation, identification, drug susceptibility, and IS6110 based genotyping and spoligotyping) was collected from those with bacteriologically confirmed pulmonary TB. Patients were followed to ascertain treatment outcome and retreatment. From 2001 to 2004, epidemiological and clinical information was collected from household and neighborhood contacts and they were followed for active TB. We estimated TB incidence and mortality rates by smoker and non-smoker population, using information from the National Survey of Addictions.

**Results:** 1062 patients with pulmonary TB and 2951 contacts were enrolled. Smoker:non-smoker incidence rate ratio was higher for men (2.74, 95%CI 2.27–3.31; 2.92, 95%CI 1.80–4.71 and 2.71, 95%CI 2.20–3.30, total, recently transmitted and reactivated disease); living in urban (2.59, 95%CI 2.12–3.17) and rural areas (2.02, 95%CI 1.02–3.79). TB mortality rate ratio among all smokers was also significantly higher (2.95 (95%CI 1.49–5.54). Overall, smoker population was more likely than non-smoker population to experience unfavorable treatment outcomes (adjusted OR 1.74, 95%CI 1.04–2.90) and retreatment (adjusted hazard ratio (HR) 2.22, 95%CI 1.32–3.73). Contacts that smoked had a higher probability of developing active TB (HR 2.57 95%CI 1.08–6.12) during follow-up. Passive smoking was not associated with development of active TB.

**Conclusion and recommendations:** Results indicate the need of incorporating smoking prevention and cessation, especially among men, into international TB control strategies.

#### PC-777-16 Smoking prevalence among pulmonary tuberculosis patients in the Republic of Georgia

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**Background:** There is growing evidence that tobacco smoking increases tuberculosis infection, disease and mortality. However, limited data exists regarding the burden of tobacco exposure among TB patients; data that is needed to determine the utility of smoking cessation interventions. We investigated the prevalence of tobacco smoking among man and woman with active TB disease in the Republic of Georgia.

**Design/methods:** A smoking prevalence survey was conducted from May 2011 to April 2012. Newly diagnosed TB patients >18 years diagnosed were interviewed within 2 months of TB diagnosis. Current smoking was defined as smoking during the interview. We report results of the first 375 participants.

**Results:** A total of 375 TB patients were interviewed; 289 (77%) were male and the median age was 35 years (IQR = 48–25). Overall, 155 (41%) patients were current smokers; 51% among males and 8% among females. Among current smokers, 145 (94%) were daily smokers. Among non-smokers 58% were past smokers (78% among males; 23% among females) and 42% were never smokers. Univariate analysis was performed to analyze the relationships between smoking and other variables. Odds of being smoker among alcohol users is 3.3 times to the odds of being smokers among those who do not use or use alcohol less than once per week. Odds of being smoker among males is 11.8 times to the odds of being smokers among females. There is no association between smoking status and incarceration.

**Conclusion and recommendations:** Prevalence of tobacco smoking is very high (over 40%) among newly diagnosed TB patients in the Republic of Georgia. Cessation efforts among this population are warranted, and has great potential to increase positive treatment outcomes in this population.

#### PC-778-16 Characteristics of patients with recurrence of tuberculosis in the state of São Paulo, Brazil (2006–2010)

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**Background:** The persistence of tuberculosis bacilli in patients considered as cured can determine the recurrence of the disease, which remains as an important issue for public health. The aim of this study was to characterize the cases of TB recurrence in the state of São Paulo (SP), Brazil, from 2006 to 2010.

**Methods:** Descriptive study conducted with patients reported as recurrence in the TB surveillance system in SP. We excluded cases with change of diagnosis, transferred to other states and with unknown information on the outcome. Socio-demographic, clinical and follow-up variables were analyzed using descriptive statistics. Of 94407 notified TB patients, 6937 (7.3%) were recurrences, from which a total of 6403 was included in the study. Calculations were performed considering the valid (complete) data for each variable.

**Results:** Most cases of recurrence consisted of men (73.7%), white (45.0%) with mean age of 41.6 years (SD = 14.3), with 4–7 years of education (32.5%) or schooling ignored (23.6%). The pulmonary form was predominant (84.3%)—66.7% of them were sputum smear positive. The cure rate was 73.1%, the dropout rate 14.3%, failure 2.6% and death 10.0%, still below WHO goals. Co-infection with HIV/AIDS was 19.4%, reaching 27.9% of the total dropouts and 42.9% among deaths. Alcohol use was observed in 15.6% of the patients and in 27.5% of the TB deaths. 63.7% of the patients had indication for DOT. However, 50.0% of the data on the attainment of treatment supervision was incomplete. Considering valid data, less than the half (46.9%) had DOT attained during TB treatment. Among the dropouts, 64.1% had no information on DOT maintenance, and from the valid data, only 13.6% had DOT maintained. Among the deaths, the situation was even poorer, with 71.1% without information, and only 9.1% of DOT attainment.

**Conclusion:** The characteristics observed reinforce the need to develop new strategies to approach TB recurrence and strengthen DOT attainment.

#### PC-779-16 Global financing of national tuberculosis programmes: value for money, additionality, impact and sustainability

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**Background:** TB control is recognized as one the most cost-effective global health interventions. Since its inception in 2002, the Global Fund Against AIDS, Tuberculosis and Malaria has increased its contribution to TB control year upon year. But in 2010 it cancelled Round 11, thereby deferring any new grants until 2014. This paper aims to inform discussions of global TB control funders around some of their core principles—value for money, additionality, impact and sustainability.

**Methods:** We analysed expenditure and notification data reported by National TB Programmes (NTPs) of more than 100 countries in the years 2002–2010. Bivariate relationships were visualized and multivariate regression analysis performed to confirm statistical significance and robustness of results. We employed multiple imputation methods and a dynamic panel estimator.

**Results:** Cost-effectiveness of first-line drug treatment by NTPs was high overall relative to WHO benchmarks based on income level. Value for money, measured by the cost per patient detected and successfully treated with first-line DOTS, varied greatly between countries. The cost per treatment success increased by 0.9% (95%CI, 0.6–1.1%) for every 1% increase in GNI per capita; it *decreased* by 0.5% (0.2–0.8%) for every 1% increase in the total num-

ber of cases. Donor allocations per case did not correlate strongly with the average cost per treatment success. We did not find evidence of foreign funding displacing domestic funding for TB control. A one-time 10% increase in real spending was associated with a 0.9% (0.2–1.6%) decrease in prevalence.

**Conclusion:** Global funders are rightly concerned about making aid unnecessary in the long run, but need to set shorter term benchmarks for NTP performance. There are relatively clear short- and long-run dynamics in value for money, additionality, and impact; benchmarks can help maximize the impact of every dollar spent on TB control today and make it less needed tomorrow.

#### PC-780-16 Cost-effectiveness analysis of a new tuberculosis diagnostic algorithm

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**Background:** New tuberculosis (TB) diagnostic technologies such as Xpert<sup>®</sup> MTB/RIF (Xp) detect TB with higher sensitivity and specificity than existing tests, but are more expensive initially and per test than Ziehl Neelsen microscopy (ZN). Cost-effectiveness analyses are needed to inform implementation of these new technologies.

**Methods:** We created a state-transition model to analyze the evolution of TB in a hypothetical country of 50 million with high TB, HIV and drug resistance prevalence over 10 years, using either a traditional diagnostic algorithm (TDA) or an advanced diagnostic algorithm (ADA). The TDA used ZN then chest X-ray when ZN was negative. The ADA used Xp as the initial diagnostic for high-risk TB suspects (drug resistant suspects and HIV-infected) and Xp after negative microscopy for low-risk TB suspects. We also modeled the effects of improving from ‘real world,’ imperfect compliance (IC) to perfect compliance (PC), and conducted a sensitivity analysis.

**Results:** With IC, ADA resulted in 213 920 fewer TB cases and 279 394 deaths than TDA over 10 years, and *reduced* the net present value of diagnostic and treatment costs by US\$17 million. PC alone improved the TDA outcomes by 214 623 cases and 670 701 deaths. The fewest TB cases and deaths were seen when PC was assumed with the use of the ADA. Univariate sensitivity analysis showed that case and death reduction depended most on infectiousness. Threshold analysis indicated that assuming a range of 4–14 infections resulting from an untreated TB case, deaths averted ranged from 136 to 433 thousand while the cost savings ranged from US\$29 to US\$5 million.

**Conclusions:** Our analysis is consistent with other models which suggest the use of an ADA with Xp

offers sufficient benefits relative to cost such that more detailed analyses for specific settings are warranted. Perfecting TDA compliance would reduce cases by a similar magnitude, but would be far more difficult to implement and sustain than the ADA.

### PC-781-16 Household costs associated with diagnosis and treatment of susceptible and multidrug-resistant tuberculosis in Karachi, Pakistan

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**Background:** Little or no published data on the cost of seeking treatment for susceptible and multi-drug resistant (MDR-TB) exists for Pakistan, a country

**Table** Household costs associated with diagnosis and treatment of susceptible and multi-drug resistant tuberculosis in Karachi, Pakistan

Type of cost	Cost per Patient			
	Susceptible TB		MDR-TB	
	PKR	USD	PKR	USD
Pre-diagnosis				
Consultation fee	571	6.27	1128	12.39
Medication	1051	11.54	3022	33.20
Transport	1112	12.22	1933	21.24
Food	117	1.28	285	3.13
Additional costs	735	8	0	0
Sub-total direct costs	3586	39.31	6368	69.96
Time lost from work days	10 hrs		20 hrs	
Sub-total indirect cost	340	3.74	680	7.47
Hospitalization				
Mean number of in-patient days in the past 6 months	1		3	
Sub-total direct costs	247	2.71	1311	14.40
Mean no. of in-patient days work lost	1		3	
Sub-total indirect costs	270	2.95	810	8.90
Anti-TB drug collection visits				
Consultation fee	96	1.05	8	0.09
Travel	124	1.4	393	4.3
Medication	5.7	0.06	0	0
Food	10	0.10	65	0.72
Other	10	0.10	101	1.1
Sub-total direct costs	245.7	2.7	567	6.21
Anti-TB drugs collection visit time lost	16 hrs		48 hrs	
Sub-total indirect costs	544	5.97	1632	17.93
Follow up visit				
Consultation fee	0	0	9	0.01
Travel	113	1.23	510	5.60
Medication	69	0.75	6	0.06
Food	9	0.09	72	0.80
Other	12	0.12	8	0.08
Sub-total direct costs	203	2.19	605	6.55
Follow-up visits time lost	20 hrs		50 hrs	
Sub-total indirect cost	680	7.47	1700	18.68
Total direct costs	4282	47	8851	97
Total indirect costs	1834	20	4822	53
Total costs	6116	67	13673	150

with the 6th-highest burden of TB. We estimated the direct and indirect household costs for TB diagnosis and treatment for patients in Karachi.

**Design/methods:** Adult patients in Indus Hospital's free community-based TB control program were interviewed between March and May 2011. We measured direct out of pocket household expenditures for consultations, diagnostic tests, non-TB medicines, hospitalization, meals and transport in the five to six months after initially seeking a diagnosis. Indirect costs from lost earnings were estimated only for the time spent on seeking medical care and based on the minimal wage in Pakistan. We extrapolated direct and indirect costs over the full course of treatment.

**Results:** The total costs of diagnosis and treatment were \$67 over 5 months for the 413 susceptible TB patients, and \$150 over 6 months for the 93 MDR-TB patients. Even when free diagnostics and treatment are being utilized through the National TB Program (NTP) partners, a TB patient in Karachi incurs on average \$107 for susceptible disease and \$600 for MDR-TB. Most costs were incurred during the pre-diagnosis period, with transport (31%) and medicines (29%) representing the highest proportion. These cost are many times over the estimated \$22 per capita expenditure on health in Pakistan. Most households also experienced a decrease in monthly income (\$122 to \$102).

**Conclusion and recommendations:** Household costs for TB treatment are substantial even in programs offering free diagnostics and care and may be a barrier to service utilization for the poorest patients. The huge costs even with 'free treatment' means that further social protection (e.g., cash transfer, food packages, travel vouchers etc.) is warranted, especially for MDR patients.

### MULTIDRUG-RESISTANT TUBERCULOSIS: PROGRAMMATIC ASPECTS

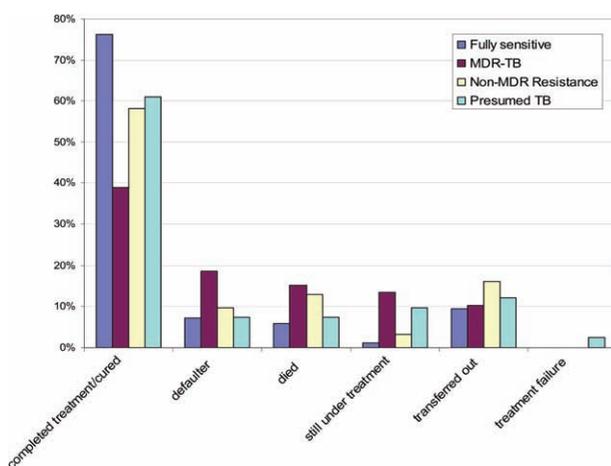
#### PC-813-16 A review of ten years of tuberculosis control in the Torres Strait between Australia and Papua New Guinea

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**Background and challenges to implementation:** Papua New Guinea (PNG) has an estimated tuberculosis (TB) incidence rate of 303/100 000, with 5% of new cases and 24% of retreatment cases reportedly having MDR-TB.<sup>1</sup> Because of limited access to health care in the Western Province of PNG, many PNG nationals from the coastal areas seek treatment on the Australian Torres Strait Islands.

**Intervention or response:** The Cairns Regional TB Control Unit has set up clinics to identify and treat infectious cases of TB in PNG nationals visiting the Torres Strait Islands. Most treatment is given on an outpatient basis, with patients being supplied with drugs and then returning to PNG.

**Results and lessons learnt:** In the 10-year period 2001–2010, 213 patients were treated for TB by the Cairns RTBCU (57% female, mean age 25.5 years, median 24, range 0–76). In this group, 38 patients (18%) had had previous TB treatment in PNG. None had had treatment in Australia before. HIV testing was done in 160 cases (75%); only five patients (3%) were HIV positive. Of 172 patients (81%) with a positive culture, 84 (49%) had fully sensitive TB, 57 (33%) had MDR-TB and 31 (18%) had non-MDR drug resistance. One MDR-TB patient had an additional capreomycin resistance (pre-XDR). Sixty-one percent of all patients completed their treatment, 11% defaulted and 10% died. One case of treatment failure had a second episode of treatment which was successfully completed. The remainder was transferred out of Australia into PNG care or is still on treatment. Outcomes according to drug sensitivities are in the Figure.



**Figure** Outcomes of treatment in Papuan patients in the Torres Strait, 2001–2010.

**Conclusions and key recommendations:** Despite difficult circumstances and high rates of drug resistance, outcomes were reasonably good. Fortunately HIV is not a problem in this region (yet). The situation in the region will have to be carefully monitored while care for these patients is being transferred to PNG.

<sup>1</sup> World Health Organization. WHO Report 2011. Global Tuberculosis Control.

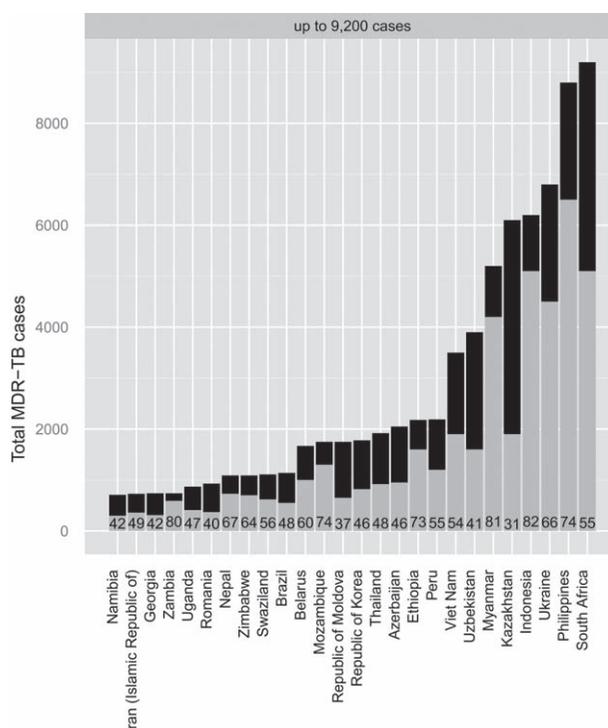
## PC-814-16 Multidrug resistance in new tuberculosis patients: burden and implications

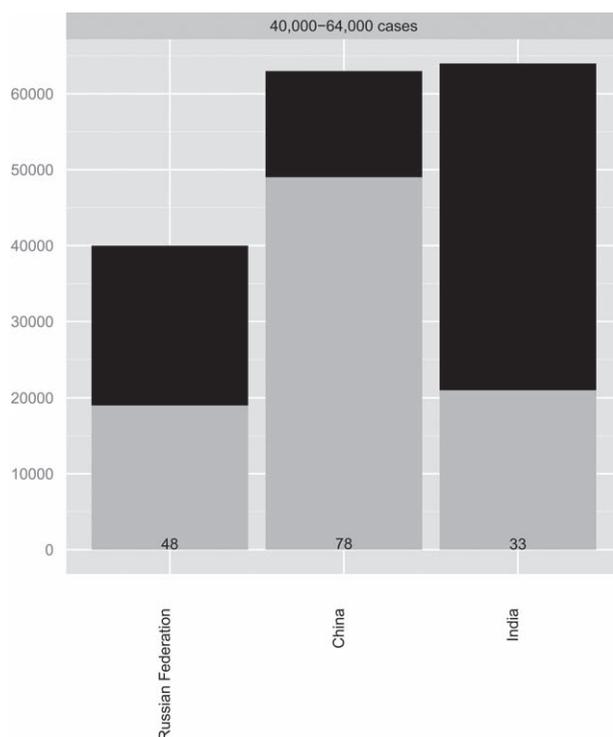
S Royce,<sup>1</sup> D Falzon,<sup>2</sup> K L Van Weezenbeek,<sup>3</sup> M Dara,<sup>4</sup> K Hyder,<sup>5</sup> P Hopewell,<sup>6</sup> D Richardson,<sup>7</sup> M Zignol.<sup>2</sup> <sup>1</sup>Global Health Sciences, University of California, San Francisco, CA, USA; <sup>2</sup>Stop TB Department, World Health Organization, Geneva, Switzerland; <sup>3</sup>Western Pacific Regional Office, World Health Organization, Manila, Philippines; <sup>4</sup>European Regional Office, World Health Organization, Copenhagen, Denmark; <sup>5</sup>South-East Asia Regional Office, World Health Organization, New Delhi, India; <sup>6</sup>Division of Pulmonary and Critical Care Medicine, University of California, San Francisco, CA; <sup>7</sup>TB, PATH, Washington DC, USA. e-mail: sarahroycemd@gmail.com

**Background:** The World Health Organization (WHO) estimates the number of incident multidrug-resistant tuberculosis (MDR-TB) cases that would be found if drug susceptibility testing (DST) results were available from all new pulmonary and retreatment TB notifications. In 2010, only 18% of the world's estimated 290 000 cases of MDR-TB were reported by national health authorities, compared to the *Global Plan 2015* target of over 50%. Using this WHO method, this study analyzes the proportion of total MDR-TB cases estimated in notified new TB cases, and discusses policy implications.

**Design/methods:** Published WHO data are used to analyze the estimated MDR-TB cases in countries located in all WHO regions that had at least 700 MDR-TB cases estimated among notified TB cases in 2010 based on representative drug resistance data.

**Results:** In the 29 countries meeting the inclusion criteria, new TB patients comprised a median of 54% (45–67% interquartile range) of the estimated MDR-TB cases.





**Figure** MDR-TB cases in notified new pulmonary (grey bars) and previously treated (black) TB cases as a proportion of total estimated MDR-TB cases, 2010 (numbers in the grey bars represent notified new pulmonary TB cases as a percentage of total estimated MDR-TB cases).

**Conclusion and recommendations** Finding that new TB patients comprise a median of 54% of these countries' MDR-TB cases shows that MDR-TB is not confined to TB patients who have been inadequately treated. The occurrence of MDR-TB in a new TB patient is a warning sign that MDR-TB is spreading in our communities. Another implication is that MDR-TB case-finding strategies limited to previously treated patients will miss the substantial number of MDR-TB cases that occur among new TB patients. However, while diagnostic capacity is limited, MDR-TB case finding should first focus on the world's previously treated patients, only 6% of whom had DST in 2010. Then countries need to quickly add other risk groups to reach universal access to MDR-TB diagnosis. Despite several limitations to this Global Plan indicator, countries can use the ratio of notified to estimated MDR-TB cases to assess progress toward universal access to MDR-TB diagnosis.

### PC-815-16 The impact of six-month sputum conversion in multidrug-resistant tuberculosis patients

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**Background:** Sputum conversion among patients with multidrug-resistant tuberculosis (MDR-TB) in the end of 6th month is an important indicator for the success of treatment. Our aim was to evaluate the potential impact factor on six-month sputum conversion of MDR-TB patients in Taiwan.

**Methods:** From May 2007 to December 2010, MDR-TB patients in Middle-Taiwan and East-Taiwan under DOTS-plus care of Taiwan MDR-TB Consortium (TMTC) supported by Taiwan CDC. After

**Table** Impact of variables to initial sputum culture conversion of MDR-TB in multivariate Cox proportional hazards regression models

	Model 1 (n = 146)*		Model 2 (n = 137)*	
	RR (95% CI)	P value	RR (95% CI)	P value
Male	0.90 (0.54–1.51)	0.699	1.00 (0.58–1.72)	0.995
Female (Reference)				
Age				
35–65	1.11 (0.60–2.02)	0.746	1.09 (0.58–2.05)	0.797
≥65	1.31 (0.64–2.66)	0.463	1.06 (0.52–2.18)	0.871
≤35 (Reference)				
BMI				
<18.5	0.56 (0.33–0.97)	0.037	0.57 (0.33–0.99)	0.047
≥24	0.49 (0.28–0.86)	0.012	0.56 (0.32–0.97)	0.038
18.5–24 (Reference)				
Aborigines	1.07 (0.63–1.81)	0.800	1.00 (0.58–1.74)	0.990
Non-aborigines (Reference)				
Alcoholic				
Yes	0.98 (0.58–1.66)	0.942	0.81 (0.45–1.46)	0.490
No (Reference)				
Smoking				
Yes	0.76 (0.45–1.28)	0.305	0.85 (0.49–1.48)	0.568
No (Reference)				
Cavity				
Yes	0.53 (0.34–0.83)	0.005	0.54 (0.34–0.87)	0.010
No (Reference)				
Previously treated for TB	0.55 (0.35–0.85)	0.007	0.64 (0.40–1.03)	0.066
Never treated for TB (Reference)				
Diabetes				
Yes	1.05 (0.63–1.75)	0.865	0.95 (0.57–1.59)	0.841
No (Reference)				
Resistance				
FQs†	0.37 (0.19–0.72)	0.003	0.40 (0.20–0.79)	0.008
Non-FQs (Reference)				
Regimen				
EMB or PZA	1.54 (0.49–4.87)	0.459	—	
EMB and PZA	3.28 (1.08–9.98)	0.036		
No EMB and PZA (Reference)				
Regimen (based on E/Z)				
SM/KM + FQs + α1‡	—		1.24 (0.51–3.01)	0.637
SM/KM + FQs + α2‡			1.94 (0.95–3.98)	0.069
SM/KM + FQs + α≥3‡			2.54 (1.08–6.00)	0.033
No enough drugs (Reference)				

\*Model 1 and Model 2: The same variables were enrolled into multivariate Cox regression analysis but regimen different.

†FQs: fluoroquinolones (levofloxacin or moxifloxacin)

‡SM/KM: (streptomycin or kanamycin)

α1, α2, α≥3: one kind of oral second-line drugs, two kinds of oral second-line drugs, three kinds of oral second-line drugs at least.

Cox proportional hazards models to estimate the hazard ratio of conversion, the relative risks (RR) were tested by Wald tests and the significance level was ≤0.05.

exclusion of patients who were loss of follow up ( $n = 7$ ), culture-negative at the start of treatment ( $n = 51$ ) and chronic case ( $n = 10$ ). A total of 146 cases were enrolled in our study to evaluate the influencing factors on six-month sputum conversion after category IV anti-TB treatment. We conducted Cox proportional hazards models to estimate the hazard ratio of conversion, the relative risks (RR) were tested by Wald tests.

**Results:** Of 146 MDR-TB patients, six-month sputum culture conversion rate was 69.2% ( $n = 101$ , mean conversion time 64.5 days). The multivariate Cox regression analysis showed that impact factors on sputum conversion were: Body mass index (BMI) of  $<18.5 \text{ kg/m}^2$  (RR 0.56; 95%CI 0.33–0.97), BMI of  $\geq 24 \text{ kg/m}^2$  (RR 0.49; 95%CI 0.28–0.86), having cavity (RR 0.53; 95%CI 0.34–0.83), previous treatment of TB (RR 0.55; 95%CI 0.35–0.85), fluoroquinolones (FQs) resistance (RR 0.37; 95%CI 0.19–0.72). Combined use of ethambutol (EMB) and pyrazinamide (PZA) (RR 3.28; 95%CI 1.08–9.98) and use of  $\geq 3$  oral bacteriologic second line agents if only EMB or PZA included (RR 2.54; 95%CI 1.08–6.00) had positive effect on sputum conversion (Table).

**Conclusions:** Except of the importance of sound regimen to including ethambutol, pyrazinamide and more of oral bacteriologic second line agent as tolerated, life style modification to maintain an ideal body mass index also a key factor to facilitate sputum conversion and better outcome of disease cure.

### PC-816-16 Control of (multi) drug resistance and tuberculosis incidence over 25 years in the context of a well-supported tuberculosis programme in rural Malawi

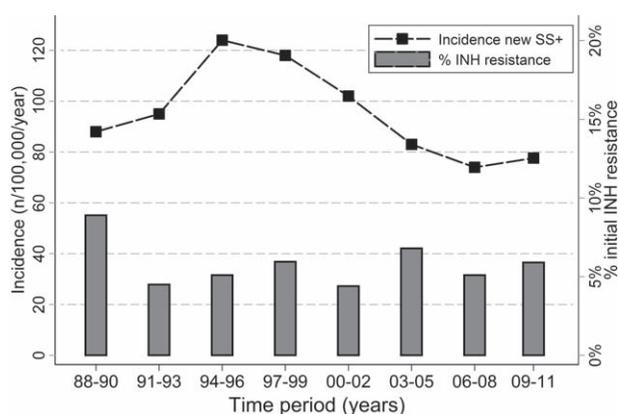
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**Background:** The rise in TB incidence following generalized HIV epidemics can overwhelm TB control programmes in resource-limited settings, frequently accompanied by rising rates of drug resistance. This has led to suggestions that a DOTS-based TB control has failed in such settings. However, there is little evidence of the impact of a sustained and well-supported DOTS programme on TB incidence and drug resistance over a long period. We present long-term trends in incidence and drug resistance in rural Malawi.

**Methods:** Karonga is a rural district in northern Malawi, current population ~270 000 with an adult HIV prevalence of ~10%. The Karonga Prevention Study collaborates with the National Tuberculosis Pro-

gramme to support core control activities. Clinical, bacteriological and demographic information of all patients starting TB treatment in the District have been recorded since 1986. A sample from each culture positive TB patient was exported for drug sensitivity testing. ART has been widely available since 2005.

**Results:** Incidence of new smear positive adult TB peaked at 124/100 000/year in the mid-90s, but has since fallen to ~75/100 000/year and is currently stable (Figure). Drug sensitivity information was available for 90% (2978/3312) of culture positive cases up to March 2010. Since 1990 initial resistance to isoniazid has consistently been below 7% (Figure). Fewer than 1% of episodes involved a multidrug-resistant strain, despite a small cluster occurring during the study period.



**Conclusion and recommendations:** In this setting with a generalised HIV epidemic and medium TB burden, a standard well-supported DOTS programme controlled drug resistance and TB incidence. Enhancing TB control programmes should include improving and strengthening the existing, sputum smear based DOTS infrastructure, and support of ART programmes, which remain the cornerstones of cost-effective, equitable and sustainable TB control in many resource-limited settings.

### PC-817-16 Obstacles hindering successful treatment of multidrug-resistant tuberculosis in rural, high HIV-prevalent settings in South Africa

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**Background:** The management of MDR-TB has always been a very complex task, with low success rates in treatment, especially in rural settings. With MDR-TB incidence increasing in high HIV prevalent regions and because successful management of MDR-TB patients is of utmost importance we sought to

look at some of the obstacles that might hinder us to achieve successful treatment rates.

**Design/methods:** Patient clinical data on previous TB history, treatment and current MDR-TB treatment episodes in Eastern Cape (EC) and KwaZulu-Natal (KZN) data were used from the 'Preserving Effective TB Treatment Study' (PETTS), which was a prospective observational study conducted from 2005 to 2008. Specific characteristics were analysed to identify obstacles that might be a hindrance to effective MDR-TB treatment.

**Results:** 224 patients were enrolled from EC and 197 from KZN. No differences between the two provinces were found for the characteristics: age, gender, HIV status and previous TB history. In KZN 52.8% cured compared to 15.2% in EC and 16.2% died compared to 38% in EC ( $P < 0.001$ ). Median time (days) from sputum collection to DST report date was 34 [IQR: 32–42] for KZN and 39 [IQR: 35–57] for EC and from DST report date to treatment start date was 37 [IQR: 22–67] for KZN and 10 [IQR: 7–21] for EC. Median number of drugs used in the treatment period were 8 [IQR: 7–10] in KZN and 8 [IQR: 7–9] in EC and the median number of effective drugs were 4 [IQR: 3–4] in KZN and 3 [IQR: 3–4] in EC.

**Conclusion and recommendations:** Time from date of DST results to treatment start date is not necessarily an indicator for successful treatment, possibly due to the patient's poor clinical condition when presented at the clinic for diagnosis. The high cure rate but longer time from diagnosis to treatment in KZN may possibly be masking fatality before treatment initiation. Active case finding must be implemented not just as an infection control strategy but also as a management tool to ensure that patients are put on treatment in the early stages of disease.

### PC-818-16 Accelerated progress towards nationwide scale-up of programmatic management of MDR-TB in India

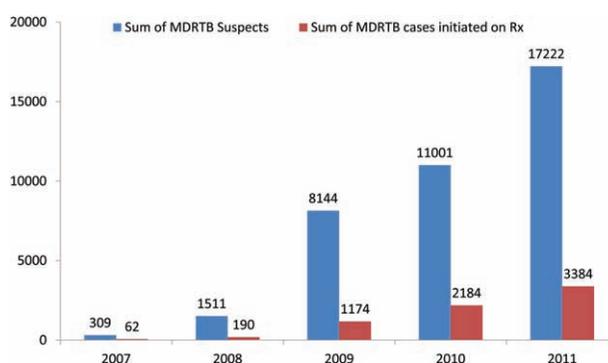
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**Background:** India has the world's highest burden of tuberculosis (TB) and multidrug-resistant tuberculosis (MDR-TB), with an estimated 64 000 MDR-TB cases among cases notified by the national programme. The programmatic management of MDR-TB (PMDT) in India began in 2007. We sought to document the progress towards nationwide scale-up, and compare with expansion plans.

**Methods:** We reviewed programme records on MDR-TB case-finding, and treatment initiation, and compared with the targets against the 2011–12 national PMDT scale-up plan. At a series of regional consulta-

tion meetings conducted in 2012, expansion challenges were systematically documented.

**Results:** From 2007 to 2011, PMDT services have expanded to all 35 states of India covering 260 districts (40%) with 512 million population (43%); 37 culture labs have been accredited, including 20 offering rapid drug susceptibility testing (DST). In 2011, 17 222 MDR-TB suspects were tested (a 57% increase from 2010) and 3384 MDR-TB cases initiated on MDR-TB treatment. The number of patients initiated on MDR-TB treatment was a 55% increase from 2010, but only 46% of the 7403 patients envisioned in national plans. Programme reviews identified delays in laboratory capacity development, disbursement of funding, and human resources and training as key expansion constraints.



**Figure** Total MDR suspects tested and cases initiated on MDR TB treatment 2007–2011.

**Discussion:** MDR-TB diagnosis and treatment availability is accelerating in India, but by 2011 remained substantially behind programme targets. Detection and treatment of MDR-TB is still limited to a fraction of the estimated burden. To recover the pace of expansion, the national TB programme is emphasizing rapid DST deployment, human resource strengthening, improved incentives, MDR-TB service integration, and better prevention through improved engagement with the private sector.

### PC-819-16 Phased implementation of Xpert® MTB/RIF technology for the diagnosis of drug-resistant tuberculosis in Nigeria

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**Background:** In December 2010 WHO endorsed Xpert® molecular technology for the rapid diagnosis of TB and rifampicin resistant TB. The National TB

Programme through the support of TBCARE 1 project initiated phased implementation of the technology with a focus on testing DR-TB suspects. The objective of this study is to assess the outcome of this new approach for the purpose of scaling up the intervention in the country.

**Design/methods:** Stakeholders' meeting was conveyed where the country GeneXpert Advisory Team (CGAT) was established. Nine sites were evaluated and selected according to WHO criteria. Training of Trainers workshop was held to develop country-specific training modules and SOPs including revision of registers and reporting formats. Laboratory personnel were trained and the machines were installed with back-up system in 8 of the sites. The sites were supported to conduct routine testing and reporting to the national programme.

**Results:** Twenty-eight national and laboratory staffs (15 males and 13 females) were trained. From December 2011 to 31 March 2012, a total of 458 tests were performed out of which 54 (12%) were rifampicin resistant. Twenty-two tests failed representing an error rate of 4.8%. Weak computer skills, unstable power supply, and inadequate cartridge storage conditions constituted challenges in implementation.

**Conclusion and recommendations:** Xpert MTB/RIF offers an entry point for routine DR-TB surveillance. The high rifampicin resistance among DR-TB suspects evaluated is a predictor of high DR-TB in Nigeria. The National Programme needs to scale up the technology to include also other risk groups.

### PC-820-16 Does conventional drug susceptibility testing guide tuberculosis case management?

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**Background:** Drug susceptibility testing (DST) in developing countries has allowed increased detection of drug resistant (DR) TB. Whereas guidelines exist for managing MDR-TB, evidence is lacking for other DR-TB. Nevertheless, correct treatment of any drug resistance is important to prevent further emergence of MDR-TB.

**Aim:** To describe drug resistance patterns and evaluate the impact of conventional DST on TB case management.

**Methods:** Retrospective analysis of routinely collected data (9/2010–1/2012) in a referral NGO-hospital in Phnom Penh, Cambodia. Culture was done on Löwenstein-Jensen medium. The indirect 1% proportion method was used for *M. tuberculosis* DST. The first 9 months (phase 1) DST was requested for re-treatment cases at the physician's discretion. From

5/2011 (phase 2), DST was done on all *M. tuberculosis* complex cultures.

**Results:** Of 263 DSTs done, 49 revealed any drug resistance: 10/21 and 39/242 in phase 1 and 2, resp. Median age was 42 (IQR 29–53), 23/49 male, 16/49 HIV positive and 10/49 had previous TB history. The most common resistance patterns were streptomycin (S) ( $n = 18$ ) and isoniazid (H) mono-resistance ( $n = 11$ ), HS-resistance ( $n = 8$ ), rifampicin (R) mono-resistance ( $n = 4$ ) (Table). In addition, MDR strains were identified in 4 cases (1 HR, 2 HRS, 1 HRSE); all were referred for second-line TB treatment. With no S-resistant cases on S, no treatment adjustments were made. For R, H, HS or other resistant cases no treatment adjustments were made. Reasons for 'no action' were the TB physicians' ignorance on the clinical relevance and management of mono- and poly-resistance, as well as transfer out or lost to follow-up of patients by the time DST results became available ( $n = 23$ ).

**Table** Drug resistance patterns and case management

Resistance pattern	Drug	n	Treatment n	Treatment adjusted n	Outcome				Comment
					Cured	Completed	Died	Transfer out/LTFU	
S		18	17	0	1	2	2	12	
H		11	6	0			3	3	
HS		8	6	0	1	1	1	3	
R		4	4	0	1			3	
HRS		2	2	2					2 on treatment
HRSE		1	1	1					1 on treatment
HR		1	1	1					1 on treatment
HE		1	1	0					1
HSFq		1	1	0	1				
HSE		1	1	0				1	
Fq		1	1	0				1	C3 smear pos

S = streptomycin; H = isoniazid; R = rifampicin; E = ethambutol; Fq = fluoroquinolone; LTFU = lost to follow-up.

**Conclusion:** Except for MDR-TB, DST results are rarely acted upon in our setting. Besides the need for rapid DST and follow-up of TB patients, more evidence on clinical relevance and management of mono/poly-DR TB is essential to benefit from culture/DST results.

### PC-821-16 Treating patients with drug-resistant tuberculosis in a disputed territory: successes and challenges to programme sustainability

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**Background and challenges to implementation:** Abkhazia is a disputed territory in the Caucasus after conflict with Georgia in 1992. Despite recent recognition by Russia, the state is politically isolated from the international community and suffers from socio-economic insecurity. It has a high burden of drug-resistant tuberculosis (DR-TB), with multi-drug resistance found in 6.9% of new and 15.6% of previously treated cases.

**Intervention or response:** Médecins Sans Frontières (MSF) has supported the local health authorities to pilot DR-TB treatment programs on either side of the disputed border in Abkhazia (2001) and Zugdidi (2006). In Abkhazia, Green Light Committee approval was gained with support from authorities on both sides of the conflict. Second line drugs and sputum samples were transported across a military checkpoint at the border of the disputed zone.

**Results and lessons learnt:** There was success in the transfer of medical knowledge and skills in case management of DR-TB patients to local staff. Vulnerable patients were able to access treatment. The challenge to the program in Abkhazia is sustainable transfer of management to local authorities. The major barriers were human resources, obtaining sustainable drug supply and laboratory capacity—all a direct result of the geopolitical context and political insecurity. Conversely, in Zugdidi, which has stability, strong national and international technical support, handover was achieved in 2010 with scale up across the country.

**Conclusions and key recommendations:** There is a need for a comprehensive programmatic approach to the management of DR-TB. Implementing this in contexts where health systems are weak is challenging. An independent humanitarian organisation was the only means to provide access to DR-TB treatment in Abkhazia. Long term partnership with local authorities and building management capacity are fundamental to ongoing program sustainability.

#### PC-822-16 Treatment outcome among patients with multidrug-resistant tuberculosis in a low-income setting, DR Congo, 2007–2008

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**Background:** The DR Congo is one of the 27 high burden countries of TB drug resistance in the world. Since 2007, the NTP used a standardized treatment for suspected patients.

**Aim:** To evaluate treatment outcome among patients with multidrug-resistant tuberculosis (MDR-TB) in

DR Congo and reports the results of this scheme of 24 months including the second line drugs following kanamycin, ofloxacin, prothionamide, cycloserine, ethambutol and pyrazinamide.

**Design/methods:** We reviewed record of patients who started treatment with second line drug from January 1, 2007, to December 31, 2008. During years 2007 and 2008. Patients were suspected on basis of retreatment failure, cultures on solid medium and sensitivity test made. MDR-TB confirmed as *Mycobacterium tuberculosis* isolates resistant to isoniazid and rifampicin at least.

**Results:** During these 2 years, 349 patients (147 in 2007 and 202 in 2008) have been enrolled, 233 had result of drug sensitivity test, 168 were confirmed to be MDR-TB (48.13%). The results of MDR-TB confirmed patients are as follows: the conversion of sputum culture was 82.3% between the 2nd and 3rd month. Therapeutic success recorded in 112, 67%, 3% failures. With high levels of death (11%) and defaulters (17%).

	Year 2007 n (%)	Year 2008 n (%)	Total n (%)
Therapeutic success	50 (65)	62 (68)	112 (67)
Failure	3 (4)	2 (2)	5 (3)
Dead	8 (10)	11 (12)	19 (11)
Defaulters	14 (18)	14 (15)	28 (17)
Transfers	2 (3)	2 (2)	4 (2)

**Conclusion/recommendations:** The treatment success is not different from global results but here no intervention other than the treatment had been funded, which did not permit a good restraint of patients in treatment because a number of abandonment was concerned of patients with negative sputum. To maximize success treatment and reduce defaulters, poor setting need not only supervised treatment but some other interventions as psychosocial and nutritional support.

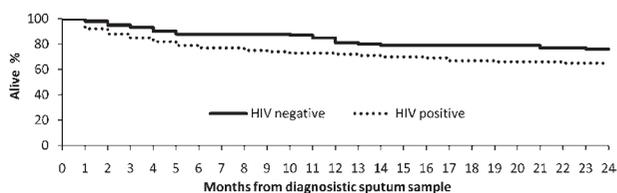
#### PC-823-16 Improved survival among HIV-infected MDR-TB patients diagnosed and treated in a community-based programme in Khayelitsha, South Africa

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**Background:** Initial reports suggest extremely high and rapid mortality among HIV-infected MDR-TB patients. Contributing factors potentially include: delayed MDR-TB diagnosis, low CD4 levels and lack of antiretroviral treatment. We aimed to assess survival among MDR-TB patients diagnosed through a decentralised programme, integrated into the existing TB-HIV system at primary care level in Khayelitsha.

**Design:** The DR-TB programme aims to increase case detection, improve treatment outcomes and reduce DR-TB transmission, through clinic staff training and ongoing individual patient counselling and social support. Standard treatment (including moxifloxacin) is initiated rapidly after bacteriological confirmation, and modified according to further drug susceptibility testing. Hospital admission is based on clinical status. Mortality was determined through clinic reports, communication with families and linkage to the South African deaths registry for a subset of patients. Life tables and Cox regression were used to analyze survival over time from MDR-TB diagnosis.

**Results:** From 2008 to 2011, 658 patients were diagnosed with MDR-TB, of which 459 (70%) were HIV positive (HIV+). Survival was significantly lower among HIV+ patients (Figure,  $P = 0.02$ ), with 73% survival at 12 months and 65% at 24 months among HIV+, compared to 85% and 76% for HIV- respectively. Death prior to DR-TB treatment accounted for much of the difference in survival; 10% of HIV+ patients died before treatment could be started (5% among HIV-). Additional factors associated with mortality among HIV+ patients included low CD4 and further second-line resistance at diagnosis.



**Figure** Survival among HIV positive and negative MDR-TB patients diagnosed between 2008 and 2011.

**Conclusions:** Although survival remains lower among HIV infected MDR-TB patients, outcomes can be dramatically improved through decentralisation and integrated HIV management, enabling earlier diagnosis and rapid treatment initiation.

#### PC-824-16 Time to treatment initiation and to switch to second-line drugs among new MDR-TB cases in Lima, Peru

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**Background:** MDR-TB (multidrug-resistant tuberculosis) management overwhelms public health systems in high prevalence areas. Identifying cases and providing them timely with appropriate treatment is particularly problematic. In Peru, rapid drug susceptibility tests (DST) are routinely performed in high risk

groups and in patients not responding to first line TB treatment. However, the real frequency of MDR-TB, the proportion of these patients receiving MDR treatment and the delays incurred are unknown.

**Methods:** From March 2010 to December 2011, all new smear-positive patients in a district in North Lima were enrolled in a prospective study and followed for at least four months. An additional sputum sample was collected just after diagnosis and cultured in Löwenstein-Jensen (LJ) media; LJ proportion method was used for DST. The dates of the first positive routine smear result, treatment initiation and possible switch to second line drugs were collected from patient's charts.

**Results:** LJ results were available for 69.4% (911/313) of patients; 7.1% (65/911) had MDR-TB. After TB diagnosis, 3 of them were lost to follow up and 19 (29.2%) did not start a MDR regimen: 5 defaulted, 2 died, 6 are still under evaluation for MDR treatment and 6 completed the first line regimen (despite LJ DST results becoming available). Of the 43 patients who received a MDR regimen, 8 (18.6%) started on it immediately and 35 (81.4%) were switched to it. Within the former group, it took 28 days (IQR 25.3–42.5) to start MDR treatment, while in the latter it took 114 days, (IQR 75–159.5).

**Conclusions:** Despite current routine NTP efforts, MDR treatment initiation is significantly delayed. The next step is to precisely identify the reasons for the delays and to find ways to solve them. MDR testing based on a narrow pre-defined set of risk factors could be one of the factors.

#### PC-825-16 Xpert® MTB-RIF diagnosis and decentralised management of drug-resistant tuberculosis in rural South Africa

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**Background:** TB-HIV Care Association (THCA) has provided support to a rural district in South Africa since 2008 to increase access to TB and HIV diagnosis, treatment and adherence support. THCA received Stop TB Partnership TB REACH funding in late 2011.

**Intervention:** THCA aims to increase TB case finding through TB symptom screening by mobile HIV counseling and testing teams at community level and by community health workers at household level. Sputum is collected from symptomatic clients and transported to the nearest laboratory. Through a mix of donor and Department of Health (DOH) funding, Xpert MTB-RIF (GXP) machines were placed in all 5 sub-district laboratories such that every TB suspect has their first sputum tested by GXP. If *Mycobacterium tuberculosis* is detected with no rifampicin (RIF)

resistance, then regimen 1 is started and if *M. tuberculosis* is detected with RIF resistance then drug resistant TB (DRTB) treatment is started and a sample is sent for culture and susceptibility. In preparation for increased and more rapid diagnosis of drug resistant TB (DRTB), the TB hospital was upgraded and staff were trained to initiate DRTB treatment in the district and outreach injection teams were hired to administer injections of anti-TB drugs in patients' homes.

**Results:** From October 2011 to March 2012, there were 3794 GXP tests performed and 128 (3.3%) were unsuccessful. Of the 3666 successful tests, MTB was detected in 433 (11.8%) of samples of which 70 (16.2%) were rifampicin resistant. It should be noted that some patients provided 2 samples and some who were already on TB treatment were retested by GXP which resulted in higher than expected RIF resistance. The national average for RIF resistance identified by GXP in South Africa is 7%.

**Conclusions and recommendations:** Partnership between THCA and DOH to procure GXP machines in a rural district helped accelerate the decentralized management of DRTB. DOH has committed to fund GXP running costs to ensure sustainability.

#### **PC-826-16 Innovative approaches to establishing and sustaining a drug-resistant tuberculosis in-patient facility in a secondary level hospital in Lagos, Nigeria**

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**Background and challenges to implementation:** Nigeria ranks 10th among 22 high burden TB countries in the world. In 2007, the case detection rate was 31%, the treatment success rate 79%. HIV co-infection was estimated at 30%. The MDR/XDR-TB burden is unknown. A national level BSL 2 laboratory linked to six regional reference laboratories is being upgraded to BSL 3 to support national DR surveillance and monitoring of treatment. There was no treatment centre to support the patients diagnosed in the laboratory in the same state. We describe the establishment of a state level in patient DR TB care centre linked with the BSL 3 laboratory in Lagos State, Nigeria.

**Intervention or response:** Processes included: Site selection with government authorities; engagement for ownership in infrastructure, staffing and provision of second line drugs; signing of MoU as well as renovations; staffing and training; development of infection control systems; M&E; sample referral and transport.

**Results and lessons learnt:** Three previous TB wards were renovated into a 40 bedded ward with special features for infection control. Dedicated medical and nursing staffs were trained and national mentorship support provided. Sample/result transport system

linkage of wards with a Biosafety level 3 lab and the state DOTS centers was established. Patients identified from these satellite surveillance centers will be managed in a community extension care centre by the local government DOTS provider under the TB Supervisor. A hospital technical working group was established to monitor infection control and second line anti-TB drugs best practices in the facility and report to government for policy control. Clinical management systems were linked with the e-TB manager for electronic patient record keeping.

**Conclusions and key recommendations:** Clinical management of MDR/XDR-TB requires sound technical support and strong government commitment at national and sub national levels.

#### **PC-827-16 Nationwide implementation of programmatic management of drug-resistant tuberculosis in a resource-limited setting: experiences from the field**

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**Background:** Namibia is sparsely populated and has a high TB incidence (589/100 000 in 2010). The 2007 XDR-TB outbreak in neighbouring South Africa sparked public alarm, and routine DST intensified in the selected patient categories according to national guidelines, and 116 MDR-TB cases were notified in 2007.

**Intervention:** A government funded DR-TB programme commenced in 2008. A circular with WHO-based technical guidelines for the MDR-TB was issued. Second-line anti-TB medicines were procured, and WHO, CDC, The Union and KNCV provided technical assistance. Liquid culture was introduced and a committee was established to advise on case management. A medical officer for DR-TB was appointed and health workers (including rehabilitation technicians, social workers and community DOT supporters) were trained. A database of treatment regimens was introduced in 2010 to track the medicine utilisation at facility level.

**Results and lessons learnt:** 1180 patients have been commenced on DR-TB treatment since 2008. The laboratory information system does not report the number of laboratory-diagnosed cases. There was a progressive decline in the number of patients commenced on treatment without consulting the committee. Hospital-based management failed in the nomadic San community due to sociocultural factors (a promising community-based treatment programme has since been established). Rapid staff turnover continues to undermine capacity building efforts. Outcome analysis for the 2009 cohort (246 patients) revealed a treatment success rate of 47%.

**Conclusions and recommendations:** Implementation of PMDT in a resource-limited setting is possible with government commitment, technical support and stakeholder engagement. Psychosocial patient support and local peculiarities in different patient populations should be addressed. PMDT should entail human resource development and retention; and strengthening the public health role of the laboratory.

## MANAGING ASTHMA IN ADULTS AND CHILDREN

### PC-858-16 Prevalence of asthma symptoms in adults in Sudan: modified ISAAC project

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**Background:** The morbidity of asthma is increasing in adults worldwide with the highest risk in the urban areas. Few data exist on the prevalence of asthma among Sudanese adults.

#### Objectives:

- 1 To determine the prevalence of asthma symptoms among Sudanese adults using a modified ISAAC approach.
- 2 To identify the common trigger factors for asthma symptoms in the affected group.

**Design/methods:** A multi-center cross-sectional study covering northern, eastern, western and central Sudan was conducted during 2006/2007 and 2009/2010. A modified ISAAC questionnaire for adults was distributed to university students, academic staff, employee and workers chosen randomly. 3974 respondents were included. Any subject with asthma symptoms was interviewed by another questionnaire and had pulmonary function and skin prick tests.

**Results:** A total of 3974 adults aged 18–77 were included. Average prevalence of current wheeze in Sudanese adults was 10%: Khartoum 10.7%, Elobeid 6.7%, Dongola 9.6% and Kassala 13%. Most of the patients have intermittent and mild persistent symptoms. Asthma was more prevalent in urban than rural areas. Skin test showed sensitivity to house dust mites, cockroach, pets, and trees.

#### Conclusions:

- 1 Asthma prevalence in adults varied among different regions in Sudan with more prevalence in urban areas.
- 2 The average prevalence depending on current wheeze in Sudanese adults was 10%.
- 3 House dust mites, cockroach, pets and trees were the most important trigger factors for asthma symptoms.

### PC-859-16 Validation of the modified ISAAC questionnaire: is wheeze alone enough for asthma symptoms prevalence?

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**Background:** The ISAAC protocol for asthma prevalence depended mainly on self-reported wheezing symptom in the past 12 months. This study aimed to evaluate the prevalence of asthma symptoms using self-reported wheezing versus combination of symptoms and spirometric criteria.

**Design/methods:** A multi-center cross-sectional study covering northern, eastern, western and central Sudan was conducted during 2006/2007 and 2009/2010. A modified ISAAC questionnaire for adults was distributed to university students, academic staff, employee and workers chosen randomly. 3974 aged 18–77 respondents were included. Any subject with asthma symptoms was interviewed by another questionnaire and had pulmonary function test (bronchodilator reversibility).

**Results:** Average prevalence of asthma symptoms depending on wheeze only was 10%: Khartoum 10.7%, Elobeid 6.7%, Dongola 9.6% and Kassala 13%. The use of combination of symptoms (wheeze + shortness of breath or nocturnal cough) correlated more with reversibility validated prevalence and doctor diagnosed asthma than wheezing alone in all study sites and total sample (Table).

**Table** Prevalence of asthma symptoms depending on wheeze only compared to combination of symptoms, reversibility validated and doctor-diagnosed asthma.

Asthma prevalence criteria	Study site				Total sample
	Elobeid	Dongola	Khartoum	Kassala	
Wheeze in the past 12 months	6.8%	9.6%	10.7%	13%	10%
Wheeze + shortness of breath (SOB)	5%	4.5%	4.5%	6.3%	5%
Wheeze + nocturnal cough	5%	5.9%	4.6%	8%	6%
Positive reversibility test	4%	4%	2.4%	4.4%	3.6%
Doctor-diagnosed asthma	5%	6.6%	7%	10.7%	7%

**Conclusion and recommendations:** Wheezing alone does not predict the true asthma prevalence and the use of combination of symptoms (wheeze plus) is essential to yield a valid asthma symptoms prevalence.

### PC-860-16 Effect of Buteyko Breathing Technique and Diaphragmatic Breathing Exercises in bronchial asthma: a prospective study from India

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**Background:** Various complementary and alternative therapies (CAT) are being studied in asthma management, with reports of varying effects. CAT includes a variety of breathing and relaxation exercises including yoga, diaphragmatic breathing, progressive relaxation, etc. If these can facilitate easy disease control, they can be utilized in bringing down the cost of asthma treatment, a major issue in resource limited countries like ours.

#### Aim:

- 1 Compare the effect of 2 CATs, i.e., Buteyko Breathing Technique (BBT) and Diaphragmatic Breathing Exercises (DBE) in asthma treatment.
- 2 Compare the effect of each to conventional treatment alone.

**Design/methods:** Prospective case-control study conducted in an allergy clinic at Alappuzha. Patients with persistent asthma aged 25–65 years were randomly grouped into 3-A-Receiving conventional therapy alone B-Above+BBT C-Above+DBE. Disease control assessed by spirometry, Mini Asthma Quality of Life Questionnaire, Asthma Control Test and  $\beta$ -agonist use during.

**Results:** Total of 60 patients, 20 in each group studied. No significant difference in FEV<sub>1</sub> among 3 groups; statistically significant improvement in quality of life (QOL) among groups B and C, with reduction in  $\beta$ -agonist use.

**Conclusion and recommendations:** CAT can be useful in improving QOL among asthmatics. Further elaborative research has to be conducted to get conclusive result.

### PC-861-16 Prevalence of asthma symptoms in children in Sudan: ISAAC project

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**Background:** Prevalence of asthma in children aged 13–14 years in Khartoum (central Sudan) has been surveyed as a part of ISAAC study-phase three in 2003 and was found to be 12.5%. Data are lacking in other regions in Sudan.

#### Objectives:

- 1 To determine the prevalence of asthma symptoms among Sudanese children using an ISAAC approach.
- 2 To identify the common trigger factors for asthma symptoms in the affected group.

**Design/methods:** A randomized cross-sectional study was performed in Gadrif (eastern Sudan), White Nile state towns (south to central Sudan) and Atbara (northern Sudan) during 2003 and 2008–2009. ISAAC questionnaire was distributed to school children aged 13–14 years old. 4401 respondents were recruited (including Khartoum). Any subject with asthma symptoms was interviewed by another questionnaire and had pulmonary function and skin prick tests.

**Results:** A total of 4401 children aged 13–14 years were included. Average prevalence of current wheeze in children was 8%: Khartoum 12.5%, Gadarif 6.3%, Atbara 4.2% and White Nile 9%. Most of the patients have intermittent symptoms. Asthma was more prevalent in urban than rural areas. Skin test showed sensitization to house dust mites, cockroach, cat, and trees.

#### Conclusion and recommendations:

- 1 Asthma prevalence in children varied among different regions in Sudan with more prevalence in urban areas.
- 2 The average prevalence depending on current wheeze in Sudanese children was 8%.
- 3 House dust mites, cockroach, cat and trees were the most important trigger factors for asthma symptoms.

### PC-862-16 Facteurs de persistance de l'asthme au Burundi

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**Objectif :** Déterminer les facteurs de persistance de l'asthme de l'adulte au Burundi.

**Matériels et méthodes :** Des dossiers de 90 patients (15–85 ans, médiane : 49 ans) admis aux urgences du CHU de janvier à juin 2011 pour un asthme persistant sont inclus et analysés à l'aide du logiciel 'épi-info'. L'analyse porte sur l'état clinique à l'inclusion et sur l'historique de leur maladie.

**Résultats :** Il s'agit de 1♂/2♀, soit une fréquence de 4,6%. Aucune autre donnée épidémiologique n'existe à tous les niveaux (Facteur 1). Le diagnostic à l'admission se limite à dire que c'est une crise d'asthme (Facteur 2). Or, il s'agit de crise aiguë grave (28%), sévère (65%) ou modérée (7%). La sévérité de l'asthme n'est pas renseignée (Facteur 3). En effet, il est persistant sévère dans 54%, modéré dans 25% et léger dans 21%. Le traitement aux urgences se limite à l'aminophylline 250 mg en IV lente (100%) et l'hydrocortisone 200 mg en IV (72%) renouvelable si besoin (Facteur 4). La durée de surveillance (Facteur 5) est moins de 1h (63%), 1–3 h (27%) ou de plus de 3 h (10%). Le traitement en hospitalisation comprend du salbutamol 3mg en perfusion dans 1/2 l de glucosé 5% en 2 à 4 perfusions/j et hydrocortisone 200 mg 2 à 3 fois/j en IVD (Facteur 6). Aucune mesure de

réversibilité n'est faite (Facteur 7). Les récurrences après la sortie de l'hôpital sont fréquentes. Les visites aux urgences sont tous les jours (7%), plus de 3/semaine (11%), 1 à 3/semaine (13%), 1 à 3/mois (33%), rares (18%) ou jugées inutiles (11%). Le traitement de fond n'est ni revu ni adapté (Facteur 8) à 64%, reconduit dans 30%, initié à 6%. Le traitement de la crise en dehors de l'hôpital est inconsciemment mal pris à 100% (Facteur 9). L'éducation thérapeutique reste à désirer (Facteur 10).

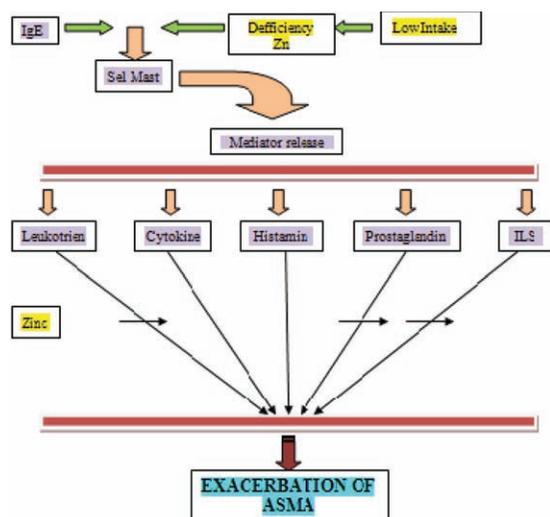
**Conclusion :** La morbi-mortalité de l'asthme n'est réduite que si ces facteurs sont évités. On n'y arrivera que par une mise à niveau régulière du personnel soignant et une standardisation de la prise en charge de l'asthme au Burundi.

### PC-863-16 Effect of zinc supplementation on partially controlled and uncontrolled bronchial asthma

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**Background:** Asthma is a reversible narrowing of airway due to airway smooth muscles contraction. Prevalence of asthma is increasing, presumably related to diet. There are some intrinsic factors related with the decreasing Zinc (Zn) level in asthma, which leads to severe and uncontrolled asthma. This study was conducted to find out the effect of Zn supplementation on partially controlled and uncontrolled asthma.

**Design/methods:** This is an experimental analytic study, performed on Pulmonary Clinic in RSUD Dr. Soetomo Surabaya, Indonesia. 98 patients were divided into two groups, 49 patients with Zn supplementation and 49 patients without it. All were given  $\beta_2$  agonist inhalation and corticosteroid inhalation. Zn dispersible tablet were given for one month (30 days). Asthma Control Test (ACT) questionnaire and lung spirometry (FEV<sub>1</sub> and FEV<sub>1</sub>/FVC ratio) test were



taken before and after the study. The result was analyzed with Kolmogorov-smirnov test and examined with Wilcoxon and paired sample *t* test.

**Results:** There were significant improvement in ACT score and percent predicted FEV<sub>1</sub> in the group of patients which was given Zn supplementation compared to those given only standard drugs. FEV<sub>1</sub>/FVC ratio were insignificantly improve on the patients with Zn supplementation.

**Conclusion and recommendations:** Zn improves ACT score and percent predicted FEV<sub>1</sub> and insignificantly improve FEV<sub>1</sub>/FVC ratio on patients with bronchial asthma. This study concluded that Zn have the benefit to improve the severity and control of asthma. A question is left regarding the role of Zn in older asthmatic patient which might has an overlapping COPD, as there was no age limitation in this study. This could open some possibilities for another study.

### PC-864-16 Association between interleukin 5 polymorphism and eosinophilia among Sudanese asthmatics

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**Background:** Eosinophil is considered a key effector cell in the pathogenesis of allergic inflammation. Interleukin 5(IL-5) may play an important part in eosinophil maturation, and activation in asthma (Tavernier J, et al. 2000).

**Objective:** To determine whether polymorphisms of IL-5 in chromosome 5 was associated with asthmatics, and to detect the level of eosinophils in Sudanese.

**Design/methods:** Seventy families (141 asthmatics and 128 non asthmatics) were included, based on sample of nuclear and extended families. Ventilatory function and skin prick test were done; eosinophil count was carried out in the whole blood sample. The subjects were genotyped for IL-5 polymorphism (rs2069812) using PCR with MALDI-TOF mass spectrometry. The data was analyzed using Haplo view Test, and  $\chi^2$  test.

**Results:** The IL5 (C-746T) rs2069812 polymorphisms showed that CC homozygous mutant gene was found to be (11.3%) in asthmatic, and (8.5%) in non-asthmatic, where CT heterozygous was found to be (40.4%) in asthmatic, and (39.8%) in non-asthmatic. TT homozygous for wild type was found to be (48.2%) in asthmatic, and (51.5%) in non-asthmatic ( $P = 0.6227$ ). The result showed that the IL5 (C-746T), rs2069812 was not associated with asthma in Sudanese. Eosinophil count was found to be (45.4%) 64\141 in asthmatics, where in non-asthmatic (21.2%) 28\128. ( $P = 0.0001$ ). Hypersensitivity symptoms to ten allergens showed positive skin test, 80% of

asthmatic patients showed skin hypersensitivity to at least one allergen ( $P = 0.00$ ).

**Conclusion and recommendations:** No association between the polymorphism in IL-5 gene and the susceptibility to asthma. There is strong correlation between eosinophilia, skin test, hypersensitivity symptoms and asthma.

### PC-865-16 The association between solid fuel smoke and prevalence of asthma symptoms in Sudanese urban and rural states

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**Background:** Most of people living in developing countries depend on coal and biomass fuel for cooking and heating. The association of smoke from biomass with lung cancer, asthma in children and adults, and tuberculosis in adults was considered scarce.

**Objective:** To investigate the association between exposure to solid fuel smoke and prevalence of asthma symptoms in Khartoum (urban state city) and two rural state cities (Dongola and Madani).

**Method:** A cross-sectional study performed in Khartoum City (the capital of Sudan), Dongola City 480 km northern Khartoum and Madani 180 km southern Khartoum during December 2009 to March 2010. A modified ISAAC questionnaire was distributed to adult university students and workers chosen randomly in Khartoum and Dongola, and asthma register card for asthmatics and controls in Madani. The questionnaire and asthma register card covered asthma symptoms, allergy symptoms and both indoor and outdoor environmental factors. A total of 4140 subjects were included (2291 in Khartoum, 1413 in Madani and 436 in Dongola).

**Results:** A total of 4140 subjects were included. 70.7% and 16.7% of asthmatic group in Madani and Dongola respectively tend to use wood coal for cooking on daily basis compared to 36.1% and 7.9% respectively in non asthmatic groups. In Khartoum City 8.2% of asthmatic group tend to use wood coal for cooking compared to 7% in non asthmatic group. Significant strong association between asthma symptoms and exposure to solid fuel smoke was found in Madani and Dongola (OR 4.26,  $P = 0.000$  and 2.8,  $P = 0.005$  respectively), whereas in Khartoum, weak and statistically insignificant association was found (OR 1.1,  $P > 0.05$ ).

**Conclusion and recommendations:** There is a possible association between exposure to wood solid fuel smoke and prevalence of asthma symptoms which was more evident in rural than urban states cities. Natural gas needs to be accessible and affordable for rural areas.

### PC-866-16 Association of asthma control with medication adherence and quality of life among out-patient adult asthmatics at the Chest Clinic, Hospital Melaka

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**Background:** The goal of asthma treatment is to achieve and maintain clinically asthma control with an adherent pharmacological intervention strategy together with a partnership between the health care provider and the patient and/or family members. This study determined the level of asthma control, medication adherence and quality of life, and their association among studied adult asthmatics.

**Methods:** In this cross-sectional prospective study, questionnaires that consist of socio-demographic and medical data, Asthma Control Test, Standardized Asthma Quality of Life Questionnaire (AQLQ(S)) and Modified Morisky Adherence Scale eight-item were distributed to recruited outpatient adult asthmatics attending follow-up appointment at Chest Clinic, Hospital Melaka, Malaysia, between July and November 2011. Both descriptive and inferential statistics were used for data analysis whereby  $P$  value  $< 0.05$  was considered as statistically significant.

**Results:** The mean + SD age of 73 subjects was  $50.6 \pm 14.9$  years old (age ranged from 19 to 80 years old). About 46.6% of subjects had at least well-controlled (ALWC) asthma. The majority were female, Malays and had completed high school education. Unemployed females including housewives ( $P = 0.001$ ) presented with ALWC or not well-controlled (NWC) asthma. About 23.5% of ALWC and 20.5% of NWC subjects had a history of smoking. Females were significantly ( $P = 0.040$ ) more obese than males in general, but not significant if based on asthma control or gender among subjects' asthma control. About 70.6% of ALWC subjects had at least one comorbidity disease ( $P = 0.020$ ). Eight percent of NWC subjects were not on controller medication. About 34.3% of subjects were highly adherence while 43.8% demonstrated low adherence toward asthma medications. Thirty six percent of subjects demonstrated overall AQLQ(S) scores  $\geq 6$ ; however 2.7% had no quality of life impairment at all. There was no association between asthma control and adherence ( $P = 0.799$ ) but significant with overall quality of life and each domain of AQLQ(S) ( $P < 0.001$ ).

**Conclusion:** This study suggests that asthma control, irrespective to degree of medication adherence, may influence the quality of life in adult asthma patients. Therefore, continuity of enhanced asthma educational program is essential in order to improve asthmatics' quality of care and life.

### PC-867-16 The patient's role in asthma management: a case study of Kerugoya District hospital, Kenya

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**Background and challenges to implementation:** It is estimated that about 3.6 million people in Kenya (10% of the population) suffer from asthma. Hospital studies also indicate that asthma is the most common reason for emergency room visits among adults. These caused by among others, inadequate health infrastructure with lack of essential equipment necessary for diagnosis and poor societal awareness of the disease leading to poor health seeking behaviors.

**Intervention or response:** In the year 2008 KAPTL, working with various partners engaged and trained a group of patients on asthma diagnosis and management practices. It then approached the Kerugoya District hospital to pilot a patient-led asthma clinic. The volunteers train the patients on the proper use of their inhalation devices, how to identify their triggers and control their asthma. The hospital has provided a clinic room and a doctor to review the asthma patients.

**Results and lessons learnt:** In the year 2010, 2163 asthma patients were booked into the clinic. 193 adults and 29 children attended as new patients. The clinic has reduced the hospital's asthma cases admission and long queues at the out-patient and casualty departments. It is important to note the support of the hospital administration was crucial to the success of this project.

**Conclusions and key recommendations:** The success of this project demonstrates the power of ACSM; which created a strong public, private and patient partnership. This project is a clear indication that patients and their relatives have a very important role to play in asthma management in the country.

## DIABETES AND TUBERCULOSIS/ NON-COMMUNICABLE DISEASE/ CO-MORBIDITIES

### PC-894-16 Diabetes mellitus in tuberculosis patients at tuberculosis control unit of Singapore and its impact on clinical presentation

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**Background:** Diabetes mellitus (DM) is a risk factor for tuberculosis. The incidence of diabetes mellitus in Singapore citizens aged 18 to 69 years has increased over the years to 11.3% in 2010.

**Methods:** We undertook a retrospective study of case records of all TB patients seen at the TB Control Unit

(TBCU) in 2010 to determine the incidence of DM and the effect on the clinical presentation of TB in these patients.

**Results:** A total of 1695 patients were seen at TBCU in 2010. Among the 1027 patients who were citizens and permanent residents, 26.2% were diabetic, of whom 22.1% were newly diagnosed at the time of diagnosis of tuberculosis. The median HbA1c of the known and newly diagnosed diabetics were 8.9% (range 5.2%–18.3%) and 10.9% (range 5.8%–16%) respectively. Pulmonary disease occurred in 93.5% and 91% of diabetics and non-diabetics respectively. The median duration of cough was 4 weeks in both groups. Diabetics had significantly more sputum smear positive (56.2% vs. 30.1%,  $P < 0.001$ ), culture positive (84.6% vs. 56.5%,  $P < 0.001$ ) and cavitary disease (33.6% vs. 17.2%,  $P < 0.001$ ) compared to non-diabetics. Diabetics with poor control (HbA1c  $> 7\%$ ) had significantly higher rate of smear positivity (65.1% vs. 40.5%,  $P = 0.02$ ), culture positivity (89.3% vs. 73.2%,  $P = 0.006$ ) and cavitary lung disease (41.1% vs. 9.5%,  $P < 0.001$ ) compared with well-controlled diabetics (HbA1c  $< 7\%$ ).

**Conclusion:** Compared to non-diabetics, diabetics had significantly higher bacterial burden and cavitary disease at presentation. Poor DM control was associated with more advanced disease.

### PC-895-16 Diabetes mellitus and risk of recurrent tuberculosis: a population-based case-control study

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**Background:** Diabetes mellitus increases the risk of developing tuberculosis (TB), and is associated with unfavorable treatment outcomes, including treatment failure and death. It remains unclear whether diabetes also increases the risk of TB recurrence among those who had completed treatment.

**Methods:** A case-control study was conducted. The study population, all confirmed pulmonary TB cases reported to Taiwan TB registry during 2006–2007 with successful treatment outcomes, was followed till December 31, 2010. Cases were defined as illnesses in patients with bacteriological or pathological confirmation of TB after having completed treatment. Controls were selected from the study population with 1:1 ratio to cases using incidence-density sampling and matched on time since treatment completion. Demographic and clinical characteristics of previous TB episodes were collected. We used conditional logistic regression analysis to measure the association between diabetes and recurrent TB.

**Results:** There were 305 (1.4%) cases of recurrent

TB found among the 22 092 pulmonary TB patients enrolled; 297 matched case-control pairs were analyzed. TB recurrence were increased among patients with co-morbid diabetes mellitus during the previous TB treatment (crude OR = 1.57, 95%CI 1.10–2.25). The association remained unchanged after adjusting for sex, age, with smear or positive status, coexisting extra-pulmonary lesions, comorbidities such as chronic kidney disease, pneumoconiosis, residual cavitation, presence of 2-month culture positive, treatment regimen adequacy, and DOT (adjusted OR = 1.64, 95%CI 1.02–2.63).

**Conclusions:** The presence of diabetes mellitus is independently associated with increased risk of developing recurrent TB. To prevent recurrent TB among this population, further studies are needed to understand whether improved glycemic control during anti-tuberculosis treatment may decrease the risk of recurrence.

#### PC-896-16 Use of inhaled corticosteroids and the risks of tuberculosis

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**Background:** Recent report suggested that inhaled corticosteroid (ICS) use could increase risk of tuberculosis (TB) in a low TB burden country. The aim of this study was to elucidate the association between the ICS use and the development of TB among patients with various respiratory diseases in South Korea, an intermediate TB burden country.

**Design/methods:** A nested case-control study was conducted based on the Korean national claims database. The eligible cohort consisted of 792 687 new adult users of inhaled respiratory medications between 1 January 2007 and 31 December 2010. Patients diagnosed with TB after initiation of inhaled medication were included. For each case individual, up to five control individuals matched for age, sex, diagnosis of asthma or COPD, Charlson Comorbidity Index, number of health care visits, and initiation date were selected.

**Results:** From the cohort population, we matched 1738 individuals diagnosed with TB with 7106 controls. ICS use was associated with increased rate of TB diagnosis (aOR, 1.25; 95%CI 1.10–1.42). In addition, ICS use increased risk of TB was dose dependently (*P* for trend < 0.0001). The odds of TB development was 2.23 (95%CI 1.80–2.75) among patients used ICS more than 75 000 µg.

**Conclusion and recommendations:** The use of ICS increases the risk of TB dose dependently in an intermediate TB burden country. Clinicians should be aware of the possibility of TB development among long-term high dose users of ICS.

#### PC-897-16 Deaths of tuberculosis patients in urban China: a retrospective cohort study

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**Background:** The case fatality rate (CFR) of Chinese patients with tuberculosis (TB) is more than 5%, which is higher than in Western countries. The purpose of the present study was to identify factors associated with TB-associated deaths and all-cause deaths of TB patients in urban China.

**Design/methods:** This was a retrospective cohort study of all pulmonary TB patients who were registered in four districts of Shanghai from 2004 to 2008. Data were derived from the China National TB Surveillance System. A total of 4271 patients were followed up in communities. Data were analyzed by Cox regression.

**Results:** The percentage of all-cause deaths in the study population was 15% after 2–6 years from the most recent TB diagnosis. TB was responsible for only 17% of all deaths and male sex was significantly associated with all-cause deaths. After adjustment for sex, age, and treatment history, four factors were significantly and independently associated with increased risk of death: psychopathy, chronic bronchitis, cancer, and presence of multiple diseases. TB was responsible for 7.2 potential years of life lost (PYLL), and PYLL was higher in females (8.2) than males (5.3).

**Conclusion:** TB remains a significant problem in urban China. Implementation of improved clinical management, prevention strategies, TB control programs, and other public health programs should target TB patients with elevated risk.

#### PC-898-16 Association of diabetes and tuberculosis: impact on outcomes and transmissibility to household contacts

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**Objective:** To determine the clinical consequences of pulmonary tuberculosis (TB) among patients with diabetes mellitus (DM) and to determine the risk of active disease among individuals with DM who are exposed to pulmonary TB patients in the household.

**Methods:** Population based cohort study of pulmonary TB patients and of their household and neighborhood contacts. Bacteriologically confirmed cases of pulmonary TB at in the Orizaba Health Jurisdiction, Veracruz, Mexico, diagnosed between 1995 and 2010 and their household and neighborhood contacts recruited between 2001 and 2004.

**Results:** 1262 patients with pulmonary TB, 900

household contacts and 889 neighborhood contacts. Prevalence of DM among TB patients and household and neighborhood contacts was: 29.64%, 6.67% and 5.40%, respectively. Patients with DM and TB had more severe clinical manifestations as determined by sputum with blood (adjusted odds ratio (aOR) 1.66, 95% confidence interval (CI) 1.26–2.20); a higher probability of sputum conversion after 45 days or more (aOR 1.43, 95%CI 1.02–2.00); of treatment failure (aOR 2.93, 95%CI 1.18–7.23); of recurrence (adjusted Hazard ratio (aHR) 1.76, 95%CI 1.11–2.79); and of relapse (aHR 1.92, 95%CI 1.07–3.43). Most of the second episodes among patients with DM were due to bacteria with the same genotype; although in 19.23% of instances reinfection with a different strain occurred. Household contacts with previous diagnoses of DM had a higher probability of developing active TB with the same bacteria as the index case (aHR 12.48, 95%CI 4.52–34.48).

**Conclusion and recommendations:** Given the growing epidemic of DM worldwide, it is necessary to add DM prevention and control strategies to the TB control programs and vice versa.

### PC-899-16 Alarming prevalence of diabetes among tuberculosis patients in Kerala, India: policy implications

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**Background:** While diabetes mellitus (DM) is a known risk factor for tuberculosis, the prevalence among TB patients in India is unknown. We conducted a cross-sectional survey of TB patients registered June–July 2011 under the National TB Program in the state of Kerala, India, to determine the prevalence of DM. **Methods:** A state-wide representative sample of TB patients in Kerala were interviewed and screened for DM using glycosylated hemoglobin (HbA1c); patients self-reporting a history of DM or those with HbA1c  $\geq 6.5\%$  were defined as diabetic. HbA1c is recommended globally as a diagnostic tool for DM which is affected least by the temporary changes in the blood glucose levels due to various factors including tuberculosis disease and does not require patient preparation like fasting.

**Results:** Among 552 TB patients screened, 243 (44%) had DM—128 (23%) had previously known DM and 115 (21%) were newly diagnosed—with higher prevalence among males and those aged  $>50$  years. The number needed to screen to find one new case of DM was just four. Of 128 TB patients with previously known DM, 107 (84%) had poor glycemic control as indicated by HbA1c  $\geq 7\%$ , which is equivalent to

**Table** Prevalence and additional yield of new cases of diabetes mellitus and number needed to screen to diagnose a new case of DM among tuberculosis patients in the state of Kerala, India, June–July 2011

Characteristic	Number of TB patients whose DM status was ascertained [a]	Number with previously known DM [b]	Number of DM newly diagnosed [c]	Additional yield [c/(b + c) × 100]	Number needed to screen [(a – b)/c]	Total number with DM [d]	Prevalence of DM (95% CI)
Total	552	128	115	47%	3.7	243	44.0 (38.8–49.3)
Sex							
Male	420	108	100	48%	3.1	208	49.5 (43.6–55.4)
Female	132	20	15	43%	7.5	35	26.5 (19.1–33.9)
Age, years							
15–24	57	3	1	25%	52.6	4	7.0 (0.6–13.4)
25–34	70	4	11	73%	6.0	15	21.4 (10.6–32.2)
35–44	114	19	25	57%	3.8	44	38.6 (29.1–48.1)
45–54	134	44	30	41%	3.0	74	55.2 (46.5–63.9)
55–64	106	38	29	43%	2.3	67	63.2 (51.7–74.7)
$>65$	71	20	19	49%	2.6	39	54.9 (42.1–67.7)
Residence							
Urban	107	37	14	27%	5.0	51	47.6 (35.8–59.5)
Rural	445	91	101	53%	3.5	192	43.1 (37.9–48.4)
Type of TB							
New smear positive pulmonary TB	307	87	70	45%	3.1	157	51.1 (44.3–57.9)
New smear negative pulmonary TB	37	4	7	64%	4.7	11	29.73 (17.7–41.7)
New extra-pulmonary TB	128	15	21	58%	5.3	36	28.1 (18.4–37.8)
Relapse	35	12	8	40%	3.3	20	57.1 (40.8–73.5)
Treatment after failure	19	7	2	22%	6.0	9	47.3 (24.5–70.2)
Treatment after default	26	3	7	70%	3.3	10	38.4 (18.3–58.5)

TB = tuberculosis; DM = diabetes mellitus; NNS = number needed to screen is defined as the reciprocal of the prevalence of newly diagnosed DM after excluding self-reported previously known cases of DM; CI = confidence interval.

preprandial capillary plasma glucose 70–130 mg/dl (3.9–7.2 mmol/l).

**Conclusion:** Nearly half of TB patients in Kerala have DM, and approximately half of these patients were newly-diagnosed during this survey. Screening of TB patients for DM yielded a large number of DM cases and offered earlier management opportunities. Routine screening of TB patients for DM under program conditions will require policy revisions.

### PC-900-16 Diabetes mellitus and time to tuberculosis sputum culture conversion among patients with multidrug-resistant tuberculosis in the country of Georgia

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**Background:** Diabetes mellitus (DM) is a risk factor for developing TB but less is known about the influence on TB treatment outcomes and TB culture conversion. We assessed the influence of DM, DM treatment, and fasting blood glucose (FBG) on time to sputum culture conversion in patients with MDR-TB in the country of Georgia.

**Methods:** A prospective cohort of patients with laboratory confirmed pulmonary MDR-TB was followed during TB treatment to assess time to culture conversion (first of 2 consecutive negative cultures  $\geq 30$  days apart). DM status, DM medication, and FBG were determined by medical record. Kaplan Meier (KM) curves and proportional hazards models were used to assess the association of DM with culture conversion time.

**Results:** Among 975 patients with MDR-TB, 73 (7.6%) had DM (TBDM). Among 51 (70.0%) of TBDM with detailed DM records, mean FBG at MDR-TB treatment start was 10.5 (mmol/L). Prior to MDR-TB treatment, 76% of TBDM received DM medications; during MDR-TB treatment all received DM medications (78.4% insulin and 21.6% metformin). Among baseline MDR-TB culture positive patients ( $n = 670$ ), 45.1% with DM vs. 43.3% without DM converted sputum cultures within 6 months, mean time to culture conversion was 4.5 months for both groups. No significant differences in time to conversion by prior DM medication, baseline FBG, or DM medication during treatment were observed in TBDM patients; in KM curves, those with FBG  $\leq 10.0$  during MDR-TB treatment converted to sputum culture negative more quickly than TBDM with FBG  $> 10.0$  (67% vs. 20% converted within 6 months,  $P = 0.05$ ). In multivariable analysis the adjusted hazard ratio of culture conversion comparing patients with DM to those without was 0.92 (95%CI 0.53–1.6).

**Conclusions:** We did not observe significant associations with DM and time to sputum culture conversion in a cohort of MDR-TB patients. In Georgia, MDR-TB patients with DM who have FBG  $\leq 10.0$  during treatment may convert to culture negative more quickly.

### PC-901-16 Intensified case finding for tuberculosis in two diabetes clinics in Western Kenya

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**Background:** Disease patterns in sub-Saharan Africa (SSA) have changed rapidly over the past 25 years. Diabetes mellitus (DM) is one of the most common chronic diseases in the world and its prevalence is expected to increase in SSA. There are many risk factors for TB: HIV/AIDS, silicosis, malnutrition and smoking. Evidence gathered show a strong association between DM and TB. Studies dating to the first half of the past century demonstrate a considerable increase in TB among patients with DM. This study aimed to show the yield of a symptom screen for TB case-finding among diabetics.

**Design/methods:** This was a prospective cross-sectional study done within two diabetes specialty clinics (Webuye and Kitale district hospitals) from September 2010 to January 2012. Patients attending the clinic were screened for TB using a previously validated cough monitor questionnaire. All who reported a history of productive cough for more than 2 weeks had spot and early morning sputum taken for smear microscopy in the hospital laboratory. Data was entered on EpiData entry (Ver. 3.1) and analyzed with EpiData analysis software (V2.2.2.178).

**Results:** 585 patients with DM were screened for TB including 354 (60.5%) females and 231 (39.5%) males. Mean age was 61.1 (55.5–66.8) years. A positive symptom screen was found in 74 (12.6%) of patients screened, of whom 45 (61%) had a history of productive cough and had sputum smear microscopy done. 4 (9%) of the 45 patients had positive smear microscopy; 2 patients had 2+ smear result and 2 had 3+ smear result on both smear results. Patients were started on treatment according to the national guidelines. 27 (4.6%) of the patients had a history of treatment for TB and 34 (5.8%) had lived in the same household with a person with TB.

**Conclusion and recommendations:** Targeted TB case finding among patients with DM is productive in a routine clinic and would be useful in TB control. History of TB and history of a household contact with TB is common among these patients.

### PC-902-16 Tuberculosis and gender, but not HIV, are universal predictors of both cholesterol levels and body composition among adults in Uganda

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**Background:** It is not known whether HIV infection affects cholesterol levels or predicts body composition among adults with tuberculosis. We determined the effect of HIV on cholesterol levels and whether HIV predicts cholesterol profiles and body composition among adults with or without pulmonary tuberculosis.

**Design/methods:** In a cross-sectional study, 131 patients were screened for pulmonary tuberculosis and HIV. Serum total cholesterol (TC); high density lipoproteins (HDL); low density lipoproteins (LDL); body mass (BMI), lean tissue (LMI) and fat mass (FMI) indices were measured using recommended methods.

**Results:** Sixty-three patients with tuberculosis had significantly lower TC (134 mg/dl vs. 158 mg/dl), HDL (32 mg/dl vs. 43 mg/dl), LDL (81 mg/dl vs. 95 mg/dl), BMI (19 vs. 23 kg/m<sup>2</sup>), LMI (16 vs. 18 kg/m<sup>2</sup>), and FMI (3 vs. 5 kg/m<sup>2</sup>) compared to 68 individuals without TB respectively. Mean HDL was the only significantly lower profile level among HIV sero-positive than HIV sero-negative individuals regardless of tuberculosis disease status. In multivariable linear regression analysis, tuberculosis disease and male sex were associated with relative decrease in TC, HDL, LDL, BMI, and FMI compared to no tuberculosis and female sex. HIV positive status was associated with relative decrease for only TC and HDL levels compared to HIV negative status. There were remarkable decreasing trends in serum TC, HDL, and LDL with increasing severity of clinical tuberculosis disease regardless of HIV status.

**Conclusion and recommendations:** Tuberculosis and gender are universal predictors of both cholesterol levels and body composition; while tuberculosis and HIV are independently associated with reduced levels of cholesterol among adults.

### PC-903-16 Major depressive episodes are associated with negative outcome in patients with pulmonary tuberculosis in Lima, Peru

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**Background:** Pulmonary tuberculosis (PTB) is an important contributor to the burden of diseases in developing countries. Negative outcomes (NO) such as treatment default and death are still frequent among PTB patients. Depressive disorders are associated with lower treatment compliance for chronic diseases. This study aimed to estimate the significance and magnitude of major depressive episode (MDE) on NO in patients with PTB in Lima, Peru.

**Methodology/principal findings:** Within a prospective cohort study in (Lima, Peru) we enrolled adult participants with culture-confirmed PTB. A validated, 5 item version of the Center for Epidemiological Studies Depression Scale (CES-D) was self-completed by the participant at enrollment. This CES-D version reported a sensitivity of 95.7% and specificity of 93.4% for MDE. Patients with MDE were referred for medical evaluation and management. Treatment outcomes were defined following World Health Organization's recommendations. Survivor function of NO according to MDEb status was estimated using Cox's Regression model controlling for age, sex, marital status and educational level.

**Results:** 344 patients were enrolled; 188 (53%) were male; mean age was 29.8 years (SD = 12.4); 24 (7%) presented a NO, and 131 (38%) presented MDE at baseline (MDEb). Significant difference was found on the survivor function of patients with and without MDEb, respectively (0.87 vs. 0.96,  $P = 0.049$ ). On the crude analysis, patients with MDEb had a hazard ratio of 3.34 (CI 95% 1.43–7.81) compared to patients without MDEb. The results of the adjusted model showed little variation in relation to the bivariate estimates (HR = 3.77; CI 95% 1.52–9.39).

**Conclusion:** The results suggest that MDEb is associated with NO in PTB patients in Lima. A baseline screening and adequate treatment for patients with MDEb may improve the outcomes.

### PC-904-16 Diabetes, pre-diabetes and tuberculosis in an Asian mega-city: Karachi, Pakistan

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**Background:** It is now established that diabetes (DM) is a major risk factor for tuberculosis (TB) in many parts of the world, and that the global burden of DM is rising. By 2030, more than 80% of DM cases will be in low- and middle-income countries (LMICs), many of which already have a high burden of TB, such that the growth of diabetes threatens further increases in TB incidence. We sought to determine the first estimation of the contribution of DM to TB in an Asian mega-city: Karachi, Pakistan.

**Methods:** TB-DM comorbidity was abstracted from medical records of Indus Hospital TB Control Program patients. These data were compared with community DM prevalence from the baseline non-communicable disease survey of the Indus Hospital Community Cohort (IHCC). Age- and sex-adjusted odds ratios were calculated for DM comparing these two populations. Diabetes was defined using HbA1c levels in accordance with the new WHO guidelines.

**Findings:** The prevalence of DM among TB patients was almost triple that measured in the surrounding community [16% vs. 7%, adjusted odds ratio: 2.9 (1.9–4.3)]. Further, a significantly higher percentage of TB cases screened for DM had pre-diabetes (HbA1c  $\geq$  5.7% and  $<$ 6.5%) compared with community members. Despite having higher rates of DM, the percentage of TB cases who were overweight or obese was lower than that in community members (9% vs. 27%).

	no-DM	DM	aOR (95% CI)
Female	1,313 (88)	175 (12)	1
Male	884 (82)	189 (18)	1.16 (0.9, 1.5)
Age Group			
15-34	1,487 (94)	92 (6)	1
35-55	494 (76)	159 (24)	5.43 (4.1, 7.2)
$\geq$ 55	216 (66)	113 (34)	8.60 (6.3, 11.8)
Community	386 (93)	30 (7)	1
TB Cases	1,811 (84)	334 (16)	2.87 (1.9, 4.3)

	Community	TB Cases	aOR (95% CI)
no-DM	268 (64)	1,071 (50)	1
pre-DM	118 (28)	740 (34)	1.653 (1.3, 2.1)
DM	30 (7)	334 (16)	3.569 (2.4, 5.4)
Underweight	98 (24)	968 (54)	
Normal Weight	202 (49)	655 (37)	
Overweight	77 (19)	119 (7)	
Obese	33 (8)	34 (2)	

**Conclusion:** We observe TB-DM rates almost triple DM rates in the corresponding community in an Asian megacity. Of additional concern is the first observation of the potential contribution of 'pre-diabetes' to tuberculosis in this population, suggesting that a large number of people with marginally elevated glycosylated hemoglobin are also at increased risk in a high TB prevalence community.

## ABSTRACT PRESENTATIONS SATURDAY 17 NOVEMBER 2012

### ORAL PRESENTATION SESSIONS

#### TUBERCULOSIS OUTBREAKS AND CONTACT INVESTIGATIONS

##### OP-193-17 Feasibility and reliability of mobile health application as an innovative M&E tool for tuberculosis contact tracing in eThekweni District, South Africa

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**Background and objective:** eThekweni District has the highest burden of TB in South Africa, thus requiring an efficient management information system.

**Objective:** To test the feasibility and reliability of using mHealth technology (combination of smart phones and Google Earth™) to provide timely information on community management of TB.

**Methodology:** TB patients' addresses were obtained from the Electronic TB Register (ETR) and this information was transmitted to tracing teams' smart phones, thereafter used for locating households, following indexes, screening contacts for TB and HIV, and adequately refer thereafter to appropriate facilities. Global Positioning System (GPS) coordinates were collected; real time data were transmitted to a centralized server via a cell phone network; Google Earth™ households mapping was generated as well as automated reports of households' data. Validation of the raw data compared with the database report and end users considerations were analysed.

**Results:** Qualitatively we found that despite a high load of information (target sample of 7436 households and 10469 contacts), the application generated an extremely high level of consistency between end point server generated reports and data entered and sent through the smart phones. The health care workers expressed a high level of acceptance of the smart phones. Quantitatively 4555 household over a target of 7436 (61%) were located, of 10469 contacts targeted, 6204 (59%) were found at the time of the tracing teams visit, 920 of them (15%) found to be TB suspect cases, of which 533 (58%) provided sputum sent to the laboratory. HIV Counselling and Testing was offered to 4738 family members, with an acceptance rate of 37%; 41 pregnant women were referred to antenatal care.

**Conclusion:** Smart phones have a huge potential to gather and transmit real time information to the TB control program for interventions at community level and to ease information workload.

#### **OP-194-17 Cost of setting up contact investigation in a high tuberculosis incidence setting in Tanzania**

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**Background and challenges:** In many low-income, high TB-incidence countries, contact investigation is often not done; there is limited information on the cost of setting up such activities. The study aimed at providing information on the annual cost of setting up an intervention for TB contact investigation in a high incidence setting in Dar es Salaam, Tanzania.

**Intervention:** March to September 2011, a randomized controlled trial was piloted using trained community health workers to conduct contact investigation. Patients with active pulmonary TB (index case) were identified at 10 TB diagnostic clinics in Kinondoni District and randomized to a control group (receiving standard care) or an intervention groups (receiving TB contact investigation in their households). Household members from both groups were followed for 6 months to ascertain whether any developed TB. The costing study was undertaken from a health provider perspective.

**Results:** 284 index cases were enrolled. 749 household contacts were elicited and followed up for 6 months. A total of 17 contacts (2.2%) out of 749 were identified as secondary TB cases by the contact investigation. No secondary TB cases were identified from the control group. The total costs of the intervention including annualized capital costs and recurrent (operating) costs for setting up contact investigation was US\$35 730 for all 10 TB clinics. The recurrent costs and capital costs incurred about 92% and 8% respectively. The unit cost per secondary case identified was calculated at US\$1050; per clinic cost was US\$3600.

**Conclusions and recommendations:** The unit cost per identified TB case in relation to per capita GDP seems to be within achievable levels. The yield (2.2%) of secondary cases was lower than expected. Study procedures were revised and yield is expected to increase which would decrease the unit cost per case identified. These data will be used in a cost effectiveness analysis of contact investigations in Dar es Salaam.

#### **OP-195-17 Tuberculosis among health care workers in KwaZulu-Natal, South Africa: a cohort analysis**

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**Background:** Tuberculosis (TB) is known to be an occupational hazard for health care workers (HCWs) and it is estimated that HCWs are more likely to develop TB than the general population. The objective of this study was to compare the difference in estimated risk of TB disease among HCWs with a history of working in TB wards with those without a history of working in a TB ward.

**Design/methods:** Retrospective cohort study for the period January 2006 to December 2010 was conducted in four district hospitals in KwaZulu-Natal, South Africa. Data were abstracted via chart review between July and September 2011 from HCW occupational health (OH) medical records. Bivariate analysis and multivariate analyses were performed. A generalized linear latent multilevel mixed (GLLAMM) regression model was used.

**Results:** Of 1380 (92.31%) medical charts reviewed which had data on location of work documented, 115 (8.59%) cases of TB were identified. HCWs with a history of working in TB wards were at statistically significant increased odds OR 2.08 (95%CI 1.02–4.22) of developing TB controlling for other factors. Findings also indicated that HCWs with a history of working in more than one ward and in non-TB wards were also at significantly greater odds of developing TB. Paramedical staff were more likely to develop TB compared with administrative staff; OR 3.28 (95%CI 1.12–9.66) and HIV-positive HCWs were at greater odds of developing TB compared with those without HIV OR 5.54 (95%CI 2.73–11.26). The odds of developing TB were greatest within the first 5 years of employment OR 1.77 (95%CI 1.40–2.24).

**Conclusion and recommendations:** HCWs working throughout hospitals, not only TB wards, are at an increased risk of developing TB. This further supports the need for improved infection control measures and occupational health services to protect HCWs.

#### **OP-196-17 Factors influencing compliance with tuberculosis contact investigation in Viet Nam**

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**Background and challenges to implementation:** Contacts of tuberculosis (TB) patients are known to be at significant risk of developing the disease, however there have been few studies assessing compliance with TB contact investigation in high prevalence settings. In Viet Nam, where prevalence of TB remains high despite achieving WHO targets for more than a decade, we are currently implementing a randomized-controlled trial of contact investigation within the Viet Nam National Tuberculosis Program. We aimed to assess the knowledge, attitudes and practices of staff, patients and their household contacts, and to identify factors associated with non-attendance by contacts.

**Intervention or response:** A contact investigation program was implemented at 37 district tuberculosis units, among household members of patients with smear positive tuberculosis. Contacts were clinically assessed and a chest radiograph was performed at baseline and after 6 months. Questionnaires were designed following focus group discussions, and were completed by 200 participating government health workers and a random selection of 150 TB patients and 300 contacts, from districts that had achieved at least a 40% follow-up rate. Contacts who were defaulters and non-defaulters were compared.

**Results and lessons learnt:** The staff, patient and contact questionnaires identified key barriers to contact investigation including cost of transportation, opportunity costs, limited understanding about the disease and perceived stigma against tuberculosis. Key components of this program's success included an initial pilot study, local engagement, strong support from a national level, and ongoing monitoring.

**Conclusions and key recommendations:** Structured questionnaires are a useful tool to understand local factors that influence compliance with TB contact investigation. National contact investigation policies should be tailored to reflect the local conditions in which they are being implemented.

#### **OP-197-17 Demographic characteristics and bacteriological status of pulmonary tuberculosis cases detected using active case finding**

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**Background:** Since 2005, the National Tuberculosis (TB) Programme, Cambodia, has been conducting active case finding (ACF) of TB cases with mobile radiography units, targeting contacts in poor and vulnerable communities in addition to routine passive case finding (PCF). The objective of this study was to

examine differences in demographic characteristics and bacteriological status of pulmonary TB cases who were detected using both approaches (active and passive case finding), and considering associated project costs.

**Design/methods:** Demographic characteristics, smear grades and treatment outcomes were compared between actively ( $n = 405$ ) and passively ( $n = 602$ ) detected patients by reviewing the existing records (including TB registers) of 2009 and 2010. Additional analyses were performed for PCF cases detected after ACF sessions ( $n = 91$ ).

**Results:** The overall cost per case detected through ACF was US\$108. ACF detected patients from older populations (by age) compared to PCF (the median age of 55 vs. 48;  $P < 0.001$ ). The percentage of smear-negative TB cases detected through ACF was significantly higher than that of PCF (71.4% vs. 40.5% in ACF and PCF groups respectively). Among smear-positive patients, lower smear grade was observed in ACF compared to PCF ( $P = 0.002$ ). After the ACF session, smear grade of TB patients continued to be low among the cases detected through routine PCF.

**Conclusion and recommendations:** The community-based ACF approach was found to be cost-effective, with additional benefits of early case finding of patients, possibly with an extended benefit for reducing secondary cases.

#### **OP-198-17 Active case finding among contacts of smear-positive tuberculosis patients: experience and key recommendations**

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**Background and challenges to implementation:** Burkina Faso is a high incidence TB country, estimation rate is 55 smear-positive pulmonary tuberculosis/100 000 habitants occur every year. To improve TB detection NTP established a partnership with Civil Society organization.

**Intervention or response:** The intervention aim to improve earlier case detection by reducing the patient delays and access delay to the health centre. The strategy included an active cases finding among contact of TB patients. During home visits to TB patients who have given their consent before, an awareness followed by chronic cough screening is performed among the contacts. This intervention has to be implemented by 20 CBOs involved in TB community-based care (permanence at DTC, home visit, defaulters tracing, DOT, TB contact investigation).

**Results and lessons learnt:** Data collected on one centre is shown in the Table. The data show a detection rate of smear+ of 268 per 100 000 among contacts

PTB+ with awareness during home visit, 2011	Number of contacts sensitized, an estimation of 8 by PTB+	Suspects refer, rate	Suspects and tested by smear exams, rate	PTB+ among contact, rate by 100 000 habitant	Notification rate PTB+/100 000
140	1120	26 2.32%	23 88%	3 268 PTB+/100 000	24.2 PTB+/100 000

11 times high more than in general population. The contribution of the active cases finding among contact of TB patient estimated by one patient is about 2.1% of total smear positive TB detected in 2011 (89/3934).

**Conclusions and key recommendations:** This finding needs to be corroborated by total national data analysis. An operational research among TB patient contact is actually ready to start. It is expected that the result will be based for future to take policy and define national approach for TB contact tracing. This will be allowed a better calculation of the impact and contribution to detection rate.

## TUBERCULOSIS HOTSPOTS: FROM THE GENOME TO THE COMMUNITY

### OP-199-17 Exposure to secondhand smoke and risk of active tuberculosis: prospective cohort study

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**Background:** Although active smoking is found to increase the risk of tuberculosis (TB), only a few epidemiological studies reported on the association between exposure to secondhand smoke and risk of TB.

**Methods:** A cohort of never smokers was assembled using participants ( $\geq 12$  years old) of two rounds (2001 and 2005) of National Health Interview Survey in Taiwan. Information on exposure to secondhand smoke at home as well as other relevant sociodemographic and behavioral factors was collected through in-person interview. The participants were prospectively followed for incident cases of active TB through cross-matching the NHIS database to the TB registry of Taiwan. Cox proportional modeling was used to estimate the effect of secondhand smoke on the risk of TB, adjusting for potential confounding factors.

**Results:** A total of 93 cases of active TB were identified among 24 655 never smokers after a median follow-up of 7.5 years. The prevalence of exposure to secondhand smoke at home was 41.8% in the study

population. Exposure to secondhand smoke was not associated with incidence of active TB in the crude and adjusted analysis (crude and adjusted HR: 0.98 (95% CI 0.65–1.49) and 0.87 (95% CI 0.55–1.36)). A potential effect modification by age ( $< 18$  or  $\geq 18$  years old) was found ( $P$  for interaction: 0.09), and the adolescents were shown to be more susceptible to the effect of secondhand smoke (adjusted HR: 4.51 (95% CI 0.76–26.77)). A separate analysis revealed that secondhand-smoke exposure was associated with increased risk of coronary heart disease (adjusted HR: 1.47 (95% CI 1.07–2.02)) in this cohort, consistent with other reports on secondhand smoke and coronary heart disease.

**Conclusions:** Exposure to secondhand smoke was not associated with risk of active TB in this cohort. However, the adolescents may be particularly vulnerable to the effect of secondhand smoke, and the results need to be further confirmed in future large-scale studies.

### OP-200-17 What is the prevalence of extensively drug-resistant tuberculosis in Andhra Pradesh, India?

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**Background:** Antituberculosis drug resistance is a major public health problem around the world. Approximately 440 000 cases of multidrug-resistant (MDR) tuberculosis (TB), defined as TB resistant to at least isoniazid and rifampicin, occur globally each year. Extensively drug-resistant TB (XDR-TB) is a subset of MDR-TB with further resistance to at least one of three injectable second-line drugs (SLD) (amikacin, kanamycin, or capreomycin) and any fluoroquinolone. India accounts for nearly 20% of the global TB burden; even small proportions of XDR-TB have a large magnitude of scale, yet it is unclear how many XDR-TB cases occur nationally.

**Objectives:** To estimate the prevalence of XDR-TB among MDR-TB isolates in Andhra Pradesh, India.

**Methodology:** As part of a statewide antituberculosis drug resistance survey (population: 86 million), we conducted drug susceptibility testing (DST) on 141 MDR-TB isolates identified from September 2008 through December 2009. Using Löwenstein-Jensen culture media, DST was conducted according to 1% proportion method for kanamycin and ofloxacin.

**Results:** Valid results of 120 *M. tuberculosis* isolates were available. 20.83% isolates were resistant to ofloxacin (13.3%, and 23% among new and retreatment cases, respectively); and 10.8% were resistant to kanamycin (20.7% and 7.7% among new and retreatment cases, respectively). Overall XDR-TB

prevalence was estimated to be 5.8% of all MDR-TB isolates.

**Conclusions:** More than 1 in 5 MDR-TB isolates from a statewide anti-TB drug resistance survey were resistant to ofloxacin, and 1 in 20 were XDR-TB. The high prevalence of resistance to ofloxacin suggests that current MDR-TB regimens may not be efficacious in all MDR-TB patients, and that routine second-line drug resistance testing should be considered to optimize treatment.

### OP-201-17 Characteristics of *pncA* mutations in multidrug-resistant tuberculosis isolates cultured from Queensland migrants and Papua New Guinea residents

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**Aim:** Pyrazinamide (PZA) is an important first-line anti-tuberculosis drug involved in treatment of multi-drug-resistant (MDR) cases. The aim is to genotype and to perform *pncA* mutation analysis of PZA resistant isolates among MDR cases cultured from Queensland (QLD) migrants and Papua New Guinea (PNG) residents and to compare with phenotypic (BACTEC 960) evidence of PZA resistance.

**Method:** Between 2005 and 2011, all 28 MDR isolates that were resistant or suspicious of PZA resistance from QLD migrants (6/28) and PNG residents (22/28) were subjected to *pncA* mutational analysis and 12 loci MIRU typing. Phenotypic and genotypic data were compared.

**Results:** Using culture drug susceptibility testing as 'gold standard' overall sensitivity and specificity of *pncA* mutational analysis was 100%. Of the 22 MDR isolates from PNG residents, 1 was susceptible to PZA and showed no mutation, 1 had point mutation at nucleotide (nt) position 36 (C36A), 13 had a point mutation at nt position 307 (T307G) and 7 had a point mutation at nt position 202 (T202C). The majority of the isolates with a mutation at nt position 307 had a MIRU pattern of 22325163544 and those with a mutation at nt position 202 had MIRU pattern of 22325163545. Of the 6 MDR isolates from QLD migrants, 2 isolates that were susceptible to PZA showed a silent mutation at nt position 195 (C195T) and 3 PZA resistant MDR isolates showed 3 mutations at nucleotide position, 28 (C28G), 174 (C174G) and 192 (T192G).

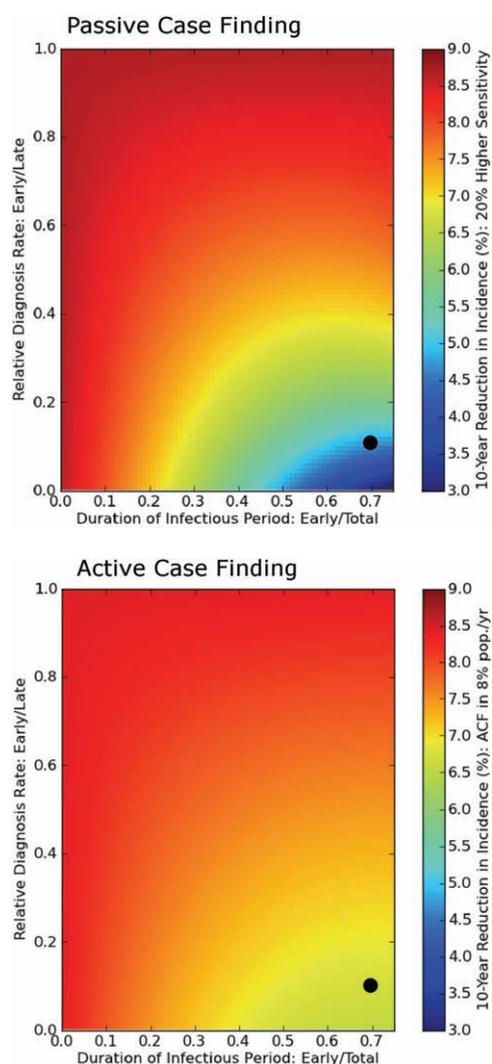
**Conclusions:** Two genotypes with distinct *pncA* mutation patterns (T202C and T307G), were seen from the PNG resident MDR isolates. A diversity of genotypes and mutations were seen in isolates from the QLD migrant population. *pncA* mutation analysis provides an excellent secondary test of the PZA culture DST with an improved result turn around time.

### OP-202-17 Are we overestimating the impact of new diagnostic tests for tuberculosis? A model-based analysis

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**Background:** Novel diagnostic tests for TB are recommended largely on the assumption that they will reduce transmission and incidence. Models of TB diagnostics often assume a constant rate of diagnosis, but many patients seek care late in the disease course after symptoms progress.

**Design/methods:** We constructed a simple compartmental model of TB transmission based on the



**Figure** Reductions in TB incidence through improved passive and active detection, according to duration and relative diagnosis rate of the early infectious period.

structure of widely cited existing TB models. We compared a model (the ‘baseline model’) simulating a constant rate of diagnosis to a second model (the ‘late care-seeking model’) that distinguishes an ‘early’ and ‘late’ infectious period. This model allows diagnostic attempts to cluster later in the natural disease course while keeping the total infectious duration constant. We varied the duration of the early infectious period from 0% to 75% of the total infectious period, and the relative rate of diagnostic attempts in the early versus late infectious periods from 0.0 to 1.0.

**Results:** In the baseline model, a 20% improvement in diagnostic sensitivity of the passive case-finding system reduced TB incidence by 8.7% after 10 years, while population-based active case-finding in 8% of the population per year reduced TB incidence by 8.4%. By contrast, the same interventions in the late care-seeking model, in which patients seek care at a relative rate of 0.1 throughout the first 70% of the infectious period, reduced TB incidence by 4.6% and 6.7%, respectively (Figure, black dots). In one-way sensitivity analysis and multivariable uncertainty analysis, the population-level impact of TB diagnostics depended more on patient care-seeking patterns than on any parameter except test sensitivity.

**Conclusion and recommendations:** By failing to account for an early infectious period during which patients—being less symptomatic—are less likely to seek care, existing models may overestimate the impact of passively-implemented diagnostics on TB incidence by a factor of two or more.

### OP-203-17 Heterogeneity in tuberculosis transmission and the role of geographic hotspots in propagating epidemics

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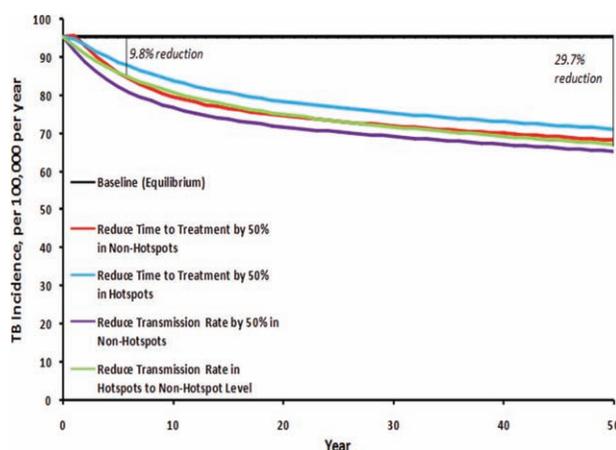
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**Background:** Tuberculosis (TB) transmission is geographically heterogeneous, but the importance of high-incidence ‘hotspots’ to population-level TB dynamics within cities is not known.

**Design/methods:** We constructed a spatially-explicit, steady-state compartmental model of TB in Rio de Janeiro, Brazil, replicating 9 epidemiological parameters within 1% of their observed values. Using city surveillance data, we identified three geographic clusters that together accounted for 6.0% of the city’s population, but 16.5% of its TB incidence. We used our model to estimate the proportion of city-wide TB transmission originating from these hotspots, and the relative impact of TB control measures targeting hotspots versus the remainder of the city.

**Results:** If each case of active TB in a hotspot caused

0.5 secondary transmissions in the general community for each within-hotspot transmission, the 6.0% of people living in the hotspots accounted for 35.3% of Rio de Janeiro’s total ongoing TB transmission. Reducing the TB transmission rate in the hotspots to that in the remainder of the city (‘equalization’) reduced city-wide TB incidence by an estimated 9.8% in year 5, and 29.7% in year 50—an effect similar to halving time-to-diagnosis for the remaining 94% of the city’s population (Figure). The importance of the hotspots to city-wide TB control depended strongly on the extent of TB transmission from hotspots to the general community; if each TB case in a hotspot generated as many infections outside the hotspot as within it, then equalizing TB transmission—i.e., reducing TB transmission rates in hotspots alone—was sufficient to eliminate TB from Rio de Janeiro in the long term (i.e.,  $R_0 < 1$ ).



**Figure** Impact on TB incidence of hotspot-focused versus population-based interventions.

**Conclusion and recommendations:** High-incidence hotspots may play an important role in propagating TB epidemics. Achieving TB control targets in hotspots containing 6% of a city’s population can have similar impact on city-wide TB incidence as achieving the same targets throughout the remaining community.

### OP-204-17 Improving tuberculosis case finding in the urban slums of a high tuberculosis burden country: what works best?

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**Background and challenges to implementation:** Project setting: Urban slums in five cities and municipalities in Kenya. Kenya has a large TB disease burden that is fuelled by both poverty and HIV. Recent national TB data suggests that cities and municipalities in Kenya are disproportionately contributing to the burden of TB notified to the NTP, reflecting the increased vulnerability of slum dwellers to TB infection and disease.

**Intervention or response:** We sought to improve and hasten TB case finding among slum dwellers in five cities and municipalities in Kenya through slum based private health care provider engagement, TB screening in outreach camps, intensified case finding among PLHIV using peer to peer screening and screening for TB in HIV care settings, door-to-door screening by community volunteers and contact investigation.

**Results and lessons learnt:** Between October 2010 and December 2011, a total of 31 806 TB patients were notified to the NTP from the project areas including 12 780 sputum smear positive pulmonary TB cases (PTB+). Our project contributed 3242 TB cases including 2412 PTB+ cases to the numbers of notified cases. In terms of yield (PTB+ cases found divided by persons screened) private provider engagement had the highest yield at 7%, followed by door-to-door screening by community volunteers at 5%, contacts investigation at 1.3%, PLHIV peer screening and screening in HIV care settings at 0.7% and 0.4% for TB screening at medical camps.

**Conclusions and key recommendations:** In a multi-faceted approach to find TB in slum dwellers, engagement of slum based private providers and door-to-door screening may yield higher numbers of TB cases with lower numbers of people screened and should therefore be prioritized for inclusion in such programmes.

#### **OP-205-17 Triage test characteristics for increasing the cost-effectiveness of Xpert® MTB/RIF in the diagnosis of tuberculosis: a decision analytical model**

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**Background:** In an economic evaluation, Xpert® MTB/RIF (Xpert) proved cost-effective for increasing TB case detection, by the GDP per capita threshold.

High diagnostic costs are, however, a limitation to scaling up in resource constrained settings. And, cost-effectiveness decreases with lower prevalence of TB among the suspects, limiting the use of diagnostics for enhanced case finding. We explored combinations of sensitivity, specificity and cost at which a hypothetical triage test would improve the cost-effectiveness of Xpert.

**Methods:** In a decision analytical model, two diagnostic pathways were compared with a base case of smear microscopy followed by clinical diagnosis for smear-negative TB: (1) a pathway in which TB suspects with a positive triage-test were tested by Xpert; (2) Xpert on all suspects. The model was parameterized for three epidemiological and cost settings, representing different levels of HIV and MDR prevalence. Costing data were used from Xpert demonstration sites, using the ingredient approach.

**Results:** If the prevalence of smear-positive TB among suspects was 5%, a triage test required at least 75% sensitivity to improve the cost-effectiveness of Xpert. A triage test with, for example, 95% sensitivity and only 75% specificity would improve the cost-effectiveness of Xpert if its per suspect cost were \$15 or below. The strategy would be highly cost-effective in low income countries by the conservative minimum care packages (MCP) threshold if per suspect triage test cost were \$6. A triage test with, e.g., 85% sensitivity and 85% specificity would improve the cost-effectiveness of Xpert if per suspect cost were \$15 or below, and meet the MCP threshold if this cost were \$8.

**Conclusion:** A triage-test strategy can improve the cost-effectiveness of Xpert at low TB prevalence ( $\leq 5\%$ ) in the suspect population. Tests and markers with lower accuracy than desired of a diagnostic test should be considered for modification into a simple triage test.

#### **OP-206-17 Costs associated with tuberculosis evaluation in rural Uganda**

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**Background:** The time and cost associated with accessing tuberculosis (TB) diagnostic services in rural Uganda is not well described.

**Design/methods:** From 11/2011 to 4/2012, we surveyed adult TB suspects at six geographically dispersed Level IV government health centers in rural Uganda and adults from randomly selected households within the sub-districts served by the health centers. We collected data on household income, costs associated with seeking care, time spent seeking care, and care-seeking patterns.

**Results:** Among 40 TB suspects surveyed at the health centers, median roundtrip transport time was 60 minutes (IQR 60–120 minutes) and median cost of the visit was 16% (IQR 2–33%) of monthly household income. Of 30 TB suspects who had sought care previously for the same episode of cough, 8 (27%) had previously visited a Level IV health center and 22 (73%) initially presented to a facility without TB diagnostic capacity. The most common reasons for not visiting the Level IV health center included distance, transport cost and belief that testing or treatment would not be available at a government clinic. Results were similar in 74 community surveys. Of 34 individuals with cough  $\geq 2$  weeks within the past year, 32 (94%) had sought care for their cough. 22 (69%) individuals first sought care at a location other than the Level IV health center and only 9 (28%) had sputum specimens collected for TB examination. The median time per care-seeking visit (including transport and waiting time) was 300 minutes (120–540) and median cost per visit was 54% (IQR 20–100%) of monthly household income.

**Conclusion and recommendations:** Obtaining TB evaluation is associated with considerable transport time and costs in rural Uganda. Presentation to facilities without TB diagnostic capacity is common and contributes to higher costs and longer delays. Patient-centered strategies such as community-based case finding are needed to reduce barriers to TB evaluation.

## TB-HIV: THE PROMISE OF LIFE BUT THE REALITY OF DEATH

### OP-207-17 Mortality among HIV-infected adults presenting for antiretroviral therapy with unexplained weight loss, chronic fever or chronic diarrhoea in Malawi

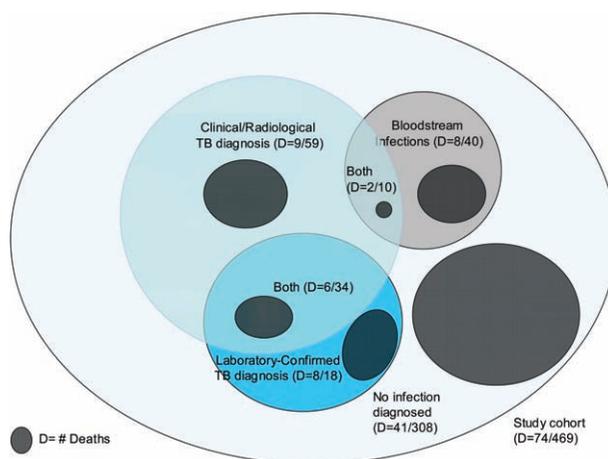
M Van Lettow,<sup>1,2</sup> A Akesson,<sup>3</sup> A Martiniuk,<sup>1,2</sup> A Ramsay,<sup>4</sup> A K Chan,<sup>1,2</sup> A D Harries,<sup>5</sup> S Anderson,<sup>6</sup> L Corbett,<sup>6,7</sup> R Heyderman,<sup>6</sup> R Zachariah,<sup>3</sup> R Bedell.<sup>1</sup> <sup>1</sup>Research, Dignitas International, Zomba, Malawi; <sup>2</sup>Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada; <sup>3</sup>Operations Research, Médecins Sans Frontières, Thyolo, Malawi; <sup>4</sup>Tropical Disease Research Programme, World Health Organization, Geneva, Switzerland; <sup>5</sup>Operations Research, International Union Against Tuberculosis and Lung Disease, Paris, France; <sup>6</sup>Clinical Research Programme, Malawi-Liverpool-Wellcome Trust, Blantyre, Malawi; <sup>7</sup>Tropical Medicine, London School of Hygiene & Tropical Medicine, London, UK. e-mail: m.vanlettow@dignitasinternational.org

**Background:** Among ART-eligible patients in Africa, undiagnosed opportunistic infections (OIs) contribute to high early mortality after ART initiation.

**Methods:** A prospective cohort study of TB and blood stream infections (BSIs) in HIV-infected adults with weight loss, chronic fever or diarrhea, and negative TB sputum microscopy, was conducted in

Malawi. ART uptake, treatment of OIs, mortality and risk factors for death were assessed 6 months after intention to initiate ART.

**Results:** Of 469 ART-eligible adults enrolled, within 6 months 74 (16%) died. 370 (79%) started ART at a median of 18 days. 103 (22%) were diagnosed with TB on clinical grounds, including 34 (33%) where TB treatment preceded laboratory confirmation. Mortality in this group was 17/103 (17%). 18 TB and 50 BSI cases were identified solely through laboratory investigations. Mortality among these 18 was significantly higher than among TB cases where decision to treat was based on clinical grounds (44% vs. 18%). There was no difference in median time to ART initiation; median TB treatment start was 25 days later than those diagnosed on clinical grounds. Among the 50 (11%) BSIs, 10 (20%) died (7 before receiving treatment). Of the 308 without any identified infection, 41 (13%) died. In multivariate analysis (adjusting for baseline characteristics and survival of >21 days), baseline weight loss >10%, low CD4, severe anemia, being diagnosed with TB solely through laboratory investigations and not initiating ART, were independently associated with increased risk of death. Additional laboratory investigations and treatment may have averted up to 42 deaths.



**Figure** Study cohort.

**Conclusions:** Mortality was high among chronically ill patients with non-specific criteria for ART initiation. Diagnostic and treatment delay among TB cases was strongly associated with risk of death. ART programs need access to rapid point-of-care-diagnostic tools for OIs. The role of early empiric OI treatment requires urgent evaluation in clinical trials.

### OP-208-17 Tuberculosis and the risk of opportunistic infections and cancers in HIV-infected patients starting antiretroviral therapy in southern Africa

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**Background:** HIV-infected patients are at high risk for opportunistic infections (OIs) such as tuberculosis (TB), cryptococcal meningitis (CM) and *Pneumocystis jirovecii* pneumonia (PCP). We aimed to study the incidence of AIDS-defining OIs and cancers, and the role of a history of TB as a risk factor for AIDS-defining conditions in HIV-infected patients on antiretroviral treatment (ART).

**Methods:** We analyzed patient data from 2000 to 2010 in five ART programs in South Africa, Zimbabwe and Zambia. Inclusion criteria were age  $\geq 16$  years and known ART start date. History of TB was defined as a diagnosis before or at start of ART. We identified risk factors for OIs using Cox models adjusted for age, sex, CD4 cell count at ART start and treatment site, presented as adjusted hazard ratios (aHR).

**Results:** A total of 175 212 patients with 320 459 person-years of follow-up were included. Median age at ART start was 35.0 years (interquartile range [IQR]) 29.8–41.6), median CD4 cell count 131 cells/ $\mu$ l (IQR 64–205 cells/ $\mu$ l), and 108 521 (61.9) were females. We analyzed 702 patients with incident CM occurring at or after ART initiation (including 205 with a

**Table** Hazard ratios for developing AIDS-defining opportunistic infections and cancers after starting antiretroviral treatment (ART) in 175 212 HIV-infected patients

Characteristic	Total number of events	Association with a history of any TB			
		HR (95% CI)	P value	aHR (95% CI)	P value
AIDS-defining respiratory and non-respiratory opportunistic infections					
Cryptococcal meningitis	702	1.64 (1.39–1.93)	<0.0001	1.28 (1.05–1.55)	0.015
<i>Pneumocystis jirovecii</i> pneumonia	487	2.34 (1.94–2.81)	<0.0001	1.61 (1.27–2.04)	<0.0001
AIDS-defining cancers					
Non-Hodgkin lymphoma	40	0.92 (0.43–2.01)	0.84	1.09 (0.45–2.65)	0.85
Kaposi's sarcoma	633	1.05 (0.87–1.27)	0.57	1.02 (0.81–1.27)	0.89

Models were adjusted for age, sex, CD4 cell count at ART start, and treatment site. P values are from Wald tests.

ART = antiretroviral therapy; HR = hazard ratios; aHR = adjusted hazard ratios; ND = not defined; TB = tuberculosis; 95% CI = 95% confidence interval.

history of TB), 487 with incident PCP (including 179 with a history of TB), 633 with incident Kaposi's sarcoma (including 139 with a history of TB), and 40 patients with an incident non-Hodgkin lymphoma (including 8 with a history of TB). A history of TB was associated with CM (aHR 1.28, 95%CI 1.05–1.55) and PCP (aHR 1.61, 95%CI 1.27–2.04), but not with non-Hodgkin lymphoma (aHR 1.09, 95%CI 0.45–2.65) or Kaposi's sarcoma (aHR 1.02, 95%CI 0.81–1.27, Table). Other risk factors were low CD4 cell counts.

**Conclusion:** A history of TB was associated with AIDS-defining opportunistic infections, but not with AIDS-defining cancers in HIV-infected patients. This was possibly due to a reduced lung function post-TB (lung as an entry port for other OIs) or shared immune deficits.

### OP-209-17 Impact of TB-HIV collaborative activities on case fatality of HIV-infected TB patients registered under the TB programme in Gujarat, India

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**Background:** Tuberculosis (TB) control efforts have been challenged by the deadly interaction of TB and HIV epidemics. To address this, all TB patients are routinely being offered HIV testing and cotrimoxazole prophylaxis therapy (CPT) and antiretroviral treatment (ART) are being provided for those found to be HIV-infected. We describe the impact of these activities on case fatality of HIV-infected TB patients.

**Methods:** We reviewed all the TB registers maintained under the national TB programme in Gujarat State and retrieved data on HIV testing, ART, CPT and treatment outcomes of TB patients registered in 2010.

**Results:** Of 77 839 TB patients registered, 59 638 (75%) were ascertained for HIV status and 2893 (4%) were HIV-infected. Of HIV-TB patients, 95% received CPT and 68% received ART during TB treatment. Case fatality among HIV-TB patients was 14% as compared to 4% among TB patients who were not HIV-infected. Among HIV-TB patients who received both CPT and ART, case fatality was 10% as compared to 37% among those who did not receive both ( $P < 0.01$ ).

**Conclusion:** TB-HIV collaborative activities have been successfully implemented with nearly three-fourths of TB patients getting tested for HIV and CPT administration to almost all HIV-TB patients.

However, ART could not be started in one-third of HIV-TB patients and needs strengthening. Even those who got both CPT and ART, case fatality was unacceptably high at 10%. Future TB-HIV collaborative efforts should focus on early diagnosis of HIV, early diagnosis of TB using higher sensitivity diagnostics and early initiation of ART to further reduce case fatality.

### OP-210-17 Elevated blood lactate is an independent predictor of mortality among hospitalised patients with HIV-associated tuberculosis in rural South Africa

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**Background:** Mortality in hospitalised patients with HIV-associated tuberculosis (HIV-TB) is high in Africa. The clinical factors associated with mortality are not well described.

**Methods:** A prospective observational study of 100 consecutive HIV-infected inpatients at Madwaleni Hospital, Eastern Cape, South Africa, who were diagnosed with TB within  $\pm 14$  days of admission was performed. Clinical and laboratory parameters were recorded and point-of-care lactate measured. Outcome was death within 2 months of starting TB treatment. Significant associations in univariate analysis ( $P < 0.05$ ) were included in a multivariate logistic regression model.

**Results:** One patient was lost to follow-up, 99 patients included in final analysis: median age 32 years; 40% male; median CD4 count 72/mm<sup>3</sup> (IQR 24–148). 22 previously received antiretroviral therapy (ART) and 29 commenced ART within 2 months. TB diagnosis was based on culture in 60, smear in 14 and clinico-radiological features in 25. 32/99 died; 28 during admission. The median duration from TB treatment to death was 8 days (IQR 2.5–38.5). The median lactate was 5.5 mmol/l in those who died and 3.1 mmol/l in survivors ( $P < 0.0001$ ). The median CD4 count was 31/mm<sup>3</sup> in those who died and 80/mm<sup>3</sup> in survivors ( $P = 0.004$ ). Other mortality-associated factors in univariate analysis were: WHO stage, performance score, cough, BMI, Glasgow Coma Scale (GCS), blood glucose, creatinine, haemoglobin, C-reactive protein and albumin. There was no mortality difference between those with microbiological

(30%) versus clinico-radiological (40%) TB diagnosis ( $P = 0.34$ ). In multivariate analysis higher lactate (aOR = 3.34 per 1 mmol/l increase, 95%CI 2.0–5.6), GCS  $\leq 14$  (aOR = 8.23, 95%CI 1.8–38.4) and CD4 count  $< 50$ /mm<sup>3</sup> (aOR = 6.21, 95%CI 1.7–22.2) independently predicted death.

**Conclusions:** One-third of patients died within 2 months. Elevated lactate independently predicted mortality. Hyperlactataemia likely reflects sepsis syndrome related to TB itself or bacterial co-infection. Studies examining aetiology of hyperlactataemia in HIV-TB and improved acute management strategies in such high-risk patients are needed.

### OP-211-17 Survival in HIV-tuberculosis co-infected patients at 48 weeks after starting antiretroviral therapy: CARINEMO trial ANRS 12146

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**Background:** Tuberculosis (TB) increases mortality of HIV infected patients requiring systematic and early initiation of antiretroviral therapy (ART) in co-infected patients. We present results of 48 weeks survival analysis of HIV-TB co-infected patients from Mozambique after starting ART.

**Methods:** Follow-up of TB-HIV co-infected patients with less than 250 CD4/mm<sup>3</sup> enrolled in a randomized control trial than compared the 48 weeks efficacy and safety of nevirapine and efavirenz combined with lamivudine and stavudine/zidovudine. ART was initiated 4–6 weeks after starting TB treatment (6 months rifampicin-based regimen). Kaplan-Meier method was used to estimate probabilities of survival. Predictors of deaths were identified among baseline patients' characteristics (sex, age, body mass index (BMI), hepatitis B and C infection, Karnofsky score, WHO HIV staging, type of TB, ART regimen, time between TB treatment and ART initiation, haemoglobin, CD4-count, HIV1-RNA) using Cox model.

**Results:** 573 HIV-TB co-infected patients were followed on ART over 24 321 person-week. Of them, 58% were male, 24.7% had extra-pulmonary TB and 21.5% (122/568) were co-infected with hepatitis B virus. Median age, BMI, CD4-count and HIV-1 RNA were 33 years, 18.8 kg/m<sup>2</sup>, 89 cells/mm<sup>3</sup> and 5.6 log<sub>10</sub> copies/ml, respectively. Median time to start ART after TB treatment was 4.9 weeks. Probability of survival at week 48 was 0.94, 95%CI [0.91–0.95]. Causes of death were TB (8), severe sepsis (6), IRIS (6), Kaposi (4), wasting syndrome (2), other (3) and

indeterminate (6). Low haemoglobin (HR = 1.46 95%CI [1.01–2.11]), CD4 < 50 cells/mm<sup>3</sup> (HR 3.5 [1.0–12.2] and BMI (HR = 0.47 [0.23–0.96]) were independently associated with the risk of death.

**Conclusions:** Despite severe immunosuppression, the survival of HIV-TB co-infected patients was high most likely due to early ART initiation and close trial follow-up conditions. Type of TB and ART regimen were not associated with the risk of death.

### OP-212-17 Cerebral toxoplasmosis mimicking tuberculous meningitis in HIV-infected patients: a cohort study from Indonesia

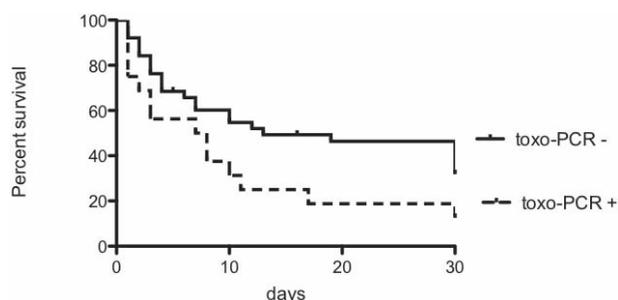
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**Background:** In our previous cohort of HIV-positive meningitis cases, tuberculous meningitis (TBM) was found in 21%, cryptococcal meningitis (CM) in 30%, while no diagnosis was made in 49% of patients. Without cerebral imaging, toxoplasmosis is generally not considered as differential diagnosis of meningitis.

**Methods:** We performed cerebrospinal fluid (CSF) real time PCR (toxoplasma-PCR) and serological (IgG) testing for *Toxoplasma gondii* in archived samples from a cohort of 57 HIV-infected patients with subacute meningitis in a referral hospital in Indonesia. Definite TBM was confirmed by CSF TB-PCR, culture and microscopy, alone or in combination; CM by CSF microscopy and/or antigen testing; and toxoplasmosis by CSF toxo-PCR. Neuroradiology was not available.

**Results:** Seventy percent of patients were male, median age 30 (IQR 28–34) years. Forty-nine (80%) of HIV infection was newly diagnosed, with a median CD4 count of 22/ml (range 2–110). 12.8% of patients were on ART, and 10.5% on PJP-prophylaxis at time of presentation. Diagnoses were toxoplasmosis ( $n = 18$ ), TBM ( $n = 18$ ), CM ( $n = 15$ ), and no confirmed diagnosis ( $n = 13$ ). Five patients had double infection of TB and toxoplasmosis. Circulating toxoplasma IgG was present in 77.2% of patients tested, including all whose toxo-PCR were positive. Clinically, toxoplasmosis was difficult to distinguish from TBM or CM, but CSF abnormalities were less pronounced. Although not significant, patients with TBM and toxoplasmosis were more frequently present with altered consciousness and motor deficit as compared to those with CM. Mortality among patients with positive CSF toxo-PCR was 2.15-fold higher (95%CI 0.99–4.72) compared to those with negative PCR (see Figure).

**Conclusions and recommendation:** Toxoplasmosis may mimic TBM and CM in patients with advanced



**Figure** Kaplan-Meier estimation of survival according to toxo-PCR result.  $P = .05$ ; hazard ratio 2.16 (95%CI 0.99–4.72).

HIV-infection in the absence of cerebral imaging. Toxo-PCR and/or empiric toxoplasmosis treatment may help improve the dramatic outcome of HIV-associated meningitis of unknown etiology.

## POSTER DISCUSSION SESSIONS

### MOLECULAR EPIDEMIOLOGY – 2

#### PC-223-17 *Mycobacterium tuberculosis* CAS1 lineage strains display a lower 15 MIRU loci based diversity as compared with non-CAS1 isolates

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**Background:** Central Asian Strain1 (CAS1) lineage of *Mycobacterium tuberculosis* is predominant in South Asia, including Pakistan. Mycobacterial interspersed repetitive unit-variable number of tandem repeat (MIRU-VNTR) typing is a useful tool to study transmission dynamics of *M. tuberculosis* strains and to study its lineages. However, there is variability in the discriminatory power of MIRU typing between strain types from different geographical location. We have evaluated the discriminatory power of MIRU-VNTR 15 loci typing for the CAS1 as compared with non-CAS1 lineages.

**Methods:** *M. tuberculosis* isolates ( $n = 200$ ) comprising CAS1 (38%), Beijing (5%) and other non-CAS1 strains (57%) were studied. Isolates were subjected to standard PCR based MIRU-VNTR 15 loci typing.

**Results:** The average Hunter Gaston Discriminatory Index (HGDI) for all isolates was 0.632. HGDI based on 15 MIRU loci for CAS1, non-CAS1 and Beijing strains was 0.469, 0.677 and 0.687, respectively ( $P = 0.02$ ). Allelic diversity of individual loci revealed that eight out of 15 loci (MIRU 10, 16, 26, 31, Mtub 04, ETRA, 4156, and Qub 26) were highly discriminatory with HGDI > 0.6. The average MIRU HGDI

based on these 8 discriminatory loci identified for all strains was 0.762. While the same eight loci based differential HGDI for CAS1, non-CAS1 and Beijing strains was 0.634, 0.791 and 0.757, respectively.

**Conclusions:** The lower DI for CAS1 observed in comparison with non-CAS1 and Beijing strains suggest a lower genetic diversity in these isolates. This indicates that CAS1 MIRU-VNTRs may be more stable over time and that they could be used to estimate phylogenetic relatedness among CAS1 strains. Furthermore, eight high HGDI MIRU loci identified could be useful in monitoring transmission of *M. tuberculosis* strains in clinical and epidemiological settings in the geographic region with high CAS1 prevalence.

### PC-224-17 Molecular diversity of *Mycobacterium tuberculosis* isolates from tuberculosis patients in Cuba

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**Background:** Tuberculosis remains a major health problem all over the world, but prevalent strains and their transmission, can vary by country and by region. Although Cuba is one of the lowest burden countries in Latin America, and in the World, there was a reemergence of the disease after 1991, basically by economic reasons. This is the first survey study to investigate the prevalence of *Mycobacterium tuberculosis* isolates in the country and its different regions.

**Methods:** A total of 312 *M. tuberculosis* isolates from 14 different provinces of Cuba during 2009–2010 period, were characterized by spoligotyping and resulting profiles were compared with the international spoligotyping database SPOLDB4.

**Results:** The four most predominant lineages observed were: Beijing (28.4%), the Latin-American Mediterranean (LAM, 19.8%); Haarlem (18.0%); and S (14.4%). By regions there was a clear predominance of Beijing and LAM genotypes in the Centre and East of the country respectively. In Havana, 30% of isolates belonged to the S family and there was a large number (22.5%) of new spoligotype patterns found.

**Conclusions:** A high percent of spoligotype diversity was found in Cuba. The prevalence of *Mycobacterium tuberculosis* isolates varied among geographic regions of the country with a large number of unknown signatures found and the globally-emerging Beijing/W genotype family predominance.

### PC-225-17 Cluster patterns of *Mycobacterium tuberculosis* DNA fingerprinting in the metropolitan area of Vitória, Brazil, and the relationship with RDRio genotype

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**Background:** Based on the hypothesis that genetic variability of *Mycobacterium tuberculosis* could influence transmission we analyzed RFLP patterns of different *M. tuberculosis* isolates in order to investigate its distribution and the relationship with RDRio genotype in Vitoria, Brazil.

**Design/methods:** A retrospective surveillance study of new TB cases in the metropolitan area of Vitoria identified between 2000 and 2010. *M. tuberculosis* isolates were analyzed by RFLP. Two or more isolates with identical RFLP patterns were defined as belonging to the same RFLP cluster. Isolates with 65%

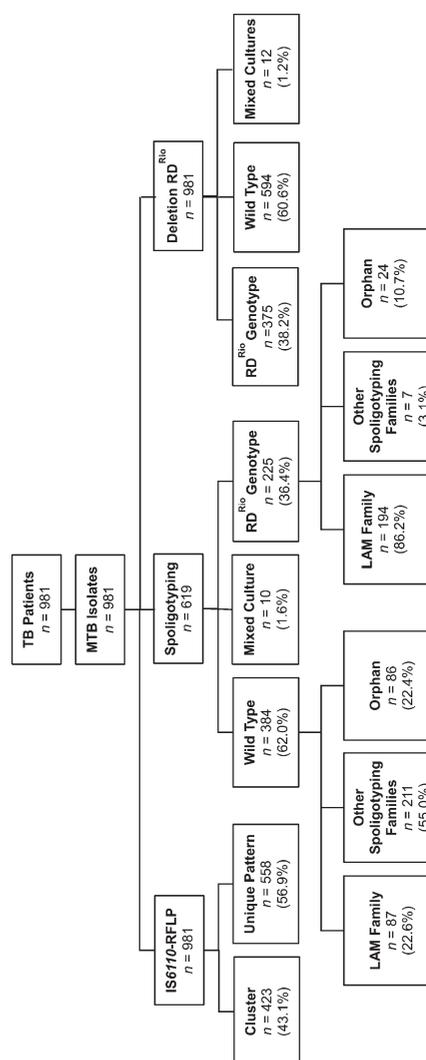


Figure Flow chart of number of isolates and genotype methods.

similarity belonged to the same RFLP family. Isolates designated as RDRio based on multiplex PCR were further analyzed according to their RFLP genotypes. Between-group distributions of genotypic clusters were compared and multivariate logistic regression was performed.

**Results:** A total of 981 *M. tuberculosis* were typed by RFLP, of these 423 (43.1%) had cluster patterns and 558 (56.9%) had unique pattern (non-cluster). There were no demographic differences between patients infected with cluster or non-cluster pattern strains and isolates from patients with pulmonary tuberculosis, smear positive were more likely to belong to cluster pattern ( $P < 0.05$ ). Of 981 isolates submitted to RDRio analysis 375 (38.2%) belonged to RDRio genotype and 594 (60.0%) WT among these isolates 178 (47.5%) and 238 (40.1%) were in cluster in each group respectively ( $P = 0.023$ ). Interestingly, through IS6110 RFLP analysis, these 178 RDRio isolates in clusters belong to 47 distinct IS6110 RFLP genotypes. Among 238 nonRDRio isolates in clusters, 83 distinct genotypes were found. The difference was not statistically significant ( $P = 0.94$ ). Multivariate analysis revealed that only RDRio genotype (adjOR 1.52; 95% confidence interval [CI] 1.12–2.05) and smear positive sputum (adjOR 1.5; 95%CI 1.01–2.21) are associated with cluster pattern genotypes.

**Conclusions:** Although RDRio genotype strains were comprised of many distinct RFLP genotypes, they were significantly likely to belong to cluster pattern RFLP strains. This observation suggests that the high prevalence of RDRio in Vitoria may be due to its recent introduction into the community rather than its intrinsic virulence or enhanced transmissibility phenotype.

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### PC-226-17 Frequency of non-tuberculous mycobacteria in pulmonary infections in Burkina Faso

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**Setting:** National Tuberculosis Center and National Tuberculosis Program in Ouagadougou, Burkina Faso.

**Objectives:** To determine the frequency of NTM in patients with pulmonary mycobacterial infections.

**Methods:** From 2005 to 2006, the AFB-positive sputum of patients in four centers were inoculated on solid medium Löwenstein-Jensen. Anamnesis information, epidemiological and clinical data (patient's cases, gender, age, inclusion center and HIV status) were collected using a questionnaire.

**Results:** 539 new patients and 110 previously treated cases were included. HIV status was positive in 29% ( $n = 338$ ) and culture in 566 (87.2%) cases. The bacteriological study was continued on 532 (82%) strains among 362 men and 170 women, mean age  $37 \pm 13$  years. The frequencies of strains were as follows: *M. tuberculosis* complex, 93.3% ( $n = 491$ ) and NTM, 7.7% ( $n = 41$ ) of NTM: 18 *M. avium*, 14 *M. intracellulare*, 5 *M. avium-intracellulare*, 01 *M. intracellulare* serotype 18, 02 *M. malmoense* and 01 *M. lentiflavum*; they were identified in bacteriological-virology laboratory of Montpellier (France) and in National Reference Center for Mycobacteria of Borstel (Germany). The number of repeated positive cultures and chest X-rays showing infiltrations or cavitations in patients indicate their pathogen role. Analysis had not revealed a significant association between the studied variables and NTM,  $P > 0.050$ . However, NTM were more frequent in previously treated patients, 12.7% vs. 7.6% in new cases,  $P = 0.94$ .

**Conclusion:** A conduct periodic study in pulmonary mycobacterial infections, especially among previously treated cases has a clinical, therapeutic and epidemiological interest. NTM are indeed resistant to common anti-TB drug.

### PC-227-17 Molecular epidemiology of tuberculosis in Swaziland

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**Background:** A drug-susceptibility study conducted in 2009 revealed a prevalence of multidrug-resistant tuberculosis (MDR-TB) in 7.7% of new cases and 34% in previously treated cases (PTC). This study aimed to describe factors contributing to the MDR epidemic including level and risk factors of MDR-TB transmission and possible associations with the diversity of circulating *Mycobacterium tuberculosis* complex (MTBC) strains.

**Methods:** 420 *M. tuberculosis* (119 MDR) strains from consecutive culture positive patients enrolled during the 2009 DST survey were included. MIRU-VNTR typing and spoligotyping were applied to determine prevalent lineages as well as the level of clustering, used as a proxy-indicator for recent transmission. To determine factors associated with clustering and MDR-TB infection, univariate and multivariate analysis were performed.

**Results:** Ten different lineages were identified, with 4 being the most dominant ones: X-type, S-type, Beijing and LAM. 287 strains (68%) belonged to 60 different

clusters ranging in size from 2 to 12 strains. Clustering (OR 7.94, 95%CI 3.48–18.1), PTC (OR 7.93, 95%CI 4.02–15.64), HIV positive status (OR 2.87, 95%CI 1.2–6.9) and S-type lineages (OR 4.66, 95%CI 1.63–13.29) were independently associated with MDR-TB, while independent factors associated with recent transmission were PTC (OR 2.1, 95%CI 1.31–3.36) and infection with Beijing (OR 9.46, 95%CI 4.35–20.56), X-type (OR 3.92, 95%CI 1.98–7.75) and S-type lineages (OR 4.68, 95%CI 2.06–10.61).

**Conclusions:** The MDR-TB epidemic in Swaziland is largely driven by transmission. Two (X- and S-type) lineages showing strong clonal expansion within the MDR-TB strain population. After adjustment on the strain lineage, being HIV positive, significantly increase the risk of MDR-TB.

#### PC-228-17 Antituberculosis drug-resistance survey in pulmonary tuberculosis cases in Ankara, Turkey

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**Background and aim:** There was no national or regional survey for tuberculosis drug-resistance in Turkey. This is the first antituberculosis drug-resistance survey (DRS) in Turkey.

**Design/methods:** This DRS was planned as a pilot study and done in Ankara Province during 1st January to 31st December, 2011. The study was carried out by participation of health facilities providing tuberculosis diagnosis and treatment services (Provincial Health Directorate Tuberculosis Coordination Department, 7 Tuberculosis Dispensaries, 1 Provincial Public Health Laboratory; 1 Chest Diseases, 6 Government and 6 University Hospitals), by coordination of National Tuberculosis Reference Laboratory (NTRL). There is a well running notification system in Ankara. This system catches nearly all TB cases. We obtained notification, data and samples of all TB cases. Sample information of tuberculosis cases notified by health facilities, have been questioned from laboratories. Positive isolates were analysed by phenotypic and genotypic first line susceptibility testing in NTRL. Ankara cases were defined as living in Ankara 3 months before diagnosis.

**Results:** Total 1277 TB cases were notified, 434 were from other provinces, 37 were patients from 2010, 65 were not TB cases. 740 of them were from Ankara Province during 2011; 405 were extra pulmonary TB. Pulmonary TB cases were 335, and their mean age

was  $43.4 \pm 20.0$ , males were 67.4% ( $n = 226$ ). Culture positives were 229 (68.3%) and 88.6% ( $n = 223$ ) were susceptible to all first line drugs. 8 cases (3.5%) were MDR-TB; 2 were new cases (2/214, 0.9%) and 6 were previously treated cases (6/15, 40%). Among MDR-TB cases 3 were from high MDR-TB countries living in Ankara more than 3 months during diagnosis.

**Conclusion:** Nearly all cases were included to the study. Drug-resistance is low in new cases, but high in previously treated cases. This is the first DRS in Turkey, and DRSs will be expanded to other provinces.

#### PC-229-17 Genotyping of *Mycobacterium tuberculosis* with RD105 and variable numbers of tandem repeat-mycobacterial interspersed repetitive unit in Eastern China

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**Background:** To explore the characteristics of epidemiology and transmission of Beijing lineage *Mycobacterium tuberculosis* (MTB) in Eastern China, and to evaluate the discriminatory power of 7 loci variable numbers of tandem repeat-mycobacterial interspersed repetitive unit (VNTR-MIRU).

**Methods:** A total of 448 MTB isolates strains were successively collected between June 1, 2008, and May 30, 2010, in three counties/districts with a population of between 0.6 and 1 million. Beijing lineage MTB strains were identified by RD105 using deletion-targeted multiplex PCR (DTM-PCR) and further genotyped by VNTR-MIRU. The allelic diversity and discrimination power of single locus were confirmed by *h* and Hunter-Gaston discriminatory index (HGI), respectively.

**Results:** A total of 393 isolates (87.72%) were identified as Beijing family strains. MIRU determined 431 genotypes from all isolates, including 417 unique patterns and 14 clusters, with 2 to 4 strains in each cluster. All the strains in clusters belonged to Beijing family. The proportion of recent transmission was estimated at 3.79%. The allelic diversity of the 7 loci MIRU varied in different strains. All loci showed highly polymorphic ( $h > 0.6$ ), and the polymorphism of locus VNTR3820 was the highest ( $h = 0.8736$ ) of all, while Qub26 was the lowest ( $h = 0.7587$ ). The discriminatory power of the 7 loci was also different, with the highest HGI of 0.8759 (VNTR3820), the lowest at 0.7609 (Qub26). It showed that the higher the polymorphism, the stronger the discriminatory power. The HGI of the combination of 7 loci was 0.9996.

**Conclusion and recommendations:** Beijing lineage strains are predominated in Eastern China. VNTR-MIRU genotyping appears a simple and fast method, with a much higher discriminatory power than that of single locus. It suggests that VNTR-MIRU typing could be used as a reliable method for MTB epidemiology and transmission analysis.

### PC-230-17 Evaluation of the GeneChip for rapid diagnosis of drug-resistant tuberculosis in China

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**Background:** Rapid diagnosis of multidrug-resistant tuberculosis is needed to identify and initiate appropriate treatment for those with this disease. We evaluated the GeneChip as part of a demonstration project to diagnose and treat drug-resistant TB.

**Methods:** In 3 cities, the sputum specimens from all new smear-positive pulmonary TB cases diagnosed at the district level public health clinic were transported to a central laboratory at a city hospital. The GeneChip test was used for rapid detection of isoniazid and rifampin resistance. Discordant rifampin results between GeneChip and DST were evaluated using sequencing of the *rpoB* gene.

**Results:** 1505 smear-positive sputum specimens were collected. Compared to DST results, the sensitivity, specificity, positive and negative predictive values for detection of rifampicin resistance were 83.0%, 98.1%, 84.7% and 97.6%, respectively. The same results for isoniazid resistance were 78.8%, 95.9%, 76.0% and 96.5%, respectively. Sequencing revealed that the GeneChip result was accurate in two-third of the discordant genechip-DST rifampin results. This suggests the actual performance characteristics of the GeneChip test for rifampin is actually much higher than the performance when compared against DST results. The turnaround time for test results was a median of 1 day.

**Conclusions:** Using GeneChip at a central laboratory, we demonstrated the accuracy and feasibility of rapid testing for drug-resistant TB, which in turn allowed clinicians to rapidly identify and treat drug-resistant TB.

### PC-231-17 Molecular epidemiology and transmission dynamics of *Mycobacterium tuberculosis* in northwest Ethiopia

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**Background:** Although Ethiopia ranks seventh among the world's 22 high-burden tuberculosis (TB) countries, little is known about strain diversity and transmission. In this study, we present the first in-depth analysis of the population structure and transmission dynamics of *M. tuberculosis* strains from northwest Ethiopia.

**Design/methods:** 244 *Mycobacterium tuberculosis* complex (MTBC) isolates were analysed by MIRU-VNTR (mycobacterial interspersed repetitive unit-variable number tandem repeat) 24-loci and spoligo-typing to determine phylogenetic lineages and perform a cluster analysis. Clusters of strains with identical genotyping patterns were considered as an indicator for the rate of recent transmission.

**Results:** The population structure was found to be highly diverse: out of the 244 MTBC isolates 59.0% were classified into nine previously described lineages: Dehli/CAS (38.9%), Haarlem (8.6%), Ural (3.3%), LAM (3.3%), TUR (2.0%), X-type (1.2%), S-type (0.8%), Beijing (0.4%) and Uganda II (0.4%). Interestingly, 31.6% of the strains investigated were grouped into four new lineages and were named as Ethiopia\_3 (13.1%), Ethiopia\_1 (7.8%), Ethiopia\_H37Rv like (7.0%) and Ethiopia\_2 (3.7%) lineages. The remaining 9.4% of the isolates could not be assigned to the known or new lineages. Overall, 45.1% of the isolates were grouped in clusters, indicating a high rate of recent transmission. Similarly, 66.7% of MDR strains were grouped in clusters.

**Conclusion and recommendations:** This study confirms a highly diverse MTBC population structure, the presence of new phylogenetic lineages and a predominance of the Dehli/CAS genotype in northwest Ethiopia. The high rate of recent transmission indicates defects of the TB control program in northwest Ethiopia. This emphasizes the importance of strengthening laboratory diagnosis of TB, intensified case finding and treatment of TB patients to interrupt the chain of transmission.

### PC-232-17 No and low IS6110 copy strains: same molecular background?

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**Background:** Molecular characterization of *Mycobacterium tuberculosis* is often done by IS6110 DNA

fingerprinting based on the detection of the IS6110 element. This element is absent in the 5–11% so-called no copy strains in Southeast Asia. No-copy and low-copy strains are usually regarded as strains with similar genetic background. Little is known about the epidemiological, clinical and molecular characteristics of these strains. We quantified the frequency of no and low IS6110 copy strains in rural Viet Nam and related this to patient factors.

**Methods:** TB patients  $\geq 15$  years from 3 adjacent rural districts submitted each 2 pretreatment sputum specimens for TB culture and molecular typing by spoligotyping, IS6110 DNA fingerprinting, and variable number tandem repeat (15 loci VNTR) analysis. PCR was performed to confirm the absence of the IS6110 elements in the no-copy strains.

**Results:** Among 2664 TB patients, 109 (4.1%) had a no-copy and 983 (36.9%) low-copy strain. Spoligotypes of no-copy and low-copy strains were distinctly different. Compared to other strains, no-copy strains were more often susceptible to anti-TB drugs, especially to streptomycin (adjOR 0.42, 95%CI 0.19–0.43) and were more often found among patients aged above 65 years (adjOR 1.96, 95%CI 1.04–3.6). The association with streptomycin susceptibility remained when all Beijing strains were excluded from the analyses. No associations with clinical symptoms, TB history or other demographic factors were found. Low copy strains were associated with susceptibility to streptomycin, male sex and age above 34, and were more frequent among new than among previously treated, also after excluding the Beijing genotype isolates (except male sex).

**Conclusion:** No-copy strains are genetically different from low-copy strains but their characteristics were largely similar. Contrary to Beijing family strains, no-copy and low copy strains are more sensitive to anti-TB drugs and associated with older age.

#### PC-233-17 The Uganda-T2 *Mycobacterium tuberculosis* genotype shows negative association with anti-tuberculosis drug-resistance but no association with HIV infection

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**Background:** Uganda-T2 genotype (previously *Mycobacterium africanum* subtype II) strains are phenotypic variants of *M. tuberculosis* with specific biochemical characteristics. We examined their epidemiological and clinical characteristics.

**Design/methods:** We extracted DNA from a representative sample of mycobacterial isolates collected

in the national anti-TB drug resistance survey (including HIV testing) and performed fingerprinting using IS6110 RFLP. *M. tuberculosis* was identified by time-PCR method with ‘melting curve’ analysis to differentiate the Uganda-T2 subtype II genotype from other *M. tuberculosis* families. The primary outcome was the prevalence of Uganda-T2 subtype II genotype and association with anti-TB drug resistance and HIV infection among smear-positive TB patients.

**Results:** A total of 1039 isolates were available for analysis, of which 1011 had PCR results. Of these, 443 (43.8%) were of the Uganda-T2 subtype II genotype, mostly distributed in the southwestern region (OR = 6; 95%CI 2.83–7.57,  $P < 0.001$ ), but occurring in other regions at varying levels, especially in the 25–34 years age group (OR = 64; 95%CI 1.12–2.33,  $P = 0.01$ ) compared to other age groups. In multivariable analysis a negative association existed between the Uganda-T2 subtype II genotype with any resistance to anti-TB drugs (OR = 0.35; 95%CI 0.20–0.61,  $P = 0.001$ ) and multidrug-resistance (OR = 0.18; 95%CI 0.05–0.70,  $P = 0.02$ ) but no association was found with HIV infection, sex, previous TB treatment and rural or urban setting.

**Conclusion and recommendations:** The Uganda-T2 subtype II, *M. tuberculosis* genotype is widely distributed in Uganda, especially in the southwestern region, less likely than other circulating genotypes to show resistance to anti-tuberculosis drugs, and not associated with HIV infection.

#### PC-234-17 Isolation of non-tuberculous mycobacteria in children investigated for tuberculosis, Cambodia

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**Background:** Data on the epidemiology and clinical significance of NTM among children in Asia are limited. The goal of this study was to evaluate NTM prevalence and clinical presentation among children investigated for TB in rural Cambodia.

**Methods:** From July 2010 to February 2011, children (<5 years) suspected of having TB were enrolled in Cambodia’s Svay Rieng Province. Enrolled children underwent physical examination, tuberculin skin testing (TST), chest X-ray (CXR), and collection of 1 induced sputum (IS), 2 gastric aspirates (GA) and 1 stool for smear microscopy and TB culture. Gen-Probe MTB, Hain Genotype Mycobacterium CM and AS were used to speciate NTM.

**Results:** 873 children with a median age of 2.1 years (IQR 1.2–3.7) were enrolled. 267 NTM isolates were obtained from 225 children; 83 (31%) from GA1, 64 (24%) from GA2, 120 (45%) from IS. The total recovery rate of NTM ( $n = 225$ ) was 25.8% (95%CI 22.9–28.8). Most common isolated NTM were *M. intracellulare* ( $n = 79$ ; 30%), *M. scrofulaceum* ( $n = 59$ ; 22%), *M. interjectum* ( $n = 34$ ; 13%), *M. fortuitum* ( $n = 14$ ; 5%) and 58 (22%) NTM not identified by Hain CM/AS. Among 126 children diagnosed with pulmonary TB, 34 (27%) also had NTM recovered. Among children with NTM alone ( $n = 191$ ), 2% had a positive TST, 59% an abnormal CXR and 65% cough. By contrast, among children with TB diagnosis without concomitant NTM ( $n = 92$ ), 28% had a positive TST ( $P = 0.001$ ), 97% an abnormal CXR ( $P = 0.001$ ), and 75% cough ( $P = 0.10$ ). None of the children with NTM received NTM-specific therapy, but all had spontaneous symptom resolution.

**Conclusion:** NTM prevalence was high among children with suspected TB and among children with TB diagnosis. Although no clinical symptoms to distinguish NTM cases from children with and without TB were identified, positive TST and abnormal CXRs may be useful in establishing a specific diagnosis of TB. In this cohort, NTM recovery did not appear to have substantial clinical significance as children recovered without targeted NTM therapy.

### PC-235-17 Prevalence and cofactors for non-tuberculous mycobacteria among newly arrived immigrants and refugees in the USA

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**Background:** Non-tuberculous mycobacteria (NTM) may cause disease but are generally non-communicable. NTM cross-react with the tuberculin skin test (TST), confounding the diagnosis of latent tuberculosis (TB) infection (LTBI). The extent of NTM cross-reactivity with interferon-gamma release assays (IGRA) is not well defined. We assessed the prevalence and cofactors for NTM infection among U.S.-bound immigrants and refugees.

**Methods:** We analyzed reports of U.S.-based TB examinations from immigrants and refugees arriving from January 1, 2008, to December 31, 2011. Individuals were defined as NTM positive when two or more sputum cultures were positive for NTM and NTM negative when no sputum cultures were positive for NTM. The number of arrivals per country was obtained from the US Department of Homeland Security.

**Results:** We included 22 639 immigrants, of whom 945 (6%) were NTM positive. Annual NTM preva-

lence was 42 per 100 000 arriving immigrants and refugees. Annual prevalence was approximately 20-fold greater for immigrants from the Philippines (314/100 000) and Viet Nam (248/100 000) than for all other countries (15/100 000). NTM positivity was significantly associated with a positive TST ( $\geq 10$  mm) (odds ratio (OR): 1.35; 95% confidence interval (CI) 1.13–1.62;  $P = 0.0006$ ) but not with a positive IGRA (OR: 1.13; 95%CI 0.91–1.39;  $P = 0.21$ ). Of those who were NTM positive, 89 (9.7%) had 1 or more sputum smears positive for acid-fast bacilli.

**Conclusions:** NTM culture positivity was unusually high for immigrants from the Philippines and Viet Nam. This finding may represent a high prevalence of NTM exposure and disease in these countries. The impact of NTM on TST and IGRA testing in this population warrants further investigation.

## TB DIAGNOSTICS: CULTURE AND RAPID DETECTION – 2

### PC-262-17 Differentiation of *M. tuberculosis* and non-tuberculous mycobacteria by gas chromatography

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The World Health Organization (WHO) has declared tuberculosis (TB) a global emergency, prompted by the resurgence of TB mostly fuelled by the HIV epidemic, and by the increasing incidence of tuberculosis drug resistance observed worldwide. The development of a fast and simple method for early diagnosis of tuberculosis has therefore become an urgent research priority. We have previously described a rapid gas chromatography-mass spectrometry (GC-MS) method for sputum-based TB diagnosis requiring minimum sample preparation.<sup>1</sup> Differentiation of *Mycobacterium tuberculosis* from non-tuberculous mycobacteria (NTM) is of clinical importance in HIV endemic countries, where HIV infected patients frequently present with low mycobacterial loads in sputum. We have therefore improved the detection limit (sensitivity) of the GC-MS tool. We have concurrently addressed specificity, in order to maintain the test's discriminatory ability between *M. tuberculosis* and NTM in sputum. Participants were enrolled from the Tygerberg sub-district of Cape Town, South Africa, where 28% of culture proven TB patients had Ziehl-Neelsen negative sputum smear. From these patients, we have used GC-MS to detect 108 *M. tuberculosis*

and 41 NTM strains. Using advanced statistical analysis, twenty compounds could be selected for the differentiation of *M. tuberculosis* and NTM. The GC-MS were analyzed by linear discriminant analysis. A sensitivity of 94% and a specificity of 83% compared with liquid mycobacterial culture (the gold standard) was found. We plan to further explore the utility of this GC-MS method and statistical analysis for the direct identification and differentiation of *M. tuberculosis* and NTM in sputum from TB suspects.

1 Kaal E, Kolk A H J, Kuijper S, Janssen H G. *Journal of Chromatography* 1216(2009) 6319–6325.

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### PC-263-17 Validation of increased blood storage times for T-SPOT®.TB with T-Cell Xtend® in individuals with different tuberculosis risk factors

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**Background:** Interferon gamma release assays for tuberculosis (TB) testing rely on the collection and use of fresh blood samples. Storage of blood for more than 8 hours leads to loss of T-cell activity. Longer storage times would also allow sample collection at any time for batching of tests or transport to a reference laboratory. We evaluated the use of the T-Cell Xtend® reagent to lengthen the storage of blood for T-SPOT®.TB between 8 and 33 hours in individuals with different TB risk factors and from different clinical settings.

**Design/methods:** A multi-center, concurrent control, matched-pair study comparing T-SPOT.TB test performed on blood within 0–3.5 hours post collection (control) with blood stored for 0–3.5, 5–8, 18–21, or 31–33 hours with the addition of T-cell Xtend (experimental).

**Results:** A total of 154 eligible subjects who were either healthy, had various risk factors for latent TB infection or had active TB disease were enrolled in South Africa, Texas and Ohio. The participants were 62% women, 34% White, 28% Black, 33% Hispanic with mean age of 35 years. 44 subjects reported a medical condition including HIV infection which could affect their immune status. Blood samples from each subject were tested under three blood storage times, yielding a total 462 T-SPOT.TB assay results. Six (1.3%) of the tests were excluded due to either high nil or insufficient cells numbers. The remaining 302 valid matched pair results (control vs. experimental) showed an overall concordance of 95.4% (95%CI 92.3–97.4;  $\kappa = 0.90$ ).

**Conclusion and recommendations:** Our findings indicate that blood stored for up to 33 hours at room temperature is suitable for T-SPOT.TB analysis when used in combination with the T-Cell Xtend reagent. This is important for rural or remote sites with no available reference laboratories. A delay of up to 33 hours from collection to testing can occur without affecting the test results.

### PC-264-17 Development of a microsphere-based suspension assay for rapid differentiation of *Mycobacterium tuberculosis* complex

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**Aim:** To diagnose children and adolescents with extrapulmonary tuberculosis (TB), we established a high-throughput assay for differentiating *Mycobacterium tuberculosis*, *M. bovis* and *M. bovis*-BCG vaccine strain among *M. tuberculosis* complex (MTBC).

**Methods:** A total of 70 paraffin-embedded tissues or other clinical specimens were analyzed. Routinely, we used a streamline algorithm including 3 tests, an IS6110 real-time PCR, an *M. bovis*-BCG specific multiplex PCR, and the *pncA* gene sequencing for differential diagnosis. Two single nucleotide polymorphisms, *fbpA*311 GGC>GGG and *fbpB*140 TTC>CTC, previously identified as robust markers for *M. bovis* family and *M. bovis*-BCG, respectively, were adopted in designing a high-throughput microsphere-based suspension assay.

**Results:** The detection limitation of the microsphere-based suspension assay was 50 fg. Of the 70 DNA samples extracted from paraffin-embedded tissues or other clinical specimens, 21 (30.0%) were MTBC positive. Of the 21 MTBC positive samples, 7 (10.0%, 7/70) were identified as BCG, 1 (1.4%, 1/70) was *M. bovis* family, 7 (10.0%, 7/70) were *M. tuberculosis*, and 6 (8.6%, 6/70) were MTBC using the microsphere-based suspension system. Discordant results were observed in 8 DNA samples between routine assays and the microsphere-based suspension assay. One MTBC-positive and one MTBC-negative samples were reclassified as *M. bovis*-BCG. Thus, no public health measures such as contact tracing are necessary to be conducted. Overall, sensitivity of the microsphere-based suspension assay was comparable to 3 consecutive assays.

**Conclusion:** The microsphere-based suspension assay was proved to be a cheaper and faster assay for differentiation of MTBC in clinical specimens with limited DNA contents, and particularly useful for identifying extrapulmonary TB.

### PC-265-17 Using surface-enhanced Raman scattering for differential diagnosis of mycobacteria

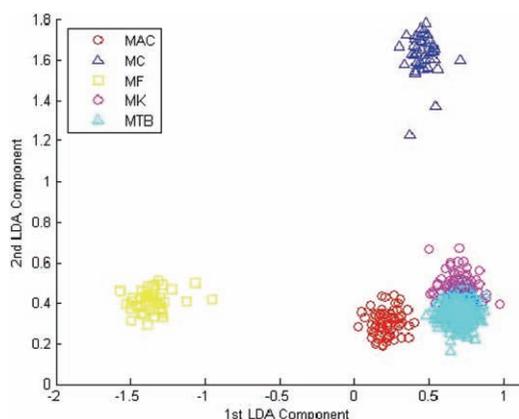
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**Aim:** The surface enhanced Raman scattering (SERS) has an extremely high sensitivity on molecular detection. Therefore, SERS is a powerful tool for detection chemical structure of one microorganism in a low quantity of samples. We evaluate the application of SERS for differentiating *Mycobacterium tuberculosis* and non-tuberculous mycobacterium (NTM).

**Methods:** A silver nanoparticle array was used as substrate for SERS detection. We applied a micro-Raman microscopy system for real-time detection the vibrational spectra of molecules on the cell-wall of the targeted microorganism(s). We have analyzed 4 NTM species (*Mycobacterium avium* complex, *M. fortuitum*, *M. goodnae* and *M. kansasii*) and 2 drug-sensitive *M. tuberculosis* isolates (ATCC27194, ATCC25177) and an isoniazid-resistant *M. tuberculosis* isolate.

**Results:** This test is fundamentally a pure culture test, and only single bacterium is required. The spectra of microorganism(s) can be recorded in a few seconds. The spectra were analyzed by the Linear Discriminant Analysis method. Distinct patterns were identified for differentiating NTM species (Figure). However, overlapping profiles for *M. kansasii* and *M. tuberculosis* isolates were observed. Based on the characteristic differences of spectra obtained, *M. tuberculosis* and NTM could be differentiated. To validate the method, we used the Support Vector Machines to verify the unknown spectrum and the positive predictive rate was approximately 90%. The test can be completed in one hour.



**Conclusion:** The SERS-based detection platform with single bacterium sensitivity could be applied for NTM species identification.

### PC-266-17 Evaluation of the *mtp* gene as a putative biomarker for *Mycobacterium tuberculosis*

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**Background:** Novel biomarkers are urgently needed for use in point of care diagnostic tests for *Mycobacterium tuberculosis*. Patients with active TB had been shown to produce antibodies against MTB pili (MTP), encoded by the *mtp* gene. The aim of this study was to determine the utility of the *mtp* gene as a diagnostic biomarker for TB.

**Methods:** The *mtp* gene in clinical isolates of *M. tuberculosis*, mycobacteria other than tuberculosis (MOTT) and other respiratory organisms was sequenced and aligned with that of H37Rv. Blast analysis of published *mtp* gene sequences of other MOTT and respiratory organisms was done.

**Results:** The *mtp* gene was present with 100% homology in the 32 clinical isolates of *M. tuberculosis* which comprised 13 strains of F15/LAM4/KZN family, 3 of the Beijing family and 14 other strains. All 29 isolates of MOTT and 10 respiratory organisms did not harbour the *mtp* gene. Alignment of mycobacteria with full genome sequences showed 100% *mtp* gene sequence homology to *M. bovis* and *M. bovis* BCG. Partial alignment was observed with a few species of MOTTs, and none with the common respiratory organisms.

**Discussion/conclusion:** The presence of the *mtp* gene suggests the potential for MTP production in clinical strains of *M. tuberculosis* irrespective of the genotype. The absence of the *mtp* gene in non-tuberculous mycobacteria and other respiratory bacteria, as well as the absence of mutations in the clinical isolates tested suggests that MTP may be a suitable target for a point of care test.

### PC-267-17 Utilisation of two real-time PCR assays for the identification of *Mycobacterium tuberculosis* complex in a high throughput laboratory

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**Background:** The Hong Kong TB Reference Laboratory is a high throughput laboratory identifying around 200 mycobacterial isolates weekly. Due to the large sample volume, an algorithm for *Mycobacterium tuberculosis* identification has to be accurate, rapid, simple, affordable and with minimum influence from human error. A 'double checking' algorithm that consists of two real-time PCR assays (RT-PCR), using region of 16s rDNA and region of difference (RD) for the identification of *M. tuberculosis* was evaluated as routine laboratory testing.

**Method:** A total of 829 clinical isolates from 4 batches of samples were tested for evaluation of this algorithm. After initial *M. tuberculosis* screening using colonial morphology in solid Löwenstein-Jensen medium, 597 isolates were selected for further *M. tuberculosis* identification. DNA was extracted independently for each RT-PCR to safeguard the risk of accidental mixing up of samples. Presence of typical RT-PCR sigmoid curve with cycle threshold (CT)  $\leq 35$  indicated a positive reading and borderline result was defined as curves with very low signal or with CT  $> 35$ .

**Results:** Among 597 selected culture isolates, 554 (92.8%) were finally identified as *M. tuberculosis* complex (MTBC). When using the 16s rDNA RT-PCR, 536/554 (96.8%) isolates were MTBC positive, 16 (2.9%) were borderline and 2 (0.3%) were misidentified as non-tuberculosis mycobacteria (NTM). RD assay recognized 547 (98.7%) MTBC isolates, which were further identified as *M. tuberculosis* ( $n = 544$ ) and *M. bovis* BCG ( $n = 3$ ). There were 6 (1.1%) borderline and 1 (0.2%) false NTM cases. When both assays were interpreted together, 551 (99.5%) of MTBC can be identified with high confidence by this 'double checking' algorithm. Running cost of reagents and consumables was approximately US\$2.50 per sample.

**Conclusion:** This 'double checking' algorithm was an accurate, fast and inexpensive way for performing MTBC identification in a high throughput TB laboratory.

#### PC-268-17 Robotics application in routine laboratory practice for molecular diagnostics of tuberculosis

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**Setting:** PCR diagnostics of TB acquired growing importance in the last decade. However, the manual extraction of *M. tuberculosis* DNA from clinical samples is very complicated, laborious, time consuming procedure. Errors made by an operator often result in contamination of samples and false-positive PCR results. To avoid this problem, implementation of robotic systems for automated DNA extraction in practice of TB labs is necessary.

**Aims:** Adapting a liquid handling platform for automated extraction of *M. tuberculosis* DNA; development of reagents for pretreatment and inactivation of samples from TB patients. The study was performed using liquid handling system Freedom Evo 150 (Tecan, Switzerland).

**Results:** 1. The inactivation reagent A was developed for liquefaction of viscous samples and rapid inacti-

vation of *M. tuberculosis* in samples. The reagent was tested on 500 sputum samples obtained from culture-positive TB patients. Sputum were mixed with inactivation reagent A, incubated for 1 h and centrifuged. After washing, sediments were inoculated on L-J medium and Bactec MGIT 960. All 500 samples under study became culture-negative and remained PCR-positive after pretreatment with inactivation reagent A.

2. Optimal protocol for DNA *M. tuberculosis* extraction and configuration of device worktable were developed.

3. LOD of the automated DNA extraction system was estimated as 25 *M. tuberculosis* cells/sample using serial dilutions of *M. tuberculosis* suspension. Sensitivity of the automated extraction system was equal to the manual one.

4. Control of cross-contamination during procedure was performed. Samples containing  $10^9$  *M. tuberculosis* cells were extracted together with negative samples in checkerboard pattern. The test was repeated 6 times. None of negative samples was detected as false-positive.

**Conclusion:** At present *M. tuberculosis* DNA extraction using robotics technology developed is implemented in routine practice of our lab. Automation of *M. tuberculosis* DNA extraction procedure allows to prevent cross-contamination, increases personnel productivity, and reduces labor hours for sample processing.

#### PC-269-17 Performance of the Determine tuberculosis lipoarabinomannan antigen test on urine for the diagnosis of tuberculosis suspects with and without HIV infection

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**Aim:** Early tuberculosis (TB) treatment in resource-constrained and high HIV settings is hindered by the lack of simple, accurate and affordable assays. In response to this, Determine TB lipoarabinomannan antigen (Determine TB LAM Ag) test is recently developed urine rapid point-of-care test and the aim of this study is to evaluate the performance of this assay for the diagnosis of TB suspects with and without HIV infection.

**Method:** This cross-sectional study consecutively enrolled 66 TB suspects (median age: 30 years and 51% were females) from September to December 2011 at three health centers in Addis Ababa. Blood, sputum and urine samples were collected and TB diagnosis was done with smear microscopy and culture (Löwenstein-Jensen). From the suspects, 23 (34.8%) were culture positives; of which 9 (39%) were HIV

co-infected and 20 (87%) were sputum smear negatives. Culture was used as gold standard for TB diagnosis to evaluate the performance of Determine TB LAM Ag test.

**Results:** Of the suspects, 7 (30%) were positive by LAM Ag test but 3 (13%) were positive by sputum smear microscopy. From the sputum smear negative cases, 5 (25%) were LAM Ag test positive. Of the culture positive HIV co-infected, 3 (33.33%) were positive with LAM Ag test. The overall sensitivity and specificity of LAM Ag test compared to culture result was 30.43% and 100%, respectively. Malnutrition ( $P = 0.002$ ), HIV status ( $P = 0.001$ ) and level of immunosuppression ( $P = 0.002$ ) were shown to have a significant association with LAM results.

**Conclusions and recommendations:** Our observation on the performance of the LAM Ag test in smear negatives and HIV co-infected cases indicated LAM Ag test to be a potential alternative for TB diagnosis. The significant association between immunosuppression and LAM Ag test results also shows the potential of this assay as a diagnostic tool in TB cases with advanced HIV infection.

#### **PC-270-17 Automated TB Microscopy: recent results and a model to increase pre-test probability with gene-based diagnostics**

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**Aim:** To describe the latest performance of the detection algorithms from the TBDx Automated TB Microscopy system and to posit the use of such a system to increase the pre-test probability of definitive results from more sophisticated but expensive diagnostics such as Xpert<sup>®</sup> MTB/RIF.

**Methods:** 181 samples from a reference laboratory which had a conventional microscopy and a culture result were processed by the TBDx automated system. The system automatically loads auramine stained slides, autofocuses, and collects images from 100 fields of view under 400 $\times$  power, and then applies an image-based diagnostic algorithm to determine a microscopy result. TBDx results were compared to culture as the gold standard.

**Results:** The sensitivity of the TBDx system in this study was 64/74 (86.5%). The specificity was 75/107 (70.1%). These results were deployed in a desktop model of using TBDx as a 'front end' to Xpert MTB using the combined performance and cost characteristics of both systems. The model demonstrated that it may be possible to reduce the cost per case detected using the dual system to a net cost similar to conventional microscopy by reducing the number of unnecessary tests being submitted to Xpert MTB. This is without losing too many cases detected.

**Conclusion and recommendations:** Using an automated TB microscopy system to process samples

can increase the pre-test probability and reduce the operational costs of a more sophisticated diagnostic system. The function of the automated microscopy continues to improve with development. Such improvement in function may lend itself to the system being rationally deployed in resource-constrained settings.

#### **EXPANSION OF THE STOP TB STRATEGY – 3**

##### **PC-295-17 Understanding factors related to health-seeking behaviour of tuberculosis patients in Madang, Papua New Guinea**

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**Background:** Most TB deaths in PNG are attributed to delayed diagnosis, referrals and poor treatment adherence. This study aims to investigate the factors related to health seeking behaviour for diagnosis, and adherence to TB treatment in Madang, PNG.

**Design/methods:** This exploratory study used qualitative research methods. There are 33 in depth interviews (29 TB patients and four health care workers), 4 focus group discussions (FGD) (TB patients, treatment supporters, health workers and members of community). This study was conducted from May to July 2010. This research was carried out at Modilon general hospital, health centres in the North Coast of Madang Province.

**Results:** Delay in seeking health care was common and traditional beliefs and perceptions for causes of illness are not consistent with 'germ' theory, their health seeking options were second or third priorities. Most TB patients started feeling better would discontinue the treatment as well as those, experiencing side effects of TB drugs, without understanding of side effect, patients discontinued their treatment. Movements of TB patients whilst on treatment greatly affected TB treatment adherence, as there is no proper transfer and follow-up system. Access to a healthcare facility for TB diagnosis and treatment was a major difficulty (the distance to health facilities, locations, and availability of transport and the costs of travel as well as long waiting times at the TB clinic, and inconvenient opening hours). Most respondents indicated various forms of stigma exist among families and households of tuberculosis patients.

**Conclusion and recommendations:** The effective referral system is urgently needed. A better understanding of factors related to the delay in seeking health care are essential steps towards an effective TB control program.

### PC-296-17 Long-term effectiveness of community participation to improve tuberculosis case detection among the urban poor in Phnom Penh, Cambodia

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**Background:** Although community based participation has been proposed as a way to increase access to TB care and enhance case finding, data on its effectiveness, especially on the long-term, are scarce. We aimed to evaluate the short (<1 year) and long-term (>1 year) impact on case detection of community participation in poor urban communities in Cambodia.

**Methods:** The study was conducted in four health centers and one referral hospital in Phnom Penh, Cambodia. In July 2009, a community DOTS (C-DOTS) program was implemented. TB C-DOTS watchers were trained to give TB education within the community, to identify TB suspects and to refer these to the health center for sputum collection. We compare the TB case detection rate during the first 12 months of the C-DOTS program (short-term effect) and the subsequent 21 months (long-term effect) with the 18 months before the implementation.

**Results:** In the 18 months before the implementation of the TB-DOTS watchers, a median of 35 PTB(+) cases/quartile and 43 PTB(-)/EPTB cases/quartile were diagnosed, yielding a median of 79 TB cases/quartile. Within the first year after the C-DOTS implementation, a significant increase of 23% to 43 PTB(+) case/quartile was documented ( $P = 0.03$ ). A non-significant increase of 7% in PTB(-)/EPTB cases to a median of 45 cases/quartile was observed as well ( $P = 0.66$ ). During the following 21 months, the effect persisted. Compared to pre-intervention, a 31% increase in PTB(+) cases (46 cases/quartile,  $P = 0.02$ ) and a non-significant increase of 23% in PTB(-)/EPTB cases (53 cases/quartile;  $P = 0.09$ ) was seen.

**Conclusion and recommendations:** The integration of TB-DOTS watchers in the community appears effective in enhancing TB case finding, mainly smear-positive cases. Importantly, the effect was maintained during the second and third of implementation.

### PC-297-17 'Are two weeks up?': media strategies for improving tuberculosis case detection

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Tuberculosis (TB) is a major public health problem in India: nearly 2 million people in India develop TB

annually, of which 0.87 million are infectious and 0.33 million fatal. The Revised National Tuberculosis Program, working to halt and reverse TB incidence in India as per MDG 6, has established over 12 000 quality-assured designated microscopy centers (DMCs) countrywide that provide sputum microscopy services. They achieve rates of approximately 70% case detection. Reaching the remaining 30% remains a challenge.

This paper looks at the 360 degree campaign, using both mass media (TV, radio, outdoor publicity, street theatre, video vans) and on ground activation (materials for frontline health workers), that has been devised to reach this unreached 30% and communicate a two-fold message, relating to the symptoms and detection of TB: that a cough that lasts for 2 weeks is the key symptom and if you have such cough then you should go to a DMC for sputum testing. At the centre of this campaign is Bulgam Bhai ('Sputum-Man'): a superhero character with a uniquely anachronistic listening device which detects coughing from all over the country. Upon hearing a cough, his superhero powers immediately transport him to the vicinity of the cougher where he asks his trademark question: 'Are two weeks up?' His appearance is simultaneously intrusive and comic, across region, socio-economic class and age, until the final call to action informs the audience about what to do if they have been coughing for two weeks. Evaluations demonstrate promising impacts with significant implications for media strategies in improving TB case detection elsewhere.

### PC-298-17 Anti-tuberculosis drug resistance profile among previously treated patients at the National Reference Laboratory in Kenya

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**Background:** Kenya ranks 15th in the 22 TB high burden countries. Of the 105 781 TB patients notified in 2010, 10% (10 503) were previously treated. In the absence of periodic drug surveillance system, data from routine drug susceptibility testing of selected high risk patients performed at the Reference Laboratory plays an essential role to inform on the burden and trends of anti-TB drug resistance. The NRL receives sputum samples of mainly previously treated TB patients from throughout the country for DST. In 2010, a total of 112 MDR-TB cases were reported.

**Methods:** A retrospective review of all samples received for DST at NRL in Kenya in the year 2010 was performed. Demographic and laboratory data available from the laboratory request form was collected and analysed.

**Results:** 7257 sputum samples were received at NRL for DST. 2423 (33%) had a positive culture for

*Mycobacterium tuberculosis* on Löwenstein-Jensen (LJ) media which was followed by DST in Mycobacterium indicator tube (MGIT). 1691 (70%) patients with DST results had available information regarding previous treatment. The most common reason—1178 (70%) for DST request was relapse status, treatment failure and return after default representing 22% (369) and 8% (142) respectively. The resistance pattern to first line antituberculosis drugs was isoniazid 20.1% (344/1689), streptomycin 9.8% (165/1689), rifampicin 9.8% (165/1689) and ethambutol 7.9% (134/1689). The overall rate of MDR-TB was 8.5% (143/1689). MDR-TB was diagnosed in 3.5% (13/369) of relapses, 6.6% (78/1178) of defaulters and 36.6% (52/142) of treatment failures.

**Conclusion:** Our data suggest that the occurrence of MDR-TB among previously treated TB patients in Kenya is high. Systematic testing of all high risk individuals (previously treated) country wide is the first step necessary for diagnosis and control of MDR-TB.

### PC-299-17 Challenge in replacing old technology: case study of introducing LED fluorescent microscopy in 200 medical college designated microscopy centres in 23 Indian states

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**Background and challenges to implementation:** According to the WHO Global TB Report 2010, 21% of global incidence of tuberculosis occurs in India. New technologies to diagnose and cure TB are important to reduce the burden of the disease and its manifestation. To establish the feasibility new technology, it is imperative to ensure its acceptance by its user. It must be simple, efficient, effective and affordable for health system and health personnel to optimise its use to improve case detection.

**Intervention:** To replace age-old ZN microscopy, LED fluorescent microscopy (FM) is being introduced in 200 DMCs of National Tuberculosis Program (NTP) across 23 states. To develop acquaintance in FM, 400 laboratory personnel working in NTP have been trained in 35 batches by The Union. After trainings, participants feedback was collected on the FM. 12 FGDs were also conducted immediately after the completion of the trainings.

**Results:** 86.5% participants have expressed their willingness to practice the FM in their work. However 12% have shown moderate commitment. Only 1.5% has not responded. On thematic analysis, majority of trainees said this technology brings ease to their work. They find it ergonomically better, easy visibility of AFB, easy identification of the scanty cases. Few participants have complaint that since FM recommends 400× for the examination, bacteria

appears in smaller size create misperception. More time required in staining process for FM technology compare to ZN technology is also a challenge. However they also stated that overall time in the complete process reduces up to 60% with FM.

**Conclusions:** The laboratory personnel appreciated the new technology and rated LED fluorescent microscopy better than the traditional ZN microscopy. All 400 lab personnel will be interviewed again to account their perception on new FM technology with ZN technology after 3 months of its usage. The findings will be shared during the conference.

### PC-300-17 Mid-term evaluation of tuberculosis advocacy, communication and social mobilisation interventions

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**Background:** Mercy Corps, jointly with the National TB Control Program, is implementing advocacy, communication and social mobilization interventions for TB control in Pakistan since 2008 with funding support from the Global Fund to Fight AIDS, TB and Malaria (GF). Activities include mass media campaign, community-based awareness-raising events for orientation of journalists, opinion leaders and healthcare providers, and formation of community coalitions. A mid-term evaluation to assess the relevance, effectiveness, and efficiency of activities was conducted.

**Design/methods:** A three-stage stratified random sampling approach was used for the KAP survey was conducted in 15 urban and 45 rural sub-sub-districts. A total of 2400 respondents were interviewed.

**Results:** Participant recall of TB was considerable with 64.6% recalling any TB information without prompts. The main source of TB information was TV/Cable (39.9%), followed by interpersonal sources [elders/family members (20.4%)]. Participants aware of TB information were found to have significantly better knowledge than those unaware ( $P < 0.01$ ). Perceptions of where people should go for treatment if they experienced symptoms of TB tended to focus predominantly on government health facilities (65.7%). TB patients would disclose their status to a spouse (43.1%), doctor or other medical worker (42.4%) or a parent (40.6%). 82% stated that they would like more information about TB. Only 31.4% had prompted recall of TB brand.

**Conclusion and recommendations:** Program evaluation showed a cohesive and technically driven approach to the delivery of a broad range of quality assured community interventions supported with a mass media umbrella. Challenges for the program moving forward include the need for strong branding of activities at community level. There is need to strengthen outcome driven ACSM activities.

**PC-301-17 Patient charter for tuberculosis care: empowering tuberculosis patients in India**

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**Background and challenges to implementation:** Basic optimal health care is the right of every citizen and it is the responsibility of the state to provide it. The Union-led Project Axshya implemented across 240 districts across the country aims to empower TB patients and community through Advocacy, Communication and Social Mobilization (ACSM) interventions such as community participation, equitable distribution of services with social and gender sensitivity. Patient Charter is one such advocacy tool adopted under the project for this common cause, for the entire TB community.

**Intervention or response:** An illustrated version of Patient Charter developed by International Standards for Tuberculosis Care, was developed by The Union under Global Fund Project Axshya. To empower TB patients on their rights and responsibilities sensitization, dissemination and promotion for adoption of the Patients' Charter was done by the NGOs partners through the leaflets which were distributed and explained to TB patients at DOTS centers and during the community groups organized under the project. Posters of Patient Charter were displayed at all major health facilities especially at waiting areas across the project districts. The TB forums formed under the project also promoted the charter and they work to ensure that the TB patients are aware of their rights and responsibilities.

**Results and lessons learnt:** The illustrated version of Patient Charter for TB care is available across all 240 project districts and displayed at all major health facilities. Awareness amongst TB patients on their rights and responsibilities has improved and has led to demand creation of quality TB services.

**Conclusions and key recommendations:** Illustrated version of patient charter is an effective advocacy tool for greater and equitable access to quality services and providing information to TB patients to reduce health inequalities and helping patients to be involved in decision-making.

**PC-302-17 Baseline knowledge attitudes and practice survey of private health-care providers on tuberculosis DOTS**

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**Background:** Mercy Corps, in collaboration with the National TB Control Program (NTP), is expanding TB-DOTS in Pakistan through public-private mix (PPM) interventions with support from the Global

Fund to Fight AIDS, TB and Malaria. A baseline survey was conducted to assess the capacity and KAP of the private healthcare providers (PHCPs) in TB diagnosis and treatment and clients' perspective on availed services.

**Design/methods:** It was a cross-sectional quantitative assessment. Multi-stage random sampling of districts and PHCPs was done. A total of 560 PHCPs and 200 clients were interviewed.

**Results:** Analysis of knowledge of PHCPs revealed that only 1 respondent correctly identified all five components of DOTS. 18% were aware of both chest X-ray and sputum examination to confirm the diagnosis of TB patients. Significant associations of KAP scores were also found with the gender of respondents (37% of male PHCPs were above mean practices score compared to only 10% of female PHCPs). Although 84% of PHCPs were aware about two phases of TB treatment but duration of treatment and number of anti-TB drugs prescribed were not in accordance with national guidelines. Only 4% of the total PHCPs interviewed were using all five standard anti-TB drugs in their practices and only 23% were treating the patients for standard duration (eight months). Interviewed clients were satisfied (94%) with quality of care provided by the PHCPs.

**Conclusion and recommendations:** Findings of the survey reveal significant gaps in the KAP of PHCPs. They should be extensively trained on TB-DOTS as per NTP guidelines; especially for female PHCPs as majority of women seek care from female PHCPs.

**PC-303-17 Pilot for developing a tuberculosis screening tool for coughers admitted for in-patient care in an area of high tuberculosis prevalence**

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**Background:** Botswana has a TB rate of 505 per 100 000 and an overall HIV prevalence of 17.6. TB remains the main cause of morbidity and mortality in persons living with HIV; WHO has encouraged facilities to adopt administrative controls to prevent nosocomial transmission. In our setting, the referral hospital opened an additional medical ward with innate structural TB infection control properties. Simple, cost-effective screening is needed to identify and separate those most infectious.

**Methods:** We recruited patients identified with cough prospectively, following admission at a referral hospital medical ward, servicing northern Botswana. For each patient, the study documented medical history, and sent two sputum samples for laboratory testing for TB via auramine stain and MGIT, liquid mycobacterial culture. TB diagnosis followed 2011 Botswana

national TB management guidelines. We estimated c-statistic on 50 signs and symptoms captured from participants, to assess probability of correct classification for a pair of patients with and without the outcome.

**Results:** Between July 2011 and March 2012, 402/1173 (34%) of medical admissions had cough. We enrolled a total of 203 coughers, including 144 (71%) who were HIV(+). A diagnosis of pulmonary tuberculosis (PTB) was made in 26% (52/203) of patients, including 17 (33%) smear positives. Having any one complaint of weight loss ( $\geq 2$  week) or fever ( $\geq 1$  week) or sickness ( $\geq 1$  week) achieved a 100% sensitivity and 100% negative predictive value. Having a known TB contact showed a low sensitivity (29%) for predicting infectious TB.

**Conclusion:** Cough is a common complaint among general medical ward admissions in our setting. Screening for weight loss, fever and length of sickness had a sensitivity and their absence a high negative predictive value in assessing transmissible TB. An infectivity-risk screening tool implemented together with rapid molecular tests like the Xpert<sup>®</sup> MTB/RIF, can reduce nosocomial transmission.

#### PC-304-17 Enhanced community-based screening in remote areas: BRAC experience in the tuberculosis control programme

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**Background and challenges to implementation:** In collaboration with NTP, BRAC aims at intensifying universal DOTS coverage with a major emphasis on a community-based service delivery model. Accordingly a special programmatic intervention for remote areas of 31 sub-districts was undertaken since October 2011 to enhance community-based screening and service linkage covering 4.8 million population. Case detection rate was low in these areas than other BRAC supported areas of Bangladesh. The aim of the program is to increase case detection and improve access to tuberculosis care services for the people living in remote areas.

**Intervention and response:** Besides routine screening services for tuberculosis, additional outreach sputum collection centers were organized monthly to enhance case detection. Locally recruited community health workers (CHWs) intensified social mobilization prior to organizing each center and disseminated TB related information through health forums. Transportation cost was provided to CHW for organizing outreach sputum collection centers. Diagnosed TB patients were treated in accordance to the national guideline. All smear-negative TB symptomatic were referred to appropriate health facilities for higher investigation and care.

**Results and lessons learnt:** Between October 2011 and March 2012, a total of 30873 suspects were screened through sputum smear microscopy. Of them, 2100 smear positive cases were identified in comparison to 1890 during the previous six months (showing an 11% increase in case detection). During the reporting period, among 2100 smear positive cases 347 (17%) were contributed by the outreach centers conducted by CHW under special intervention.

**Conclusion:** Intensive and focused effort for remote areas contribute in strengthening TB services and such interventions need to be continued with sustain programmatic inputs.

#### PC-305-17 Improving capacity for implementing tuberculosis operational research in Indonesia: achievements and challenges

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Indonesia has 240 million population and 4% of the global TB burden. DOTS has been implemented widely in public health facilities. Case detection rate target has been reached in 2007, but it has then stagnated ~76% with wide variation among the provinces. Program achievement is hampered by the lack of basic data on TB prevalence, limited systematic evidence on operational issues and the great proportion of TB patients accessing private providers.

Since 2004, The National TB program has established a TB operational research group (TORG) consisting of 16 researchers from 8 academic institutions with a mandate to increase capability and facilitating implementation of operational researches (OR) that support improvements of TB program. Routine bi-monthly meeting is conducted for coordination, facilitation and reviews of study proposals. The group actively conduct courses for implementing OR for provincial research teams.

Within this period, the group has trained and supervised 24 research teams (120 participants) selected from 23 provinces to implement OR. Topics mostly focused on ways to increase TB case detection rate. As a result, 23 research reports and policy briefs have been completed and 3 articles published internationally. Other outcomes were observed among the program staff such as willingness to implement their recommendation, more creative ways on problem solving and increased appreciation for research. Academicians showed their eagerness to continue their research activities with the TB program.

Implementation of TB OR in Indonesia still faces many challenges which encompass variation of local

capacities, limited fluency in English language and difficulties in managing time to conduct research. While its wide scale impact still needs to be assessed, small changes shown after OR activities revealed the great potential that can be mobilized. With continued network support and link to adequate resources, sustainable increase in OR capacity will be established.

### PC-306-17 Meso-level multi-disciplinary approach for reduction of initial defaults in Revised National Tuberculosis Control Programme, Delhi, India

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**Background:** Universal coverage mandate of TB program emphasizes on early detection and initiation of treatment for all pulmonary TB patients. It is essential that the magnitude of initial defaults be curbed so that it ceases to compound disease transmission chain in the community.

**Objective:** Devise an intervention model to reduce initial defaults.

**Method:** A questionnaire based cross sectional study was conducted from November 2011 to March 2012 in Delhi. 340 initial defaulters were interviewed by trained field investigators. Focused group discussions with paramedical providers using a topic outline guide, patient interviews using semi-structured questionnaire and brainstorming of program managers was conducted to elicit reasons, suggestions and health seeking behavior among initial defaulters.

**Results:** Patient interview revealed preference for private practitioners (64.4%) as the most common cause of initial default. Lack of trust in government health system (26.7%), inconvenient time of DOT centre (18.5%) and wrong patient address (14%) were other reasons. Multivariate analysis showed no significant association between the reasons elicited and the profile of initial defaulters. Focused group discussion with paramedical providers showed tendency of initial defaults in addicts and shelter less patients. Brainstorming with program managers revealed lack of trust in allopathic system of medicine and human resource constraints.

**Recommendation:** A meso-level multi-disciplinary model was devised with community participation through Resident Welfare Associations (RWA). In the model, mutual collaboration between government and non government agencies through RWAs involvement was emphasized.

**Conclusion:** Multi-disciplinary approach is beneficial for reducing initial defaults and increasing efficiency in TB program.

### PC-307-17 Successful community-based tuberculosis directly observed treatment: a case study in southern Brazil

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**Background:** The directly observed treatment (DOT) strategy is recommended since 1993 by the WHO. In Brazil, one of the 22 high-burden countries, DOT for tuberculosis is recommended by the national guideline, but its implementation has been uneven in the country. In addition, municipalities adopt different frequency of supervision. The aim of the present report is to analyze the impact of DOT implementation in Paranaguá, a city with 144 000 inhabitants and a TB incidence rate of 99/100 000 inhabitants, one of the highest in Paraná State.

**Design/methods:** Paranaguá's health department implemented community-based DOT in July 2009. Until then, treatment was self-administered. DOT in Paranaguá consists of every day visits to patients' residence or the place of their preference (work or any other) by a nurse aid or health agent, including weekends and holidays. Homeless patients also define their preferred place for DOT. We compared programmatic indicators before and after (from January to December 2010) community-based DOT implementation in Paranaguá.

**Results:** Before DOT implementation, cure rate of TB was 73.1% and default rate was 5.1%, as compared to 79.4% and 0%, respectively, after DOT implementation, representing an increase in 8.6% [95% confidence interval (CI) 7.3–9.9] of cure rates, mainly due to a reduction of 100% (95%CI 85.4–114.6). All patients were HIV-tested, compared to 44% before DOT implementation.

**Conclusion and recommendations:** The community daily-based DOT improved not only the adherence of patients to treatment, but also the compliance of healthcare workers with the national guidelines, suggesting that commitment of the team is equally important to TB control.

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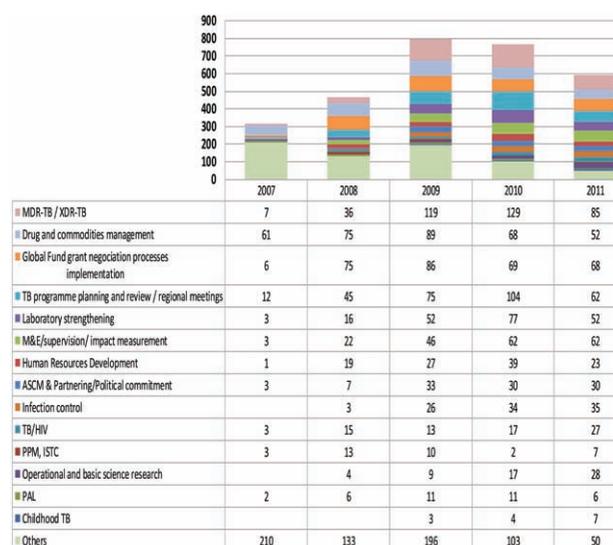
### PC-308-17 The TBTEAM global database: a tool to examine global trends in technical assistance

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**Background and challenges to implementation:** The Global Plan to Stop TB includes external TA provision to countries. There is a need to monitor and report on this. The TBTEAM secretariat manages the TBTEAM database, which records technical partners external TA missions to countries. Between 2007 and 2011, this database has captured 2938 completed mission events. TBTEAM is exploring the possibility of using the database to measure the global trends in TA provision.

**Intervention or response:** 18 variables from the database were exported and analysed in Excel. Analysis included cross tabulation of time trends of missions by partner organization, topic of mission, mission reports uploaded, funding source and WHO region.

**Results and lessons learnt:** The number of missions entered peaked in 2009 (around 66/month) and by 2011 had fallen back to 50/month, showing an overall decrease in contributions to the database by major partners. More partners have become active in reporting over the last two years. For technical areas such as MDR/XDR-TB and laboratory capacity strengthening, missions completed peaked in 2010, while paediatric TB, operational and basic science research and infection control, continue to show an upward trend. There is great variation in partners uploading mission reports (79% to 0%). The number of missions generally mirrors TB burden by region. Completeness of data has improved over time.



**Figure** Global trends in tuberculosis technical support missions by subject area: 2007–2011. Source: TBTEAM website database.

**Conclusions and key recommendations:** The TB TEAM database can be analysed to show and examine global TB TA trends. Potential reporting biases, completeness of data need to be addressed through regular data validation processes.

## TUBERCULOSIS IN PRISONS

### PC-335-17 Active case finding results and early tuberculosis detection during 2008–2011 in the penitentiary system of Azerbaijan

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**Aim:** To study all SS+/C+ and SS-/C+ TB cases against various identification means during active case finding.

**Methods:** The retrospective study data analyses were employed. Estimated inmates number was 16 000 annually. Throughout the years regular examination against tuberculosis infection according to the standardised active case finding procedure increased from 41% to 74% constituting the main TB suspects pool. However, around 250 laboratory positive (simple smear and/or culture positives) suspects firmly were recommended for the TB treatment a year.

**Results:** Nearly 1.6% of the general prison population have been recorded as approved TB cases throughout given period of time (~1.54% a year). The survey confirmed the good practice of the early case detection. The culture positive cases (SS-/C+) significantly exceeded the number of simple smear positive (SS+/C+) ones. Moreover, the number of SS+/C+ decreased almost two times among suspects (2008:2.5%; 2009:1.1%; 2010:0.5%; 2011:1.2%), although the number of SS-/C+ slightly decreased (2008:7.7%; 2009:8.7%; 2010:7.5%; 2011:5.0%) throughout the years while the lab workload increased almost two times. The study revealed the most effective TB suspects' identification mean in terms of early detection. The use of mobile X-ray unit declared as most appropriate mode. MMR identified the major number of laboratory positive TB cases in comparison with questionnaire and composition of questionnaire + MMR methods.

**Conclusion:** Significant exceed of SS-/C+ cases judged against SS+/C+ indicates an early detection and, from epidemiological point of view, is quite distinctive. As advanced identification procedure becomes as more suspects are reached and early TB detection is recorded. MMR use and sputum *in vitro* cultivation for effective TB suspects' identification suggested as most appropriate and efficient in prison settings.

**PC-336-17 Implementation of tuberculosis activities in prisons in Cambodia**

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**Background:** Enclosed settings such as prisons promote TB transmission where effective TB control services are often lacking. FHI 360/USAID/TBCARE I support the Cambodia government to provide TB-HIV services in prisons.

**Intervention:** Prison health post staff were trained to identify TB symptoms in prisoners, collect and prepare sputum smears; sending to a TB microscopy laboratory for diagnosis. All positive prisoners were offered HIV testing. Smear negative TB suspects, seriously ill TB patients with/or HIV co-infected were referred for diagnosis and management to hospitals. In addition to routine case finding, mass screening of all inmates was conducted annually using symptom screening, chest X-ray and sputum smear microscopy. The project expanded from three prisons (3034 inmates) in 2009 to seven prisons (4901 inmates) in 2011.

**Results:** TB case notification rates in prisons declined from 5175/100 000 in 2009 to 3128/100 000 in 2010 and 1977/100 000 in 2011. Compared to the national TB programme case notification rates, these are 18 times higher than the NTP in 2009, 11 times higher in 2010 and seven times higher in 2011. Treatment success rate of over 85% were maintained throughout the period 95% in 2009, 87% in 2010 and 95% in 2011. The death rate declined from 4% in 2009 to 2% in 2010 and 0% in 2011.

**Conclusions and key recommendations:** It is effective to provide quality TB-HIV services in prisons using existing staff. Routine TB case finding, coupled with annual mass screening of all inmates, lead to rapid decrease in TB case notification rates in prisons. Despite the decline in the past three years, the case notification rate in prisons is still seven times higher than in the general population.

**PC-337-17 HIV and tuberculosis prevalence in Salemba Prison, Jakarta, 2011**

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**Background:** In 2011, there were approximately 900 inmates in Salemba Prison, nearly 300% over its official capacity. More than 30% of prisoners were drug users. These conditions are conducive to the spread of TB and HIV, which were two leading causes of death. In response, the prison clinic initiated screening of inmates for TB and HIV based on TB symptoms and HIV risk behaviors.

**Intervention:** All inmates were screened for TB symptoms and HIV risks during September–October 2011. Sputum samples were obtained from all TB suspects and microscopy was performed at a public health center nearby the prison. All inmates who had HIV risks were tested for HIV. All HIV-positives who were TB suspects with negative AFB smear got chest X-ray.

**Results:** Among 900 inmates, 855 (95%) received TB and HIV screening, and 72 (8.4%) had TB symptoms. Fourteen active TB cases were detected (3 sputum positive, 5 X-ray positive and 6 extrapulmonary). TB prevalence was 1.6%. A total of 464 (54.2%) of inmates had HIV behavioral risks, and 36 new HIV cases were found. Including the 60 inmates already known to be HIV-positive, HIV prevalence was 11.2%. Among the 14 active TB cases, 10 also had HIV. All TB and HIV cases detected received treatment.

**Conclusions:** Salemba prison assigns priority to TB and HIV screening and treatment in response to the challenging prison health environment. Collaboration with local health facilities and other partners to facilitate treatment continuation post release are crucial to program success.

**PC-338-17 Partnering with prisons in curbing tuberculosis: a case from Bhandara District Jail**

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**Background:** Overcrowding is one of the main reasons of spread of tuberculosis (TB) in high burden countries. Jails generally host large number of population living together. Having one TB case not treated would be detrimental to the health status of all other inmates of the jail as chances of transmission of TB will be higher. Current study attempts to explain the importance of involving jails in RNTCP's (Revised National Tuberculosis Control Program) strategy of universal coverage.

**Intervention:** Catholic Health Association of India (CHAI) has conducted series of awareness programs in the District Jail of Bhandara in the state of Maharashtra, India as part of Project AXSHYA which envisages strengthening civil society in expanding the reach of RNTCP through involvement of various public, private and civil society sectors to work towards the cause of TB care and control in India. A total of 268 prisoners (253 male and 15 female) along with prison authorities were involved through mass awareness programs, focus group discussions during January–March 2012.

**Results:** The inmates and the prison authorities were

given awareness about TB disease, care and control. All the inmates were screened for TB symptoms and 9 suspects tested for sputum positivity of which none found positive for TB. Prison authorities understood the importance of regular screening for TB symptoms and agreed to initiate a sputum collection centre and made an agreement with an NGO (Aditya Bhabuudeshiya Sanstha) for transporting the sputum to DMC (designated microscopy centre) for TB testing. The NGO was given approval to conduct regular awareness programs within the jail premises. TB messages were displayed within the jail premises.

**Conclusion:** Towards achieving the goals of Stop TB Partnership, sustainable efforts from various sectors with felt mutual responsibility and collaborations are required. Jails if involved through local collaborations can contribute towards achieving the goals of universal coverage.

### PC-339-17 High tuberculosis burden in prisons of Tajikistan

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**Background:** Tajikistan remains high tuberculosis (TB) burden country with an average 6000 new TB cases notified yearly. In 2007, the full DOTS coverage was achieved in civilian, and in 2008, with the support of the Global Fund and Caritas Luxemburg in prison sector. The aim of the study was to compare TB burden in prison and civilian sectors.

**Methodology:** The TB- and human immunodeficiency virus (HIV)-related data recorded in the central TB register during the period 2009–2011, were analyzed.

**Results:** TB incidence was 10–17 times higher in prisons than in civilian sector. TB incidence in prison increased from 930 per 100 000 population in 2009, to 1140 in 2010, and to 1390 in 2011. During the same period, the proportion of new TB cases among all notified cases in prisons increased by 14.3%, being 57.5% in 2009 and reaching 71.8% in 2011. During the period 2009–2011, TB incidence was 80.3, 80, and 78.7 per 100 000 population respectively in civilian sector. During the same period, the proportion of new TB cases among all notified cases in civilian sector increased by 3%, being 74.9% in 2009; 77.4% in 2010 and 77.9% in 2011. During the study period, the proportion of TB-HIV co-infected persons increased more than 3.5 times in prison, and 0.3 times in civilian sector.

**Conclusions:** The TB incidence in prisons remains up to 17 times higher than in civilian services in Tajikistan. Considering increase in TB-HIV co-infection urgent actions are needed to revert TB incidence in both, civilian and prison sectors.

### PC-340-17 Control of pulmonary tuberculosis in Dhaka Central Jail, Bangladesh

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**Background:** Tuberculosis (TB) in prison populations still remains an important issue that has not been adequately addressed, especially in countries like Bangladesh. Data regarding TB among prisoners is also scarce in the country.

**Intervention:** An active screening system for pulmonary TB inside the prison cells of Dhaka Central Jail was established in October 2005 by icddr,b. Based on the study experience then we established active screening of the inmates at the entry point of the prison since January 2009 along with the screening inside the prison cells. From October 2005 to December 2011; 22 288 inmates were screened inside the prison cells and from January 2009 to December 2011; 93 147 inmates were screened at the entry point. Three sputum specimens were collected from all the TB suspects (who have cough for three weeks or more and/or body mass index less than 16 kg/m<sup>2</sup>) for acid fast bacilli (AFB) microscopy, culture and anti-TB drug susceptibility testing. Positive cases were immediately isolated and brought under treatment inside jail hospitals under DOTS.

### PC-341-17 Scaling up tuberculosis services at prison for care and referral in Bangladesh

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**Background and challenges to implementation:** BRAC, an NGO has been implementing community-based TB services since 1984 in collaboration with National Tuberculosis Control Programme (NTP). BRAC expanded TB services in 7 prisons as pilot intervention in 2004 and gradually expanded the program at 41 prisons by 2011. Prisoners are one of the vulnerable groups to develop TB and can infect other inmates easily; incidence is also high among them. The aim of the programme is to identify tuberculosis status among prisoners in BRAC supported areas.

**Intervention or response:** BRAC staff goes to prison 2/3 times in a month to identify prison inmates with TB symptoms. Prison authority also informs BRAC staff about presumptive TB patients in prison. Diagnosed cases are registered under NTP. Treatment initiated by prison medical officer and DOT is ensured by prison pharmacist. BRAC staff follows up patient

weekly and fortnightly to establish referral network after releasing or transfer to other prison.

**Results and lessons learnt:** In 2010, total 230 patients were diagnosed in 36 prisons. Among them, 75.7% new smear positive, 12.2% extra pulmonary, 7.4% smear negative and 4.8% retreatment cases. Treatment success rate was 57%, which is lower than other population. Transfer rate was high as 40%. In 2011, total 367 cases were detected, among which 84% male and 16% female. Of them, 82.6% new smear positive, 4.1% retreatment, 6.3% smear negative and 7.1% extra pulmonary cases.

**Conclusions and key recommendations:** High transfer rate is a reason for low cure rate. Early detection and strong referral linkage need to be developed, to ensure treatment continuation and notify treatment outcomes where patient are registered.

### PC-342-17 **Epidémiologie de la tuberculose en milieu carcéral au Bénin**

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**Background :** Peu de données existent sur l'ampleur de la tuberculose dans les prisons en Afrique subsaharienne. Nos objectifs étaient de déterminer l'incidence de la tuberculose pulmonaire bacillifère en milieu carcéral et de décrire le profil épidémiologique des patients tuberculeux diagnostiqués dans les prisons du Bénin.

**Design/methods :** Il s'agissait d'une étude rétrospective qui a porté sur les patients tuberculeux bacillifères dont le diagnostic a été posé au cours de l'année 2011 dans les neuf prisons civiles du Bénin. L'effectif de la population carcérale au Bénin en 2011 a été obtenu auprès de la direction de la planification du ministère de la justice du Bénin.

**Results :** Au cours de l'année 2011, 37 cas de tuberculose pulmonaire à microscopie positive (TMP+) ont été diagnostiqués dans les prisons au Bénin pour une population carcérale de 7148 détenus, soit une incidence de 500 patients pour 100 000 prisonniers. La tuberculose bacillifère dépistée en milieu carcéral représentait 1% (37/3593) de tous les cas de TMP+ diagnostiqués au Bénin en 2011. Les patients étaient jeunes avec une moyenne d'âge de 32 ans (CI95% 29–35 ans). La majorité était de sexe masculin (97%). 33 patients (89%) étaient des nouveaux cas de TPM+. La prévalence de la séropositivité VIH était de 14% (5/37). La durée moyenne de détention avant le diagnostic était de 25 mois (CI95% 12–39 mois).

**Conclusion and recommendations :** L'incidence élevée de la tuberculose en milieu carcéral nous impose d'accorder plus d'attention aux populations vulnérables qui y vivent.

### PC-343-17 **Lack of continuity of care undermines tuberculosis treatment success in Zambian prisons**

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**Background:** In the Zambian prison system there is paucity of information on treatment outcomes for inmates with tuberculosis (TB). We report treatment outcomes for inmates diagnosed during a TB REACH-funded screening program implemented by the Zambia Prisons Service and the Centre for Infectious Disease Research in Zambia (CIDRZ).

**Design/methods:** In April 2011 we reviewed national TB treatment records for inmates diagnosed in one prison between November 2010 and November 2011.

**Results:** Of 206 inmates diagnosed with TB, 87 (42%) were bacteriologically confirmed and 119 (58%) were clinically diagnosed. Mean age (SD) was 36.1; 191 (95%) were male, and mean BMI was 21.7. 81/167 (48%) TB patients who accepted HIV testing were co-infected with HIV; 60 (29%) had history of prior incarceration, and 57 (28%) had history of prior TB. No evidence of TB treatment initiation was found for 53 inmates (26%), due to transfer to another prison or release prior to receiving their TB diagnosis. Of the remaining 153 inmates who initiated treatment, 5 (3%) were still on treatment at the time of data collection, 65 (42%) were cured or had completed treatment, 1 (0.7%) had defaulted and 8 (5%) had died. The remaining 74 (48%) were transferred or released during treatment. These inmates may have continued treatment, but communication with receiving clinic was not documented.

**Conclusions and recommendations:** Continuity of TB care is undermined by systemic factors that are unique to the prison environment including unexpected release, frequent transfers and inadequate communication to and from receiving clinics and the community. For prison TB screening programs to be successful referral to care, patient tracking and follow-up services must first be strengthened to cope with increases in case load. Integrated inmate information management and tracking systems are urgently needed in the Zambian prison system.

**PC-344-17 Incidence rates of tuberculosis and associated risk factors in Cameroonian prisons**J Noeske,<sup>1</sup> S Mbondi Mfondih,<sup>1</sup> E Dopico,<sup>2</sup> F Bekang.<sup>1</sup><sup>1</sup>Health/AIDS Program, German Development Cooperation (GIZ), Yaounde, Cameroon; <sup>2</sup>Mycobiology, Catalan Institute of Health, Barcelona, Spain. e-mail: juergen.noeske@giz.de

**Background:** While tuberculosis (TB) is acknowledged as a major issue in prison inmates worldwide, quantifying the problem remains a challenge. Incidence rate is supposed to be the appropriate measure; a recent review, however, identified only nineteen available published studies, most of them from the last century and all but two from low (-middle) income countries. The objectives of this study were to contribute to the quantification of epidemiologic knowledge of TB by determining the TB incidence rate in Cameroonian prisons and to identify associated risk factors.

**Design:** A prospective study was done in a convenience sample of ten prisons with comprehensive TB prison programmes in the different regions of the country, representing urban and rural as well as crowded and spacious prisons, and comprising about 10 000 prisoners at any time. TB and HIV data were extracted from standard TB laboratory and patients registers (WHO format) comprising prison entrance date. As incident case were counted all prisoners with incident TB after a length of stay of >90 days. For the person-time of inmates inside the prison the monthly count of inmates was added up. As comparison for the HIV infection rate in TB incident cases HIV infection rates of new entrants were used. The main risk factors controlled for were length of stay, malnutrition, HIV infection and crowding.

**Results:** TB incidence was 2.9 and 2.3 cases per 100 person-months for all TB cases confounded and for PTB+ cases, respectively. HIV infection rates in PTB+ and all other TB cases were 7.1% (range 4.3–11.1%) and 10.9% (range 5.9–18.1%), respectively. Neither length of stay nor malnutrition was associated with the incidence of TB. HIV infection was positively associated only with other than PTB+ forms of TB. Crowding appeared to be the only major risk factor.

**Conclusions:** Our study confirms in a methodologically controlled way the results of a series of TB point prevalence studies undertaken during recent years, i.e., high TB transmission and incidence in Cameroonian prisons notwithstanding an existing TB control programme according to international recommended standards, including active case finding and mass screening. As long as imprisonment conditions and in particular extreme crowding do not change in this setting, prison TB control cannot succeed.

**PC-345-17 Public and private partners contributing to improvements in TB-HIV interventions in Thai prisons**N Ngamtrairai,<sup>1</sup> C Charuenporn,<sup>1</sup> S Jittimane.<sup>2</sup> <sup>1</sup>Medical Services Division, Department of Corrections, Ministry of Justice, Muang, <sup>2</sup>TB Bureau, Department of Disease Control, MOPH, Bangkok, Thailand. e-mail: sxj47@yahoo.com

**Background:** TB and HIV remain prevalent in Thai prisons. Thus, enhancing access to interventions known to save lives is crucial even though these HIV infected TB patients are housed in prisons where resources are extremely limited. The objective of this study was to assess results of TB-HIV interventions in 41 prisons in Thailand.

**Design/methods:** Between 2008 and 2011, TB-HIV interventions were implemented by funding of the GFATM Round 8 through strong collaborations of Department of Corrections (DOC) Ministry of Justice, Ministry of Public Health (MOPH), and National Catholic Commission on Migration and Prisoner (NCCM) a faith-based organization for the post release care. Interventions contained indicator development, quarterly meeting for public and private partners, and training for prison staff. Prison nurses performed 3 month TB-HIV reports and forwarded to the DOC. These TB-HIV reports of 4674 TB patients were used to assess the result of TB-HIV interventions.

**Results:** There was an improvement of HIV testing for 87% (1010/1163) in 2011 better than the 75% (844/1127) in 2008. Among TB patients knowing their HIV status, 36% were HIV positive in 2011. CPT was considered weak due to the reduction from 72% in 2008 to 67% in 2011. However, a substantial improvement in ART provision was observed from a very low level as 17% in 2008 to 42% in 2009.

**Conclusion and recommendations:** Evidence showed that involvement of public and private partners contributed to an impressive improvement of TB-HIV interventions in prisons. This public private partner model should be replicated to support other TB interventions in prison settings especially MDR-TB.

**PC-346-17 Case finding of multidrug-resistant tuberculosis in prison populations in Thailand**S Homkeaw,<sup>1</sup> W Akeplakorn,<sup>2</sup> S Jittimane,<sup>3</sup>N Ngamtrairai.<sup>4</sup> <sup>1</sup>Thailand Business Coalition on AIDS, Bangkok, <sup>2</sup>Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, <sup>3</sup>TB Bureau, Department of Disease Control, MOPH, Bangkok, <sup>4</sup>Department of Corrections, Ministry of Justice, Muang, Thailand. e-mail: sxj47@yahoo.com

**Background:** Increasing MDR-TB cases in Thai prisons have been reported. Thus, improving the coverage of testing for MDR-TB is urgently needed especially in closed settings. The objectives of this study were to assess the proportions of MDR-TB and factors associated with MDR-TB.

**Design/methods:** A retrospective study was conducted

to enroll 439 pulmonary TB patients registered between 2008 and 2010 at the Medical Correctional Institution (MCI), Department of Corrections in Bangkok. The MCI with 350 beds is only one hospital providing tertiary care for prisoners across the country. Routine culture and DST were performed for all TB patients at this institution by a laboratory of the Thai Anti-TB Association. TB register of these patients were reviewed. Multiple logistic regression was used to assess the associations.

**Results:** Among 439 cases, 21% had resistance to at least one drug and 6% had MDR-TB. Proportions of resistance to at least one drug were 21% among 343 new cases and 21% among those previously treated ( $n = 96$ ). Proportions of MDR-TB were 4% and 11% among new cases and previously treated, respectively. There was a significant association between history of TB treatment and MDR-TB, while HIV infection was not related to MDR-TB.

**Conclusion and recommendations:** The proportion of combined MDR-TB appeared to be declined when compared to the 2000 study as 20%. It is observed that MDR-TB in new cases was high. Careful consideration should be focused on ensuring the true information about history of TB treatment in patients in prison settings.

#### PC-347-17 Continuation of care after being released during the course of treatment in prison settings, Thailand

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**Background:** About one fifth of TB patients are released before their treatment completion. Interventions to help these patients to continue the medication are the most important. This study was to assess the treatment outcomes of those who were released from prisons during their treatment.

**Design/methods:** Discharge planning records of new smear positive patients registered during 2009–2011 in 41 prisons were reviewed. National Catholic Commission on Migration and Prisoners (NCCM) provided assistance to patients who were released through the discharge planning activities. The NCCM staff met patients known to be released inside the prison to assess patient's needs for continuing medications. Assistance contained service arrangement, transportation, negotiation with hospitals for free service if the patient was uninsured, and emergency house if needed.

**Results:** About 508 new smear positive patients were enrolled. Among these patients, 23% were released before the treatment completion. About 91% (106/117) visited the hospital for the first appointment. It showed that about 66% (69/106) had treatment completion, while six had died, six were repeatedly

housed in prisons, 11 had treatment default, and 25 remained on the medication.

**Conclusion and recommendations:** Interventions improved the continuation of care after the patients were released during their treatment. Collaborating with civil society partners was important to help the prison program to provide high quality of care.

#### EPIDEMIOLOGY: TUBERCULOSIS IN HIGH- AND LOW-BURDEN COUNTRIES – 3

##### PC-379-17 Mathematical modelling of tuberculosis prevention in the foreign-born population of Canada

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**Background:** In 2009, foreign-born people contributed 63% of all tuberculosis cases in Canada while representing 20% of the Canadian population. Transmission of tuberculosis in the foreign-born population is relatively infrequent and these active cases primarily result from the progression of latent tuberculosis infections that were acquired prior to immigration. A proposed intervention approach to prevent this progression is evaluated using a deterministic mathematical model.

**Methods:** The intervention strategy was based on screening of new immigrants within the first year of residence in Canada for latent tuberculosis using interferon-gamma release assays (IGRAs) and treat positive reactors with nine months of daily isoniazid (standard treatment). Model validation is conducted retrospectively using data between 1986 and 1996 from Citizenship and Immigration Canada and the Canadian Tuberculosis Reporting System.

**Results:** Modeling indicates that the most cost-effective strategy is targeting foreign-born persons less than 35 years old who arrived from countries with tuberculosis incidence rates higher than 50 cases per 100 000 population. Assuming treatment effectiveness of 75%, the intervention strategy predicts that the screening and treatment of latent tuberculosis infection among new immigrants from countries with tuberculosis incidence rates higher than 15 per 100 000 population between 1986 and 1996 would have reduced the national tuberculosis incidence rate in Canada from 5.8 to 3.6 per 100 000 population in 1997.

**Conclusion:** The National Tuberculosis Elimination Strategy, which set as a target an incidence of 3.6 per 100 000 population or less by 2015, would have been

possible under the proposed approach before the year 2000. The use of mathematical models integrated with epidemiological information can provide useful insights into issues of public health importance.

### PC-380-17 Analysis of the population structure of *Mycobacterium tuberculosis* in Saudi Arabia

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**Background:** Saudi Arabia is the third biggest Arab country in the world with a moderate tuberculosis (TB) incidence rate (24/100 000 populations) and highly diverse human population which includes 8.4 million expatriates mainly from TB endemic countries among the total population of 26 million. In addition to the massive number of expatriates, the country annually receives almost 10 million visitors for the Islamic rituals. However no studies were conducted to find the active transmission and the association with different ages of patients. We sought to study the molecular dynamics of TB associated with age, gender and site of the infection.

**Method:** A collection of 908 isolates from different regions of the country were genotyped by using 24 loci based MIRU-VNTR typing and spoligotyping. Demographical and genotyping data were analyzed collectively.

**Results:** The three lowest age categories (16–29, 30–44 and 45–59 years) reveal maximum cases predominantly caused by the lineages Delhi/CAS (25.6%, 29.1%, 27.5%), EAI (13.9%, 16.4%, 14%) and Haarlem (13.6%, 12.7%, 9.4%), respectively. The clustering rates in these three age groups amounts up to 34%. In contrast the elderly (>60 years) population revealed predominance of Delhi/CAS (22.1%), Ghana (10.6%), S (11.2%), TUR and Uganda-I (8.6%) with no clustered cases. As cases among the elderly seem to be caused by endogenous reactivation, the deviating distribution of genotypes in this age group is a reflection of the ancestral population structure of *M. tuberculosis* in the country. In addition the PGG-1 strains showed an affinity towards extra pulmonary infections when the PGG-2 and 3 has significant association with pulmonary infections.

**Conclusion:** The results clearly indicate an ongoing transmission in the younger age groups. This observation indicates the causative agent of TB in Saudi Arabia has changed and drastic measures are needed to interrupt the ongoing transmission.

### PC-381-17 Incidence and risk factors of pulmonary tuberculosis using health checkup programme

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**Background:** It is aimed to estimate the incidence and relative risk factors of pulmonary tuberculosis (PTB) for the general population through the health checkup (HC). National health insurance cooperation provides annual or biannual HC to the all employees, self-employees with dependents at least 40 years, and civil servants.

**Design/methods:** It is retrospective cohort study using biannual HC program. Subjects showed normal chest X-ray in 2006 HC and no previous history of TB was followed until next HC in 2008. New active PTB cases developing between 2006 and 2008 in subjects receiving HC has been identified from the HC in 2008, TB surveillance data, information on reimbursement charge with anti-TB drugs, and laboratory registry of the Korean Institute of Tuberculosis.

**Results:** A total of 4 902 453 out of 15 198 112 subjects to receive HC was available for investigation. Mean followed up period was  $2.00 \pm 0.27$  years. Active PTB was found in 11 699 cases. 64.4% of the cases were only detected through the 2nd HC in 2008. Sputum smear and culture positive cases were only identified in 1171 and 1567 cases because of low coverage of sputum examinations. Overall annual PTB incidence rate adjusted to the whole population was 117/105 (95%CI 116–118). It was higher in male (131/105, 95%CI 129–132) than female (103/105, 95%CI 102–104). The incidence rate was increasing with age after 45 years old. Higher blood glucose level, lower BMI, abnormal AST increased the incidence. High cholesterol level, abnormal ALT, and regular exercise decreased the incidence.

**Conclusion and recommendations:** TB is still a serious health problem in Korea considering such high PTB incidence rate.

### PC-382-17 Influence of earthquake and tsunami on tuberculosis control in East Japan in 2011

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**Background:** Three prefectures were affected in East Japan by earthquake and tsunami on 11 March 2011. Objective is to describe the influence of the disaster on tuberculosis control in affected areas.

**Method:** Data on TB notification were obtained from national TB surveillance system. Information on case finding and case holding were collected through cohort analysis of TB patients.

**Results:** Mortality rate from tsunami was more than 0.6% in 7 coastal PHC areas (Table), where tsunami severely hit. Six TB patients were killed by tsunami and the direct death rate was 15.4% in these PHC areas. In addition 2 TB deaths caused by delayed diagnosis due to disaster were observed. Three cases developed TB immediately after the tsunami while they stayed in cold environment. Among TB patients on treatment in March 2011, there were no defaulters. In one PHC area, 9 out of 10 TB patients were confirmed to continue treatment. Two were transferred to other hospitals. Continuation of treatment of 7 patients, temporarily evacuated was reported to the PHC in different ways from shelter, clinic and a relative. The numbers of TB patients reported in the 7 PHC areas are 120 and 102, respectively in 2010 and 2011.

**Table** Number of TB patients in public health centre area with high mortality (more than 0.60%) in northeast Japan before and after earthquake and tsunami in March 2011

Public health centre (prefecture)	Death or missing by earthquake and tsunami	Population	%	No. TB patient	
				2010	2011*
Ofunato (Iwate)	2219	64040	3.47	8	5
Kamaishi (Iwate)	2328	54855	4.24	15	5
Miyako (Iwate)	1320	92714	1.42	12	10
Ishinomaki (Miyagi)	5755	213663	2.69	32	18
Kesennuma (Miyagi)	2201	90925	2.42	5	16
Shiogama (Miyagi)	2429	357872	0.68	26	35
Soso (Fukushima)	1181	149110	0.79	22	12
Subtotal	17433	1023179	1.70	120	101
Total of 3 prefectures	18939	5707257	0.33	549	455

\*Provisional.

**Conclusions:** With destruction of medical service system due to disasters, delay of case finding may have occurred. But case holding was well maintained through routine TB control program with networking of PHCs, medical facilities and well oriented patients and families. There is no tendency of increase in TB cases in affected areas.

### PC-383-17 Risk factors for treatment default among tuberculosis patients in three provinces of South Africa

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**Background:** Persons who default from TB treatment are at risk for developing additional drug resistance and death. The objectives of the study were to identify risk factors associated with treatment default among TB patients in three provinces of South Africa (SA).

**Design/methods:** We analyzed data collected among

1339 patients as part of a national surveillance evaluation in SA. Treatment default was compared with favorable outcomes, including cure and treatment completion. A multivariate regression model was developed to estimate risk ratios and 95% confidence intervals.

**Results:** Of 881 (65.8%) patients with final treatment outcomes recorded, 87 (10%) were children <8 years of age. Overall, 110 (12.6%) patients defaulted from treatment: 10 (11.5%) children and 100 (12.6%) patients aged  $\geq 8$  years. Independent risk factors for default among adults included receiving no or partial DOT (vs. full; aRR = 4.3, 95%CI 2.5–7.3,  $P < 0.0001$ ) and receiving treatment in a rural setting (vs. urban; aRR = 3.1, 95%CI 1.9–5.2,  $P < 0.0001$ ). Children who were treated with the SA standard adult Regimen 1 were significantly more likely to default than those prescribed the SA standard regimen 3 for children (aRR = 5.6, 95%CI 1.9–16.0,  $P = 0.002$ ).

**Conclusion and recommendations:** Factors associated with default differed between age groups. Regimen 1 treatment was associated with default among children aged <8 years, while treatment in a rural area with incomplete DOT was associated with default in those aged  $\geq 8$  years. Providers should recognize the importance of DOT throughout the course of TB treatment, especially in rural settings, and of treatment according to national guidelines, especially in children. Addressing default in all age groups is critical to overall program success.

### PC-384-17 Are patients who have recovered from tuberculosis still at risk of premature death? Results of a 10-year follow-up of all Israeli patients

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**Objective:** To estimate excess in mortality among TB patients that completed treatment and to identify their causes of death.

**Methods:** All Israeli citizens reported with TB between 2000 and 2010 were crossed-matched with the Civil Registry to identify those who died after recovery. Death certificates and/or last hospital reports of all fatalities were reviewed. Standardized mortality ratio (SMR) and hazard ratio (HR) were calculated and Cox analysis was performed.

**Results:** Of all 3394 tuberculosis patients who were followed for 21503 person-years, 412 (12.1%) died in an average of 2.1 (SD = 2.5) years after treatment completion, with 41% dying within the first year. Overall, patients recovered from tuberculosis had 3.4 (95%CI 3.1–3.7) times greater risk of dying than the

general Israeli population. SMR was highest in males and females aged 25–44 (6.7 [95%CI 4.5–9.6] and 4.9 [95%CI 2.0–10.1], respectively), and then decreased with age in both genders. Males had a higher risk of dying than females (HR = 1.4, 95%CI 1.2–1.7,  $P = 0.01$ ), those born in Europe/North America higher than Israeli-born (HR = 2.8, 95%CI 1.9–4.1,  $P < 0.001$ ) and HIV-positive more than HIV-negative (HR = 1.5, 95%CI 1.2–2.0,  $P = 0.04$ ). Each 5-years decrement increased HR in 1.35 (95%CI 1.3–1.4,  $P < 0.001$ ). Adjusted-HR model demonstrated that being male (HR = 1.5, 95%CI 1.1–1.8) and older age >65 (HR = 1.4 95%CI 1.3–1.4) had additional risk of dying. The leading causes of death was malignancy ( $n = 81$ , 19.7%), mostly lung, followed by septicemia ( $n = 57$ , 13.8%), cardiac diseases and pneumonia ( $n = 52$ , 12.6% each).

**Conclusion:** Patients recovered from TB are at higher risk of mortality compared with the general population adjusted for age and sex, mainly in males and in the ages of 25–44. The overall most common diagnosis for death was malignancy.

#### PC-385-17 Tuberculosis disparity in a high burden province of Thailand

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**Background:** TB in Sisaket is continuously high and raising. This study aims to enhance an understanding of the host-related factors of TB in Sisaket Province.

**Design/methods:** This cross sectional study described TB incidence and examined relationships of TB and demographic and district characteristics including age, gender, and selected clinical data. District characteristics included population density, predominant ethnic population, household size, income, literacy rate, and access to basic information. Data were obtained from Office of Education, Tuberculosis Control Unit of the Sisaket Public Health Office, and census database. TB incidences were analyzed by clinical classifications, gender, age groups, income, and ethnic groups. The association of TB with aforementioned characteristics was examined.

**Results:** The overall rates of pulmonary and extrapulmonary TB were 140 and 34 cases per 100 000 population, respectively. TB patients were more likely to be males ( $P < 0.0001$ ) and in the older age groups, especially those who were older than 65 years of age ( $P < 0.05$ ). District poverty was associated with TB incidence ( $P = 0.0218$ ). Districts in which Suai ethnicity were prominent had higher odds of TB than those from districts largely populated by Khmer and Lao groups (OR = 1.28,  $P > 0.05$ ). Income, literacy rate, access to information, and household size negatively influenced TB morbidity. Lower income districts

had higher odds of TB than those with higher incomes. Additionally, total population and household size were positively significant predictors of pulmonary TB ( $P < 0.05$ ).

**Conclusion and recommendations:** Demographic and district characteristics were associated with TB incidence. Consequently, targeting intervention in these areas as priority would be beneficial for the provincial TB control. Further study utilizing demographic and socioeconomic characteristics of individual patients in order to verify the association of these variables with TB incidence at the district level is suggested.

#### PC-386-17 Calculating the annual risk of infection with *Mycobacterium tuberculosis* among adolescents in Western Kenya in preparation for tuberculosis vaccine trials

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**Setting:** Siaya District, Western Kenya, with the highest TB notification rates in Kenya (400/100 000).

**Objective:** To determine the annual risk of TB infection (ARTI) with *M. tuberculosis* in 12–18 year adolescents.

**Design:** Adolescents aged 12–18 years of age were enrolled from an area under continuous health and demographic surveillance. At enrolment clinical and demographic data was collected, study participants were screened for tuberculosis including administration of tuberculin skin tests (TST).

**Results:** Out of 5004 adolescents enrolled, a total of 4808 (96%) came for TST readings. The overall prevalence of infection was 32.1% (95%CI 29.2–35.1) with a corresponding ARTI of 2.67% (95%CI 2.37–2.96). Being male ( $P = 0.0001$ ), having a BCG scar ( $P = 0.001$ ), being enrolled in school ( $P = 0.004$ ), residing in a rural area ( $P = 0.0001$ ), having both parents deceased ( $P = 0.022$ ) and a positive HIV test ( $P = 0.022$ ) were significantly associated with a positive tuberculin skin test. They remained strong predictors of a positive tuberculin skin test in a multivariate model.

**Conclusion:** We found a high ARTI indicating quite high TB transmission rates among adolescents. This high transmission rate may indicate a high TB incidence making this an attractive population for prevention studies including TB vaccine trials.

### PC-387-17 Implementation of a field epidemiology research protocol to screen households for tuberculosis infection and disease

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**Background:** In 2006, we were funded to conduct a prospective cohort study of 4000 households of TB patients in Lima, Peru. The aim was to examine the relative ability of drug-resistant *M. tuberculosis* strains, compared to susceptible organisms, to cause infection and disease in household contacts. These outcomes were to be measured when the TB patient initiated TB treatment and during the following 12 months. **Design/methods:** We developed and implemented the following new components: a study protocol, a manual of procedures, and a quality management plan. We also developed and tailored the following components building on baseline organizational capacity: a logistics and financial system, a laboratory referral system, and a medical informatics system.

**Results:** We recruited, hired, and trained 281 individuals as study staff to implement this protocol. Enrollment began on September 1, 2009. By March 31, 2012, the field team had screened 18 118 individuals and enrolled 16 722 (92.3%) as study subjects: 4032 TB patients and 12 699 of their household members. Among household members tested at baseline, 39.5% (4312/10 930) had a positive tuberculin skin test. Nearly 1 in 50 (1.8% [222/12 699]) had active TB. Twelve-month follow-up has been completed for 95.9% (5083/5300) of eligible participants.

**Conclusion and recommendations:** We have developed a complex research infrastructure that has successfully recruited and retained >4000 TB patients and >12 000 household contacts. The human resource and infrastructure capacity built for this study is well prepared to implement large observational or intervention protocols in the near future.

### PC-388-17 Validation of approaches to estimate recent transmission of tuberculosis in three US states, 1998–2000

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**Background:** Tuberculosis (TB) genotyping data is frequently used, when epidemiologic data is not available, to estimate the amount of recent TB transmission (RT). However, the geographic unit used for analysis of RT estimates has varied. We validated estimates of RT based on three geographic

approaches—state, county, and geospatial scan statistic (SaTScan)—by comparing them to RT confirmed by epidemiologic investigation.

**Design/methods:** Isolates from culture-positive cases of TB reported in three US states during 1998–2000 were genotyped using IS6110 RFLP; cases with <6 RFLP bands were excluded. Genotype clustering was defined as a case with an RFLP pattern matching that of  $\geq 1$  other case in the same state, county, or by SaTScan. Sensitivity and specificity were calculated by comparing these classifications to epidemiologic evidence of RT, defined as identification of a source case  $\leq 2$  years prior with a matching RFLP pattern.

**Results:** Of 1188 cases, 265 (22.3%) were part of a genotype cluster within the state, 172 (14.5%) were part of a cluster within a county, and 151 (12.7%) were part of a SaTScan cluster. The sensitivity of clustering by state, county, or SaTScan for RT was 100.0%, 80.6%, 80.6%, respectively, and the specificity was 87.3%, 93.3% and 94.8%. Of cases with epidemiologic evidence of RT but not clustered by county or SaTScan, 77.8% and 75.0%, respectively, were geographically proximate (<50 km) to the identified source case.

**Conclusion and recommendations:** Estimates of RT vary widely according to the geographic unit over which genotyping data is evaluated. While specificity is higher when a smaller geographic unit is considered, this comes with lower sensitivity. County and SaTScan-based methods miss some transmission between cases that are geographically proximate. Alternative approaches to estimating RT that maximize both sensitivity and specificity for RT are needed.

### PC-389-17 Assessing TST and QFT for tuberculosis screening among population with a high prevalence of tuberculosis

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**Background:** Approximately 1 million persons are granted permanent USA residency visas each year after screening for tuberculosis (TB). We evaluated the effectiveness of TB screening with Mantoux skin test (TST) or QuantiFERON®-TB Gold In-Tube Assay (QFT) (Cellestis, Inc) prior to the required chest radiograph (CXR) of all adult visa applicants.

**Methods:** We assessed the association of a positive TST and QFT with having a normal CXR, abnormal CXR and negative sputum culture, and culture-confirmed TB among U.S.-bound immigrant applicants from Viet Nam, a country with high TB prevalence and universal BCG vaccination at birth. From December 2008 until January 2010, applicants

were recruited in a 2:1 ratio of abnormal CXR suggestive of TB to normal CXR. The sensitivity for culture confirmed TB was compared for QFT and TST using thresholds of 5 mm (TST-5), 10 mm (TST-10), and 15 mm (TST-15). We estimated the specificity for latent TB infection by comparing the age-specific annual rate of increase in positive results.

**Results:** 1475 applicants 15 years and older were enrolled. Of these, 479 had a normal CXR, 864 were TB-CXR, and 132 had TB. The sensitivity for culture confirmed TB was 86.4% (95%CI 79.3%–91.7%) for QFT, 89.4% (82.8%–94.1%) for TST-5, 81.1% (73.3%–87.45%) for TST-10, and 52.3% (43.4%–61.0%) for TST-15. Overall, we estimated that the percent QFT positive increased 2.05% (1.29%–2.81%) per year of age compared with 0.73% (0.07%–1.40%) per year of age for TST-10. Two-step screening with QFT compared to TST-10 instead of universal CXR would have required CXR in 37% and 51% of applicants, respectively.

**Conclusions:** In this population, the sensitivity of QFT and TST-10 in detecting TB in for culture-positive TB was similar for QFT and TST-10, but fewer overall were QFT positive, and the age specific prevalence suggests this is due to greater specificity for QFT.

### PC-390-17 Risk of ever having had tuberculosis disease is associated with self-reported diabetes and lower body mass index in a transitional community in Peru

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**Background:** Diabetes is increasingly prevalent within transitional communities and is associated with active tuberculosis (TB) disease. Routine diabetes testing is recommended in TB patients. Despite this, in Peru, diabetic prevalence amongst TB patients in impoverished transitional communities remains largely unknown, the TB-diabetes association unclear and diabetes education limited. We aimed to measure self-reported diabetes in TB patients, their contacts and healthy controls and to examine effect of body mass index (BMI) and self-reported diabetes on likelihood of ever having had TB disease.

**Design/methods:** 1106 microbiologically-confirmed TB patients, 2037 household contacts, and 490 healthy controls were enrolled from the study-site, an impoverished peri-urban transitional community of

16 contiguous shantytowns on the outskirts of Lima, Peru. Volunteers were asked whether they had existing diabetes. Volunteers were defined as ever having had TB if they had previous history of TB, were a current TB patient, or developed secondary TB at follow-up. Inference for proportions of diabetes between groups and logistic regression were performed using STATA.

**Results:** Overall diabetes prevalence was 1.5%. A significantly greater number of TB patients had diabetes compared to their contacts (25/1106, 2.3% vs. 22/2010, 1.1%,  $P < 0.009$ ). 1.6% of healthy controls reported diabetes. Amongst contacts, diabetics had higher BMI (median 28.3 units vs. 24.4,  $P = 0.0009$ ). Lower BMI and self-reported of diabetes were strongly associated with ever having had TB (see Table).

**Table** Risk of ever having TB disease vs. never having TB disease with respect to diabetes and BMI

	<i>P</i> value	Odds ratio (95%CI)
Self-reported diabetes	0.002	2.6 (1.4–4.8)
Body mass index	0.000	0.8 (0.8–0.9)

**Conclusions:** Prevalence of self-reported diabetes in our cohort was low but was more common in TB patients than TB contacts. A volunteer who self-reported diabetes had 2.6 times higher odds of ever having had TB. TB control programs need to actively promote diabetes testing and may need to consider integrating TB and diabetes services in dual-affected people. In Peru and other relevant settings, larger cohort studies are required to establish the true prevalence of diabetes in transitional communities and its independent effect on acquisition of TB infection and progression to TB disease.

### PC-391-17 Probabilistic record linkage to identify individuals with multiple episodes of treatment for smear-positive tuberculosis in a high-incidence setting

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**Background:** This study was conducted in a setting with high tuberculosis (TB) incidence in South Africa. Its objective was to make use of treatment register data, in order to describe the number of subsequent episodes of treatment for smear-positive TB per individual person over a 13 year period.

**Design/methods:** Data from the 1996–2008 treatment registers of the two local TB clinics were captured in an electronic database. Registry Plus/Link-Plus probabilistic linkage software was used to determine

the number of treatment episodes for smear-positive TB per individual person. First- and surname, sex and year of birth were chosen as matching variables. Matches of treatment episodes were classified into certain, highly probable and probable matches. All matches were verified via a manual review using the original treatment registers and patient files as a reference.

**Results:** A total of 2613 independent episodes of treatment for smear-positive TB were recorded in the treatment registers 1996–2008. Record linkage and manual review resulted in a total of 442 matches of treatment episodes, 381 (86%) of which were initially certain, 23 (5%) highly probable and 38 (9%) probable matches. The number of individual persons treated in the study period was 2245, of whom 1936 (86.2%) had one, 262 (11.7%) had two, 38 (1.7%) had three, 6 (0.3%) had four and 3 (0.1%) had five subsequent episodes of treatment for smear-positive TB recorded in the study period.

**Conclusion and recommendations:** Record linkage reveals that a small proportion of TB patients experience multiple episodes of treatment for smear-positive TB. We speculate that this group of individuals may play an important role for both, transmission of TB and the evolution of drug-resistant disease in this high-incidence setting. Limitations apply to the methods of this study as record linkage may not be sensitive if individuals changed names, and it does not capture TB episodes untreated or treated outside the study area.

## MEDICAL MANAGEMENT OF TUBERCULOSIS – 3

### PC-424-17 Analysis of factors associated with delayed diagnosis of tuberculosis

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**Background:** Delay in diagnosis of pulmonary tuberculosis worsens results of treatment, increased severity, mortality and transmission. The analysis factors delaying tuberculosis diagnosis may help tuberculosis control programs to diagnose and treat patients more effectively.

**Design/methods:** Medical reports of 123 patients with pulmonary tuberculosis were analyzed. Clinical presentations, radiological, laboratory data of all patients were collected. The chances for establishment of diagnosis and influencing factors were estimated.

**Results:** Males 66% mean age  $35 \pm 13.3$  yrs. The period from the disease manifestation up to establishment of final diagnosis was  $56.7 \pm 57.3$  (mean  $\pm$  SD) days. The average patient delay was 21.6 days. 51 (41.5%) patients with pulmonary tuberculosis

nonspecific antibiotic therapy were used because of misdiagnosis and it increased the duration of the period of diagnosis. Factors associated with increase of diagnostic delay: old age (OR 0.13), dyspnea (OR 0.36), revealing of individual foci (OR 0.38) and pulmonary dissemination (OR 0.45) on chest X-ray, monocytosis (OR 0.17), lymphocytosis (OR 0.04) in the hemogram, increase of level CRP (OR 0.06). Factors, associated with decrease of diagnostic delay: an accessory of patients to city dwellers (OR 2.35), unemployed (OR 2.32), contact TB patients (OR 2.07), being in prison (OR 3.33), increase of level fibrinogen (OR 4.81), infiltrative changes in the X-ray (OR 3.26), positive culture MBT (OR 95.93).

**Conclusion and recommendations:** At suspicion on TB it is expedient to consider factors influencing on duration diagnostic period. Reducing diagnostic delay may reduce the transmission of infection in the community and to improve results of treatment.

### PC-425-17 Diagnostic delay in tuberculosis in Yemen: a cross-sectional study

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**Background:** Diagnostic delay is an important indicator of access to tuberculosis (TB) diagnosis and treatment. Analyses of patient delay and health care system delay can aid in modifying policies to improve access to treatment. Delay in diagnosis of new smear-positive pulmonary TB patients, and the risk factors for delay were evaluated in this study.

**Methods:** A cross-sectional study of newly diagnosed TB patients, was conducted in referral tuberculosis center, Sana'a, Yemen. A total of 505 new TB patients were interviewed on the same day of diagnosis using a questionnaire. The study period was from 2008 to 2010. The  $\chi^2$  and Fisher's exact tests were used to compare differences in proportions in total delay between subgroups. Uni-variate and multi-variate logistic regression analyses were conducted to identify risk factors associated with long delay.

**Results:** The significant risk factors ( $P < 0.05$ ) for long total delay were male, old age ( $>60$  years), employment status, a pharmacy as the first place visited by TB patients, improper treatment with antibiotics, number of visits to a health care unit, and cauterization as traditional treatment. The significant risk factors for long patient delay were old age ( $>60$  years), improper treatment with antibiotics, the pharmacy as the first place visited by TB patients, economic status, absence of husband, and transportation difficulties. Then, the significant risk factors for long health care delay were improper treatment with antibiotics, number of visits to a health care unit, and high level of TB bacilli in smears of the TB patient.

**Conclusions and recommendations:** Patient and health care system-related factors contribute significantly to delays of TB diagnosis. The findings revealed the importance of health education for patients and health care providers. Collaborative effort should be made to assist in early recognize and diagnose for the symptomatic TB patients.

#### PC-426-17 Treatment outcomes in a cohort of new cases of pediatric tuberculosis in Lima, Peru

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**Background:** Since 1991 Peru has administered pediatric TB treatment per a fully supervised, two-phase 2RHZE/4R2H2 regimen. 1st phase dosage (RMP: 10 mg/kg, INH: 5 mg/kg, PZA: 25 mg/kg, EMB: 20 mg/kg) is taken 6 days per week, while 2nd phase dosage (RMP: 10 mg/kg, INH: 15 mg/kg) is taken twice per week. The WHO has recently recommended new dosages for anti-TB drugs in children, but treatment outcomes under the present regimen are not well documented.

**Objective:** Determine regimen efficacy and program efficiency in pediatric pulmonary TB treated through the TB program in central Lima, Peru.

**Methods:** Retrospective cohort study of treatment outcomes in new, smear ( $\geq 1+$ ) or culture ( $\geq 10$  colonies) positive, pulmonary TB cases. Pediatric cases under age 15 were consecutively recruited from patients treated between 2005 and 2008 in 44 primary health centers (HC) in Lima Ciudad. Data were collected from TB program treatment registries and an existing electronic TB record system. Cure was defined as success or treatment completion, failure was any positive culture after the fourth month of treatment, and default was at least one month of treatment interruption.

**Results:** Efficacy: 95.2%, efficiency: 83.2%. 10 patients were excluded; 7 did not have registered outcomes and 3 transferred to different regimens. All failures and the death were either in direct contact with an MDR-TB index case or received care at high-MDR-burden HCs. When the highest-MDR-burden HC is excluded, efficacy and efficiency increase to 98.6% and 89.0%, respectively.

**Table** Treatment outcomes in new cases of pediatric TB in central Lima, Peru

Total	Included	Cure	Failure	Died	Default	Transfer
105	95	79	4	1	6	5
	100%	83.2%	4.2%	1.1%	6.3%	5.3%

**Conclusion:** Decreased regimen efficacy was likely due to undetected primary MDR-TB. Default and

transfer accounted for 11.6% of lost efficiency. Accordingly, treatment efficacy is unlikely to improve by changing the dosage. Our data add to growing evidence that currently defined MDR-TB risk factors are insufficient to detect MDR-TB in high-burden zones of Lima and that DST should be expanded.

**Acknowledgement:** Thanks to all Lima Ciudad TB program personnel.

#### PC-427-17 Treatment of drug-resistant tuberculosis in Azerbaijan

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**Background:** Treatment of drug-resistant tuberculosis (DR-TB) patients in the civilian sector has been started since 08/2008 with financial support of the GFATM. The project was implemented by MOH. Treatment of the 1st and 2nd cohorts of DR-TB patients (26 and 79 patients) started in 08/2008 and 12/2010, respectively. It should be noticed that more severe patients were involved to the 1st 2 cohort treatment. Patients received intensive phase treatment in the department of the TBD #4 and ambulatory phase was continued at home. All patients were provided with social support within the framework of the project. Out-patient treatment was carried out in the DOT points. It should be noticed that the DOT + points have been established within the project for the first time in the composition of PHC services. For lab investigations there have been used L-J method and Bactek-960.

**Purpose:** Analysis of the first 2 cohort MDR-TB patients enrolled to treatment with 2nd line drugs in Azerbaijan.

**Materials and Methods:** With this purpose there have been used data base (R8R) of the SRILD, the laboratory results of the NRL.

**Findings:** According to gender 81 patients (77%) were males and 24 (33%) are females. % of patients between the ages of 15 and 24 were 19% (20 patients), percentage of patients more than 45 year were 23% (24). More illness is identified between the ages of 25 and 44 (58%). 31 (29, 5%) patients out of 105 were diagnosed infiltrative TB with destruction phase (4 out of them have 2 side process), 2 (2%) patients have cavernous TB, 72 (68, 6%) patients have fibrous-cavernous TB (19 out of them have 2 side process), and 1 patient have focal TB.

**Treatment outcome:** 5 (4.8%) patients are continuing their treatment, 55 (52.4%) patients completed treatment, 21 (20%) patients died, 2(1.9%) patients refused treatment, 22 (20.9%) patients' failed treatment.

**Conclusion:** Two-thirds (77%) of patients were men, patients' ages mainly were 25-44. All patients were

retreated. FK TB (68.6%) is dominant forms of TB. All of the 1st line anti-tuberculosis drugs, and NAA, PTH and Oflo from the 2nd line TB drugs have the highest resistance. High level of XDR-TB (37%) and existence, even total DR draw attention to the problem and is a reason to worry and require strengthening of epidemiological surveillance in the country.

#### PC-428-17 Delay from diagnosis to treatment among tuberculosis patients in Burundi

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**Background and challenges to implementation:** Burundi is an enclosed country in central Africa and characterized by a high relief with difficult access to health facilities. Access is specifically tough for tuberculosis case finding and treatment supervision.

**Intervention or response:** A socio-anthropological survey has been led in Burundi in 2011 to show perceptions, attitudes and practices about tuberculosis. Data had been collected among a sample of 2024 people from general population and TB patients.

**Results and lessons learnt:** Time spent between apparition of first symptoms of tuberculosis and care seeking in a health facility is lower or equal to one month for 64.96% of TB patients and 35.4% from 2 to more than 5 months after the apparition of the first symptoms. Among TB patients who had been asked to give sputum for an exam, 20.3% achieved it the same day, 18.4% 2 days later, 11.4% 3 days later and about 26.6% achieved the exam between 3 and 7 days later. 17.7% patients achieved their sputum exam one week after consultation but 5.7% of the patients didn't achieve it at all. About returning sputum results from laboratory, 46.8% of patients re-

ceived their results the same day, 19.0% one day after giving sputum, 10.8% 2 days after giving sputum and 4.4% beyond 3 days. The indirect expenses bound up to TB diagnosis vary between 3600 and 9000 burundese francs (Fbu) (US\$2.48–6.20) for 78.4% of the patients.

**Conclusions and key recommendations:** The time between the first symptoms and care seems to be long in Burundi, 50.1% of TB patients are achieving the sputum exam from one day to 3 days. Fortunately, 80.% of patient receive their results in less than 3 days. Delay in the diagnosis of tuberculosis in Burundi seems to be affected by patient's care seeking behaviors.

#### PC-429-17 Health-seeking behaviour among people with cough of two weeks or more in India

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**Background:** In India (a high TB burden country), for promoting early diagnosis of pulmonary TB (PTB), efforts are being made through multiple strategies to raise awareness in the population, that cough of  $\geq 2$  weeks is a symptom of PTB and they should seek appropriate health care. A large Global Fund Project is being implemented since 2010 in 374 out of the 650 districts to supplement and support the National TB Programme (NTP) in raising this awareness.

**Objectives:** A baseline survey was conducted to assess the present level of awareness among the general population on the various aspects of TB (cause, symptoms, diagnosis, treatment, curability, about NTP's services). As a part of this survey, people were asked whether they had cough of two weeks or more in the past 2 months and assessed whether they have sought care from any health provider.

**Methodology:** 4562 people were interviewed by trained field investigators using a semi-structured questionnaire from 30 Global Fund Project Districts. The selection of districts and individuals within the districts was done by multistage cluster random sampling methodology.

**Results:** 437 (10%) informed that they had cough of  $\geq 2$  weeks in the past 2 months prior to the survey. The proportion of people who had cough was 8% in the south and west zones, 11% in the north zone and 12% in the east zone of the country. Overall, 131 (31%) of the people who had cough had visited a health care provider for their symptom. The proportion of people who had visited a health care provider was highest in the south zone (55%), when compared to the west (41%), north (25%) and east (17%) zones.

**Table** Delay from the diagnosis to treatment among TB patients in Burundi

Indicators	%
Delay from first symptoms to care seeking ( <i>n</i> = 158)	
Less than a month	43.7
One month	20.9
2 months	13.9
From 3 to 5 months	18.3
More than 5 months	3.2
Delay in giving sputum to laboratory ( <i>n</i> = 158)	
The same day	20.3
From 1 to 3 days later	29.8
From 3 to 7 days later	26.6
More than 7 days	23.3
Delay in returning laboratory results ( <i>n</i> = 149)	
The same day	43.0
From 1 to 3 days later	18.8
From 3 to 5 days later	35.6
More than 5 days	2.6
Delay from results to TB treatment ( <i>n</i> = 158)	
The same day	46.8
From 1 to 3 days later	48.8
More than 3 days	4.4

**Conclusions:** This survey showed that large number of people in the community suffered from cough of  $\geq 2$  weeks. Very few of them had visited any health care providers. This has huge implications for early diagnosis of TB and highlights the need for mobilising the community to seek appropriate care and enhancing the reach of TB diagnostic services.

### PC-430-17 Improving quality of infection control at Engels Tuberculosis Dispensary, Saratov Oblast, Russia

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**Background and challenges to implementation:** Engels TB Dispensary covers Engels and 11 nearby regions. TB nosocomial infection is a big concern for the medical community, as the incidence of TB in medical staff in 2010–2011 was 3 people out of 100.

**Intervention or response:** In November 2011, we trained the deputy chief physician in IC and established an in-facility QI team, consisting of administrative, lab staff, chief nurse and engineer, to analyse the current IC system, identify barriers, and design an IC program for the dispensary.

**Results and lessons learnt:** The QI team designed

**Table** Changes made by the QI team in Engels TB Dispensary, Saratov Oblast, Russia, to address administrative, environmental and respiratory infection control

Type of IC control	Changes proposed	Micro-indicators
Administrative control	Develop infection control (IC) Prikaz <sup>1</sup> on delimitation of authority regarding in-facility IC control; Develop job category-specific instructions on IC policies for each staff member including lay workers; Train personnel in accordance with their job category-specific instructions; Separate patients into different rooms according to their smear status; Separate the flow of patients at Rn-office according to their smear status;	IC Prikaz issued;  Job category-specific instructions developed;  # of personnel trained;  Rooms for SS- and SS+ patients are created;  Flow of patients is separated according to their smear status;
Environmental control	Analyze possible ways to separate bacteriological lab into high and low risk zones; Check installation of ultraviolet (UV) lamps and biosafety cabinet class II in accordance with IC standards; Check lab mechanic ventilation with the smoke tube;	Bacteriological lab is divided into high and low risk zones;  UV lamps and biosafety cabinet class II are checked and reinstalled according to IC standards (if needed);  Lab mechanic ventilation is checked and fixed if needed;
Respiratory control	Allocate funds to purchase the needed amount of respirators; Train personnel working at high risk zones to fit-test respirators and use them daily.	# of personnel provided with respirators;  # of personnel trained.

<sup>1</sup> Prikaz is an administrative order issued by oblast health authorities detailing a practice or procedure that should be implemented by providers in the oblast health system.

changes addressing administrative, environmental and respiratory IC measures (see Table). Each dispensary staff member received job-specific IC instructions and was trained to fit-test respirators. Patients with SS+ and SS- were separated in rooms and at X-ray. Bacteriological lab was divided into high- and low-risk zones by constructing a barrier wall and adjusting mechanic ventilation. Ultraviolet (UV) lamps were placed at high-risk lab zone and at MDR department. Incorrect installation of biosafety cabin class II was identified and fixed. From November 2011 through March 2012, TB incidence rate among medical staff was 0 people out of 100, microbiological tests of wipe sampling were negative (in 2010–2011 there were 5 positive results/1000 samples weekly).

**Conclusions and key recommendations:** Remarkable improvements in IC control can be achieved through minimum material investments by means of active staff involvement into the process of identifying and implementing local changes in work processes.

### PC-431-17 Development of a model of community DOTS in Pyinmana Township, Myanmar

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**Background:** National TB prevalence survey conducted in 2009 revealed that the prevalence of TB is more than WHO expected. Therefore, NTP needs to strengthen all measures of case finding. In July 2011, NTP decided to introduce community DOTS in order not only to treat but also to find more TB cases in the communities. The most distinctive feature of this community DOTS is no monetary incentives for the community health volunteers (CHVs) even though some INGOs already working on community DOTS in Myanmar provide high monetary support.

**Objective:** To identify facilitating and hindering factors at the initial phase of development of community DOTS.

**Method:** NTP gave advocacy and training in accordance with the guideline for referral of TB suspects, health education and provision of DOT. Total (29) CHVs (10 from rural, 19 from urban) were trained. Monthly evaluation meeting, supervisory visits were regularly conducted.

**Results:** During the first (7) months, (21) TB suspects were referred while health education was given to the total of 838 people in their community. Out of 21, 12 (57%) were confirmed as TB cases and provided DOT. Only one patient was found out of (77) TB suspects by doing contact tracing. During evaluation meeting, we found that activities of CHWs are limited because sputum transport charges from their villages

to township were needed. Selection criteria for the volunteer are crucial to present the drop out and yield of TB cases.

**Conclusion and recommendation:** Technical support by the NTP staff facilitates CHVs activities in the initial stage of community DOTS. Some CHVs face the challenges to gain the trust of TB patients and the communities. Selection of the CHVs is vital role in successful community DOTS.

### PC-432-17 The timing of nucleic acid amplification tests considering cost and effect on the diagnosis of tuberculosis in a chest hospital

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**Background:** Within the guidelines for nucleic acid amplification tests (NAAT; PCR-based rapid identification) of *Mycobacterium tuberculosis* (MTB), each TB control or treatment program should evaluate the overall costs and benefits. Thus, we investigated the value of NAAT in addition to experts' opinions.

**Design/methods:** Our physicians made decisions to do NAATs if the diagnoses were not sure before or after anti-TB treatment. A questionnaire was designed for our physicians to fill in while the NAATs were arranged. Data from these cases were collected if NAATs were done from April to June in 2009.

**Results:** The positive predictive value by the physicians was 50.0% before the suspected patients were treated as TB (under the prevalence of 16.4%). With the assistance of NAAT, the PPV was 91.7% and the NNT was 2.4, (i.e., to increase PPV by NAAT in addition to acid-fast smear and physician's judgment).

	Sensitivity	Specificity	PPV	NPV
<b>Before Rx</b>				
Doctor	8/11 72.7 (39.0-94.0)	48/56 85.7 (73.8-93.5)	8/16 50.0 (24.7-75.3)	48/51 94.1 (83.8-98.8)
NAAT	11/11 100.0 (71.5-100.0)	55/56 98.2 (90.4-100.0)	11/12 91.7 (61.5-99.8)	55/55 100.0 (93.5-100.0)
p-value	0.21	0.03	0.04	0.11
<b>Initial phase</b>				
Doctor	38/39 97.4 (85.5-99.9)	1/5 20.0 (0.5-71.6)	38/42 90.5 (77.4-97.3)	1/2 50.0 (1.3-98.7)
NAAT	38/39 97.4 (85.5-99.9)	5/5 100.0 (47.8-100.0)	38/38 100.0 (90.7-100.0)	5/5 83.3 (35.9-99.6)
p-value	1.00	0.05	0.12	0.46
<b>Cont. phase</b>				
Doctor	6/9 66.7 (29.9-92.5)	3/9 33.3 (7.5-70.1)	6/12 50.0 (21.1-78.9)	3/6 50.0 (11.8-88.2)
NAAT	9/9 100.0 (66.4-100.0)	9/9 100.0 (66.4-100.0)	9/9 100.0 (66.4-100.0)	9/9 100.0 (66.4-100.0)
p-value	0.21	0.01	0.02	0.04

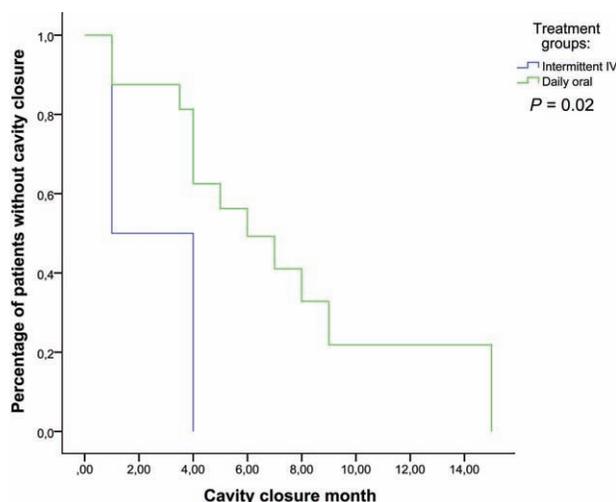
**Conclusion and recommendations:** In this condition, NAAT are of great value to assist diagnoses, rule out the possibility of non-tuberculous mycobacteria (NTM) and avoid unnecessary use of public resources in this setting. There are still limitations in our study. This is not a clinical trial. NAAT was not applied to all specimens. Recently, routine NAATs were applied to all first specimens of our patients once culture media (MGIT) showed positive. The average prevalence of TB was 35.7% (p.s. by different commercial kits). Thus, the NNT may be adjusted under this prevalence.

### PC-433-17 Intermittent intravenous chemotherapy in new cases of pulmonary tuberculosis

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**The purpose:** To compare the efficacy and tolerability of intermittent intravenous and daily traditional treatment in patients with new cases of pulmonary tuberculosis.

**Methods:** We have conducted a randomized comparative prospective study of daily per os vs. intravenous intermittent chemotherapy for 74 new cases TB with smear positivity (MBT+). We have randomized those patients into 2 groups: Group #1—23 people—received standard chemotherapy every day; Group #2—51 people—received intravenously two times a week isoniazid 12 mg/kg, rifampicin 7.5–10 mg/kg, intramuscular streptomycin 16 mg/kg, per os pyrazinamide 25 mg/kg. Groups were identical sex, age, and form of disease. There were 5 patients in the first group and 9 patients in the second with MDR-TB. **Results:** Cavity closed in 18 patients of the group #1 and 45 of the group #2 ( $P < 0.05$ ), sputum negativation occurred in 20 and 45 ( $P > 0.05$ ) correspondingly. Toxic reactions occurred in 16 and 4 patients accordingly (RR = 8.9, 95%CI 6.9–10.8;  $P = 0.000001$ ). It was found that at patients with toxic reactions to chemotherapy at the group #1 cavity closed in  $7.3 \pm 1.3$  months, and in the group #2 at  $2.5 \pm 0.9$  months ( $P = 0.02$ , log-rank test Mantel-Cox).



**Figure** Probability of cavity closure in TB treated patients with toxic reactions.

**Conclusions:** The intermittent intravenous chemotherapy for new patients with pulmonary tuberculosis is effective and preventive with occurrence of toxic reactions in comparison with a daily treatment per os: toxic reactions in group of TB patients with the daily per os treatment were worse than in group of patients on intermittent intravenous treatment.

### PC-434-17 Multidisciplinary interventions for successful TB-HIV integration in 178 South African health facilities

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**Background:** South Africa ranks 3rd in the highest TB burden countries worldwide, with a high mortality especially in people living with HIV. The Presidential Emergency Plan for AIDS Relief funded component of the USA Agency for International Development TB project run by University Research Corporation identified and followed up facilities with integration challenges over the October 2009 to September 2011 period. We evaluated performance progression of the 178 clinics identified since 2009.

**Intervention:** The 178 facilities from 6 South African provinces were visited twice a month and joint quality improvement interventions conducted. A baseline assessment revealed facility staff and management weak knowledge on TB-HIV integration, complex patients' flow between TB and HIV services, lack of job aids and community and patients' awareness. Interventions ranged from TB-HIV collaborative trainings, support to HIV counseling and testing (HCT) integration within TB services, simplification of patients' flow, integration of HIV indicators in TB register, development of tools for isoniazid preventive therapy, patients leaflets, community dialogues on TB-HIV, to districts support in regular supervision and feedback for action TB-HIV meetings. TB-HIV facilities data were entered into Excel format

**Results:** Data analysis showed a 26% and 7% increase in the TB screening and TB treatment initiation rates, 51 fold increase in IPT uptake in HIV patients, 30% and 25% increase in HCT and cotrimoxazole uptake rates in TB patients (all rates currently hovering over 90%); the antiretroviral uptake rate shows a slower increase and we are conducting root cause analysis in the cadre of the new PEPFAR realignment.

**Conclusion:** TB-HIV integration has exhibited noticeable achievement at management levels; translation into quality performance at facility levels has been facilitated by high level collaboration with provinces districts sites and community.

### PC-435-17 Stubborn tuberculosis knowledge and skills gaps among health care providers in Kenya: how can the ever-escalating training needs be addressed?

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**Setting:** Kenya is a low income country with a high TB disease burden that is fuelled primarily by poverty and HIV.

**Background:** To effectively provide TB care and control services, an adequate health care workforce that has appropriate knowledge and skills of the disease is imperative. Many NTPs invest heavily in training programs. It is important that training programs focuses more on the needs of the health care workers in the delivery of health care services.

**Objective:** To identify knowledge, attitudes and practices of health care workers both in the public and private sectors in order to identify knowledge and practice gaps that need to be tackled in training and technical support programmes.

**Methods:** This was a cross sectional survey that was carried out in Kenya in 2011 targeting all health care providers in both public and private health facilities. A total of 299 health facilities were randomly selected from all health facilities in the country and 1146 health care workers was enrolled into the study. All health care workers working in the sampled facilities who consented were interviewed using a structured questionnaire by research assistants.

**Results:** A total of 1146 health care workers were recruited into the survey. The distribution was as follows: 220 (19%) were medical doctors, 205 (17.4%) were medical assistants, 483 (42.2%) were nurses and 198 (17%) were other health care providers. Knowledge gaps were common with 54% of respondents choosing a diagnostic approaches not recommended by the NTP, 83% unaware of newer molecular tests for the diagnosis of drug susceptible and drug resistant TB, 32% selecting the recommended drug regimen for new previously untreated patients and 35% indicating that they had no knowledge of the drug regimens recommended for the treatment of MDR-TB. The knowledge gap were common across all cadres of health care workers.

**Conclusion:** Despite massive investments in training programmes for health care workers in clinical services, knowledge gaps still persist. New ways of training health care workers need to be developed and implemented to address this challenge. There is urgent need to revise the training methods and curriculum in training institutions to capture modern knowledge and practises.

### PC-436-17 A partnership to reduce the rate of pulmonary tuberculosis cases initiated on treatment without smear microscopy, Motheo District, South Africa

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**Background:** South Africa has the third highest TB incidence worldwide. Despite national improvements in TB control, the bacteriological coverage (BC) remains under 90% in some areas. In the Free State, Motheo, a district supported by the USA Agency for International Development (USAID) TB project run by University Research Corporation (URC) had a 68.8% BC (40.9% of new PTB cases being initiated without microscopic confirmation). We conducted interventions to identify, conduct root cause analysis and support a corrective action plan addressing this finding, in close collaboration with the district and facilities staff.

**Intervention:** In 2011, jointly with district, we identified 4 high caseload facilities initiating TB treatment without microscopic confirmation. A root cause analysis was conducted with facility staff and management; a critical analysis identified the nurses' reluctance to collect sputum after down referral viewed as additional workload, and poor recording of microscopy results. After sharing the assessment results, a partnership was established with district, sub district TB coordinators and facilities, established and trained TB focal points at the hospital, capacitated and involved medical wards supervisors on TB control performance, trained the 3 other facilities nurses on TB management and sensitized operational managers on the importance of pretreatment smear microscopy, followed by monthly facility visits and review of TB case findings data jointly for the development of challenge-based improvement plan.

**Results:** Over 2011 the rate of lack of pretreatment microscopic confirmation for new pulmonary TB cases decreased (National Hospital from 60.4% to 18.0%; Heidedal HC from 24.3% to 14.2%, Kagisanong from 14.5% to 1.4% and Bloemspruit from 20.0% to 12.6%).

**Conclusion:** Partnering with district and facility staff in quality improvement plans is a key to TB control.

### PC-437-17 User interaction with an interactive two-way SMS medication reminder system for tuberculosis patients

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**Background:** The treatment for tuberculosis is long with uncomfortable side-effects. Some patients fail to complete their full course of treatment and increase their risk of developing and transmitting drug-resistant TB. We measured TB patients' user interaction with Zindagi SMS, an interactive SMS medication reminder system in Karachi, Pakistan to understand the proportion of patients who will respond to the system and the characteristics associated with higher response rates.

**Methods:** We analyzed response rate data of participants in an ongoing randomized control trial measuring the impact of Zindagi SMS on drug compliance and treatment outcomes of patients with drug susceptible tuberculosis. Zindagi SMS is an interactive system that sends daily SMS reminders to patients on treatment and requires them to respond back after taking their medication, either through SMS or a missed (unbilled) call. Patients that do not respond are sent up to three reminders a day; those non-responsive for seven days are followed up over the phone.

**Results:** We analyzed response rates of 115 patients during their first 180 days of treatment. Patients had an average response rate of 39% over this period. 95% of patients responded at least once to the system. Response rates were higher amongst those who were literate (47% vs. 29%,  $P < 0.01$ ), those that reported having someone reminding them to take their medication (49% vs. 30%,  $P < 0.01$ ), and those who reported knowing how to send SMS at the time of enrollment (53% vs. 28%,  $P < 0.01$ ). While response rates were not significantly different for those who

**Table** Characteristics associated with response rates to the Zindagi SMS medication reminder system for TB patients

Patient characteristics	Response rate		
	% (SD)	95%CI	Pr( T  >  t )
Total (N = 115)	39 (34)		
Gender			0.16
Male (n = 60)	34 (30)	27-42	
Female (n = 55)	43 (37)	33-53	
Literacy			0.00
Can read (n = 63)	47 (32)	39-55	
Cannot read (n = 52)	29 (34)	19-38	
Reminder support			0.00
Patient reminded by someone (n = 52)	49 (33)	39-58	
Patient did not have someone to remind (n = 63)	30 (32)	22-38	
SMS familiarity			0.00
Can send SMS (47)	53 (33)	44-63	
Cannot send SMS (68)	28 (31)	21-36	
Mobile ownership			0.11
Mobile owned by patient (n = 54)	44 (33)	35-53	
Mobile not owned by patient (n = 61)	34 (34)	25-43	
Mobile ownership for males			0.00
Males who own mobile (n = 37)	41 (30)	31-51	
Males who do not own mobile (n = 23)	15 (18)	7-23	

owned a mobile phone versus those who did not, they were significantly higher amongst males who owned a mobile phones than those who did not (41% vs. 15%,  $P < 0.01$ ).

**Conclusion:** This data suggests that a two-way SMS reminder system is feasible for TB patients in low-literacy environments such as Pakistan. Most patients will, at some point, respond rather than ignoring the messages.

#### **PC-438-17 Community-based organisations as key players in tuberculosis control: a success story from uThungulu District, South Africa**

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**Background:** South Africa ranks third of the high TB burdened countries worldwide. The USAID for International Development (USAID) TB project run by the University Research Corporation provide technical assistance to national Department of Health and National TB Program at all levels of management. To increase the demand for TB services the project run a small grants program aimed at local CBOs working in community TB activities. Monitoring and evaluation of community activities have often been undermined leading to a limited knowledge of their impact on TB control.

**Intervention:** In 2011, 2 CBOs were selected as beneficiaries of the project small grants program in uThungulu District. A basic TB management training, and mentoring on the national TB signs and symptoms tool were conducted. As a result the 2 CBOs expanded their activities of TB awareness to screening household members through door to door interventions as well as to collecting and sending sputum for microscopy or referring symptomatic patients to nearby facilities.

**Results:** Each CBO member saw an average of 3 households per day between August 2011 and March 2012; 515 households were visited and 4945 individuals were screened for TB allowing the identification of 559 TB suspects; sputum were collected from 327 people, while 232 were referred to clinics. To date, 18 clients were confirmed with TB and started on treatment and 269 TB contacts were further identified and screened for TB.

**Conclusion:** This intervention shows that capacitated CBOs activities can be critical in controlling TB; their role should be emphasized and acknowledged by integrating them into the health system.

#### **STOP TB STRATEGY PUBLIC-PRIVATE MIX-2**

##### **PC-462-17 Completeness of tuberculosis case registrations: evaluation of a surveillance information system, São Paulo State, Brazil (2006–2010)**

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**Background:** For TB control, an accurate patients recording means better information to plan control programs. This study aimed to determine data completeness of TB registration in a state surveillance information system.

**Methods:** We considered data of all new cases of TB notified under the public health surveillance system of the 645 cities of São Paulo (SP) State, Brazil, from 2006 to 2010. The surveillance system—*TBWeb*— is an online system implemented throughout SP in 2006. Completeness indices were calculated according to the percentage of non-completed data and evaluated as excellent (less than 5%), good (5–10%), fair (10–20%), poor (20–50%) and very bad (50% or more). Variables were classified as mandatory or essential. *CDC Updated Guidelines for Evaluating Public Health Surveillance Systems* were used as the methodological framework.

**Results:** The dataset comprised 81 143 patient records. Mandatory variables completeness was evaluated as excellent for age, sex, disease form, case type and sputum smear testing—only DOT record was considered as poor. However, an increase in recording of DOT indication was observed: from 62.8% of completed data in 2006 to 90.2% in 2010. The majority of essential variables was also determined as excellent (HIV testing, information of other diseases) or has shown an increase of completeness (schooling, race, number of contacts). Records of the attainment of treatment supervision have also improved, but are still poor (from 35.3% of completed data in 2006 to 63.2% in 2010). Completeness of health service responsible for DOT and patient employment status has shown decrease, being evaluated as very bad and poor, respectively.

**Conclusion:** This study has demonstrated satisfactory recording information in São Paulo and an effort to increase completeness of essential data regarding cases characteristics and management. An evaluation of data consistency is also recommended in order to evaluate the surveillance system.

### PC-463-17 Urban DOTS contribution to treatment outcomes of new sputum smear-positive tuberculosis cases in Kabul City, 2008–2011

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**Background and challenges:** Kabul with around 5 million population and poor health infrastructure was in critical situations especially for TB service delivery. Treatment success rate for new TB SS+ cases was very low (46%) with high transfer out rate. In 2009, Urban DOTS model program introduced by support of USAID/TB CAP to engage public-private sectors in DOTS implementation, referral system, patient follow up, training of staff and timely supervision. Moreover, supply of TB drug, lab reagent and community events conduction. We assessed impact of Urban DOTS approach on treatment outcome of new SS+ TB patients.

**Intervention:** TB data from 2008 to 2011 from 56 health facilities were collected and a technical team from NTP/TB CARE I compared treatment outcome of 2011 with 2008–2009 and 2010.

**Results:** In 2008, the treatment success rate for new TB SS+ cases were 46%, transfer out rate was 47%. In 2009, treatment success rate dropped to 44% and transfer out rate to 46%. In 2010, following urban DOTS implementation treatment success rate for new TB SS+ cases increased to 62% (18% improvement), transfer out rate declined to 26%. In 2011 (1st quarter), treatment success rate ascended to 70% and transfer out decreased to 23%. There are no big differences in death, failure and defaulter rates between 2008, 2009, 2010 and 2011.

**Table** Treatment outcome of new sputum smear positive cases trend by Urban DOTS, 2008–2011

Year	2008 (n = 875) n (%)	2009 (n = 871) n (%)	2010 (n = 1022) n (%)	2011 (1stQ) (n = 240) n (%)
New TB SS+ success rate	410 (46)	383 (44)	642 (62)	170 (70)
New TB SS+ transferred out rate	397 (46)	387 (46)	270 (26)	55 (23)
Death rate	17 (2)	18 (2)	22 (3)	2 (1)
Failure rate	23 (3)	41 (4)	31 (5)	3 (2)
Defaulter rate	28 (4)	42 (4)	57 (4)	10 (4)

**Conclusions:** Based on data analysis, Urban DOTS contributed significantly in improving treatment outcome for new sputum smear positive TB patients. Thus, we strongly recommend the expansion and application of this model to similar settings.

### PC-464-17 Driving sustainability through involvement of corporate sector in handling tuberculosis in uncovered areas

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**Background:** Most of the people working in private and corporate sectors might not get time and permission to attend to the health needs at government facilities though they will be provided with in-house medical aid which at times might not be on par with national programs thus not providing the quality services to the staff and their families. The corporate sector can be easily roped into becoming satellite centres for Public Health Programs like RNTCP (Revised National Tuberculosis Control Program) through sensitization, awareness and perseverance.

**Intervention:** Through Project AXSHYA, Catholic Health Association of India (CHAI) in collaboration with The Union (International Union Against Tuberculosis and Lung Disease) has organized a sensitization workshop at Suzlon Energy Ltd. Satara on 17th Dec 2011. Suzlon Energy Ltd. is a multinational energy production company with more than 500 wind mills in Satara District of Maharashtra. By shared contribution from Suzlon to the project initiative a workshop was conducted for the benefit of the staff, their family members and residents from the surrounding villages on tuberculosis (TB), RNTCP and the way forward in mutual partnership for TB Care and Control.

**Results:** A total of 80 participants including the staff, their families and the villagers attended the workshop. The RNTCP provided technical guidance. There was also a participation of 45 SHG (self-help group) members representing SHGs from the surrounding 6 villages. This activity led into clear understanding of the need of involvement of Suzlon in TB Care and Control for the staff's benefit which indirectly results in increased production for the company. This resulted in a DOTS centre, sputum collection centre within the premises.

**Conclusion:** Increased awareness and understanding the need of the TB Care and Control among corporate sector can result in public private collaboration which can be the way for sustainable response against TB with local responsibility.

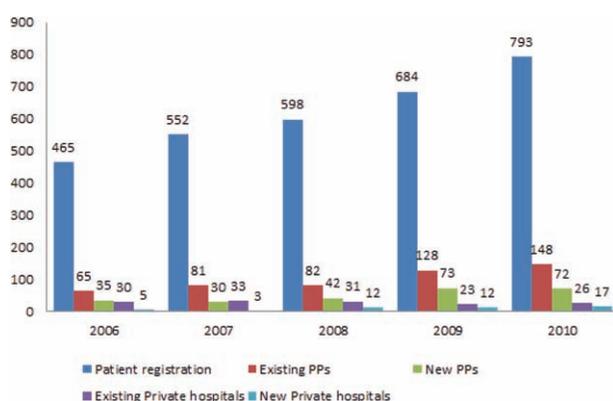
### PC-465-17 Sustaining involvement of private practitioners in public-private mix initiative in Chennai, India

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**Background:** Public Private Mix (PPM) Partnerships have been recognized as very crucial in TB control. While studies have demonstrated the feasibility of setting up a PPM for TB control, it is always considered that much effort and investment is needed in sustaining these models. We would like to report our experiences in involvement of private practitioners (PPs) in PPM initiative in a sustained manner.

**Intervention:** A PPM initiative was started (1999) in Chennai (about 6 million population), India, between the urban government TB control program and the private healthcare providers with an NGO (Non-Government Organization) acting as an intermediary, that encouraged PPs to participate in the TB control program while allowing them to retain their patients. In phase 1 (2003–2006) there had been an intense and focused sensitization for PPs through workshops and one to one approach, followed by provision of support services only (phase 2006–2008). In phase 3 (2008–2011), we only conducted yearly programs (updates on TB) for PPs along with provision of support services.

**Results:** About 5939 patients had been registered through PPM initiative over 12 years period. Subsequent to the intense campaign, TB patients registered through the PPM after 2006 were provided by steadily increasing number of PPs (65 to 148) in the existing network along with newly joined PPs (35 to 72). After 2006, both these groups had not received focused sensitization (Figure).



**Figure** Participation of PPs and private hospitals in PPM.

**Conclusion:** The present finding has highlighted the sustained involvement of PPs in PPM initiative subsequent to the period of focussed and intense sensitization of PPs along with new PPs joining the initiative. While the earlier finding could be due to the spillover effect of sensitization, the latter finding could probably be due to peer to peer communication between providers. This adds impetus to the fact that the PPM initiative has sustained and strengthened in a cost effective manner.

### PC-466-17 Medical association as a manager of public-private mix in the RNTCP, India

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**Background and challenges to implementation:** Even though it is accepted in general that private sector doctors do contribute to the national TB control program (RNTCP), absence of an effective mechanism to quantify the contribution and give proper feedback to the practitioners is still a challenge. Role of Indian Medical Association (IMA)—the largest association of doctors as an intermediary not only in facilitating the partnership but as a step above in managing the partnership—is gaining attention these days.

**Intervention or response:** To address the issue of quantifying contribution, IMA has devised a specially designed sputum referral and feedback form, by which the practitioner can refer for sputum test, and the DMC lab technician can easily identify (peculiar color) it as referred by a private doctor. Once a request is identified, when the information is recorded in lab register care is taken to note the name of the referring physician so that they can be intimated the result of the test promptly. This is being piloted in many states including Kerala (three districts). At the end of the month when the data is compiled, care is taken to segregate the data related to referral from private doctors and do the analysis. The recently introduced lab technician scheme by IMA in Kerala using support from RNTCP had added human resources at the sub-district level to do line-listing and mapping of private doctors in his/her assigned area, to contact them at least once in a week to update the results, remind follow up sputum test of patients etc.

**Results and lessons learnt:** In Kerala, private practitioners are using the sputum referral form regularly and the lab technicians are recording the information in registers as well.

**Conclusions and key recommendations:** IMA can play the role of managing the PPM component in RNTCP by effectively coordinating the private and public sector, by training private doctors, and above all as advocates for standards of TB care for the medical fraternity.

### PC-467-17 Role of informal health care providers in tuberculosis control in selected township, Myanmar

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A cross-sectional descriptive study was conducted in Bago Township, Bago Region of Myanmar, to explore the role of voluntary health workers (VHWs) and untrained health care providers in TB management and

control. It determined how this part of the private sector diagnose and treat TB, and how they collaborate with the formal health sector. A total of 137 participants were involved in quantitative survey, which included 24 quacks. In-depth interviews were conducted with 14 quacks. About 75% of quacks and 15% of volunteers are practicing private health care for their main earning. About 87% believed TB is a major health problem in their region. Majority of the respondents had correct knowledge regarding TB transmission but there are still misconceptions. Chronic cough (73%), fever (62.8%), weight loss (52.6%) are the most mentioned symptoms. Low knowledge on TB treatment was found. According to qualitative findings, quacks are giving TB treatment to some extent in rural areas. About 85% stated they have collaboration with local health centers, mostly for referring TB suspect cases. About 78% desired to undertake training on TB. VHWs and quacks may have a key role in identifying TB suspects and timely referral for effective treatment. Based on the findings, it is recommended to engage these health care providers in community based TB care and control, to provide training focusing on case detection, health education, referral and DOT provision, to reinforce the existing drug legislation (emphasizing on anti-TB drugs), and to establish the monitoring mechanism for informal health care providers.

Responses for TB diagnosis among the respondents Diagnostic tests for TB	Total (N=137)	Quacks(N=24)	Volunteers(N=113)
Sputum examination	128(93.4)	21 (87.5)	107(94.7)
Chest X ray	62 (45.3)	16 (66.7)	46(40.7)**
Blood test	29 (21.2)	9(37.5)	15(17.7)**
Others	5 (3.6)	2 (8.3)	3(2.7)

Knowledge on TB symptoms by respondents TB symptoms	Proportion (%) Total (N=137)
Chronic cough	73
Productive cough	26.3
Blood in sputum	33.6
Tiredness	19.7
Fever	62.8
Weight loss	52.6
Night sweats	15.3
Chest pain	26.3
Loss of appetite	24.1
Others	18.2

Participants' response on how to take TB drugs N=135	N(%)
To take all simultaneously	5(3.6)
To take one hour apart from food	67(49.6)
To take drugs regularly	58(43)
Others	25(18.5)

Initial response in first contact with a TB suspect Initial response (N=137)	N(%)
Traditional medicine	1(0.7)
Refer to health staff or health centre	110(80.3)
Refer to private health care provider	1(0.7)
Refer to NGO clinic	1(0.7)
Refer to GP clinic	3(2.2)
Advise for self treatment	3(2.2)
Give symptomatic treatment	14(10.2)
Others	4(2.9)

### PC-468-17 Driving and engaging non-allopathic health care providers in tuberculosis care and control: a sustainable approach

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**Background and objectives:** Population Services International (PSI) is currently implementing GFATM 9 'Project Axshya' across thirty districts in the states of Bihar, Punjab, Haryana, Maharashtra, Karnataka and Rajasthan. As a part of the PPM activities, non allopathic providers are being engaged and trained in TB care and control in the implementing districts as a sustainable model.

**Methodology:** The main objective of the modular training is to develop and enhance the capacities of non allopath providers on TB diagnosis and treatment and engage them as DOT providers. The trainings are provided by technical personnel from PSI including the state and district RNTCP staff. RNTCP referral cards are also provided for referral of TB suspects to the nearest Designated Microscopy Center (DMC).

**Results:** A total of 940 non allopathic health care providers were trained from April to December 2011—154 in Maharashtra, 203 in Punjab, 111 in Haryana, 215 in Karnataka, 96 in Rajasthan and 161 in Bihar. These providers were followed up for referrals of TB suspects from July 2011 onwards. Out of the 2016 identified TB suspects that reached the DMC for sputum testing, 337 were found to be positive for TB. A total of 308 of the trained providers also became DOT providers.

**Conclusion:** This model of partnership with non allopathic health care providers in TB care and control has yielded positive results. Training and capacity building of the providers on TB including follow-up for continuous monitoring and supportive supervision is vital to the sustainability of the model.

### PC-469-17 Sustainable tuberculosis control effort of Bangladesh through partnership

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**Background:** Bangladesh adopted the DOTS strategy since 1994 and expanded the services to cover the country in collaboration with NGO partners. National Tuberculosis Control Programme and its NGO partners continued the momentum of this control effort with limited resources.

**Intervention:** Tuberculosis services are integrated in the basic health care services. That made the services

available throughout the country with limited resources. The same approach was followed by the partner organizations. BRAC the major partner NGO providing the TB services to two thirds of the country in collaboration with NTP. BRAC also applied integrated approach of health service delivery. That enabled to minimize the resource need. Partnership of government and NGOs also helped to make it sustainable by avoiding duplication of resources, joint planning and monitoring.

**Results:** Countrywide coverage of tuberculosis has been established. The current case notification and treatment success rate of the country is more than 70% and 92% respectively which was achieved gradually since 1992 and has got a sustainable level. More than 45 partners are involved with NTP which represents different sector. Community involvement played a critical role. The enhanced capacity of the community remained with this sector which helped to refer cases and improve compliance.

**Conclusion and recommendation:** Mutual partnership, community involvement and integrated approach helped to achieve and continue the success of tuberculosis control. The new and emerging areas need to be faced with the same effort and it should also be in a sustainable way during development of strategy.

#### **PC-470-17 Linking public, private and civil society networks to strengthen tuberculosis control in Bangladesh**

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**Background and challenges to implementation:** Historically, tuberculosis (TB) has been a major public health problem in Bangladesh. The Government of Bangladesh, with many partners, is committed to further strengthening TB control. The USAID/Bangladesh's Smiling Sun Franchise Program (SSFP), aims to expand the availability of sustainable, NGO-provided health services through an Essential Service Delivery package including TB control program.

**Intervention or response:** The SSFP is building NGO capacity to deliver DOTS in urban areas. Eight SSFP NGOs provide DOTS through 56 SSFP Clinics in four city corporations in Dhaka, Chittagong, Rajshahi and Khulna. In addition, 33 of these clinics have microscopy centers to diagnose TB by sputum examination, and one has an external quality assurance center to ensure quality of laboratory services. SSFP clinics identify TB suspects, refer them near-by lab facilities for sputum tests and up to higher centers in case of complications. SSFP works with Global Fund for AIDS, Tuberculosis and Malaria (GFATM) to improve services in their catchments areas. SSFP Clinics strengthened referral networks and adopted

community based TB interventions as well as special TB interventions for garment workers, pharmacists, HIV/AIDS workers, and religious leaders to promote TB services.

**Results and lessons learnt:** Implementation of the TB Control Program within SSFP has helped improve the case detection and treatment of TB in Bangladesh. The number of cases detected and successfully treated within the network has increased each year. In 2011, SSFP served 5378 TB cases, of which 2204 were new smear positive cases, 275 were smear positive relapses, 1400 were smear negative cases, and 1581 cases were extra pulmonary.

**Conclusions and key recommendations:** Implementing an effective TB control program in Bangladesh requires working jointly with the government, other donors, and local civil society to strengthen national response and secure ownership and sustainability.

## **COMMUNITY CONTRIBUTIONS TO TUBERCULOSIS CONTROL**

#### **PC-500-17 Optimising enrolment and retention through community engagement in an adolescent tuberculosis incidence cohort study in Western Kenya**

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**Background:** Adolescents are expected to be a critical target population for new TB vaccine candidates. An optimized approach to enroll both in- and out-of-school adolescents in clinical trials is needed to maximize participation and adherence to study procedures. KEMRI/CDC conducted a TB incidence cohort study targeting enrollment of 5000 adolescents aged 12–18 years within one year in an area under continuous health demographic surveillance (HDSS). The study aimed to demonstrate the capacity to recruit, follow and retain an adolescent cohort and to determine the optimal way to enrol adolescents. It also estimated the prevalence of pulmonary TB disease.

**Methods:** Community engagement was done through the provincial administration, Ministries of Health and Education. The approach involved meetings and trainings the divisional head, chiefs and their assistants, government officials and heads or representatives of schools. The community was engaged through village meetings, parents and teachers meetings and community based organizations. We used a mobile field site (MFS) for enrollment and follow up of the adolescents.

**Results:** We enrolled 5004 (90.3%) out of 5541 adolescents approached in 12 months. 95.1% came back for the Mantoux reading within 4 days. Over 86.3%

completed the first 4 monthly follow up visits while 78.5% month 8 visits and 77.4% month 12 visit. There were 38 prevalence and 22 incidence TB cases. **Conclusion:** Our community engagement approach contributed to faster enrollment, adherence to study procedures and high retention. The MFS eliminates the need of taking participants to hospitals and ensures that the research services are more accessible to community.

### PC-501-17 Engaging well-to-do Thai women volunteers to support the poorest patients with tuberculosis

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**Background and challenges to implementation:** Poverty, HIV stigma, hilltribe minorities and illegal migrants are complicated issues in Chiang Rai that cause high default and low tuberculosis (TB) treatment success. To improve treatment outcome for poor patients, we obtained an international grant for establishing a TB patient fund in Chiang Rai hospital. This patient fund supports transportation expense and/or livelihoods for patients who were identified as 'very poor'. In order to sustain this patient fund, as well as to support patients with psychosocial difficulties, we have involved women with high social and economic status (well-to-do women) from the existing women organizations in Chiang Rai, Thailand.

**Intervention or response:** Women volunteers raise the fund for TB-patient fund and perform home-visit to patients who are very poor or/and encounter psychosocial problems.

**Results and lessons learnt:** Majority of the woman volunteers are aged over 60 years (range 37–79). They are retired senior government officers, business owners, or wives of high-level officials. The volun-

**Table** Treatment outcome of tuberculosis patients classified by ethnicity and receiving financial supports from patient funding (raised by the women volunteers)

Patients' ethnicity	Number of patients receiving support (yes/no)	Tuberculosis treatment outcome				Relative risk to be treatment success (95%CI)	P value
		Success %	Died %	Failure %	Default %		
Thai	yes 104	72.1	23.1	0	4.8	1.42 (1.24–1.67)	<0.000
	no 443	50.1	37.4	2.3	10.2	Reference	
Hilltribe minorities	yes 75	72	10.7	2.7	14.7	1.12 (0.94–1.47)	0.1
	no 85	61.2	16.5	4.7	17.7	Reference	
Migrants	yes 13	30.8	7.7	0	61.5	0.75 (0.31–1.84)	0.5
	no 39	41	36	0	23.1	Reference	
Total	yes 192	69.3	17.2	1.0	12.5	1.35 (1.20–1.53)	<0.000
	no 567	51.6	34.2	2.5	12.2	Reference	

teers raised the fund by several ways including self-donation. The Table shows treatment success of the overall and Thai patients receiving financial support are significantly higher than not-receiving groups. In addition to receiving support from patient-fund, 36 patients (23 Thai, 5 hilltribe, and 8 migrants; 16 HIV positive) were visited by women volunteers at home. Treatment success rates of these groups are 91.3% for Thai and 100% for hilltribe and migrants. **Conclusions and key recommendations:** Women volunteers with high social and economic status potentially sustain TB-patient fund and improve treatment success. Thai, hilltribe and migrant patients receiving home-visit from women volunteers achieved very high treatment success.

### PC-502-17 A novel community-based strategy for increasing adherence to tuberculosis treatment: experience from the Kenya Wildlife Service clinic in Isiolo, Northern Kenya

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**Background and challenges to implementation:** Because of the highly mobile nature of the Kenya Wildlife Service Anti Poaching Unit (KWS APU) and stigma surrounding TB and HIV, the Directly Observed Therapy (DOT) program in Isiolo has not met with sufficient adherence to TB treatment. In the hard-to-reach areas in Kenya that includes Isiolo, DOT by health care worker in the *manyatta* system entails hospital admission for the treatment period; an intervention that is limiting for the KWS APU staff that are required to be out in the wild for duty. Anecdotal reports indicated that patients on retreatment skipped their daily injections due to self perception of 'no harm' and 'feeling well'.

**Intervention or response:** The APU dispensary in Isiolo District in collaboration with Operation AIDS Response In Forces in Uniform (Operation ARIFU) project found a creative strategy to improve adherence to treatment by organizing 'TB clubs' for persons with TB disease for community TB care. Club members partnered to promote treatment adherence. Membership for this program is voluntary for TB patients. Those that have completed treatment graduate to TB ambassadors they distribute health promotion materials, refer TB suspects from the community and trace defaulters. Feedback meetings in the facility and updates by health staff provide information on the extent of treatment adherence.

**Results and lessons learnt:** Club membership gradually increased by overcoming perceived stigma to currently near universal through monthly meetings and peer encouragement. This program has provided treatment support to TB patients. No further reports of

treatment lapses are reported among TB patient/club members.

**Conclusions and key recommendations:** Health promotion through 'TB Clubs' may effectively promote adherence to TB treatment. There is need for a scientific evaluation of effectiveness of this community model.

#### PC-504-17 A tuberculosis patients association in Afghanistan

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**Aim:** Despite the high incidence rates of tuberculosis (TB) in many countries, including Afghanistan, there is inadequate knowledge in many communities about disease and inadequate support for patients by community members. In Afghanistan an association has been established to emphasis patient rights and the responsibilities of people with TB and to empower and support people with TB.

**Objective:** To support the NTP for improvement of TB case finding and treatment outcome through engagement of cured TB patients to increase community knowledge about TB and support patients.

**Methods:** In 2009 TB Patient Association was established at a series of meetings attended by cured patients, community members, staff of health facilities, universities students and scholars. The meetings emphasized the role of patients and community members in spreading correct information about TB and its socio-economic impact, and in participating in treatment support (DOT).

**Result:** After the establishment the TB Patients Association 600 people with presumptive TB were referred by previous TB patients and community members to TB diagnostic centers. Fifty-eight of these were diagnosed with smear positive TB. The outcome of these 58 patients was available in 2011. Fifty of them (86%) had successfully completed their treatment under observation of association members.

**Conclusion:** This study shows that the Afghanistan TB patients association has increased the detection of TB cases, improving the knowledge of the community about TB. It has also played a role in the successful treatment outcomes of patients.

#### PC-505-17 Barriers to accessing tuberculosis treatment in a refugee settlement in Masindi District, Uganda: perspectives from patients and the community

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**Background:** Tuberculosis (TB) is an important health problem in refugee populations. Successful TB pro-

grammes require high case detection and adherence rates. Programme success in refugee settings is varied and often below target. To improve case detection and adherence, barriers to these must be addressed. Refugee-specific data regarding these is limited, despite their potentially unique needs. This research aims to identify barriers and motivating factors for accessing TB treatment in a refugee settlement in Uganda.

**Methods:** Qualitative data was collected to identify perceived barriers to diagnosis and treatment adherence. This was collected through in depth interviews with TB sufferers selected through purposive sampling, and focus group discussions with community members, selected through convenience sampling. A thematic framework for adherence factors from the International Standards for Tuberculosis Care was used for data analysis.

**Results:** Perceived barriers to treatment were frequently associated with a lack of knowledge and understanding, alongside negative attitudes of patients and the community. Other commonly cited issues were transport, health-worker related problems, stock outs and food insecurity (exacerbating side effects). Encouragement, patient comfort, a change in perceptions and easier access to drugs were suggested to improve initiation and adherence. Financial issues and repatriation were not cited.

**Conclusion:** Factors identified in Kiryandongo largely reflect those in non-refugee settings. More unique barriers included food insecurity and the vast range of knowledge and attitudes within the community. TB interventions should reflect these population-specific barriers. Therefore, recommendations include educational programmes, increased food provisions for TB patients, and greater health worker accountability. Further research in similar settings is needed before generalisation of these results to other settlements.

#### PC-506-17 Community systems strengthening initiatives promote tuberculosis care and control across 16 Project Axshya districts of Karnataka

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**Background:** Global funded Project Axshya with a specific objective of strengthening civil society involvement in TB care and control is currently operational across 16 districts in Karnataka State. Goal of universal access to quality diagnosis and treatment for all TB patients will need the engagement and involvement of community systems.

**Intervention:** Project Axshya has identified 4 Mother Non-Government Organizations (MNGO) in each of the 16 districts ( $n = 64$ ) to advance implementation of TB control activities. Key CSS initiatives targeting

64 MNGOs included technical/programme skills transfer for service delivery, providing financial/material support, and promoting their advocacy/leadership for TB control. MNGOs further promoted community partnerships/networking at village level by engaging village health and sanitation committees, self-help groups, and Panchayati Raj institutions in a systematic manner.

**Results:** Project Axshya led efforts have resulted in strengthening community based structures at sub-district level while fostering partnerships for TB care and control in a unique manner at the village/community level. The 64 MNGOs now lead implementation of TB control ACSM activities with each covering 200 000–500 000 population, with funding support from state level NGOs.

	Total districts (31)	
	Axshya districts (16)	Non-Axshya districts (15)
Prior to Project Axshya Involvement of MNGOs at district level in implementing TB control	0	0
	64	0

**Conclusions:** Creating an enabling and leadership environment for TB control among community structures at sub-district level is possible through systematic capacity building and materials support to promote TB care and control. Sustaining these NGOs beyond the project period will need their direct collaboration with the TB control programme through existing NGO schemes. Replication of similar efforts in remaining non-Axshya districts of Karnataka and impact of their engagement over long term (>3 years) may need a detailed analysis.

#### PC-507-17 Tuberculosis control among a tribal population in Eastern India: key learning of 5 years

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**Background and challenges to implementation:** Vanavasi Seva Kendra is an NGO working in a tribal area of Bihar, known for insurgency. NGO provides Tuberculosis Unit (TU) services under Revised National TB Control Program services (RNTCP). The population covered is 435 000, spread across 470 villages in the hilly terrains of Babhua District. In 2007, when TU services were started, case notification among all TB, NSP, cure rate and defaulter rate was 61, 32/100 000, 60% was 19% respectively.

**Intervention or response:** The NGO provides services for microscopy, treatment, direct observation, defaulter retrieval, recording and registration, supervision. Besides, skilled human resources to microscopy centres in the area, strengthened ACSM and com-

munity system activities. They built capacity of general health care staff and engaged them in RNTCP activities.

**Results and lessons learnt:** After four years of intervention, new cases detection increased to 84, 52 among all and NSP respectively (year 2010). The default rate decreased to 9% in 2009 for the first time in the TU with cure rate increasing to 82% in 2010. However, management of retreatment failure cases and HIV testing is still the most challenging due to distant location of ICTCs.

**Conclusions and key recommendations:** The result showed that an NGO by strengthening basic services and community involvement is able to contribute significantly to improve case detection, decrease defaulter rate and cure rate even in tribal areas. However, possibility of strengthening HIV-TB services and linkages to social welfare schemes need to be done.

#### PC-508-17 Community involvement in tuberculosis care and control in England

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**Background:** Tuberculosis programmes in England are largely managed through a medical model of health, without sufficiently addressing the complex social aspects of the disease. In response to rates of TB rising for over 20 years, health services are increasingly responsive to managing TB within a paradigm that addresses the wider social and economic determinants of health. As has been demonstrated in high burden countries, this can be achieved through the engagement of community-based organisations (CBOs) as partners in TB control programmes.

**Intervention:** The UK's national TB charity, TB Alert, is building the capacity of CBOs representing affected communities to integrate TB into their programmes. This will allow them to partner health services in designing and delivering local TB services. A programme of 25 national awareness seminars and training workshops for CBO staff were delivered in 2010/11. These were delivered in partnership with local health services and people affected by TB, who, together with local communities, are key stakeholders in addressing TB through a social model of health.

**Results:** Over 400 delegates attended awareness seminars and 280 delegates were trained through workshops. Delegates at the workshops developed action plans on how they would incorporate TB into their work and key CBOs are now delivering TB awareness activities in affected communities.

**Conclusion:** Delivering awareness activities is the entry point for CBOs to become engaged in other TB

management activities including referrals to clinics, case management, contract tracing, DOT and peer support. TB Alert is working towards the realisation of community involvement in TB care and control in England through the creation of local TB partnerships involving statutory health services, CBOs, and people affected by TB.

**PC-509-17 L'intérêt des visites à domicile réalisées par les organisations à base communautaire dans le succès du traitement des malades de tuberculose**

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**Background and challenges to implementation :** Le Burkina Faso est un pays à haute incidence de tuberculose, 55 TPM+ pour 100.000 habitants en 2011. Le taux de succès au traitement de nouveaux cas TPM+ de 77,4% pour la cohorte de 2010 et reste inférieur aux objectifs nationaux et ceux de l'OMS et ceux du partenariat halte à la tuberculose qui est fixé à 90%. Pour renforcer la riposte efficace, le Programme d'Appui au Monde Communautaire et Associatif (PAMAC) et le Programme National Tuberculose (PNT) ont établi un partenariat pour la mise en œuvre d'une stratégie d'accompagnement communautaire des patients tuberculeux au cours de leur traitement. Une des activités de la stratégie était les visites à domicile des patients par un volontaire communautaire.

**Intervention or response :** Les associations d'accompagnement communautaire visitent à domicile les patients qui ont donné leur accord ; chaque patient reçoit au moins une visite par mois du relais communautaire pour lui apporter un soutien moral, faire le suivi du traitement.

**Results and lessons learnt :** Au cours du 1er trimestre 2012, 62% des patients ont été accompagné sur 4CDT.

- taux de succès au traitement chez 72 patients est de 90,2% alors qu'il est de 70,6% chez ceux qui ne sont pas accompagnés pour la cohorte 2011 dans 4 CDT
- succès au traitement chez les accompagnés est 15% fois supérieur à ceux qui ne sont pas accompagnés
- aucun perdu de vue chez les patients accompagnés alors qu'il est de l'ordre de 8,2% chez ceux qui ne le sont pas.

**Conclusions and key recommendations :** Cette étude ponctuelle a permis de constater de meilleurs résultats de traitement chez les patients qui ont reçu des VAD. Ce qui veut dire que les malades tuberculeux en plus du traitement ont besoin d'un soutien psychologique, d'une éducation thérapeutique au quotidien pour être plus observant.

**PC-510-17 Tuberculosis services for the high-risk groups of HIV programmes through targeted intervention-tuberculosis collaboration: good practices from South-East Asia**

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**Background:** In Asia, HIV epidemic is mostly concentrated within HRGs (sex workers, IDUs, MSM/transgender, migrants, prisoners). They are equally vulnerable to TB due to unhealthy and over-crowded living conditions, poor socio-economic status, lack of nutrition, sheer ignorance and poor infection control in overcrowded health facilities, especially within high TB burden and concentrated HIV epidemic settings. But TB case detection efforts and expanding services are still limited for those groups, who are already covered under HIV programs despite unmet TB case detection targets.

**Methods:** The 'targeted intervention' (TI) HIV prevention projects of HRGs give platform for dissemination of key TB messages, TB case detection in HRGs and linkage development with local TB services through existing peer outreach of HIV programs. The STI clinics marked for HRGs perform regular TB screening among clinic attendees and referral. Selected peer educators of TI projects function as community DOTS providers through training and motivation.

**Results:** In 2001, Sonagachi STI/HIV Project, Kolkata, India, initiated TB case detection in sex workers and their clients with the assistance of City RNTCP Office and CARE West Bengal with encouraging results. In 2005, a pilot project of TI-TB collaboration in Allahabad by CARE India detected 33 TB cases in 18 117 high risk population including 10 co-infected cases in 6 months. In 2004–2005, similar pilot project in Bangladesh, the attendees of a STI clinic, which was established for HRGs were also screened for TB and 135 TB cases detected within a year. The success of Avahan project in establishing TI-TB collaboration (2006–2007) in India prompted creation of TB-HIV schemes in RNTCP for the NGOs, though this scheme has, so far shown grossly insufficient utilization rate.

**Conclusion:** The TI-TB collaboration initiative needs good advocacy efforts to put realistic strategy and guideline in place to saturate HIV TI projects with optimal TB services.

## INTEGRATION AND CO-LOCATION

### PC-539-17 Adverse events among HIV and MDR-TB co-infected patients receiving antiretroviral and second-line anti-tuberculosis treatment in Mumbai, India

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**Background:** Significant adverse events (AE) have been reported in patients receiving medications for multidrug-resistant tuberculosis (MDR-TB). However, there is little prospective data on AE in MDR-TB-HIV co-infected patients on antituberculosis and antiretroviral therapy (ART) in programmatic settings.

**Design/methods:** Médecins Sans Frontières (MSF) is supporting an outpatient community-based program for MDR-TB in HIV-infected patients in a slum setting in Mumbai, since 2007. Prospective data were analysed to determine the occurrence and nature of AE.

**Results:** Between May 2007 and September 2011, 67 HIV/MDR-TB patients were treated; 43.3% were female, median age was 35.5 years (interquartile range: 30.5–42) and the median duration of anti-TB treatment was 10 months (range 0.5–30). Overall, AE were common in this cohort: 71%, 63% and 40% of patients experienced one or more mild, moderate or severe AE, respectively. AE occurring most frequently included gastrointestinal symptoms (45% of patients), peripheral neuropathy (38%), hypothyroidism (32%), psychiatric symptoms (29%) and hypokalaemia (23%). Eleven patients were hospitalized for AE and one or more suspect drugs had to be permanently discontinued in 27 (40%). No AE led to indefinite suspension of an entire MDR-TB or ART regimen.

**Conclusion and recommendations:** AE occurred frequently in this Mumbai HIV/MDR-TB cohort but not more frequently than in non-HIV patients. Most AE can be successfully managed on an outpatient basis, even in a resource-limited setting. Concerns about severe AE in the management of co-infected patients are justified, however, they should not cause delays in the urgently needed rapid scale-up of antiretroviral therapy and second-line anti-TB treatment.

### PC-540-17 Adherence to concurrent tuberculosis treatment and HIV antiretroviral treatment regimens among people with tuberculosis and HIV in South Africa

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**Background:** Adherence to tuberculosis (TB) treatment and antiretroviral therapy (ART) reduces TB and HIV-related morbidity and mortality. We measured adherence to concurrent treatments and associated factors among people with TB disease and HIV (TB-HIV) in TB-HIV integrated clinics in two South African provinces.

**Design/methods:** Persons receiving concurrent TB and HIV treatment between January 2008 and December 2010 in a convenience sample of 35 TB-HIV integrated clinics in North West and Western Cape Provinces were included. Adherence was defined as: 1) taking  $\geq 80\%$  of TB doses by directly observed therapy or self-administration, or if these data were not available, had a TB outcome recorded as cured, treatment completed, or treatment failure (i.e., persons who were adherent on treatment, but sputum did not convert) in the standardized TB medical record; and 2) taking  $\geq 90\%$  of ART doses as documented in the ART medical record during the concurrent treatment period (i.e., duration that a person was on both TB treatment and ART). We examined demographic, clinical, and psycho-social factors for associations with adherence.

**Results:** Among 1459 persons receiving concurrent treatments, 1291 (89%) were adherent. Median age of persons adherent to concurrent treatment was 36 years (interquartile range [IQR]: 31–43), and 56% were female. Compared to persons not adhering, persons that adhered were more likely to attend a support group or have a treatment partner, defined as a person responsible for checking on the patient and picking up medications, (odds ratio [OR]: 3.7, 95% confidence interval [CI] 1.1–12.3) and less likely to have a history of ART interruption (OR: 0.4, 95% CI 0.2–0.7).

**Conclusions and recommendations:** A high proportion of persons with TB-HIV were adherent to concurrent TB treatment and ART in two South African provinces. Providing support through groups and treatment partners may improve adherence among persons with TB-HIV.

### PC-541-17 Overlapping risk factors but no association between HIV and drug resistance among tuberculosis patients in Kazakhstan

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**Background:** Kazakhstan has a high prevalence of multi-drug resistance (MDR) and a low, but growing, HIV prevalence among tuberculosis (TB) cases. We describe the epidemiology of MDR and HIV among TB cases and its association.

**Design/methods:** Data from the national electronic TB register on 2007–2009 are described (during the conference, updated data will be presented).

**Results:** Among all TB patient HIV prevalence increased from 0.6% to 1.2%, and MDR prevalence remained 34%. Although there are variations in HIV and MDR prevalence between oblasts, there was no association between HIV and MDR prevalence, neither overall, by oblast, nor by patient characteristics. HIV prevalence was the highest among patient returning after default. Characteristics associated with HIV were drug use (odds ratio (OR) = 51.2, 95%CI 41.3–63.6), prison history (OR = 5.3, 95%CI 4.0–7.0), alcoholism (OR = 3.1, 95%CI 2.6–3.7), and homelessness (OR = 2.6, 95%CI 2.0–3.5). Risk factors for MDR-TB were drug use (OR = 1.3, 95%CI 1.0–1.7), prison history (OR = 2.2, 95%CI 1.9–2.6), and homelessness (OR = 1.2, 95%CI 1.1–1.4).

**Conclusion and recommendations:** Among TB patients in Kazakhstan, risk factors for HIV and MDR are largely overlapping. However, MDR-TB prevalence was not associated with HIV-status.

### PC-542-17 Models of TB-HIV integration and accomplishments in Nyanza Province, Kenya

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**Background:** Kenya HIV and TB programs previously functioned separately. To save lives, integration of services is being promoted. We describe successful models of integration in a high burden setting and report on accomplishments and challenges.

**Setting:** Nyanza Province bears the brunt of the TB-HIV syndemic. Services in public health facilities (PHFs) are structured into hierarchical levels: L1–community; L2–dispensary; L3–health center; L4–district hospital; L5–provincial hospital.

**Methods:** Following formation of coordinating bodies, integration of decentralized services started in

2007. Resources were mobilized to support capacity, infrastructure, supply chains and service delivery. Different models of integration were described through field visits while accomplishments and challenges were monitored through progress reviews.

**Results:** Fully integrated ‘one stop’ model was observed in 36 (65%) L4, 151 (100%) L3 and 445 (100%) L2 PHFs constituting 96% of all. Partially integrated model was observed in 11 (20%) L4 and 2 (100%) L5 PHFs constituting 2% of all. Separate co-located model was observed in 8 (15%) of L4 PHFs constituting ~1% of all. HIV testing for new TB patients rose from 74% in 2007 to 95% 2011. CPT and ART uptakes for HIV+ TB patients rose from 80% to 97% and from 34% to 62%, respectively. TB screening for PLWHA increased from 20% to 60%. Challenges include weak infrastructure, inadequate manpower and donor-dependent funding.

**Conclusions:** Decentralization of 3 models of integration led to remarkable accomplishments in interventions that protect TB patients from HIV. Nyanza plans using these platforms in the next phase to expand interventions that protect PLWHA from TB, to expand linkages with community (L1) activities and to address challenges.

### PC-543-17 Integration of TB-HIV/PMTCT services in a rural district of South Africa: healthcare providers and patients’ perspectives

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**Background:** This study sought to identify and understand the views of both healthcare providers and TB-HIV/PMTCT patients in order to develop measures to enhance provision of these services.

**Design/methods:** A cross-sectional study was conducted in one of the rural districts in KwaZulu-Natal, South Africa. A convenience sample of 200 Health care workers (HCWs) and 360 patients was drawn proportionately from each category of patients. Self-administered questionnaire approach was used for HCWs and exit interviews for patients. The data was subjected to bivariate tests and content analysis of open ended questions. Ethical clearance was sought from Ethics Committee, University of the Western Cape.

**Results:** HIV patients were significantly more likely to be offered TB services such as TB symptoms screening (OR = 14,  $P = 0.000$ , 95%CI 5.46–37.46) than PMTCT patients. The majority of the patients (84%) across all categories of patients preferred to have TB-HIV/PMTCT services at the same place and 57% of patients preferred to be seen by the same clinician.

Less than 50% of PHC clinic staff were trained on TB and HIV management yet the proportion of TB-HIV co-infected patients seen per day by PHC clinics was statistically significant based on the level of care ( $P < 0.02$ ) and this effected the quality of care provided by PHC clinics. Patients' level barriers identified amongst others include lack of money for transport to attend services on different schedules, fear to disclose HIV status to more than one HCWs and stigma. Most of HCWs perceived increase in staffing norms and training of HCWs in TB-HIV co-infection management, and strengthening of the facility and community referral system as potential facilitating factors to enhance provision of integrated TB-HIV/PMTCT services.

**Conclusion and recommendations:** The findings of this study suggest that TB-HIV services were partially integrated and key services for TB prevention were not integrated into PMTCT program. Training of HCWs at PHC clinics on management of TB-HIV including ART and mentoring of HWCs is paramount for quality is improvement. There is also a need to strengthen facility-community linkages for continuum of care. Finally, to enhance integration of TB-HIV/PMTCT services, effective strategies tailored to address providers' and patients' barriers levels as well as health system barriers are required.

#### PC-544-17 Adherence to antiretroviral therapy in the Federal Capital Territory, Abuja, Nigeria

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**Background:** High level adherence ( $\geq 95\%$ ) to ART is required for effective HIV suppression. We described adherence and the factors that constrain and motivate adherence among patients on highly active antiretroviral therapy (HAART).

**Design/methods:** Structured questionnaires were administered to patients receiving HAART at the University of Abuja Teaching Hospital. The outcome of measure was self-reported adherence, validated using viral load. Bivariate and multivariate analyses were performed.

**Results:** Of the 537 patients, 35 participants were excluded (6 did not have viral load test data, 28 had incomplete prescription refill data and 1 was younger than 18 years). Among the 502 participants analyzed, 53.6% had total optimal adherence by self-report as compared with 62.5% who had adherence by prescription refill. Most (80.3%) participants achieved virologic suppression at a level of  $< 400$  copies/ $\mu\text{l}^3$ . Adherence barriers were: forgot (43%); travelled away from home (21%); ran out of medication (16%); busy at work (13%); lack of food (5%) and medication snatched by armed robbers (2%). Adherence facilitators were: health condition improved

(40%); desire to live (30%); family support (22%); and support group (8%). Total self-reported adherence was positively associated with age (OR = 2.5; 95%CI 0.8–6.16;  $P = 0.023$ ) and viral load (OR = 6.6; 95%CI 1.6–11.07;  $P = 0.001$ ).

**Conclusion and recommendations:** Participants were persistent in treatment and achieved satisfactory viral suppression; yet low adherence to ART persisted. This suggests an urgent need for new adherence models.

#### PC-545-17 Integrated TB/ART clinics in Lusaka, Zambia: an evaluation of enrollment into HIV care and early initiation of ART in TB-HIV co-infected patients

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**Background:** In Zambia, 65% of new tuberculosis (TB) patients are HIV-infected. Management of TB-HIV co-infected patients in vertical care programs has been associated with diagnostic and treatment delays, leading to increased morbidity and mortality. To increase rates of enrollment in HIV care and early initiation of antiretroviral therapy (ART) we implemented a model of integrated TB and HIV care in TB clinics at two Lusaka health centers.

**Design/methods:** All newly diagnosed TB patients were offered opt-out HIV testing. Those found to be HIV-infected were offered immediate enrollment into HIV care with ART initiation within 2–4 weeks if eligible. Both TB and HIV care were provided in the TB clinic. We collected programmatic data from TB registers, treatment cards and the national electronic HIV care database to evaluate uptake of HIV services in a cohort of patients under the integrated system compared to a historical cohort from the same clinics.

**Results:** The number of HIV-infected TB patients enrolling into HIV care within two months of TB treatment initiation increased from 19% (45/242) to 31% (59/192),  $P = 0.03$ . The number of HIV-infected patients initiating ART within two months of TB treatment initiation increased from 10% (25/242) to 23% (45/192),  $P = 0.0002$ .

**Conclusion and recommendations:** Despite challenges of staffing shortages, space constraints and lack of health care worker 'buy-in', preliminary results of this integrated program demonstrate a significant increase in the proportion of TB patients accessing HIV services and initiating ART within two months. Further improvement in these indicators can be expected once challenges have been addressed. Similar program interventions should be considered in other settings.

### PC-546-17 Patient outcomes and delays prior to starting antiretroviral treatment among HIV and tuberculosis co-infected adults in Cape Town, South Africa

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**Background:** Although data exists on pre-antiretroviral treatment (ART) losses and delays for HIV cohorts in sub-Saharan Africa, there is relatively little information available for HIV and tuberculosis (TB) co-infected cohorts. We, therefore, conducted a study at an integrated TB/ART service in Cape Town.

**Design/methods:** In a retrospective observational cohort study, all ART-naïve co-infected patients aged  $\geq 18$  years that commenced TB treatment in 2010 were included. Data were analyzed using basic descriptive statistics and log-linear regression analysis.

**Results:** TB treatment was initiated among a total of 274 co-infected ART-eligible patients (median age, 34 years; median CD4 count, 158.5 cells/ $\mu$ l). ART was subsequently initiated by 220 patients. Of the remainder, 23 patients were lost (i.e., deaths and lost to follow-up) prior to screening at the ART clinic; 12 were lost after having been screened for ART; 3 patients had transferred out; 2 were referred elsewhere for ART but treatment initiation was unknown and 14 initiated ART after TB treatment. The median delay between starting TB treatment and starting ART was 51 days (IQR 29–77). The proportion of patients with CD4 cell counts  $< 50$  cells/ $\mu$ l who started ART within 2 weeks was 12.7%. In multivariate analysis, starting ART after 8 weeks was associated with having recurrent disease and CD4 cell counts  $> 50$  cells/ $\mu$ l.

**Conclusion and recommendations:** The losses and delays identified in our programme require corrective interventions. In particular, interventions addressing obstacles to losses occurring prior to screening and to timely initiation in those with recurrent disease and CD4 cell counts  $> 50$  cells/ $\mu$ l.

### MPOWER AND TOBACCO CONTROL POLICIES–2

#### PC-563-17 Reasons underlying the lack of interest in quitting smoking among current smokers from Romania and implications for health education

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**Background:** Studies from numerous countries show that although a large proportion of smokers want to quit, only few of them succeed in quitting long-term. Increasing tobacco cessation in Romania would be critically important to improve public health. The aim of this study was to identify the reasons that prevent large proportion of smokers to attempt quitting and to outline the public health approach to overcome these impediments.

**Design/methods:** This study is based on data gathered for GATS Romania 2011, a nationally representative household survey of persons 15 years of age or older. 4517 individuals representing an estimated 18.17 million persons aged 15 and over were interviewed. Complex survey data analysis was performed to obtain population estimates and their 95% confidence intervals using the sample module of a statistical package, SPSS 17.

**Results:** Among current smokers not interested in quitting (33.6%) we analyzed the main reasons that prevent them considering quitting as overall and stratified by gender, age, educational level and a tobacco dependence indicator. Overall, 85.8% reported ‘enjoying smoking’, 61.5% thinking that smoking reduces stress, 39.2% thinking that smoking is not bad for their health, 38.3% considering they cannot quit. The highest percentages of smokers not interested in quitting (48.1%) along with lowest interest to quit within next 12 months (11.0%) were noticed among those who are nicotine addicted.

**Conclusion and recommendations:** Findings from this study highlighted the main reasons underlying the lack of interest in quitting smoking among current smokers from Romania. Among the most frequent reasons were those related to the addictive nature of nicotine, the fear of losing a way to handle stress and the underestimation of risks. Our data point to the necessity of providing the public with complete and relevant information on health consequences of tobacco use, including the nicotine dependence.

### PC-564-17 Effectiveness of smoking cessation skills-building workshops in educating physicians about smoking cessation techniques

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**Introduction:** Physician advice to quit smoking is an effective component of a smoking cessation strategy. Previously published data clearly demonstrated that education smoking cessation skills to physicians improves physicians' smoking cessation practices and increases smoking cessation rates among their patients.

**Objective:** To determine the effectiveness of smoking cessation skills-building workshops in training of smoking cessation techniques to Pakistani physicians.

**Methods:** Five full day smoking cessation skills-building workshop have been arranged in different parts of the country in which 113 physicians participated including general practitioners (GPs), chest physicians, cardiologists, residents, and house officers. A validated questionnaire regarding the attitude and knowledge about smoking is filled by the doctors at the registration desk before the start of the workshop. After the completion of the workshop same questionnaire was again filled by the attending doctor to record the response.

**Results:** Total of 113 doctors attended the workshops in which 90 were males and age ranged from 22 to 61 years (mean age  $\pm$  SD is  $37 \pm 11$ ). Out of these 113, 33 doctors were GPs, 11 chest physicians, 11 cardiologists, 8 consultant physicians and 11 were house officers. After the workshop the physicians felt very confident about their knowledge to treat nicotine dependence 15.9% (pre-workshop) vs. 64.6% (post-workshop); they (physicians) seemed very confident is discussing the smoking cessation issue with their patients 52.2% vs. 80.9% and also they themselves felt them very knowledgeable regarding pharmacotherapy 9.7% vs. 49.1%. Regarding the technical knowledge of the subject response was also favorable, e.g., the 5As approach answered correctly by 17.7% vs. 69.9% in pre and post workshop respectively; regarding nicotine replacement therapy correct answer given were 39.8% vs. 61.1% in pre and post workshop respectively; while regarding Bupropion adverse effects 46.9% vs. 71.1% physician gave correct answer in pre and post workshop questionnaire respectively.

**Conclusion:** After attending one full day smoking cessation skills-building workshop physicians felt more confident in discussing the anti-smoking issue with their patients and their smoking cessation knowledge also increased significantly.

### PC-565-17 The development and effectiveness of a smoke-free policy in taxis in Tianjin, China

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**Objectives:** To create a smoke-free environment among the taxi companies through communication and policy development; and to establish a smoke-free city and protect the health of the public by searching for and promoting effective strategies for tobacco control in various sectors of the society.

**Methods:** Various strategies have been used to educate the public on the harmful effects of secondhand smoke. In collaboration with the mainstream media, the project team released a series of reports, which have helped the Tianjin City Transport Administration to promulgate the Public Notice on a Smoking Ban on Taxis. The whole Tianjin taxi sector was required to implement what were stipulated in the Notice. A survey was conducted on the tobacco use of the taxi drivers and their knowledge on the harmful effects of tobacco both before and after the promulgation of the Notice to assess the effects of tobacco control on Tianjin taxis and a sample was taken of the PM<sub>2.5</sub> level to verify their self-reported tobacco use behavior.

**Results:** Compared with 2008 before the promulgation of the Public Notice on a Smoking Ban on Taxis, the percentage of taxis whose drivers smoked and in which cigarette butts and smell of tobacco were found or detected decreased from 77.0% to 15.3%

Index	2008 before % rate (95%CI)	2010 after % rate (95%CI)	c <sup>2</sup>	P value
Behavior				
Smoking	57.2 (50.5, 63.9)	47.7 (43.4, 52.0)	5.38	0.02
Drivers smoke in taxis	25.2 (17.4, 33.0)	7.6 (4.3, 10.9)	21.71	0.00
Dissuade passengers from smoking in taxis	17.8 (12.6, 23.0)	96.0 (94.3, 97.7)	470.62	0.00
Attitude				
Support smoke- free in taxis	87.0 (82.5, 91.6)	91.2 (88.8, 93.6)	2.93	0.09
Think smoking is negative to the business	84.1 (79.2, 89.1)	81.9 (78.6, 85.2)	0.53	0.47
Phenomenon				
Has cigarette ends or ash in taxi	77.0 (71.2, 82.7)	15.3 (12.2, 18.4)	256.85	0.00
Has cigarette advertisement in taxi	1.9 (0.1, 3.8)	4.4 (2.6, 6.1)	2.55	0.11
Has no-smoking sign in taxi	9.1 (5.2, 13.0)	96.4 (94.8, 98.0)	557.11	0.00

in 2010 ( $P < 0.05$ ). The percentage of taxi drivers who advised their customers against smoking inside the taxi increased from 17.8% to 96.0% ( $P < 0.05$ ). More than 85.0% of the drivers received information on the harmful effects of tobacco and 91.2% of the taxi drivers supported the smoking ban in taxis. The level of  $PM_{2.5}$  was  $51.0 \mu\text{g}/\text{m}^3$  which is lower than the level inside smoke-free hospitals and government office buildings.

**Conclusions:** The model of the smoking ban in taxis in Tianjin was to create an environment supportive of the development and implementation of the smoke-free policy through comprehensive communication and education, followed by the promulgation of a public notice. These efforts played an essential role in the promotion of smoke-free taxis. Moreover, the Public Notice was implemented by the taxi sector itself, which helped to reduce enforcement cost and produced fairly good results. This model should be adopted by other sectors of the society so as to establish a smoke-free city.

#### PC-566-17 Analysis of cigarette affordability and increasing tax impact in Indonesia

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**Background:** Tobacco taxation is a policy instrument to control cigarette consumption. Increasing tobacco tax will increase cigarette price, decrease cigarette affordability and decrease cigarette consumption. The research questions of this study are how affordable is cigarette price in Indonesia? How would cigarette tax and price increases affect the government revenue, cigarette consumption, and smoking prevalence?

**Methods:** In studying the affordability of tobacco, we use relative income price (RIP) as developed by Blecher and van Walbeek (2009). In studying the fiscal and public health impact of tobacco taxes, a simulation model introduced by van Walbeek (2010) was used (<http://www.commerce.uct.ac.za/TETSIM>).

**Results:** The findings in this study indicate that cigarettes in Indonesia are becoming more affordable. In 2002, the relative income price of cigarettes was 0.07 while in 2010 decreased to be 0.03. It means that for the periods of 2002–2010 cigarettes became 2 times more affordable. Concerning increasing cigarette excise from the current 38% to 57%. At 57% excise tax burden, the price of one pack of cigarettes will be US\$1.65, and will decrease 12.6% cigarette consumptions. From the health point of view, if the government applies this increase to the entire tobacco product, then it is estimated to save 1.04 million lives.

**Conclusion:** The government should increase and simplify tobacco tax system in Indonesia to decrease cigarette affordability, to decrease cigarette consumption, to increase government revenue and to save lives.

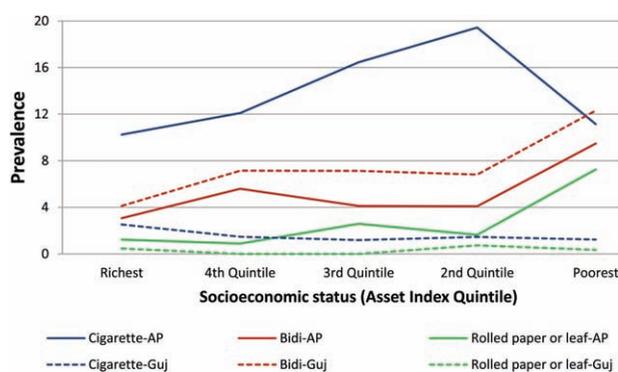
#### PC-567-17 Socio-economic differences in consumption of different smoking products in India

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**Background:** Socioeconomic differences for smoking are well known worldwide and also in Indian context. Our objective in this study is to access not only the socioeconomic differences of smoking prevalence but also for different smoking products in India.

**Methods:** Project STEPS (Strengthening of Tobacco Control Efforts Through Innovative Partnership and Strategies) is a three year multicomponent intervention being implemented in two states of India; Gujarat and Andhra Pradesh (AP) to comprehensively control tobacco menace. The data included 4838 participants of more than 15 years of age at baseline of Project STEPS. Smoking, overall and product wise are main outcome variables. Asset index was used as the measure of socioeconomic status (SES) and divided into quintiles. Multiple logistic regression models were applied to estimate the association between SES and smoking controlling for age group, gender and occupation.

**Results:** As compared to respondent from the highest asset index quintile, the lowest quintile was 2.2 times more likely to smoke in AP and 2.5 times more likely in Gujarat, respectively. In AP compared to highest quintile, people belong to 2nd quintiles were 1.7 times more likely to use cigarettes. People from lowest quintile were 2.9 times more likely to use bidi and 4.5 times more likely to smoke tobacco in rolled paper or leaf than those from highest quintile. In Gujarat overall smoking is less prevalent than AP and only bidi is significantly associated with SES.



**Figure** SES-wise prevalence of different smoking products in Andhra Pradesh and Gujarat, India, 2011. AP = Andhra Pradesh; Guj = Gujarat.

**Conclusion:** The higher prevalence of smoking among socioeconomically disadvantaged group may be due to easy affordability of bidis as the taxation rate on bidis is very low in India. Strong policy and higher

taxation rate are needed to prevent the bidi consumption among lower SES groups. Also the intervention strategies to tobacco control should target different products according to their prevalence in different states.

### PC-568-17 Promoting smoke-free homes in India

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**Introduction:** Secondhand smoke (SHS) is responsible for over 600 000 premature deaths annually, one third of these are among children. The rising smoking patterns in low and middle income countries (LMICs) would lead to a vicious cycle as children and adolescents exposed to SHS in homes are doubly likely to initiate smoking. The WHO-FCTC through its MPOWER strategy supports protecting people from SHS, but its implementation is weak in LMICs. This study explores the prevalence and perceptions of SHS in homes and the need to promote smoke-free homes (SFH) in India.

**Methods:** A total of 4838 households were surveyed as baseline for the Project STEPS (Strengthening of Tobacco Control Efforts Through Innovative Partnerships and Strategies) in two states of India; Andhra Pradesh and Gujarat. The questionnaire included GATS variables along with other related study variables. Analysis has been drawn from SHS related questions of the questionnaire.

**Results:** A 27.8% of the households have family members who smoke at home. Low education and socio-economic status was significantly associated with smoking in homes. Only 55.3% of the respondents had heard about SHS and among those 61.2% of the respondents were concerned about the adverse health effects of SHS.

**Discussion:** The SFH interventions across the world have provided evidence that shared responsibility facilitates smoking reduction. These are yet to be widely adopted in countries like India.

**Conclusions:** Interventions informing people about protecting non-smokers at home should be integrated into national tobacco control programme. A multi-pronged approach needs to be adopted involving active participation of allied stakeholders and concurrent community mobilization efforts to curb SHS in homes.

### PC-569-17 Prevalence of exposure to passive smoking among health care professionals in Chennai, India: a cross-sectional study

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**Background:** As one of the components of MPOWER is to 'Protect people from tobacco smoke, this study focused on exposure among the Health Care professionals in Chennai. The primary objective to estimate prevalence of exposure to tobacco smoke among health professionals including the place and frequency. Secondary objective, to determine attitude towards passive smoking and awareness of ill-effects and of current tobacco control policies.

**Design/methods:** 180 health care professionals were recruited using stratified random sampling, stratified on the type of health profession and from each stratum, simple random sampling was used to select subjects. Questionnaire was given and responses were recorded.

**Results:** 77.8% of the health professionals are exposed to passive smoking, of them 49.4% are exposed occasionally, 67.8% are exposed outside, 2.8% at home and 7.8% at both places. When exposed, majority of them (58%) move away from the place. 96% supported the ban of smoking in public places. 95% of the health professionals are aware of the dangers of passive smoking. There is a significant association between occupation and frequency of exposure to passive smoke; majority of the dentists are exposed occasionally and doctors are exposed on a daily basis (d.f. = 6,  $\chi^2 = 19.068$ ,  $P = 0.004$ ). Nurses reported that they are exposed at public places (23%), dentists at home (2%) and doctors at both the places (5%).

**Conclusion and recommendations:** Health professionals—vital tobacco control advocates, themselves are silent victims of passive smoking and are apathetic, so they should be empowered to become powerful tobacco control advocates.

### PC-570-17 Smoke-free rule enforcement in India: importance of leadership and networking

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**Background and objectives:** Under Cigarette and Other Tobacco Products Act, 2003, Indian government has framed detailed Smokefree Rules which came into force October 2, 2008 and revised again by adding more authorized persons who can take action against the violators. The smokefree rules requires that all public places including workplaces to

be smokefree. India is the largest country in the world to implement a nationwide smoke-free law. However, it will not have the desired benefits unless the government effectively enforces it.

**Methods/description:** This study reviews the successful enforcement models of smokefree jurisdiction, i.e., Sikkim State, Kottayam District, Bhubneshwar City and Shimla City. The study aims to identify importance of leadership and networking in creating smoke-free jurisdiction. In the study, various steps taken for creating smokefree jurisdictions have been reviewed. The study highlighted considerable differences in the process initiated and adopted at various setting.

**Results/outcomes:** Sikkim State, Kottayam District, Bhubneshwar City and Shimla City have been declared smokefree however the process followed was different, general administration was the lead agency in smokefree Kottayam, whereas political motivation followed by administrative actions was instrumental in making Shimla smokefree. Smokefree Bhubaneswar was mainly the outcome of police department efforts. Smoke-free Sikkim State is an exemplary model of activeness of bureaucracy in health ministry. Technical support and collaboration of civil society was the only common feature across all models.

**Conclusions/lessons learnt:** In spite enactment of smoke-free rules, leadership of at least one stakeholder and networking with the key partners is vital for creating smokefree jurisdiction in India.

#### PC-571-17 Creative communication for strategic advocacy on tobacco control

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**Background and challenges to implementation:** The tobacco epidemic is spreading faster in the developing world due to low levels of public awareness and social acceptance of tobacco use. The FCTC outlines (Article 12) that each party shall promote and strengthen public awareness of tobacco control issues, using all available communication tools, as appropriate. Communication has a critical role in advocacy in distilling essential information for audiences, demolishing social acceptance of tobacco and spread knowledge and awareness to help consumers and new users make an informed choice.

**Intervention or response:** Authentic information from various sources, inputs and guidance of senior public health specialists, communication and advocacy experts were used to develop innovatively packaged, target-oriented messages. Dissemination process ensured that information is marketed and communicated, not just distributed, for parliamentarians, policymakers, public health officials, partner agencies, media, civil society, public, healthcare providers and researchers across India.

**Results and lessons learnt:** VHAI succeeded in developing a creative communication package for advocacy on tobacco control. Printed materials included study reports, fact sheets, manuals, guidebooks, earned, paid media messages and best practice documents. Also developed were a web portal, a photo library and short films. This package succeeded in capacity building and sensitization of target audiences. This was assessed by public opinion survey results, number of hits on the web portal, demand for advocacy materials by stakeholders, news in the media and parliament questions raised.

**Conclusions and key recommendations:** Creative communication mediums are effective in increasing public awareness on health hazards of tobacco use, instill behaviour change, change the socially accepted and glamourized image of tobacco. They are also useful to share new ideas about internet use and innovative tools in health communication.

#### PC-572-17 Secondhand smoke exposure of health care providers and implementation of smoke-free policy at the health facility

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**Background:** Exposure to secondhand smoke (SHS) causes an estimated 5% of the global burden of disease, slightly higher than the burden from direct use of tobacco. The burden of morbidity from SHS exposure is higher in low-income countries in south-east Asia region. The WHO's FCTC and India's Cigarettes and Other Tobacco Products Act, 2003 laid emphasis on ensuring smoke-free public places including the health facilities. The present study captured the self-exposure of medical officers to secondhand smoke and implementation of smoke-free law at the health facility.

**Methods:** Cross sectional survey of 238 physicians using a semi-structured questionnaire was conducted in two Indian states—Andhra Pradesh and Gujarat from January to April 2011 covering 200 health facilities. We assessed implementation of smoke-free policies in health facilities and validated it through observation by interviewer.

**Results:** Most medical officers (95%) never allowed smoking inside their house. However the majority of doctors were exposed to SHS everyday (56%) or weekly (25%) at other places. Almost all (97%) medical officers stated that there is official policy restricting use of smoking tobacco products inside hospital building or premises. Although 76% of medical officers stated that there was enforcement of smoke-free policy, interviewers observed that 90% of public health facilities where the interview took place had displayed no smoking sign with or without violation penalty sign board.

**Conclusions:** The smoke-free policy yet to be fully enforced in public health facilities. The chances of SHS exposure are also high outside resident or office building. The premises in which health facilities operate need to be 100% smoke-free. Implementation of smoke-free policy in their health facility premises should be a priority for the health department.

#### **PC-573-17 Smoke-free district headquarters: results of a compliance survey in Himachal Pradesh, India**

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**Background:** State of Himachal Pradesh (population 7 million, area 55 000 km<sup>2</sup>) presents a good model for tobacco control in India. Article 8 of FCTC and Section 4 of COTPA prohibits smoking in public places in India. Present study was conducted to assess the compliance with the smoke-free rules and assess the respective district headquarters preparedness for smoke-free declaration.

**Design/methods:** An unobtrusive cross-sectional survey was done in 1330 public places across 11 district headquarters. Sampled public places was evaluated for five core criteria, i.e., presence of signage, absence of active smoking, smoking aids, tobacco odour and smoking ash and cigarettes butts and bidi ends. The bench mark of 80% compliance was kept for the smokefree declaration.

**Results:** In seven district headquarters, compliance to signage was observed in more than 80% public places. All (11) district headquarters demonstrated more than 80% compliance in other four core indicators. Hospitality venues, bus and taxi stands and markets were the common places of violation.

**Conclusions and recommendations:** Seven out of the eleven district headquarters qualified for smoke-free status. The display of signage is a crucial indicator. This survey also identified the areas/potential points of violations in each jurisdiction which requires urgent attention from enforcement agencies. The ongoing activities have to be augmented.

#### **PC-574-17 Activities for the development of smoke-free public places in Bangladesh**

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**Background and challenges to implementation:** Exposure to secondhand smoke (SHS) is a risk for contracting diseases. The only way to protect people from SHS is to completely eliminate smoking in indoor spaces. To assist achieving this goal, declaration of smoke-free places, compliance monitoring, capac-

ity building and campaign for law amendment and tax raise are the major activities organized by four Non Government Organizations (NGOs) in Bangladesh.

**Intervention or response:** Taskforce committee meeting, mobile court operation, sensitization meeting with authorities, installation of signboards and 'No Smoking' signage and distribution of posters, stickers and leaflets were the measures for the development of smoke-free environment. Compliance monitoring, formation of community vigilance team (CVT) and follow-up meetings with CVTs were the measures for declaration of smoke-free places. Capacity building and campaign for law amendment and tax raise were the other measures.

**Results and lessons learnt:** More than five hundred taskforce committee meeting and more than two hundred mobile court operation were organized by four NGOs. About 8000 large and medium sized signboards were installed in activity areas. About 18 000 'No Smoking' signage were installed and 2.5 million posters and stickers distributed. More than 4000 public places and 77 000 public transports were declared smoke free. More than 100 sharing meetings with taskforce members, government officials, NGOs, CBOs, civil society and media people on tobacco control act were done for capacity building.

**Conclusions and key recommendations:** Extensive sensitization meeting, compliance monitoring in public places and public transports, capacity building and campaign for amendment of tobacco control law and tax raise in national, divisional, district and sub-district level are the effective activities in Bangladesh.

#### **PC-575-17 Cost of nicotine replacement therapy provision under the RNTCP, India: policy implication for developing countries**

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**Background:** Nicotine replacement therapy (NRT) is cost effective, safer and increases the rate of long-term quitting by 50–70%. NRT with effectiveness 1% is predicted to result in avoidance of 3.5 million deaths in the world. NRT has been successfully practiced over 30 years in developed countries. India with one million smoking attributable deaths, unevenly affecting poor, urgently requires adopting NRT as a public health measure in order to prevent near-term deaths of current smokers. There is proven public provision of DOTS, EPI vaccines, etc., under various national health programmes in India. This systematic review estimated the cost of NRT provision for smoking cessation under National Tobacco Control Programme (NTCP) of India and its implication.

**Methods:** Systematic review of NRT treatment guide-

lines and tobacco surveillance data was done. Considering the recommended treatment regimen of World Health Organization, we projected the cost of NRT for smoking cessation using current market price of nicotine gum in India.

**Results:** The estimated cost of NRT per person per 12 wk session treatment is US\$116–142. The cost of NRT for high ND is 26% higher. The annual budgetary allocation required for treatment of 3/4th of current smokers willing to quit is US\$2.95 billion. Second model based on experience of NRT practitioners, the average cost of NRT to cover the current smokers is US\$1.5 billion.

**Conclusion:** The absolute budgetary requirement for NRT under NTCP far exceeds the annual budget of NTCP. NRT induced reduction in smoking prevalence would require less resources in subsequent fiscal years. Although bulk purchase may reduce the cost, it may not be possible for public provision of NRT for all smokers. NRT price regulation with phase wide implementation, social marketing and public private partnerships may be opted for NRT provision. Creation of GAVI like agency for availing low cost NRT in developing countries should be envisaged.

### PC-576-17 Strategic advocacy to generate evidence to support the government of India in implementing strong graphic health warnings

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**Background and challenges to implementation:** Picture health warnings on tobacco product packages communicate health hazards of tobacco use to consumers. They encourage users to quit and discourage non-users from initiating use. Evidences prove that effective health warnings include graphic images, are large and use strong, clear and specific language. But the first warnings in India, which appeared from June 2009 after a court order were weak and ineffective.

**Objective:** Strategic advocacy to generate evidence to support and facilitate the government of India in implementing stronger, effective warnings.

**Target Audience:** Policymakers, Expert Committee Members and very senior bureaucrats of the Ministry of Health and Family Welfare, India.

**Intervention or response:** The methodology involved two phases:

**First phase:** Pre-testing to select most effective warning—11 pictograms were used to field test their efficacy in communicating the harmful effects of tobacco use. The pre-testing was carried out in 8 states with a sample of 734 participants. Focus group discussions (FGDs) were conducted with men, women, youth, tobacco users, non-users and retailers.

**Second phase:** Visual documentation to create a

graphic databank of health warnings to suggest and advocate for stronger health warnings for the next rounds.

**Results and lessons learnt:** Out of the 11 pictures, 98% respondents rated the 'Mouth Cancer' picture as the most effective warning. This was notified by the Health Ministry of Health and Family Welfare, Government of India.

**Conclusions and key recommendations:** Due to industry pressure and threat to close production, government failed to get the warning implemented. However, strategic advocacy and close networking resulted in new notified, effective warnings for smokeless tobacco products being chosen from the VHAI databank.

### PC-577-17 Garnering multi-stakeholder support for effective implementation of smokefree policies: promoting lung health in districts of Orissa, India

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**Background:** Exposure to secondhand smoke (SHS) is a leading tobacco related adversity causing high risk of lung diseases and deaths. In India, 52.3% adults are exposed to SHS at home and 29% at work. Indian Government has issued comprehensive smoke-free regulation under Indian tobacco control law (COTPA) and has notified a gravid list of enforcement officers to penalize smoking in public places. Inadequate awareness and sensitization of officials and public at grassroots remain causes of non-compliance. To strengthen enforcement of COTPA, HRIDAY with partner IIPH, Bhubaneswar, under a grant from Bloomberg Initiative to Reduce Tobacco Use implemented a project in 5 Indian states Bihar, Haryana, Karnataka, Odisha and Uttarakhand.

**Intervention:** Focus of the activities under the project was to strengthen the enforcement of smokefree regulations. These included **capacity building** of multi-sectoral stakeholders; **upstream** (participation in state level meetings and making formal requests) and **downstream** (rallies with school students and celebrities) **advocacy**; **public awareness** exhibitions; **institutionalization of enforcement mechanism**; **violations reporting** by NGOs and youth; **media engagement** to garner policy maker and public support for enforcement of smokefree policies.

**Results:** Bhadrak District and Bhawanipatna Town in Kalahandi District were declared smokefree as a result of sustained multilevel advocacy. Official directives were issued by district administration to comply with smokefree rules. Effective interdepartmental coordination, NGO and media engagement supported

the environment for policy enforcement. The future phase of the project will include assessing compliance in these districts and replicating the model in other project districts.

**Conclusions:** Capacity building of enforcement officers, government-NGOs partnership with media engagement is a recommended and sustainable model for promoting smokefree policies at grassroots. Such policy focused advocacy can serve well to promote lung health in India.

### **PC-578-17 Smoke-free Budgam District: first district in Jammu and Kashmir State where all public places declared smoke free**

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**Background and challenges to implementation:** The Cigarette and Other Tobacco Products Act 2003 prohibits smoking in public places. A city can be declared smoke free when the smoke-free law is complied, there is a systematic reporting mechanism to lodge complaint against violation of the rules of the law. The city/jurisdiction can be declared smoke free by an appropriate government authority. A compliance monitoring study was conducted to assess the level of compliance of smoke-free law in Budgam District. On the basis of the study finding the declaration of smoke-free Budgam District was made.

**Objectives of the study:** The compliance monitoring study was conducted with the following objectives: To assess the compliance level of smoke-free law in the public places.

- To observe presence of signages with warning.
- To assess presence of signages with the details of reporting authority. To observe smoking in and around the building.
- To assess provision of smoking aid such as ashtrays, matchboxes, lighters, etc. To assess effectiveness of enforcement mechanism.

**Study area:** The compliance monitoring study of smoke-free law and rules was organized in Budgam District. The study covered 352 public places in total in the district such as state government offices, hotels, banks, shopping malls, auditoriums, public sector undertakings, industrial corporations, hospitals, education institutions.

**Results and findings:** The study conducted in all the 352 public places. The data collected in the study were compiled and analyzed. The broad heads of the analysis and results thereof are:

- Signage with warning at entrance. Signage confirming prescription of law. Warning in English or any Indian language. Board size 60 × 30 cm.
- Signage prominently displayed at entrance.
- Signage prominently displayed at conspicuous place. Designated person detail displayed.

- In the district of Budgam there is a strong enforcement mechanism to report and take action against the violation of smoke-free law and rules.

### **PC-579-17 Compliance with smoke-free laws: an over-reported status**

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**Background:** Existing smoke-free laws (SFLs) in different countries have gaps. Actual implementation of even the existing laws is questionable, especially in developing countries, where implementation of SFLs is weak. The paper investigates the difference between reported compliance to SFLs by hospitality venues in India and the actual compliance.

**Design/methods:** Data on implementation of smoke-free laws was collected in the state of Andhra Pradesh (AP) in India. In AP, the Bill & Melinda Gates Foundation funded tobacco control Project STEPS is being implemented. Two sets of data from 401 hospitality venues were collected: one, as reported by a responsible person at the venue and another, as observed by the interviewer. Standardized questionnaires and check-lists were administered by well-trained interviewers. Data were entered in an SPSS database and analyzed for the comparison.

**Results:** While 18.4% of respondents at hospitality venues reported having 'No Smoking' signage, actual existence of it was found only at 14.7% of venues. Though 41.4% of venues claimed to have a designated person authorized to take action for non-compliance with SFLs, only 3% of venues actually had such designated person. Tobacco products were found to be sold in 10% of venues, even though only 5% of venues had reported such activity. Similarly, only 9% of venues reported providing tobacco products from outside to customers. However, 29% of venues were observed to extend this facility to customers.

**Conclusion and recommendations:** The data reveals huge gaps in actual implementation of smoke-free laws at hospitality venues. Actual compliance with SFLs is even much weaker than the poor implementation status as self-reported by someone responsible at the venue. Analysis of self-reported data on compliance with tobacco control laws should be made in the backdrop of this discrepancy with actual status. Similar analysis should be extended to states within India and in other developing countries where implementation of SFLs is weak.

## MANAGEMENT OF MULTIDRUG-RESISTANT TUBERCULOSIS AND CONTACTS

### PC-596-17 Poor prognostic factors for tuberculosis-related mortalities in hospitalised patients

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**Background:** Despite effective treatment regimens available, tuberculosis (TB) stands among one of the leading causes of death in Pakistan. Factors associated with TB-related mortality in the region include non-compliance to therapy, multidrug-resistance, and immunocompromised states. We evaluated factors concerned with in-hospital deaths in patients admitted with tuberculosis at a tertiary care centre.

**Methods:** A retrospective case-control study was undertaken at the pulmonology department of the largest public tertiary care centre in Karachi, Pakistan. For patients hospitalised with TB, sixty of those who were discharged were compared with sixty of those who could not survive during hospitalisation. Radiological findings, clinical indicators and laboratory values were matched between the two groups to locate poor prognostic factors.

**Results:** Factors concerned with in-hospital mortality listed late sequels of disease ( $P < 0.01$ ), not taking anti-tuberculosis therapy (ATT,  $P < 0.01$ ), smoking ( $P < 0.01$ ), longer duration of illness ( $P < 0.01$ ), low weight ( $P < 0.00$ ), female sex ( $P < 0.01$ ), and low haemoglobin levels ( $P < 0.02$ ). Extrapulmonary TB, dissemination of disease, bilateral radiological findings, co-morbidities and multidrug-resistance were not implicated in higher mortality. Most deaths occurred during the first week of admission ( $P < 0.00$ ) indicating late referrals and late presentation as important factors related to in-hospital fatalities.

**Conclusion and recommendations:** Poor prognosis in TB patients was associated with non-compliance to therapy, anaemic and undernourished states, late presentation of disease, and development of complications. Patients not taking ATT and hence having longer duration of illness showed higher mortality and so a more radically effective treatment regimen is required to eliminate TB early on during the onset of disease.

### PC-597-17 Feasibility of a centralised mechanism for management of multidrug-resistant tuberculosis patients at the peripheral level in the Tibetan community in India

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**Background:** Tibetan settlements, each with its own healthcare facility, are scattered throughout India, but very few have a resident general doctor. Management of MDR-TB at the peripheral level had usually been the responsibility of the settlement doctor or TB nurse, but many have minimal training on MDR-TB. As a result, patients often had to travel long distances to get an expert opinion.

**Intervention:** In June 2011, a panel of doctors with experience managing MDR-TB was established at the Tibetan Delek Hospital in Dharamsala, the main hospital of the Tibetan community-in-exile. A computerized consultation form was prepared, which includes clinical information, previous medical history, lab test, and radiology reports. The peripheral clinics were requested to consult the TB panel before starting an MDR regimen, for treatment modification or interruption, and in case of side effects of other management issues. After a consensus was reached by the expert panel, treatment and other management recommendations were communicated to the consulting doctor.

**Results:** 21 new MDR-TB cases were submitted to the TB panel for review from June 2011 to January 2012. All received a treatment regimen in accordance with WHO guidelines. 16 episodes of medication side effects were identified and submitted to the TB panel, and recommendations were given for further management. Feedback from the peripheral healthcare staff was very positive. The expert panel also enabled more experienced physicians to provide on-the-job education to healthcare workers through direct supervision and discussion of cases.

**Conclusions and recommendations:** MDR-TB treatment is complex and requires specialized training for effective management under the supervision of experienced personnel. The establishment of a standardized mechanism for consultation with a TB expert panel is an effective and efficient way to guarantee appropriate management of MDR-TB at the peripheral level.

### PC-598-17 Incorporation of GeneXpert® MTB/RIF assay in the tuberculosis diagnostic algorithm in a sub-district hospital in a high MDR area in India

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**Background:** The Tibetan population in-exile in India has a high incidence of TB. MDR-TB is common in both new and previously treated cases. This is of particular concern given that the majority of patients are students, monks, and nuns living in congregate settings, increasing the likelihood of primary transmission of resistant strains.

**Methods:** In July 2010, a GeneXpert IV (GXP) was installed at the Tibetan Delek Hospital, a sub-district hospital in Dharamsala. GXP MTB/RIF assay has been routinely used as part of the diagnostic algorithm on sputum smear positive cases for detection of rifampicin (RIF) resistance and on sputum smear negative cases for confirmation of TB diagnosis. GXP was also used to diagnose different forms of extrapulmonary (EP) TB.

**Results:** Between April 2011 and March 2012, a total of 322 tests were performed on 278 patients. Of those, 25 tests gave 'no result' or 'error' and were repeated, and 35 tests were EP samples. 243 tests were performed on pulmonary samples, of which 144 were positive for *M. tuberculosis* and 99 were negative. Culture and DST results were available in 124 and 106 patients, respectively. One patient was GXP-/culture+ for *M. tuberculosis*, and 13 were GXP+/culture-. RIF resistance was detected by GXP in 19 cases, and 17 of those were confirmed by DST (2 patients were GXP RIF resistant with negative culture). In 2 cases GXP failed to detect a DST-confirmed RIF resistance. Comparison of different techniques for TB diagnosis is summarized in the Table.

**Table** Xpert® MTB/RIF compared to culture and smear microscopy

	Culture+		Culture-		Total
	SS+	SS-	SS+	SS-	
GXP+	91	15	7	6	119
GXP-	0	1	1	3	5
Total	91	16	8	9	124

**Conclusions:** GXP use at a sub-district level in a high-MDR population is a highly effective tool for TB diagnosis. It provided early detection of RIF resistance so that appropriate treatment and isolation measures could be implemented. Our data also suggests it may be more effective compared to culture in some settings. However, the high cost of car-

tridges and high number of errors may limit GXP use in the absence of ongoing research projects or external funding.

### PC-599-17 Prevalence of drug-resistant tuberculosis in retreatment cases and implications for treatment with the Kenya standardised national retreatment regimen

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**Background:** There is limited data both on the epidemiology of mono- and poly-drug resistant tuberculosis (TB) and their treatment outcomes in Kenya. Despite national guidelines that require all retreatment TB patients undergo sputum culture testing, only 69% of eligible patients in 2012 had their specimens sent. Present national retreatment guidelines call for the addition of streptomycin to the standard 4 drug regimen as well as a prolongation period prior to moving to a 3 drug continuation phase (8 month total retreatment regimen: 2SRHZE, 1RHEZ, 5RHE).

**Objective:** To report the prevalence of mono- and poly-drug resistant tuberculosis among retreatment cases tracked through the TB Projects Office at Moi Teaching and Referral Hospital in Eldoret, Kenya, and to predict probable outcomes if the patients were treated with the national retreatment regimen.

Resistance pattern	Recommended regimen by WHO (2008)	Predicted outcome if treated per national guidelines	No. of samples with this pattern
Isoniazid	6-9 RZE	Relapse	44
Streptomycin	2RHEZ/4RH	Cured	4
Rifampicin	Treat as MDR TB	Treatment failure	2
Ethambutol	2RHEZ/4RH	Cured	4
SR	Treat as MDR TB	Treatment failure	2
HS	6-9RZE	Relapse	7
HR (MDR-TB)	MDR-TB regimen	Treatment failure	4
HE	9-12 RZ + fluoroquinolones	Treatment failure with MDR-TB risk	4
HRS (MDR-TB)	MDR-TB regimen	Treatment failure	5
HRE (MDR-TB)	MDR-TB regimen	Treatment failure	4
HSE	9-12 RZ + fluoroquinolones	Treatment failure with MDR-TB risk	6
HRSE (MDR-TB)	MDR-TB regimen	Treatment failure	6

H = isoniazid; S = streptomycin; R = rifampin; E = ethambutol; Z = pyrazinamide.

**Design:** Retrospective analysis of data on retreatment samples collected between February 2007 and December 2010 by the TB drug surveillance tracking program.

**Results:** 1358 sputum samples from patients being started on TB retreatment regimens were sent to the national laboratory for culture and drug resistance testing. 290 specimens grew *Mycobacterium tuberculosis* and underwent first line drug resistance testing. 198 (68%) samples were sensitive to all drugs. 92 (32%) were found to be resistant to at least one drug. Evaluation of predicted treatment outcomes for the drug resistant cases are presented in the Table. 91% (82/92) of all patients who were resistant to at least one drug are predicted to receive an inadequate regimen with the empiric national retreatment regimen.

**Conclusion:** Without drug resistance information coupled with the development of national treatment guidelines for cases in the middle of the spectrum between drug susceptible and multi-drug resistant isolates, there is risk for national programs to be amplifying resistance or at least contributing to repeated treatment failures.

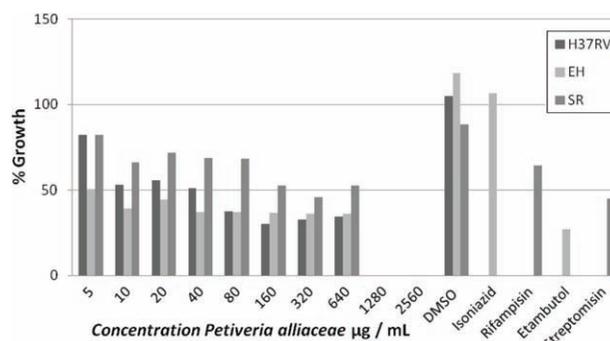
#### PC-600-17 *Petiveria alliacea* a new alternative for treatment of susceptible and multi-resistant *Mycobacterium tuberculosis*

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**Background:** *Mycobacterium tuberculosis* has infected one-third of the world's population, including Indonesia. These bacteria become resistant easily to one or several types of anti-tuberculosis standard drugs, so often treatment is not successful. There is also a need to alleviate drug regimens by developing a safer, more effective and more affordable drug. The purpose of this study is to determine the activity of *Petiveria alliacea* extracts against drug-sensitive and resistant strains of *M. tuberculosis*.

**Method:** *P. alliacea* was extracted with ethanol using the maceration method. Extracts dissolved in dimethyl sulfoxide were tested at concentrations of 5, 10, 20, 40, 80, 160, 320, 640, 1280 and 2560 µg/ml against the LJ medium. Inoculation was performed on drug-sensitive and resistant strains H37Rv *M. tuberculosis*. Each bacteria was suspended to obtain a turbidity of McFarland (MCF) 10-3 and 10-5. All tubes were incubated at 37°C. The growth of bacterial colonies was observed weekly starting week 4 to week 8. *M. tuberculosis* strains were H37Rv bacteria-sensitive, bacteria-resistant EH (resistant to ethambutol and isoniazid) and SR (resistant to streptomycin and rifampicin).

**Results:** The ethanol extract of *P. alliacea* leaves have anti-mycobacterial activity against drug-sensitive and



resistant strains H37Rv of *M. tuberculosis*. The minimum inhibitory concentration (MIC) for all types of *M. tuberculosis* is 1280 µg/ml, which is shown by the absence of bacterial growth shown in the Figure.

**Conclusion and recommendations:** The ethanol extract of *P. alliacea* was found to be active against *M. tuberculosis* at concentrations of 1280 and 2560 µg/ml. We conclude that activity of *P. alliacea* inhibits the growth of *M. tuberculosis*. Further testing is needed to identify its beneficial components.

#### PC-601-17 To find an equilibrium point of the quality and quantity of MDR-TB treatment: an evaluation of a standardised MDR-TB medical service package

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**Background:** In order to control the cost of MDR-TB diagnosis and treatment service, a service package was introduced onto the prefectures which implement China MOH-Gates Foundation hospital-CDC cooperation sub-project which focus on PMDT (programmatic management of drug-resistant tuberculosis) as intervention. Species and frequency of diagnosis and treatment services were defined in a limited set according to the WHO recommendations. Surveys were conducted before and after the implementation of project to evaluate the impact of the service package.

**Methods:** Baseline survey and the survey during the project implementation were conducted. 157 MDR-TB cases of 4 prefectures were sequentially enrolled during January and September 2011. All data of medical care costs during patient's hospitalization period were collected, including total medical cost, medical cost reimbursed by health insurance and project, out-of-pocket cost by patients, etc. These costs were stratified carefully by medical service category and funding sources. All data analyzed by descriptive statistical methods. And some of the data were compared by non-parameter statistic methods, such as the proportion rate by service categories before and after the project and daily cost of hospitalization.

**Results:** By the implementation of the service package,

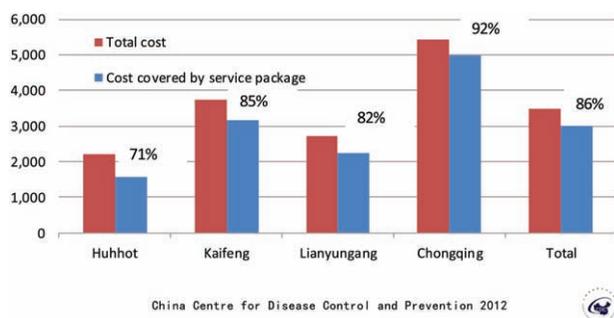


Figure 1 Cost covered by service package.

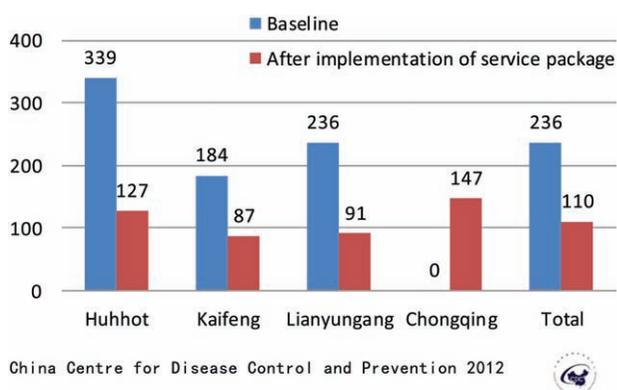


Figure 2 Comparison of daily cost of hospitalization before and after implementation of service package.

the proportion of drug cost with medical services declined from 60% to 16%. Also average daily cost for hospitalization strongly reduced from 236 CNY per day to 110 CNY per day. The patient's out-of-pocket cost reduced to 16%, significantly lower than the 70% before the project implementation.

**Conclusions:** By implementing the standardized service package, the phenomenons of overdiagnosis and overtreatment were significantly lessened, and the quality of medical services were maintained on a proper level at the same time. And patients' economic burden for MDR-TB treatment mitigated effectively.

### PC-602-17 Tuberculin skin testing and chest X-ray for tracing tuberculosis contacts: costs and practicality

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**Background:** Tuberculin skin testing (TST) and chest X-ray are the conventional methods adopted for tracing a tuberculosis (TB) suspect. The purpose of the study was to calculate the cost incurred by Penang

General Hospital on performing one contact tracing procedure by activity based costing approach. We also aimed to highlight the practical value of this conventional contact tracing procedures in local setting.

**Design/methods:** Contact tracing record from March 2010 until February 2011 was obtained from TB contact tracing record book, retrospectively. Human resource cost was calculated by multiplying the mean time spent (in minutes) by employees doing specific activity to their per-minute salaries. The costs of consumables, purified protein derivative vial and clinical equipments were obtained from the procurement section of the Pharmacy and Radiology Department. The cost of the building was calculated by multiplying the area of space used by the facility with the unit cost of public building department. Straight-line depreciation with a discount rate of 3% was assumed for calculation of equivalent annual costs for building and machine.

**Results:** Out of 1024 contact tracing procedures, TST was positive ( $\geq 10$  mm) in 28 suspects. However, anti-TB treatment was started only in 5 contacts solely based on typical sign and symptoms of TB. Total unit cost of chest X-ray and TST was MYR 9.20 (US\$3.00) and 11.80 MYR (US\$3.90), respectively. Total cost incurred on single contact tracing procedure was MYR21.03 (US\$6.90).

**Conclusion and recommendations:** Our findings suggested that only those contacts were registered as active TB patients showing particular signs and symptoms of TB irrespective of their TST result. With these figures it seems totally irrational to recommend chest X-ray and TST for every close contact of TB patients. Conventional contact tracing methods should be replaced with more accurate and specific methods only in those suspects exhibiting typical signs and symptoms of tuberculosis.

### PC-603-17 Active case finding among contacts of smear positive patients in a high tuberculosis burden country using Xpert® assays

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**Background:** Cambodia has the second highest prevalence rate for TB among the 22 high TB burden countries. However, WHO estimates that the program may be diagnosing only 65% of the TB patients (all forms). Hence, CENAT launched an active case-finding project in February 2012 with support from TBREACH to screen and diagnose TB among 27 500 contacts of about 9600 smear positive patients registered for treatment in the past two years.

**Design/methods:** We are using quasi-experimental cluster randomized design with control and intervention arms. We selected 30 target operational districts

(ODs) that have poorest health access rates and highest household poverty rates. Out of these 30 target ODs, we randomly allocated 15 ODs to the intervention arm and 15 ODs to the control arm. Intervention includes screening 27500 contacts of about 10000 smear positive cases using TB symptoms and chest X-ray, followed by diagnosis of TB using Xpert® MTB/RIF assay.

**Results:** The participation rate in the first four operational districts has been 122% of the target. We found that 2.4% of those screened have bacteriological positive TB. We found that 4.8% have TB of all forms. About 21% of the Xpert tests that we performed were MTB+/RIF-. Results of all 15 intervention and 15 control districts will become available by 30 September 2012.

**Conclusion and recommendations:** Preliminary findings of this nine-month project indicate high yield of Xpert MTB+/RIF- tuberculosis cases among contacts of smear positive cases. Full results will become available by 30 September 2012.

## NEW APPROACHES TO TUBERCULOSIS PREVENTION IN CHILDREN

### PC-634-17 Increasing uptake of INH prophylaxis for children under 6 of tuberculosis contacts through task shifting: case study, Gombe State tuberculosis programme, Nigeria

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**Background:** Prophylaxis with isoniazid (INH) has an early survival benefit and reduces incidence of tuberculosis (TB) in children especially with HIV in areas with a high prevalence of TB. Owing to the concern that administering INH preventive therapy (IPT) to persons with active TB will promote the development of INH-resistant TB, screening of children for prophylaxis in Nigeria is restricted only to doctors. However, doctors are hardly available to offer such services at all levels due to their shortage especially in rural areas and that contributes to low IPT uptake.

**Objective:** To explore enrolment of children under 6 years on IPT by DOTS providers instead of doctors.

**Design/methods:** It was a prospective, observational cohort study for a period of 3 years (2009–2011). Training on the use of TB score chart and symptoms checklist for exclusion of active TB among under 6 years was done for nurses and other health workers. All children enrolled were evaluated as a cohort for outcomes.

**Results:** Of 497 children who were screened as con-

tacts of 303 smear positive cases registered over the period (2009–2011), only 259 (52%) were enrolled for IPT compared to 77 children enrolled between 2007 and 2008. Most of them 247 (95%) were enrolled by DOTS providers and only 12 (5%) by doctors. Of those enrolled, 234 (94.7%) completed their course of isoniazid therapy, and 88.5% (207) were fully adherent compared to an average of 31% completion rate before the task shifting. Only four (4) children developed TB and 13 children defaulted. The use of symptoms checklist, double check by staff and kitting of INH ensure good responses and better outcome.

**Conclusion and recommendations:** IPT uptake among under 6 children in Nigeria could be increased through task shifting of the enrolment from doctors to DOTS providers.

### PC-635-17 Using homeopathy to prevent latent and active tuberculosis infection in children living in households with tuberculosis patients

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**Background:** High proportions of children living in households with TB patients have a latent tuberculosis infection (LTBI). Despite the substantial morbidity and mortality caused by childhood LTBI, there has been no preventive strategy especially in resource poor areas.

**Methods:** We conducted a multicenter, randomized, double-blind, placebo-controlled trial of six months of prophylactic homeopathic treatment in children under the household contact of DOTS category I pulmonary tuberculosis patients. In Jaipur rural, 166 tuberculosis patients on DOTS were selected and their 210 children in household contact were included in the study. Children up to the age of 16 were randomly assigned to receive homeopathy or placebo as a prophylactic treatment. A tuberculin skin test, sputum examination for acid-fast bacilli (AFB), and chest radiography were conducted to confirm LTBI.

**Results:** 196 (95 in homeopathy and 101 in placebo) children completed the intervention. The incidence of clinically defined LTBI was significantly lower in the homeopathy group (8 participants; 8.4%) compared with the placebo group (39 participants; 38.6%). The incidence of laboratory-confirmed tuberculosis infection was reported in 2 children (1.98%) whereas there was no active infection reported in homeopathy group. Children reported no side effects of medication.

**Conclusion:** Preliminary study data suggest that homeopathy could be effective prophylaxis in children with household contact of active case of tuberculosis especially in low cost setting.

### PC-636-17 Yield of contact tracing among household contacts of children diagnosed with TB in Gaborone, Botswana

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**Background:** Diagnosing a child with tuberculosis (TB) suggests within household transmission. Contact tracing (CT) using pediatric index cases has not been investigated in high prevalence HIV-TB settings, such as Botswana (HIV 17.6%, TB notification rate 505/100 000). Traditional CT using smear positive adult index cases reveals a new TB case yield of 2.2% and number needed to screen (NNS: total contacts/total new TB cases diagnosed) of 45. We aimed to determine the yield of CT in household contacts of pediatric index TB cases.

**Design/methods:** This operational research project included all new pediatric ( $\leq 13$  years) TB admissions from January 2009–December 2011 to Botswana's largest referral hospital. A CT team identified index cases, conducted home visits, symptom screened contacts and referred those with  $\geq 1$  TB symptom. The primary outcome was newly diagnosed TB in a contact, reported using descriptive statistics and 95% confidence intervals (CIs).

**Results:** From 163 pediatric index cases, 548 contacts were screened (median 3 contacts/case, IQR 2–4). Of these, 49 (9%) were referred for positive symptom screen and 27/49 (55%) were screened by a doctor or nurse for active TB. Twelve secondary TB cases were diagnosed (12/548 = 2.2%). Of these, 11 (92%) were smear positive; HIV-status was known in 10 (83%) and 7 (70%) were HIV positive. Median age was 31 years (IQR 23–38) and included 2 children under 5—both smear positive. Among index cases, HIV-status was known in 83 (51%) and

58 (70%) were HIV-positive. CT was done within 1 month of index case diagnosis in 75% of cases. The table shows results.

**Conclusion and recommendations:** Our yield of new TB cases by CT of pediatric index cases is similar to that of the traditional adult index case based approach. Improving the proportion of symptomatics screened by a doctor or nurse may increase yield further.

### PC-637-17 Improving uptake of isoniazid prophylactic therapy among under-6 children contacts of index cases in Nigeria from 2010 to 2011; 'protecting the child of today'

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**Background and challenges to implementation:** Given the high burden of tuberculosis in Nigeria, an effective National TB Programme will ensure fewer children exposed to infectious TB cases develop TB. Owing to this, Nigeria reviewed its data capturing tools to monitor the implementation of isoniazid (INH) prophylactic therapy (IPT) for children under the age of six who have had contact with infectious TB cases.

**Objective:** To assess the quarterly trend of IPT uptake among children under 6 yrs who are contacts of index cases between 2010 and 2011 and identify challenges to implementation.

**Methods:** A retrospective data review was carried out between 2010 and 2011 in which records of TB case notification were analyzed according to all smear positive cases; TB screening among under 6 child contacts and IPT uptake among under 6 contacts. In addition analysis of perceived barriers to uptake of IPT was done. Subsequently, data capturing tools, supplies of IPT and training of health care workers were provided.

**Results:** As at the end of 2010 there was no documentation on the implementation of IPT among children at national level. Within the period of 2011 with 52 257 smear positive cases registered, 7597 children were screened (15% relative to the number of smear positive cases registered, estimating 3 in every 20 smear positive case presented a child for screening). An incremental rate for TB screening by 31% was observed between quarter (Q)1 and Q2, 11% increment between Q2 and Q3 and 3% between Q3 and Q4. Overall, screening rate increased by 50% by the end of 2011. Out of the 7597 children screened, 65% were placed on IPT.

**Conclusions:** All DOTS centers should be linked to at least a clinician for TB screening and GHCWs

**Table** Yield of contact tracing of 548 contacts from 163 pediatric index cases

Metric	Index case approach used	
	Pediatric (95%CI)	Adult smear positive, data from the literature
New TB case yield, %	2.2 (1.1–3.8)	2.2 [range: 0.01–14.5]
New TB incidence, per 100 000	2.19 (2.100–2.282)	2.2
Number needed to screen	46 (26.4–88.0)	45

should be empowered with the skill of excluding TB among child contacts in order to allow prompt initiation of IPT.

### PC-638-17 Evaluation of a quality assurance tool used for the identification of child contacts for isoniazid preventive therapy in Cape Town

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**Background:** Monitoring of implementation of programme guidelines enables the assessment of quality, coverage and delivery of health services. In the absence of a standardised reporting tool, this may be accomplished using routine quality assurance audits, if these are validated. The city of Cape Town conducts routine annual quality assurance audits of HIV, AIDS, STI and TB (HAST) services, systematically sampling 10 records at each facility. Isoniazid preventive therapy (IPT) delivery is included in these HAST audits, but has not been validated.

**Intervention:** A random sample of 15% of all facilities stratified by TB case load, resulted in the sampling of 7 high and 7 low-burden TB facilities to enable a systematic review of all infectious TB cases in a six-month period. Data on the identification of child contacts for IPT from this review was correlated with HAST audit data.

**Results:** 1186 index cases were reviewed from April 1 to September 30, 2010. Of these 386 (49.3% of eligible clinical records) had contacts identified for IPT compared to 75.3% of records reported in the HAST audit. An intra class correlation (ICC) demonstrated no correlation ( $r = 0.6245$ ,  $P = 0.0536$ ) and the ICC (consistency) coefficient demonstrated a positive association 0.618 (95%CI 0.025–0.889) with a consistent discrepancy between the two data sources.

**Conclusions and key recommendations:** The failure to correlate the systematic review with the routine HAST data raises concerns regarding the validity of the routinely available HAST audit data for programmatic evaluation. Discrepancies are most likely due to consistent under reporting in the HAST audit, although over reporting in the clinical record review could have occurred. Where data on IPT for children remains invalidated, the monitoring of this service remains difficult. There is a critical need to develop strategies and identify shortfalls for IPT delivery; this requires the establishment of mechanisms for rigorous routine monitoring.

### PC-639-17 Improving case finding for childhood tuberculosis in Cambodia: contact tracing for childhood tuberculosis

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**Background:** Cambodia National Center for Tuberculosis and Leprosy (CENAT) developed guidelines for the management of childhood TB in 2008 which were aimed at strengthening case finding, diagnosis and treatment of childhood TB. Although the guidelines contain provisions for contact screening and management, they have seldom been implemented. Childhood TB cases detected before intervention were mostly from active case finding activity.

**Intervention:** The implementation of childhood TB focusing on contact tracing by CENAT and JATA/TB CARE I/USAID started in quarter 2 of 2011 in 14 operational districts of 77. The main activities of the childhood TB initiative are: orientation workshops, clinical trainings for diagnosis, tuberculin skin testing trainings, contact tracing by health centers and community DOTS partners, referral of TB contacts, diagnosis, treatment and supervision. Health centers and community DOTS workers conduct home visits of registered TB patients to identify and refer children with TB symptoms to hospitals for diagnosis on the pre-appointed day.

**Results:** Within one year, the data shows an increase in number of referral and TB cases. The referral number in 2011 was 282, 2784 and 2795 in quarter 2, quarter 3 and quarter 4, respectively. This number increased to 7526 in quarter 1 of 2012. Among this number of symptomatic children, 107, 609 and 559 TB cases were detected in quarter 2, quarter 3 and quarter 4, respectively in 2011. In quarter 1 of 2012, the TB cases increase to 973. The factors contributing to the success are: 1) improving clinical skill for diagnosis, 2) referral coordination by community DOTS partners, and 3) commitment of hospital team.

**Conclusion:** Contact tracing and diagnosis at hospitals for childhood TB plays an important role in TB case detection for TB in children and Cambodia NTP should expand this intervention to other districts.

### PC-640-17 Timing of tuberculosis source case contact information and tuberculosis in HIV-infected and HIV-exposed, non-infected children from southern Africa: IMPAACT P1041

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**Background:** Identifying a source case for TB-exposed children is challenging. TB can be prevented with post-exposure prophylaxis once a source case is identified. We examined the timepoint of obtaining source case TB contact information in HI and HEU participants in P1041, a randomized, placebo-controlled trial of pre-exposure isoniazid prophylaxis.

**Design/methods:** 543 HI and 808 HEU infants participated in 4 Southern African sites. This secondary analysis included data until 108 weeks from study entry. TB exposure was associated with endpoint type: definite, probable, possible TB and death or endpoint free. Caregivers of study participants were asked about TB contact at study entry and 12 weekly thereafter.

**Results:** Mean baseline age was 100 (91–120) days. 128 cases of TB disease and 40 deaths were recorded, 19% (105/543) for HI and 8% (63/808) for HEU, 229 TB contact occasions were reported in 205/1351 (15%), the majority (83%: 189/229) in the household. 53% of household contacts (108/189) had microbiological evaluations, 81% (87/108) were positive. The proportion of participants with TB contact was similar for HI- and HEU infants. A TB contact was reported in 48% who developed definite TB, 58%—probable TB, 43%—possible TB, 8% of deaths and 12% without endpoint. Among 128 children with TB, 59 had reported TB contact, with 29/59 (49%) only identified *at or after* TB diagnosis in the child.

**Conclusion and recommendations:** TB contact source cases are often identified only when TB is diagnosed in a child. More research on identifying children in contact with a TB source case is needed.

### PC-641-17 Risk factors for tuberculosis infection in children living with a sputum-positive case in Indonesia

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**Background:** Children living with a tuberculosis case are at high risk of TB infection and disease. Therefore the WHO recommends all children aged less than five years, who live with a sputum positive case, be screened for TB disease. This is rarely conducted in high burden countries where resources are focused towards infectious cases. Identifying risk factors for tuberculosis infection may aid in streamlining screening policy.

**Methods:** Sputum and chest X-ray positive adult TB patients were invited to bring their children (6 months–9 years) for screening. Children were assessed for TB disease and infection according to symptoms, QuantiFERON® Gold In-Tube assay (QFT-GIT), tuberculin skin test (TST) and chest X-ray. Children with TB disease were excluded. Risk factors for infection were collected using a structured questionnaire and were calculated separately for the TST, QFT-GIT and for the tests combined.

**Results:** Of 304 children eligible for inclusion in the study, 145/302 were positive by TST, 152/299 by QFT-GIT and 180/304 were positive by either or both tests. Test positivity was associated with infectious load, (compared to AFT1+, AFB2+ OR 1.57 95%CI 0.78–3.12; AFB3+ OR 2.44 95%CI 1.24–4.80) and exposure (child contact's parent is the index case OR 4.08 95%CI 1.75–9.49). QFT-GIT was also associated with older age (>36 mo OR 2.58 95%CI 1.53–4.34). Of children whose parents were 3+ sputum positive 72% were positive by either or both tests. Neither the TST nor QFT-GIT showed superior correlation to infection risk factor gradients.

**Conclusion:** TB infection according to either test was high and supports screening and preventive therapy. Children whose parents are sputum positive should be prioritised for screening but all child contacts of sputum positive cases are at high risk of infection.

### PC-642-17 Pulmonary tuberculosis screening in antenatal clinics in Lusaka, Zambia

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**Background:** Tuberculosis (TB) is highly prevalent in sub-Saharan Africa and previous studies have shown

that TB is common among pregnant women. TB is a cause of non-obstetric maternal deaths and is associated with poor obstetric outcomes, particularly when diagnosed at an advanced gestational age. This study was done to determine the feasibility of including TB screening in routine antenatal care and to estimate the prevalence of TB among pregnant women in three out-patient antenatal care (ANC) primary health care clinics in Lusaka, Zambia.

**Design/methods:** All women >18 years of age attending their first ANC visit were offered HIV testing and TB symptom screening. All HIV-positive women regardless of symptoms and all HIV-negative women presenting with one or more TB symptoms (*weight loss, cough, hemoptysis, fatigue, fever, night sweats, chest pain, loss of appetite, or swollen lymph nodes*) were asked to submit two sputum samples for LED fluorescence microscopy as well as liquid and solid culture. Patients found to be smear or culture positive were initiated on TB treatment through the National TB Program.

**Results:** 384 women presented for screening of whom 65 (17%) were HIV-infected. 37% of HIV-infected and 29% of HIV-uninfected women reported one or more TB symptoms. Sputum samples were collected for 143 (37%) women, of whom 1 was smear and culture positive and 1 was smear negative, culture positive. This resulted in an overall TB prevalence of 521/100 000. Both TB cases were HIV-negative.

**Conclusion and recommendations:** This is the first TB screening survey to be performed among pregnant women in Zambia and was found to be feasible and acceptable. A high proportion of women were symptomatic yet the overall cases detected were comparable to the national prevalence. Early TB detection is important in pregnant women but further studies are needed to determine if this activity should be included in routine care.

#### PC-643-17 Reasons for non-attendance for assessment for child contacts of multidrug-resistant tuberculosis

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**Background:** Local policy advises that children exposed to drug-resistant (DR) tuberculosis (TB) should be assessed in a specialist clinic.

**Aim:** To explore reasons why children referred as DR-TB contacts are not brought to these appointments.

**Methods:** Following a focus group discussion, in which themes and barriers were explored, a data capture tool was developed to explore reasons for non-attendance at clinic appointments. From 1st Septem-

ber 2011 the first 50 children who had been referred to the specialist paediatric DR-TB clinic at Tygerberg Children's Hospital, Cape Town, South Africa (or associated outreach clinics) and who then attended their clinic appointment were recruited. The first 50 children referred but who did not attend were also identified and traced. Home visits were performed and patients then recruited. Differences in patient and carer demographics, obstacles to access of care and perceptions of disease were compared between the two groups.

**Results:** Median age of children was 35 months, 48 (48%) were boys and 4 (4%) were HIV-infected. Forty-seven (47%) were of coloured ethnicity, 52 (52%) were black and one (1%) child was white. Significant demographic risk factors for non-attendance at clinic were: coloured ethnicity (OR: 0.35; 95%CI 0.15–0.83;  $P = 0.01$ ), the mother being the source case (OR: 0.26; 95%CI 0.09–0.78;  $P = 0.009$ ), smokers in the house (OR: 0.42; 95%CI 0.04–0.99;  $P = 0.04$ ), distance ( $P = 0.02$ ) and cost ( $P = 0.03$ ) of travelling to local clinic and the time ( $P = 0.002$ ) and cost ( $P = 0.03$ ) required to get to the specialist clinic. Perceptions that affected clinic attendance were: concern that MDR-TB cannot be treated ( $P = 0.04$ ) and fear of being infected whilst waiting to be seen (OR: 0.41; 95%CI 0.18–0.93;  $P = 0.03$ ).

**Conclusion:** Reasons for non-attendance at clinic appointments are complex and are influenced by demographic, social, logistic and cultural influences. Health programmes need to address these issues in order to improve uptake of services.

#### PC-644-17 Risk factors for infection in child contacts of multidrug-resistant tuberculosis

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**Background:** Young children exposed to *M. tuberculosis* (*M. tb*) have a high risk of disease progression following infection. There are limited data on risk factors for infection in children exposed to drug-resistant (DR) *M. tb* strains.

**Aim:** To determine the risk factors for *M. tb* infection in child contacts of adults with multidrug-resistant (MDR)-tuberculosis (TB).

**Methodology:** Prospective study; all children aged <5 years, routinely referred to the provincial specialist DR-TB clinic, Western Cape Province, South Africa, identified as a contact of an infectious MDR-TB source case, were eligible for enrolment from May 2010 to April 2011. Data collected on the child and the source case included demographic, clinical and

social characteristics, and exposure data. All children underwent HIV and tuberculin skin testing (TST). *M. tb* infection was defined as having a TST response  $\geq 10$  mm if HIV negative ( $\geq 5$  mm if positive). Informed consent and ethical approval were obtained.

**Results:** 193 children were included (median age 30 months); 100 (52%) were boys and 72 (37%) were TST-positive. 105 (54%) were of coloured ethnicity, 86 (45%) were Xhosa. Median age of the source cases was 33 years; 114 (59%) were female and 61 (32%) HIV positive. In multivariable analysis, HIV infection in the source case (adj OR: 0.42; 95%CI 0.18–0.97) and age  $>35$  years of the source case (adj OR: 0.43; 95%CI 0.19–0.98) were associated with lower odds of TST positivity in the child; coloured ethnicity in the child was associated with higher odds of infection (adj OR: 2.44; 95%CI 1.19–5.04).

**Discussion:** HIV status and the age of MDR-TB source case appear to influence the risk of infection in child contacts; children of coloured ethnicity are at increased risk of developing infection. Ethnicity is likely to be a surrogate for multiple socioeconomic factors. In order to manage the epidemic, these factors require further investigation.

#### PC-645-17 Isoniazid preventive therapy in HIV-infected children, Nairobi, Kenya

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**Background:** Isoniazid preventive therapy (IPT) is recommended by the Kenya Ministry of Health (MOH) for HIV-infected infants  $<12$  months of age with known tuberculosis (TB) contact and  $>12$  months of age regardless of TB contact. We describe the Eastern Deanery AIDS Relief Project (EDARP) experience with IPT provision to children in an urban slum in Nairobi.

**Design/methods:** We conducted a retrospective evaluation of children aged 0–14 years who received IPT for a two-year period between March 2008 and November 2009. Eligibility for IPT was based on negative symptom screening, physical examination and chest X-ray to exclude TB disease. We evaluated adherence to a six month course of IPT, compared incidence of TB disease and death among children who completed IPT and those who did not complete IPT.

**Results:** Two hundred fifty-five HIV-infected children were initiated on IPT, 43 were lost to follow and 6 transferred out of the clinic before the end of the two-year follow-up period. Of the 206 who had 2 years of follow up, baseline characteristics included a median age of 6.22 [IQR 4.24–9.05] years, 39% with WHO stage III and median CD4% of 28.2%

(IQR 22–36). Seven (3.4%) of 206 developed active TB disease, 3 (1.5%) died during the study period, 108 (52.4%) completed six months of IPT and 98 (47.6%) did not complete six months of IPT. There were no statistically significant differences in the number of TB diagnoses or deaths between children who completed IPT and those who did not ( $P = 0.48$ ).

**Conclusion and recommendations:** Provision of IPT is feasible in this resource-limited setting. Although fewer than half of children completed a full six-month course of IPT, there were no significant differences in TB incidence or death compared to those who completed IPT. No data were available regarding reasons for noncompliance with the full IPT regimen. As the MOH scales up routine provision of IPT to children, additional focus will be needed to promote IPT adherence and retention in long-term care.

#### PC-646-17 Toxicity and tolerability of multidrug-resistant tuberculosis preventive treatment in children

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**Background:** There is no clear consensus regarding preventive treatment for child contacts of multidrug-resistant (MDR) tuberculosis (TB). Concerns exist that regimens are toxic and poorly tolerated.

**Aim:** To document the toxicity and tolerability of MDR-TB preventive therapy.

**Methods:** All children seen in the drug-resistant TB clinic, Tygerberg Children's Hospital, Cape Town, South Africa, were included if they had been exposed to MDR-TB and placed on a preventive treatment regimen from May 2010 until April 2011, with at least one follow up appointment attended. If the source case had MDR-TB with susceptibility to the fluoroquinolones, the child was given ofloxacin (15–20 mg/kg daily), ethambutol (20–25 mg/kg daily) and isoniazid (15–20 mg/kg daily) for 6 months. Those exposed to MDR-TB resistant to a fluoroquinolone were given isoniazid (15–20 mg/kg daily) alone for 6 months. Children were seen at 2, 4 and 6 months with reported adverse events graded using DMID grades following history and clinical assessment.

**Results:** 193 children were included with median age 31 months and median weight for age z-score of  $-0.61$ . 103 (53%) were boys and 9 (4.6%) were HIV-infected. For preventive therapy, 173 were given three drugs and 21 were given isoniazid alone. The most severe adverse event experienced by each child is demonstrated in the Table. Three of the grade 3 events were associated with accidental misdosing.

	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Total
Joint, muscle or bone pain*	183	5	1	0	0	189
Skin rashes	144	42	6	1	0	193
Itchy skin	151	33	8	1	0	193
Headache*	155	3	2	0	0	160
Sleeping/mood	177	9	4	3	0	193
Lethargy	190	3	0	0	0	193
Visual problems	193	0	0	0	0	193
Vomiting	161	31	1	0	0	193
Diarrhoea	174	18	1	0	0	193
Jaundice	193	0	0	0	0	193
Appetite/nausea	164	17	10	2	0	193

\*Unable to determine in some children.

**Discussion:** Preventive treatment is well tolerated and associated with few significant adverse events. A regimen including a fluoroquinolone can be considered a safe treatment option for children exposed to MDR-TB.

## ENVIRONMENTAL AND OTHER DETERMINANTS OF LUNG HEALTH

### PC-673-17 Fatal case of pulmonary cryptococcosis in an immunocompetent host

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**Introduction:** *Cryptococcus neoformans* results in opportunistic infection in patients with cell mediated immune deficiency leading to localized or disseminated disease. Pulmonary cryptococcal infection could become disseminated in immune suppressed hosts especially HIV patients. Few reports describe cryptococcosis in immunocompetent patients. This case report discusses a fatal pulmonary cryptococcosis in an immunocompetent patient.

**The Case:** 55-year-old male with no known comorbid presented with low grade fever, weight loss and dyspnea for past two months. He was started on antituberculous therapy (ATT) empirically with no improvement and developed right sided pleural effusion, cardiac tamponade and after pericardiocentesis developed pneumothorax and subcutaneous emphysema. CT chest showed bilateral patchy lung consolidation in apical segment of right lower lobe. Biopsy from the lesion was sent for histopathology, TB and fungal culture. AFB and fungal smear were negative. 48 hours later there was growth of *Cryptococcus neoformans*. Histopathology also showed round budding yeast cell. Serum cryptococcal antigen was negative. Patient refused for CSF examination and work up for decreased immunity, except HIV testing, which was negative. He was started on intravenous amphotericin B and initially improved, however 2 weeks later was readmitted and succumbed to the disease.

**Conclusion:** This case highlights a rare case of pulmonary cryptococcosis in an apparently immunocompetent host. HIV status was negative and other common risk factors leading to cryptococcosis were absent. However as complete work up for immunodeficiency was not done therefore subtle defects in the immunity of patient could not be ruled out.

### PC-674-17 Oxidative stress is first effect of coal dust exposure followed by metaplasia of rats lung

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**Background:** Previous study was found that coal dust inducing oxidative stress, but the effects of which on lung metaplasia pathway as early carcinogenesis step are still unknown. The purpose of the present study was to evaluate the effect of coal dust on MDA level, epidermal growth factor (EGF) expression, epidermal growth factor receptor (EGFR) expression and MUC5AC expression in rats.

**Methods:** An experimental study was done on Wistar male rats divided into the following groups: control, 14 days coal dust exposure (dose 6.25 mg/m<sup>3</sup>, 12.5 mg/m<sup>3</sup> and 25 mg/m<sup>3</sup>), and 28 days coal dust exposure (dose 6.25 mg/m<sup>3</sup>, 12.5 mg/m<sup>3</sup> and 25 mg/m<sup>3</sup>) for one hour per day. Coal dust was obtained from Carsurin Coal Laboratories Banjarmasin. Size of coal dust particle is less than 10 micrometer (PM<sub>10</sub>). Exposure was done by equipment model 2010, available in Department of Pharmacology, Faculty of Medicine, University of Brawijaya, Malang. MDA level was measured by spectrophotometer. EGF expression and MUC5AC expression were measured by ELISA. EGFR expression was measured by Confocal Laser Scanning Electron Microscope.

**Results:** There are not significant different of EGF and EGFR expression in all days exposure ( $P > 0.05$ ). MDA level in all days exposure is increase significantly ( $P < 0.05$ ). MUC5AC expression in 14 days is not different significantly, but decrease significantly than control in 28 days exposure ( $P < 0.05$ ).

**Conclusion:** Oxidative stress is first effect of coal dust exposure then followed by metaplasia effect. Future research focus on the effect of exposure cessation or antioxidant application to inhibit metaplasia early carcinogenesis step.

### PC-675-17 The early lung cancer detection initiative in Corby, Northamptonshire, UK

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**Background and challenges to implementation:** Survival rates for patients diagnosed with lung cancer in the UK are amongst the worst in Western Europe due to a range of factors, including late diagnosis. UK clinical guidelines recommend a chest X-ray (CXR) in all patients over 50 yrs with respiratory symptoms lasting over 3 weeks however patients fulfilling these criteria are not always referred, either because they do not consult their general practitioner (GP) or because their GP does not refer them. Lung cancer is a particularly serious problem in Corby, Northamptonshire, UK.

**Intervention:** This study examined the implementation and impact of a new service whereby patients meeting the recommended clinical guidelines for a CXR can attend a walk-in service without requiring a referral from their GP. A social marketing campaign designed to increase awareness of the symptoms of lung cancer was associated with the service implementation. This project used a mixed-methods approach, including analysis of routinely collected data (drawn from the walk-in service, UK cancer registries, non-identifiable CXR interventional data and social marketing data); an (optional) patient questionnaire; a survey inviting general practitioner views; service user telephone interviews and face-to-face stakeholder interviews.

**Results and lessons learnt:** Findings show that the service implementation was successful and had the support of local GPs. A large initial increase in CXR numbers correlated closely with social marketing activities but dropped off quite quickly, indicating the need for constant reinforcement. Only a small number of those attending for X-ray were recommended to do so by their GP, indicating that it is not duplicating existing provision.

**Conclusions and key recommendations:** A self-requested CXR service is an effective, sustainable and cost-effective way of involving communities in managing their own lung health.

### PC-676-17 Does prolonged exposure to high levels of fluoride in drinking water affect the lungs?

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**Introduction:** Fluorosis is dental and skeletal tissue changes due to increase fluoride exposure also resulting in systemic and biochemical changes. Pulmonary

involvement is established as a result of toxic exposure to inhaled fluoride. Animal studies have shown chronic fluorosis causes by ingested fluoride can cause marked destruction in lung tissues. This can result in impairment of spirometry results.

**Objective:** The study was done to observe the spirometry changes in effected population and compare it with control and correlate it with skeletal changes.

**Method:** People from Sammo Rind village with underground water fluoride concentration of 6–8 ppm were taken as cases, and from Gadap where level of flouride in drinking water is not high (1 ppm) were included as controls. Clinical examination hematology and biochemical tests were performed spirometry was done in all and results were analyzed using SPSS 16.

**Results:** 121 cases and 121 controls were included in the study. Mean age was 30 and 33.47 in cases and control respectively. Males were 90 (74.4%) and 84 (69.4%) and females were 31 (25.6%) and 37 (30.6%) in cases and controls respectively. Ventilator function was normal in 54.54% controls and 22.31% cases. Restrictive pattern was in 47.1% and 23%, obstructive defect was in 23% and 6.6% and combined defect was in 8.6% and 15.7% cases and controls respectively. This was related to dental changes and serum, plasma and urinary fluoride levels but not related chest wall deformity.

**Conclusion:** Study show lung function impairment in effected population independent of skeletal deformities.

### PC-677-17 Correlation between high-resolution computer tomography findings and lung function in stable bronchiectasis

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**Background:** To evaluate the correlation between the HRCT findings and lung function in patients of stable bronchiectasis.

**Design/methods:** 80 adult patients were included in study. Quantification of HRCT finding was done by HRCT scoring system. Lung function parameters recorded were peak expiratory flow rate (PEFR) in L/min, forced expiratory volume in 1 sec (FEV<sub>1</sub>) in litre, forced vital capacity (FVC) in litre, and FEV<sub>1</sub>/FVC. Pearson's correlation between HRCT score and the lung function parameters was calculated.

**Results:** FEV<sub>1</sub>, FVC and PEFR were found to be negatively correlated with number of bronchiectasis segments ( $P < 0.01$ ), number of emphysematous segments ( $P < 0.01$ ), and total HRCT score ( $P < 0.01$ ). In addition FEV<sub>1</sub> was also found to be negatively correlated with bronchial dilatation ( $P < 0.05$ ), number of bulla ( $P < 0.05$ ). The relation of HRCT score was also found to be negatively correlated to FEV<sub>1</sub>/FVC, bronchial wall thickness ( $P < 0.01$ ), number of

bronchiectatic segments ( $P < 0.01$ ) and HRCT score ( $P < 0.01$ ). Male patients had higher HRCT score ( $1.00 \pm 0.97$ ) as compared to female ( $0.40 \pm 0.68$ ) ( $P < 0.01$ ).

**Conclusion and recommendations:** HRCT scores were found to be main predictor of ventilation parameters and a large number of bronchiectatic segments were highly relevant to functional impairment.

### PC-678-17 La sarcoïdose médiastino-pulmonaire au CHU Tokoin de Lomé : à propos d'une étude prospective sur trois ans (1er janvier 2008 au 31 décembre 2010)

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**Cadre :** Les données sur la sarcoïdose médi-astino-pulmonaire sont limitées en Afrique. Nous en rapportons six cas diagnostiqués au CHU Tokoin de Lomé.

**Schéma et méthodes :** Il s'agissait d'une étude prospective qui a concerné tous les cas de sarcoïdose prouvés histologiquement qui ont été diagnostiqués dans le service de pneumophtisiologie entre le 1er janvier 2008 et le 31 décembre 2010.

**Résultats :** Six cas de sarcoïdose ont été diagnostiqués en trois ans sur un total de 5106 patients, soit une fréquence hospitalière de 0,1%. Le sex ratio était de deux hommes pour une femme. L'âge moyen était de 46 ans avec des extrêmes de 39 et 53 ans. La symptomatologie était dominée par la toux, la dyspnée et l'asthénie. Le stade II radiographique était retrouvé chez quatre patients. Sur le plan biologique, la NFS était normale sauf chez un patient qui avait une lymphopénie. La calcémie était augmentée dans 02 cas. L'IDR à la tuberculine était négative chez 02 patients. Une hypergammaglobulinémie était retrouvée chez 2 patients. La preuve histologique a été apportée par biopsie cutanée dans 02 cas et par biopsie per fibroscopie bronchique dans 04 cas. L'évolution a été favorable sous corticothérapie chez la plupart d'entre eux sauf chez le patient qui était au stade IV. Un cas de rechute a également été constaté.

**Conclusion et recommandations :** En dépit des ressources limitées qui ne permettent pas souvent de réaliser toutes les explorations nécessaires, la prise en charge de la sarcoïdose est possible sous nos cieux.

### PC-679-17 Role of measurement of C-reactive protein in the rational use of antibiotics in primary health care centers

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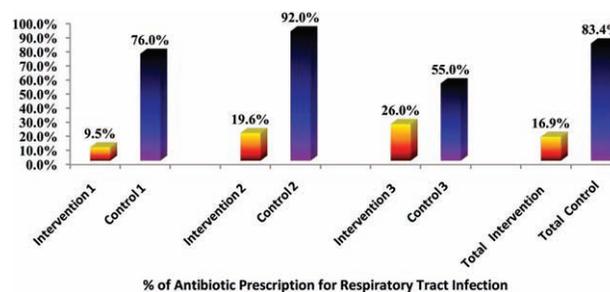
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**Background and objectives:** In most patients presenting to primary health care centers (PHCs) with respiratory tract infections (RTIs), particularly upper RTIs, viruses are the causative organism. Despite this, many of these patients are inappropriately prescribed antibiotics. This study aimed to test the effect of measuring CRP in patients presenting with RTI on antibiotic prescriptions in PHCs in Khartoum State.

**Methodology:** We conducted a controlled trial in all patients with RTI, who visited six PHCs during the period from May to June 2011. In three centers we implemented an intervention in which C reactive protein (CRP) was measured in patients presenting with RTI. In the remaining three centers, the control group, there was no change to usual care. We compared the proportions between groups using  $\chi^2$  test.

**Analysis:** SPSS, v 16.

**Results:** Of a total of 2713 patients, 1630 were in the intervention group and 1083 in the control group. There were more females in both groups (59.5% intervention group, 52.9% control). Cough (70.3%) and fever (60.5%) were the most common symptoms among both groups. Upper RTI was common among both groups (88% intervention group, 81.5% control). Antibiotics were prescribed for only 16.9% of patients in the intervention group and for 83.4% in the control group ( $P = 0.007, 0.00, 0.00$ ).



**Figure** Role of measurement of C reactive protein (CRP) in the rational use of antibiotics in primary health care centers (PHC). Control1 Intervention1 ( $P = 0.007$ ), Control2 Intervention2 ( $P = 0.00$ ), Control3 Intervention3 ( $P = 0.00$ ).

**Conclusion and recommendations:** RTIs were more common among females. The measurement of CRP has greatly reduced the rate of antibiotic prescription among patients presenting with RTI. It is recommended to apply this test on a larger scale, to validate its incorporation into national guidelines for antimicrobial use.

### PC-680-17 A comparison of laboratory polysomnography and a home sleep study in the diagnosis of obstructive sleep apnoea syndrome (OSAS)

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**Background:** The gold standard for diagnosis of OSAS is the sleep laboratory polysomnography (Lab-PSG), which is technically demanding, labor-intensive, and time-consuming. Thus, screening of large undiagnosed population for OSAS may be cost efficient only by means of ambulatory devices suitable for home recording. The aim of our study was to validate the role of a home sleep study (HSS) in the diagnosis of OSAS.

**Design/methods:** One hundred thirty six consecutive adults referred for PSG at the sleep disorders center. The sleep studies were carried out in the laboratory and at home on two different nights and with a maximum interval of 48 h. The HSS was designed to record nasal and oral flow, snoring, blood oxygen saturation and heart rate. Sensitivity, specificity and positive and negative predictive values at AHI cut-off values of 5 and 15 events/hour were calculated.

**Results:** There was a strong correlation between apnea-hypopnea syndrome (AHI) from the HSS and PSG recordings ( $P < 0.001$ ,  $r = 0.73$ ). Compared to lab-PSG for detecting  $AHI > 5$ , the HSS demonstrated the sensitivity of 91.6%, the specificity of 33.3%, positive predictive value of 91.6%, negative predictive value of 33.3% and diagnostic value (accuracy) of 85%. Compared to lab-PSG for detecting  $AHI > 15$ , the HSS demonstrated the sensitivity of 67%, the specificity of 84%, positive predictive value of 87.7%, negative predictive value of 60% and diagnostic value (accuracy) of 73.3%.

**Conclusion and recommendations:** These data suggest that the HSS is accurate in confirming the diagnosis of OSAS where there is a suspicion of the disorder.

## MULTIDRUG-RESISTANT TUBERCULOSIS: FOCUS ON SOCIAL AND COMMUNITY SUPPORT

### PC-710-17 Community-based approach to management of DR-TB in Nigeria: perception of MDR-TB patients

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**Background and challenges to implementation:** Access to rapid DR-TB diagnosis had led to increase in the number of DR-TB patients diagnosed in Nigeria

beyond the available beds. The NTBLCP is exploring the possibilities of a community based treatment approach.

**Intervention or response:** A descriptive cross-sectional study conducted in 2011 to assess the perception of MDR-TB patients on their views on community MDR treatment. An interview guide and questionnaire were developed and used to collect information from the respondents.

**Results and lessons learnt:** A total of 35 MDR-TB patients participated; 20 males and 15 females. Overall mean age for the study population was  $35.7 \pm 8.9$  years. Majority of the patients were married (62.9%) and had at least secondary education (74.2%). Most respondents 30/35 (85.7%) opted for hospitalization for a shortened intensive phase, and ambulatory continuation phase of treatment. Reasons for this choice include: difficulty to maintain strict adherence in the community, especially for injections, challenges of managing adverse events, extreme pain from the injection site and support in terms of feeding which was provided at the hospital at no cost. In addition, there is associated stigma and discrimination at community which may be a barrier to treatment adherence at home. Availability of treatment supporters and DOTS officer for supervision of treatment may also be a challenge. Despite the above, a few feel that community DR-TB is a good initiative as it allows the patient to remain within family support system while on treatment but feared that such activity may attract stigmatization from the community.

**Conclusions and key recommendations:** The view of the patients should be considered and concerns addressed while developing a community based DR-TB approach that will fit into the overall social and cultural context in the country for successful implementation of DR-TB management.

### PC-711-17 Characteristics of MDR patients and preferences for social support: descriptive study

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**Background:** Pakistan ranks 4th in MDR high burden countries of the world. According to WHO estimates the prevalence of MDR-TB is 2.9% in new cases and 35% in retreatment cases. From 2010 three pilot sites were engaged including Indus Hospital, Ojha Institute in Karachi, Gulab Devi Hospital Lahore and ICD Kotri. These institutes are successfully managing MDR patients and the adherence of patients is ensured by giving social support/food baskets to patients and treatment supporters with following standard composition: 20 kg flour, 5 kg rice, 4 kg lentils, 4 kg sugar, 5 ltr oil, 1 kg powdered milk. There was a need to assess preference of patients for social support.

**Design/methods:** A baseline assessment of need for reassessing the preferences of the MDR patients was done in June 2011 by interviewing 47 MDR patients in Indus Hospital Karachi.

**Results:** The results show that the treatment supporters of majority of the patients were health workers and their relatives. Males had a high rate of MDR occurrence, i.e., 53.2% then females (46.8%) and were between the ages of 15 and 24 (43.8%) which is the reproductive age group and 40.4% were illiterate that shows a link with poverty with monthly earning less than Rs 6000. 31.9% had history of contact with other TB patients. Transportation cost was not sufficient as patients travelled from far areas. Out of 47 patients 40 were satisfied with the food basket but carrying of food items was difficult while the remaining demanded for cash to utilize it for other purposes.

**Conclusion and recommendations:** The assessment is useful for planning future MDR social support, the transportation incentive need to be increased since patients had to travel long distances for the treatment and social support and there is a need to devise some strategy so that food basket is available close to patient's home.

#### PC-712-17 Experience of implementation of interferon tiloron for comprehensive treatment of patients with pulmonary multidrug-resistant tuberculosis

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**Background and challenges to implementation:** Tuberculosis has a tendency to progress and suppress the immunological reactivity more and more frequently against the background of resistant forms. The objective of the study was to determine the effectiveness of implementing the tiloron for comprehensive anti-TB treatment under DOTS-Plus regimen in patients with MDR-TB.

**Intervention or response:** IL-2, IFN- $\gamma$ , CD3, CD4, CD8 and antituberculosis antibodies titer were studied in 2 groups: experimental group (20 patients) and control group (19 patients). Tiloron was administered to the patients of experimental group in dose of 0.125 g by schema during 15 days per os associated with 4–5 anti-TB drugs of the second line. Infiltrative pulmonary tuberculosis was predominated in both groups (75.0% and 53.0% accordingly).

**Results and lessons learnt:** It has been observed that the implementation of tiloron during 1.5 months for comprehensive MDR-TB treatment led to the reliable increase in IFN- $\gamma$  ( $12.2 \pm 0.6$  vs.  $22.8 \pm 1.0$ ), CD3 ( $41.2 \pm 0.8$  vs.  $53.1 \pm 1.2\%$ ), CD4 ( $24.3 \pm 1.4\%$  vs.  $34.3 \pm 1.8\%$ ) and decrease in lymphocytes CD8 ( $23.6 \pm 1.6\%$  vs.  $14.1 \pm 1.1\%$ ). Reliable increase in CD3 ( $39.1 \pm 0.7\%$  vs.  $48.8 \pm 1.5\%$ ) and unreliable tendency for all other indicators were observed in patients of control, while in patients of the experi-

mental group the faster involution of intoxication symptoms, positive dynamics in roengenological and laboratory indicators were marked by us.

**Conclusions and key recommendations:** Implementation of tiloron for comprehensive MDR-TB treatment is a safe and effective method that improves immunity and consequently the treatment efficiency.

#### PC-713-17 Counseling practices on anti-tuberculosis drugs among community pharmacies in Manila

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**Background:** Patient counseling is an integral part of community pharmacy practice. It has been an important service by pharmacist which helps improve the knowledge and understanding of patients on drugs

**Table** Description of counseling received by simulated patients presenting prescriptions in the three scenarios used

Scenarios used	Rifamax* (n = 31)	Myrin P (n = 35)	Bifix† (n = 23)	Total (n = 89) n (%)
No questioning	27	29	21	77 (86.5)
No information provision	0	0	0	0
No counselling (i.e., no questioning and no information)	1	4	1	6 (6.7)
Questioning about				
Whether had taken this medicine before	3	2	1	6 (6.7)
Why the medicine was prescribed	0	0	0	0
How the medicine should be taken	1	0	0	1 (1.1)
If other medicines taken	0	0	0	0
If allergic to any medicines	0	0	0	0
If have any questions or concerns about this medicine?	0	0	0	0
If there is anything else you want to ask?	0	0	0	0
Information given about				
The name of the medicine	29	19	6	54 (60.7)
How to take the medicine‡	19	18	8	45 (50.5)
The purpose of the medication§	31	29	23	80 (89.9)
Duration of the medicine	6	17	12	35 (39.3)
Possible side effects of the medicine	0	1	5	6 (6.7)
Precautions about the medicine	0	0	1	1 (1.1)
Special instructions for the medicine	5	2	0	7 (7.9)
Given written information¶	4	2	0	6 (6.7)

\* 4 aborted as the pharmacy did not have Rifamax stock.

† 2 aborted as the pharmacy did not have Bifix stock.

‡ 2 simulated patients were also given incorrect information.

§ 1 simulated patient was also given incorrect information.

¶ In addition to mandatory package insert with price of the drug.

requiring longer duration of regimen. This is particularly important in the tuberculosis (TB) control where lack of knowledge and understanding can lead to drug resistance.

**Design/methods:** The study aimed to measure the frequency of verbal counseling in community pharmacy and to determine the types of information provided. Three phases were done in 95 randomly selected community pharmacies. The first phase was face to face counseling of simulated patient (SP) with prescription, second was telephone counselling and the last phase was survey questionnaire using an 11-point Likert scale which measured the practices of community pharmacists in patient counseling.

**Results:** During Phase I, most of the pharmacists and staff provided insufficient information on anti-TB drugs. In Phase II, some pharmacists provided only little information needed by the SP. In Phase III, a mean of 6.15, interpreted as 'often' showed that pharmacists and staff provided counseling on anti-TB drugs but was limited to common information like name of the medication, indication and the dosage of the drugs. The results of the study suggest that good counseling practices on anti-TB drugs should be improved.

**Conclusion and recommendations:** Patient counseling as a specific role of pharmacists in community pharmacies is very vital in the TB control. This will help the government in educating the patients on anti-TB drugs to prevent the occurrence of drug resistance. A policy on strengthened and improved patient counselling practices on anti-TB drugs should be acted upon for better TB control.

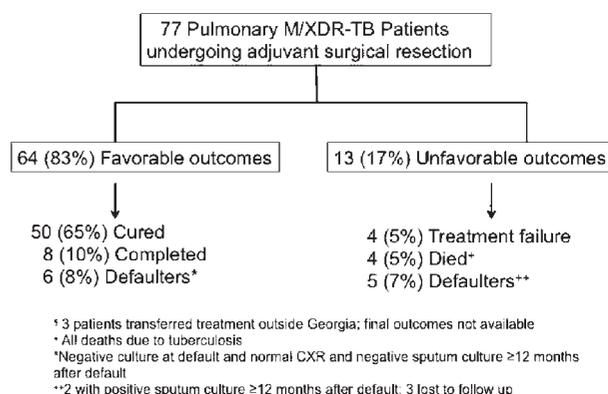
### PC-714-17 Favorable outcomes among highly drug-resistant pulmonary tuberculosis patients undergoing adjunctive surgery

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**Objective:** MDR- and XDR-pulmonary TB (PTB) are serious public health problems associated with high morbidity and mortality. We sought to evaluate the role of surgery in the treatment of M/XDR-PTB in the setting of DOTS-Plus implementation.

**Methods:** Medical records were reviewed for M/XDR-PTB patients undergoing thoracic surgery at the National Center for TB and Lung Diseases in Tbilisi, Georgia between July 2008 and January 2010. Indications for surgery included localized pulmonary disease, fit to undergo surgery, and either medical treatment failure or such extensive drug-resistance that failure was likely. Second-line anti-tuberculosis medical therapy was administered per WHO recommendations.

**Results:** 80 PTB patients (55 MDR, 25 XDR) with a median age of 30 years and mean length of medical treatment of 350 days had thoracic surgery. The following surgical procedures were performed: pneumonectomy (10%), lobectomy (51%), segmentectomy (33%), and thoracoplasty (6%). 77 patients had final outcomes and average postoperative follow up time was 372 days. A favorable outcome was achieved in 64 patients (83%) (Figure) including a favorable outcome in 90% of MDR and 68% of XDR-TB patients. There was no postoperative mortality and postoperative complications occurred in 7 patients (9%); 6 were major complications (bronchopleural fistula 4, empyema 1, hemorrhage 1). Risk factors ( $P < 0.05$ ) for poor outcomes in univariate analysis included bilateral infiltrative (OR 4.1) and cavitary disease (OR 5.1), XDR-TB (OR 4.4), increasing effective drugs received (OR 1.8), a positive preoperative sputum culture (OR 20.4), and the occurrence of a major postoperative surgical complication (OR 6.1).



**Figure** Treatment outcomes for M/XDR-PTB patients undergoing surgical operation.

**Conclusions:** Thoracic surgery was associated with a high rate of favorable outcomes and a low rate of complications when used as adjunctive therapy in M/XDR-PTB patients. Adjunctive surgery may play an important role in the treatment of selected patient with highly drug resistant PTB.

### PC-715-17 Anti-tuberculosis drug resistance in Nairobi, Kenya

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**Background:** Drug resistant tuberculosis (TB) which is a state when *Mycobacterium tuberculosis* organisms are resistant to antimicrobial agents at the levels attainable in blood and tissue pose a serious threat to TB control programs. Limited information exists on

the exact prevalence of resistance to anti-tuberculosis drugs in populations with high rates of tuberculosis and the human immunodeficiency virus (HIV) co-infection such as those in Nairobi, Kenya.

**Setting:** A cross-sectional study was conducted among new and previously treated consecutive sputum smear positive pulmonary tuberculosis (PTB) patients of 14 years and older at 16 diagnostic and treatment facilities in Nairobi, Kenya, between February and August 2010.

**Objective:** To determine the magnitude of drug resistance to first line antituberculosis drugs among *M. tuberculosis* isolates obtained from a study addressing the diagnosis and epidemiology of drug resistant tuberculosis in Nairobi, Kenya.

**Methods:** Sputum samples from patients with bacteriologically confirmed PTB on microscopy were cultured on Löwenstein-Jensen (LJ) media. Participants were offered diagnostic testing and counselling for HIV testing. Strains of *M. tuberculosis* complex from Löwenstein-Jensen (LJ) slopes were subjected to drug susceptibility testing (DST) to isoniazid (H), rifampicin (R), streptomycin (S), and ethambutol (E) using the proportional method on the Mycobacterium Growth Indicator Tube (MGIT) conventional method.

**Results:** A total of 595 TB patients had their *M. tuberculosis* strains DST done. Of the 568 (95.4%) patients who had valid results for analysis, 369 were new and 199 previously treated. About eighty-five percent and seventy-seven percent of the strains from new patients and previously treated patients were fully sensitive to all the drugs tested respectively. Any resistance to isoniazid, streptomycin, ethambutol and rifampicin was 10.3%, 4.3%, 5.1% and 0.81% respectively among new patients. Among previously treated patients any resistance to isoniazid, streptomycin, ethambutol and rifampicin was 18.1%, 10.5%, 7.03% and 9.04%, respectively. The prevalence of multidrug resistant tuberculosis (MDR-TB) defined as resistant to at least both isoniazid and rifampicin was 0.54% and 8.54% among new and previously treated patients respectively.

**Conclusion:** The study found high levels of drug resistant TB in Nairobi compared to other previous studies done in the country. MDR-TB in Kenya is now a reality and the situation in Nairobi being the largest cosmopolitan city is worrying. The upward trend of MDR-TB in Nairobi is cause of concern. This calls for urgent concerted efforts to address the problem especially the strengthening of the implementation of the comprehensive framework of the DOTS-Plus strategy for appropriate management of MDR-TB.

### PC-716-17 Nutrition supplementation helps in increasing adherence among tuberculosis patients on treatment

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**Background:** Eating good food is the suggestion given very often by the physicians to the patients on treatment for tuberculosis (TB) as the appetite gets better with the treatment and drug toxicity may be higher without sufficient nutrition. Most of the TB patients are poor and neglect the diet. Most often heard reasons for lack of adherence for TB treatment are side effects, pill burden, economic constraints and poor nutrition. Current study tries to analyze the improvement in adherence with the provision of nutrition.

**Methods:** St. Mary's Tuberculosis Units (TU) started functioning in 2001 under PPM (public-private mix) model in Tamilnadu. Since 2004 the TU started providing nutritional supplementation mobilized locally to the TB patients along with free medication as part of RNTCP. The support included was 10 kg of rice and 2 kgs of nutritional mix every month per patient till the treatment is complete. Supplementation was provided to below the poverty line, HIV+ve, widows and underweight patients irrespective of the type of TB or category of treatment. Data on default rate was collected from the above TU from the period of inception of the supplementation. Data of 2004–2010 was analyzed as before 2004 there was no nutrition supplementation and 2011 patients did not complete the follow-up. Comparative analysis default among the patients with nutrition supplementation against those without was done to identify the role of nutrition on treatment default. Further analysis on the 4 defaulters with nutrition support showed that 3 stopped DOTS within 1 month and 1 migrated to Mumbai after tested as HIV+ve.

**Results:** Data analyzed from 2004 to 2010 shows

Year	Nutrition supplementation	No. of patients	No. of defaulters
2001	Without	641	5
2002	Without	694	3
2003	Without	1206	8
2004	With supplement	239	1
	Without	903	6
2005	With supplement	186	0
	Without	610	36
2006	With supplement	169	1
	Without	723	44
2007	With supplement	151	0
	Without	694	40
2008	With supplement	200	1
	Without	544	15
2009	With supplement	182	0
	Without	470	27
2010	With supplement	150	1
	Without	432	33

that there was significant reduction ( $\chi^2 P < 0.001$ ) in default rate among those patients with nutrition supplementation (4 of 1277; 0.31%) against those without (201 of 4376; 4.59%).

**Conclusion:** Our study suggests that provision of nutrition supplementation will have an incremental effect on adherence to the TB treatment.

#### PC-717-17 *In vitro* antimycobacterial activity of new potent (R)-2-aminobutanol derived acyl thioureas

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**Background:** The long current drug regimens, the emergency of drug resistant strains and HIV co-infection have resulted in resurgence in research efforts to address the urgent need of new anti-tuberculosis drugs. Ethambutol (EMB) is one of the frontline agents recommended by the WHO for the treatment of tuberculosis.

**Objectives:** To evaluate the effect of *in vitro* antimycobacterial activity of a series of new (R)-2-aminobutanol derived acyl thioureas as novel structural EMB analogues.

**Methods:** Susceptibility testing for series of new (R)-2-aminobutanol derivatives was carried out by the recommended by WHO proportional method of Canetti. The critical concentrations for the compounds were 5, 2, 1, 0.2 and 0.1 mg/ml.

**Results:** Using cheap and commercially available chemicals, five new (R)-2-aminobutanol derivatives bearing acyl thiourea moieties have been synthesized and obtained in pure form. The choice of the acyl groups was based on their pharmacophore properties studied in our previous article (Dobrikov G., et al. Eur. J. Med. Chem, 2012). The *in vitro* activity of the compounds against *Mycobacterium tuberculosis* H37Rv was evaluated. All compounds showed remarkable activity—10 to 20 fold higher than activity of EMB (in microgram scale) in combination with insignificant cytotoxicity (IC<sub>50</sub> more than 354  $\mu$ M toward human embryonal kidney cell line).

**Conclusion:** These results can be considered an important starting point for design of new leads for anti-TB compounds.

**Acknowledgement:** This work was supported by National Science Fund, Ministry of Education and Science, Bulgaria (DMU 02/3; DMU 01/0135).

#### PC-718-17 Evaluation of the GenoType® MTBDRs/ assay in a cohort of multi- and extensively drug-resistant tuberculosis patients in South Africa

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**Background:** In 2006 South Africa documented its first outbreak of XDR-TB. Delayed diagnosis of XDR-TB increases mortality, emphasizing the need for rapid diagnostics. The MTBDRs/ assay rapidly identifies resistance to fluoroquinolones (FLQ) and aminoglycosides/capreomycin (AG/CP).

**Design/methods:** A prospective cohort study was performed in patients admitted to an M/XDR-TB hospital. Admission sputum specimens were collected. MTBDRplus Ver 1 and MTBDRs/ assays were performed on these direct sputum and cultures.

**Results:** From April 2011 to January 2012, 150 participants were recruited. 75 (50.0%) were female, 92 (61.3%) were HIV positive and 8 (5.33%) had an unknown HIV status. Of cultures obtained; 71 (47.3%) were positive, 40 (26.7%) contaminated and 31 (20.7%) negative. The proportion of smear negatives in HIV positive patients was not statistically significantly different to the smear negatives in HIV negative patients (57.5% vs. 46.0%;  $P = 0.139$ ). On phenotypic drug susceptibility tests; 51 (68.9%) were MDR only, 15 (20.3%) pre-XDR (FLQ), 1 (1.35%) pre-XDR (AG/CP), 3 (4.05%) XDR, 1 mono rifampicin (RIF) and 1 mono isoniazid (INH) resistant.

**Direct assay:** Sensitivity and specificity were 71% and 56% for RIF; 98% and 100% for INH; 100% and 95% for FLQ; 33% and 96% for AG/CP. For FLQ and AG/CP acid fast bacilli smear positives, the sensitivity and specificity were 100%, 96.0% and 50.0%, 96.9%, respectively. Smear negatives were 50%, 100% and 33.3%, 92.9%.

**Culture assay:** Sensitivity and specificity were 98% and 100% for RIF; 94% and 100% for INH; 100% and 95% for FLQ; 33% and 100% for AG/CP.

**Conclusion and recommendations:** The detection of resistance to RIF and/or INH with the MTBDRplus Ver 1 correlates with other publications. On direct, smear positive sputum the MTBDRs/ assay is a good rule-out test for detection of resistance to AG/CP and FLQ. For FLQ, it's a good rule-in test. As predicted, it does not perform well on smear negatives. On cultures the assays perform well.

### PC-719-17 Resections of lung in cases of cavitary multidrug-resistant tuberculosis

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**Introduction:** In most cases of first examination of patients with MDR tuberculosis, the cavitary form has diagnosed. If patient have good compliance for therapy, he has chance to cure. But more often fibrous wall of cavity—is a serious problem for proper treatment. That is why more than 40% of patients died per year from time of diagnosis and rate of success treatment near 40%. (Cox H, 2006)

**Objectives:** To assess the effect of surgery of MDR lung TB cases with cavities (LTBC) on their clinical recovery.

**Material and methods:** Retrospective analysis of 400 lung resection in patients with LTBC in Saint-Petersburg Research Institute for Phthisiopulmonology in 1990–2012. Segment resections (SR) were in 30%, lobectomy (LBE) and bilobectomy (biLBE) in 40%, pneumonectomy in 30% of all cases. All patients were after 6 to 8 months of chemotherapy, smear and culture conversion or in smear and/or culture positive cases, after intensive course of anti-TB chemotherapy.

**Results:** Mortality after SR was less than 1%, the rate of full recovery from TB 95–97%, the average postoperative period in hospital was 7–10 days. Mortality after LBE and biLBE was 2–3%. Postoperative period in hospital was 2–3 weeks, disability period 2–3 months. Complete recovery was achieved in 85–95% cases, mortality was 10.7%. Physical working capacity Mortality was caused by pleuropulmonary complications in 6.6% from and by systemic complications in 4.1%. Long-term results. The cumulative cure rate for patients with extensive severe fibrous lung lesions 55% and 48% after 3 and 5 years respectively, but without surgery, 20% and 15% respectively. The maximal recurrence incidence was 30% 2–3 years after the operation when long-term chemotherapy was provided for the whole period.

**Conclusions:** Use of surgery in MDR LTBC additional to chemotherapy increases their cure rate up to 55%.

### PC-720-17 Aminocoumarin derivatives as potential candidate drug against multidrug-resistant tuberculosis

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**Background:** The current status of the problem associated with treatment of tuberculosis clearly mani-

festes in the need to develop new inhibitory molecules that could help not only in shortening the duration of the therapy but also provide effective treatment of MDR, XDR and latent tuberculosis.

**Design/methods:** A series of coumarin derivatives were synthesized and screened against *Mycobacterium tuberculosis* H37Rv strain using Microplate Alamar Blue Assay. Scanning and transmission electron microscopy was carried out to observe changes in cellular morphology.

**Results:** The effective series of compounds having MICs in the range of 1–3 µg/ml was further screened against a sensitive and a multi-drug resistant clinical isolate, strain 3426 and strain 591, respectively. The lead compound, a specific amino coumarin derivative was found to display the lowest MIC of 1 µg/ml against all the aforementioned strains and further evaluated to determine their MBCs, FIC indices and cytotoxicity. The sub-inhibitory concentrations of the candidate molecule was found to induce a significant increase in the antimycobacterial activity of isoniazid (INH) and rifampicin (RMP) against *M. tuberculosis* H37Rv leading to decrease in MIC of INH up to 30-fold and that of RMP up to 20-fold.

**Conclusion and recommendations:** These results open up further avenues for incorporation in the standard treatment regimen. Scanning and transmission electron microscopy analysis revealed marked differences in the morphology of normal and drug-treated cells thereby strengthening the prospects of this molecule being developed as a drug endowed with cell-wall attacking property. Fluorescence microscopic analysis highlighted that mycolic acid could possibly be the target of drug action. The active series of compounds was further subjected to in silico ADMET for ascertaining relevant pharmacokinetic parameters taking INH as the standard. The test compounds were found to lie more or less within the acceptable ranges.

### PC-721-17 Evaluation of the impact of line probe assay on time to treatment initiation for smear-positive multidrug-resistant tuberculosis cases in the Archangelsk region of Russia

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**Background:** In Archangelsk region of Russia MDR-TB rates among new cases are amongst the highest in the world. Line probe assay (LPA) is a new rapid diagnostic tool that could speed up the time to initiation of MDR-TB treatment. The PROVE-IT LPA project aims to assess the impact of LPA on treatment initiation. Secondary outcomes will define economic and other parameters needed to facilitate the

implementation of LPA within health systems. We report preliminary analyses of the primary outcome measure and part of the health economic analysis.

**Objectives:** To evaluate the influence of LPA on time from first sputum sample collection to initiation of MDR treatment for smear-positive patients in civil sector.

**Methods:** A concurrent study design was used for a cohort of patients for whom both LPA and Bactec MGIT were performed to diagnose MDR-TB. Time difference between result of LPA and MGIT was calculated. Seventy-two smear-positive MDR-TB patients diagnosed by LPA were enrolled between April 2011 and March 2012, 61 of them successfully started treatment, 5 died, 4 did not start treatment, 2 had discordant DST results for LPA and MGIT and were excluded. Health system costs for the hospitalization of smear-positive patients were analyzed.

**Results:** Preliminary results show that LPA introduction lead to a median decrease in time to initiation of MDR-TB treatment of 21 days. All smear positive patients diagnosed by LPA started MDR treatment at least 7 days earlier ( $P < 0.005$ ), 48 (79%) started MDR treatment at least 14 days earlier compared to diagnosis by MGIT. Mean (median) reduction in cost of hospitalisation per person is rub 9883 (7919); SD = 5499, equivalent of US\$335 (268).

**Conclusions and recommendations:** LPA speeds up MDR-TB treatment initiation and reduces health system costs for smear positive cases compared to culture based DST using BACTEC MGIT. Further research is needed to assess the impact of LPA for smear-negative patients in civil sector and prisons.

#### PC-722-17 A decentralised community-based multidrug-resistant tuberculosis model of care in northern Uganda

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**Background:** Multidrug-resistant tuberculosis (MDR-TB) is emerging globally. In Uganda treatment is not yet available. Médecins Sans Frontières (MSF) initiated MDR-TB treatment in Kitgum and Lamwo Districts in December 2009 in decentralized community based approach in collaboration with Ministry of Health.

**Intervention:** We describe the community-based model, components and interim treatment outcomes of the MDR-TB program in northern rural Uganda from 2009 to April 2012. Data from routine programmatic conditions.

**Results:** A total of 13 MDR-TB patients were enrolled in the decentralized and community based pro-

gram during the study period. Hospitalization criteria were restricted. The components of the model of care include medical follow up, strict direct observed therapy, implementation of infection control, counseling and psychosocial support to patients and care takers, all implemented mainly at community level. Diagnosis, care and follow-up were based on international recommendations. Contact tracing activities were done and identified 1 patient. Sputum samples were sent through Ugandan courier system to the national reference laboratory. All patients had microbiological confirmation. Four MDR-TB (31%) were HIV positive, all on antiretroviral therapy. A total of 3 patients completed treatment. Of the 9 patients that converted culture, average time to conversion was 79 days (range 59–130 days); mean length of intensive phase was 7.8 months (range 6–9 months). Average missed days treatment was 2 (range 0–14 days). Main side effects observed were: nausea/vomiting 53.8%, abdominal pain 38.5%, hearing loss 30.8%, arthralgia 23.1%. Clinically evident hypothyroidism was seen in 3/13 (21%). None of the patients died or defaulted.

**Conclusions:** A decentralized community based model of care for MDR-TB treatment is feasible in rural Uganda. It allows follow-up, side effects monitoring, adherence to treatment, infection control, and favorable treatment outcomes.

#### PC-723-17 Building partnerships for project sustainability: the case of multidrug-resistant tuberculosis diagnostic and treatment centres in Nigeria

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**Background and challenges to implementation:** Over nine million people develop TB annually; about 1.8 million die from the disease. Nigeria ranks 10th of the 22 high-burden countries. While weak health systems impede the government's capacity to diagnose and treat TB effectively, the emergence of MDR/XDR-TB further compounds the burden. Through US funding, national capacity was strengthened to establish modern facilities for providing sustainable MDR-TB diagnostic and treatment services in four regions in Nigeria. Intervention or response MoUs between FHI360, the NTBLCP and state governments specified roles for ensuring functionality of the centers. Project management teams established, service providers trained and long term business plans developed. Stakeholder's quarterly meetings held to assess progress and stakeholder contributions.

**Results and lessons learnt:** Three BSL 3 laboratories and three MDR-TB wards have been established. Stakeholder support was realized and sustained till completion of activities. Synergies were realized from pooling different donor resources. Duplication of

activities was avoided and roles and responsibilities streamlined. All four state governments provided financial, human and material resources critical for operationalization; while NTBLCP supported the identification of patients. Two of the wards and one lab have been commissioned. Currently, eight patients are on admission in the Lagos ward, relevant facility staffs have been trained while laboratory support is available from the activated labs. Additional funds for operational costs and patient welfare have been attracted from the Global Fund.

**Conclusions and key recommendations:** Involvement of stakeholders in planning and implementation enhances stakeholders' motivation to contribute resources towards sustainability of activities.

#### PC-724-17 Rifampicin mono-resistant tuberculosis and pre-XDR-TB in Johannesburg: implications for testing algorithms and treatment guidelines

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**Background and methods:** GenoType MTBDR<sub>plus</sub> assay (LPA) results for *Mycobacterium tuberculosis* isolates, routinely tested for susceptibility as per the South African National TB Control Programme between August 2009 and January 2010, were analyzed in conjunction with corresponding first and second-line MGIT proportion method drug susceptibility testing (DST) results to inform testing algorithms and treatment guidelines.

**Results:** LPA results of 524 isolates with DST results were analyzed. By LPA, 47%, 33% and 20% were resistant to both INH and rifampicin, rifampicin alone and INH alone, respectively. Alterations in the *rpoB* gene were detected in 81% of isolates, of which 59% were identified as MDR-TB by the LPA. DST confirmed that 67% of isolates with alterations in *rpoB* gene were MDR-TB, 21% were resistant to rifampicin but susceptible to INH and 12% were susceptible to rifampicin. Of isolates with alterations in *rpoB* gene and no alterations in either *katG* or *inhA* promoter genes only 30% were confirmed MDR-TB by DST, and 51% were rifampicin mono-resistant by DST. Of the isolates with alterations in *rpoB* gene that were susceptible to rifampicin at a critical concentration of 1mg/L, 84% had absent wild type probes with no corresponding mutation probes. Ninety-two percent of the MDR isolates identified by the LPA were confirmed by DST; 12% were resistant to kanamycin, 18% were resistant to ofloxacin and 9% were XDR-TB.

**Conclusions:** Alterations in the *rpoB* region are commonly found in newly identified drug-resistant

*Mycobacterium tuberculosis* isolates in Johannesburg. Alterations in the *rpoB* gene, if not associated with a mutation in the *katG* or *inhA* promoter genes as detected by the LPA, correlated with MDR-TB in only 30% of isolates. If only *rpoB* information is available from a molecular screening test, alterations would correlate with MDR-TB in only 67% of isolates. Rifampicin-mono-resistance is present in a significant number of drug resistant TB isolates. A high proportion of newly identified MDR-TB isolates are resistant to aminoglycosides or fluoroquinolones, with 9% identified as XDR-TB.

#### TUBERCULOSIS MANAGEMENT: LABORATORY, MONITORING AND SURVEILLANCE

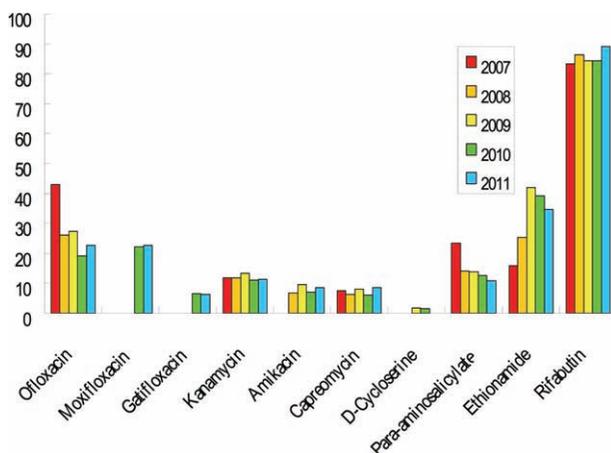
##### PC-754-17 Surveillance of second-line drug resistance among multidrug-resistant tuberculosis in Taiwan, 2007–2011

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**Aim:** 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.

**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 1108 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.

#### PC-755-17 Pattern of drug resistance among tuberculosis patients with and without HIV infection in Ibadan, Nigeria

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**Background:** Tuberculosis drug resistance is a major public health concern, particularly in TB endemic countries like Nigeria that are HIV burdened.

**Methods:** Between June–August 2010 and April–October 2011, we recruited patients with culture-confirmed pulmonary TB from 11 DOTS centers in Ibadan, Nigeria. Drug susceptibility testing using the proportion method with Löwenstein-Jensen medium was conducted with rifampicin (RIF) (40 µg/ml), isoniazid (INH) (0.2 µg/ml), streptomycin (SM) (8.0 µg/ml), ethambutol (EMB) (2.0 µg/ml) and pyrazinamide (PZA) (100 µg/ml).

**Results:** Seventy-five patients were recruited: 49 HIV uninfected (44 treatment-naive; 5 relapsed); 26 HIV co-infected (9 treatment-naive; 5 relapsed; and 12 unclassified). Multidrug-resistance (MDR) was observed in 5 (10.2%) HIV uninfected patients, and 5 (19.2%) HIV co-infected patients. Drug resistance to 1, 2, 3, 4, or 5 drugs was found in 22 (44.9%), 6 (12.2%), 6 (12.2%), 0 (0%) and 8 (16.3%) HIV uninfected

Table Demographic data of TB patients

	Number screened	
	HIV infected TB patients	Non-HIV infected TB patients
Age		
0–19	0	3
20–39	18	26
40–59	6	15
≥60	2	5
Sex		
Male	11	26
Female	15	23
Cases		
New	9	43
Relapse	5	5
Unclassified	12	1
Total	26	49

patients, respectively; and in 4 (15.4%), 2 (7.7%), 2 (7.7%), 4 (15.4%) and 2 (7.7%) HIV co-infected patients, respectively. Resistance to individual drug was RIF 11 (22.4%), INH 12 (24.5%), SM 11 (22.4%), EMB 7 (14.4%) and PZA 16 (32.7%) respectively among HIV uninfected patients; and RIF 7 (26.9%), INH 10 (38.5%), SM 8 (30.8), EMB 6 (23.1%) and PZA 11 (42.3%), respectively among HIV co-infected patients. No difference was detected in resistance between HIV co-infected and uninfected patients ( $P = 0.70$ ).

**Discussion:** Tuberculosis drug resistance including MDR-TB is prevalent in our population, regardless of HIV co-infection. More active case finding for resistance particularly MDR-TB is needed to optimize patient care and public health.

#### PC-756-17 Blood levels of tuberculosis drugs and affecting factors of drug levels

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**Aim:** Therapeutic drug monitoring (TDM) is used to optimize dosing that maximizes therapeutic benefit while minimizing toxicity. The aim of this study is to analyse drug levels and effecting factors to drug levels, during tuberculosis treatment.

**Method:** Treated tuberculosis patients who had no co-morbidity, except diabetes, were included in the study between April and October 2011. Pharmacokinetic tuberculosis drug levels of 21 patients were evaluated after 2 hours of drug administration; 85 patients after 2 hours on the 14th and 30th day. Drug levels were measured and compared with the reference for therapeutic drug levels. Effecting factors of drug levels were evaluated. (Demographic factors, previous treated history, smoking, radiology, initial

smear results, diabetes, use of additional drugs, biochemistry results).

#### Results:

Drug	14th day			30th day		
	Low	Normal	High	Low	Normal	High
INH	60 (70.6)	24 (28.2)	1 (1.2)	54 (62.1)	29 (33.3)	4 (4.6)
RIF	70 (82.4)	15 (17.6)	0	72 (83.7)	14 (15.2)	0
PZA	26 (30.6)	58 (68.2)	1 (1.2)	26 (30.6)	57 (66.3)	3 (3.5)
EMB	38 (44.7)	37 (43.5)	10 (11.8)	30 (34.9)	43 (50)	13 (15.1)

Drug levels were determined on the 14th day: RIF was low for male ( $P = 0.02$ ), EMB and PZA was low for the younger age ( $P = 0.04$ ), PZA was low at high liver function tests ( $P = 0.006$ ). On the 30th day, INH was low for diabetes ( $P = 0.001$ ) and use of additional drugs ( $P = 0.05$ ), high weight ( $P = 0.04$ ).

**Conclusion:** Patients who had diabetes, use of additional drugs and abnormality of biochemistry is useful for TDM monitoring of therapeutic drug levels.

#### PC-757-17 Pharmacokinetic analysis of tuberculosis drugs

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**Aim:** Monitoring plasma drug levels is useful and necessary to achieve maximal effect and avoidance of toxic side effects of drugs. Knowledge of changing blood levels is necessary for drug level monitoring. The aim of this study is to determine the changes in tuberculosis drug levels over a period of time.

**Methods:** 21 tuberculosis patients who had no comorbidity disease (11 male, 10 female; average age  $38.1 \pm 17.0$ ) were included in this study between March and May 2011. Blood was drawn after administering INH (5 mg/kg), RIF (10 mg/kg), EMB (25 mg/kg) and PZA (25 mg/kg) on the 1st hour, 2nd hour, 4th hour, 6th hour, and 24th hour. Plasma drug level was measured with liquid chromatography. Drug levels are expressed with means  $\pm$  SD.

**Results:** After oral administration of all drugs, drug levels increased rapidly and maximum levels were achieved on the 2nd hour. After the 2nd hour, INH drug level rapidly decreased, and RIF, PZA, EMB slowly decreased. Drug levels are shown in the Table.

Time, hour	INH ( $\mu\text{g/ml}$ )	RIF ( $\mu\text{g/ml}$ )	PZA ( $\mu\text{g/ml}$ )	EMB ( $\mu\text{g/ml}$ )
1st	$1.98 \pm 1.53$	$1.67 \pm 2.51$	$19.43 \pm 9.29$	$3.24 \pm 2.25$
2nd	$2.48 \pm 2.02$	$4.26 \pm 2.93$	$24.41 \pm 10.35$	$4.00 \pm 2.93$
4th	$1.09 \pm 1.25$	$4.19 \pm 2.37$	$20.13 \pm 10.23$	$3.98 \pm 2.26$
6th	$0.54 \pm 0.66$	$3.56 \pm 1.97$	$18.35 \pm 7.67$	$2.41 \pm 0.99$
24th	$0.06 \pm 0.26$	$0.46 \pm 0.75$	$7.00 \pm 2.99$	$0.82 \pm 0.56$

**Conclusion:** These results show INH, RIF, EMB and PZA increased maximal level on the 2nd hour after oral administration of the drugs. The 2nd hour is an appropriate time for monitoring four of the therapeutic drug levels.

#### PC-758-17 Comparing suspect identification criteria for tuberculosis case detection in low HIV prevalence settings

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**Background:** In many resource-limited settings, financial and operational constraints require a subset of tuberculosis (TB) suspects to be prioritized for testing, particularly with regards to new molecular diagnostic tests. This study compares the smear microscopy and Xpert<sup>®</sup> MTB/RIF (GXP) case-finding yield of different suspect identification criteria in Pakistan and Bangladesh.

**Design/methods:** All individuals presenting at 7 private laboratories (PLs) across Karachi and 4 across Dhaka were screened for symptoms of TB. Individuals were classified as TB suspects if they had any of the following: >3 weeks of non-productive cough; >3 weeks of productive cough; 2–3 weeks of productive cough; history of TB only (no cough) or family member with TB only. Suspects were instructed on sputum expectoration techniques and those submitting an adequate specimen on visual assessment received a smear microscopy test and chest X-ray. Smear-negative suspects with TB-suggestive X-rays received a GXP test.

**Results:** Of 6087 suspects identified from October 2011 to March 2012, the majority of suspects (62%) and cases (72%) had >3 weeks of productive cough. While sputum submission was significantly higher in suspects reporting productive cough, 61% of suspects

**Table** Smear and Xpert<sup>®</sup> yield from 5 different suspect identification criteria

Suspect identification criteria	A	B	B/A	C	C/B
	Suspects	Suspects submitting sputum	Sputum submission yield % (95% CI)	Smear-positive cases	Smear positivity yield % (95% CI)
>3 weeks of non-productive cough	432	263	60.9 (56.3–65.5)	18	6.8 (3.8–9.9)
>3 weeks of productive cough	3787	3192	84.3 (83.1–85.4)	209	6.5 (5.7–7.4)
2–3 weeks of productive cough	1624	1341	82.6 (80.7–84.4)	55	4.1 (3.0–5.2)
Past history of TB*	184	46	25.0 (18.7–31.3)	3	6.5 (0.0–13.7)
Family history of TB*	60	9	15.0 (6.0–24.0)	0	15.0 (6.0–24.0)
Total	6087	4851	79.7 (78.7–80.7)	285	5.9 (5.2–6.5)

	D	E	F	G	G/F
	X-rays done	X-rays suggestive of TB	Xpert tests performed	Xpert positive cases	Xpert positivity yield % (95% CI)
>3 weeks of non-productive cough	227	57	51	10	19.6 (8.7–30.5)
>3 weeks of productive cough	2867	803	747	157	21.0 (18.1–23.9)
2–3 weeks of productive cough	1255	368	354	50	14.1 (10.5–17.8)
Past history of TB*	39	17	16	3	18.8 (0.0–37.9)
Family history of TB*	7	1	1	0	—
Total	4122	1171	1169	220	18.8 (16.6–21.1)

\*Past and family history of TB were used as suspect identification criteria when patient didn't report productive cough > 2 weeks or non-productive cough > 3 weeks

reporting >3 weeks of non-productive cough could also provide sputum after guidance. This group had similar microscopy and GXP yield to the productive cough group. Both microscopy and GXP yield was significantly lower in suspects with 2–3 weeks of productive cough as compared to suspects with >3 weeks of productive cough.

**Conclusion and recommendations:** In low HIV-prevalence settings, suspects with TB-suggestive X-rays and >3 week of cough may be prioritized for GXP testing, irrespective of whether they report productive or non-productive cough. Suspects reporting non-productive cough should be instructed on sputum expectoration techniques, as this study shows that majority was able to produce sputum after guidance.

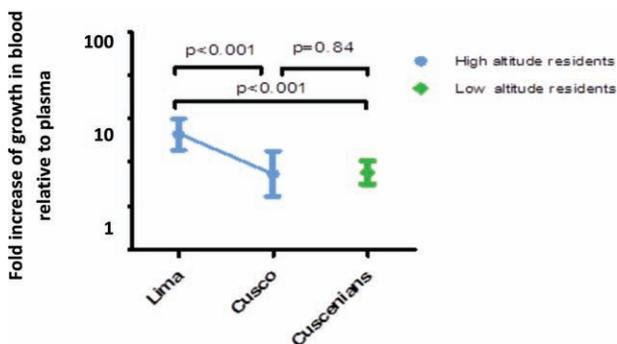
### PC-759-17 Whole blood killing of mycobacteria is greater at high altitude than at sea-level

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**Background:** Historically, sanatoria at high altitude were used to treat pulmonary tuberculosis and the disease remains relatively uncommon in high altitude areas today. With the emergence of increasingly drug-resistant strains there is renewed interest in alternative strategies for TB treatment.

**Design/methods:** We used an *in vitro* assay to measure growth of bioluminescent *M. bovis* BCG in human whole blood after 96 hours incubation. Growth of mycobacteria in whole blood was compared against simultaneous plasma and culture-medium controls. We compared the growth of mycobacteria in low altitude residents ( $n = 15$ ) at sea-level (Lima, Peru) and after ascent to high altitude (Cusco, Peru, at 3400 m) and compared data from low altitude residents with that of permanently high altitude residents in Cusco ( $n = 52$ ).

**Results:** At sea-level, mycobacteria grew 20 times more in blood than in plasma ( $n = 15$ ) whereas after



**Figure** Mycobacterial growth in blood relative to plasma.

ascent to high altitude or in subjects permanently resident at high altitude ( $n = 52$ ) mycobacterial growth in blood was restricted to only 7 times that seen in plasma ( $P < 0.001$  for both comparison groups).

**Conclusion and recommendations:** High altitude is associated with a greater restriction of mycobacterial growth in blood compared to plasma. This could suggest augmented anti-mycobacterial cellular immunity at high altitude. The immune mechanisms underlying altitude-related restriction of mycobacterial growth in whole blood should be studied further as they may offer novel approaches for treatment of drug-resistant strains of tuberculosis.

### PC-760-17 An attempt to identify biomarker(s) in urine of pulmonary tuberculosis patients

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**Background:** In the absence of a sensitive and specific diagnostic modality capable of detecting all forms of tuberculosis (TB), an effort at identifying specific *M. tuberculosis* proteins in urine, with a potential as biomarkers was made.

**Design/methods:** For identification of biomarker(s) in urine of pulmonary TB patients (PTB), proteome profile was compared with non-disease (healthy controls) and disease controls (infectious pneumonia). Second morning urine samples from 24 PTB patients (treatment naive, culture confirmed for *M. tuberculosis*), 24 age matched non-disease controls and 8 disease controls, were collected befitting the inclusion criteria. Proteomics tools such as two-dimensional difference gel electrophoresis (2D-DIGE) and mass spectrometry (reverse phase chromatography coupled to ESI-Q-TOF-MS/MS) were used.

**Results:** Eleven host proteins were identified as differentially expressed; eight proteins were upregulated in PTB: leucine rich  $\alpha$ 2-glycoprotein, zinc  $\alpha$ 2-glycoprotein 1,  $\alpha$ 1-microglobulin protein/bikunin precursor, orosomucoid-1, prostaglandin H2-D isomerase,  $\alpha$ 1-antitrypsin, immunoglobulin lambda and kappa chain. Three proteins were down regulated in PTB patients, namely serum albumin, Kininogen 1 and CD14 Antigen Precursor. Most interestingly, eighteen novel proteins corresponding to *M. tuberculosis* complex were identified in the urine of TB patients.

**Conclusion and recommendations:** Human origin proteins were analyzed in context of previous published studies and were found to be differentially expressed host proteins of acute phase/inflammatory origin. Since most of the identified human proteins were also expressed in other diseases of microbial and non-microbial origin, our initial data does not support the role of human proteins in differential diagnosis of PTB. Identified novel *M. tuberculosis* proteins

could potentially be useful candidate biomarkers to aid diagnosis/prognosis of tuberculosis. Work is ongoing to design a point of care test using these novel potential biomarkers.

**PC-761-17 An evaluation of the Genotype MTBDR+ assay for the rapid and accurate detection of *Mycobacterium tuberculosis*/MDR-TB in extra-pulmonary specimens**

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**Background:** The HIV/AIDS *Mycobacterium tuberculosis* syndemic has led to increased extrapulmonary manifestations of tuberculosis. In 2009 there were 53 411 new cases of extrapulmonary disease in South Africa. High rates of morbidity and mortality are associated with extrapulmonary tuberculosis emphasizing the need for prompt diagnosis and treatment. Diagnosis is hindered by the poor sensitivity of microscopy and the delays in obtaining a culture result. For smear positive sputum specimens, the Genotype MTBDR+ assay has shown to have a sensitivity and specificity of 98.9% and 99.0% respectively for MDR-TB compared with conventional results. To date little data is available on the performance of this assay on extrapulmonary samples.

**Design/methods:** The Genotype MTBDR+ assay was performed on 98 samples comprising 22 smear positive culture positive and 76 smear negative but culture positive extrapulmonary samples, consisting of fluids from sterile sites and lymph node aspirates. Results were compared with the MPT64 antigen assay for *M. tuberculosis* identification and conventional indirect susceptibility testing performed on Middlebrook 7H11 agar.

**Results:** The Genotype MTBDR+ assay identified *M. tuberculosis* in 21 of the 22 (95%) smear positive extrapulmonary samples. The MPT64 antigen assay confirmed the presence of *M. tuberculosis* in 21 of the 22 cultures. Of the 76 samples that were smear negative, 26 were culture positive and 50 were culture negative. The Genotype MTBDR+ assay identified *M. tuberculosis* with in 19 of the 26 (73%) smear negative, culture positive samples. The MPT64 antigen assay confirmed the presence of *M. tuberculosis* in all 19 cultures. The Genotype MTBDR+ assay has a sensitivity of 95% for the detection of *M. tuberculosis* in smear positive fluid aspirates and 73% for smear negative fluid aspirates.

**Conclusion and recommendations:** PCR assay has shown to be useful for the diagnosis of *M. tuberculosis* in extrapulmonary fluid aspirates. The above results represent preliminary data for the sensitivity of detection of *M. tuberculosis* in extrapulmonary samples.

**PC-762-17 Evaluating the performance of the new version 2 Genotype MTBDR+ assay for the rapid detection of multidrug-resistant tuberculosis**

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**Background:** Dual epidemics of HIV infection and *Mycobacterium tuberculosis* infections have hampered the diagnosis of pulmonary tuberculosis due to the increased occurrence of sputum smear negative tuberculosis. Conventional laboratory methods using the sputum smear microscopy for acid fast bacilli (AFB) are less sensitive in patients with HIV associated pulmonary tuberculosis. It is therefore critical to investigate the performance of available molecular methods in diagnosing *M. tuberculosis* (drug resistant or susceptible) in smear negative, culture positive sputum samples.

**Aims:** Evaluate the performance of the version 2 PCR assay.

**Design/methods:** The Genotype MTBDR+ version 2 assay was performed prospectively on 47 smear positive sputum samples and retrospectively on 58 smear negative culture positive sputum samples. Testing was performed in a busy routine NHLS, TB laboratory, KZN, South Africa. Results were compared to the standard methods used in the laboratory.

**Results:** Preliminary data: The version 2 Genotype MTBDR+ assay identified *M. tuberculosis* in 45 of the 47 (96%) smear positive sputum samples. The remaining two samples that were inconclusive by the version 2 Genotype MTBDR+ assay were confirmed to be non-tuberculosis mycobacteria (*M. intracellulare*) by the Genotype CM assay. Of the 58 sputum samples that were smear negative, the PCR assay identified *M. tuberculosis* in 48 of the 58 (82%) sputum samples.

**Conclusion and recommendations:** The version 2 genotype MTBDR+ assay showed a sensitivity of 96% for the detection of *M. tuberculosis* in smear positive sputum samples and 82% for smear negative culture positive sputum samples in this study. The above results represent preliminary data for the sensitivity of detection of *M. tuberculosis* in smear positive and smear negative culture positive sputum samples. Sensitivity for detection of MDR-TB, rifampicin and isoniazid mono-resistant strains of *M. tuberculosis* in smear positive and smear negative culture positive sputum samples will be presented in the final presentation.

### PC-763-17 Two-month sputum non-conversion trends among male and female tuberculosis patients in the Free State, South Africa

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**Background:** Because of its high rate of TB (second only to its neighbour Swaziland at 981 per 100 000 population in 2010), South Africa and its provinces have scaled up DOTS. The purpose of this study was to examine sex differences in the trend of sputum smear non-conversion over a period of seven years (2003–2009) in the Free State, one of nine South African provinces and the one with the fourth highest TB burden.

**Design/methods:** Population-level data from an electronic TB treatment record system were used. The patients included were all those eight years or older who had initiated 2HRZE 4HR–Reg1 treatment. This regimen remained unchanged over the period observed. Patients who transferred out, defaulted or died before 2 months after initiation were excluded. The outcome variable was the percent still smear-positive at 2 months of treatment. 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:** A total of 21 444 male and 18 543 female new pulmonary smear-positive TB patients had at least one 2-month sputum smear result recorded. Totals of 12.5% of male and 9.3% of female patients had not converted. After controlling for age, sputum smear grade, delay from (sputum smear) diagnosis to treatment (days), HIV status, and pulmonary only vs. pulmonary plus other types of TB, the decline in the rate of non-conversion (% still smear positive at 2 months) was statistically significant ( $P \leq 0.001$ ) for both females (–45.5% decline) and males (–32.1% decline) over the period 2003 to 2009, however, significantly ( $P < 0.001$ ) more male than female patients non-converted. Present specific findings to date.

**Conclusion and recommendations:** The improvement was more pronounced in females, which might be explained by their greater attendance of PHC facilities and being more exposed to TB health education and counselling. More attention needs to be paid to sex differences in treatment needs. It is recommended that the province should consider possible solutions such as extra clinic hours and outreach to more effectively target TB services to males.

### PC-764-17 Detection of DNA extracted from AFB smears with Xpert MTB/RIF assay (preliminary data)

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**Background:** The Xpert MTB/RIF assay has been proved to have high sensitivity and specificity in detecting mycobacterial DNA in native sputum specimens and allows for rapid detection of *rpoB* mutations. It has been demonstrated that *M. tuberculosis* complex DNA present in Ziehl-Neelsen or auramine-stained smears can be extracted and used in molecular tests. In this study, we attempt to prove that the MTB/RIF assay can be applied to DNA extracted from microscopy-positive stained sputum smears.

**Design/methods:** We selected stored AFB positive ZN stained slides, removed oil with xylene and scraped smears off the slides after adding phosphate buffer. The resulted solution was mixed and MTB/RIF sample reagent was added. After 15 minutes of incubation the content was transferred into the MTB/RIF cartridge, which was inserted into the GeneXpert system. In total, slides from 80 patients will be tested. Here we present preliminary data from 16 patients. The data of remaining slides will be available by July 2012.

**Results:** Out of four AFB3+ and five AFB2+ smears all 9 were found to be *M. tuberculosis* positive by MTB/RIF assay. Out of seven AFB1+ smears 3 were *M. tuberculosis* positive and 4 *M. tuberculosis* negative. None of the *M. tuberculosis* positive specimens were harboring *rpoB* mutation. More AFB1+ and scanty slides will be tested as part of remaining 64 slides.

**Conclusion and recommendations:** With the ready availability of stained smears in routine diagnostic laboratories, and their easy transport and storage at room temperature, this approach may be useful for optimizing the definitive diagnosis of TB and especially of MDR-TB.

### PC-765-17 Validation of a uniform scoring system for tuberculous meningitis in a hospital setting in Indonesia

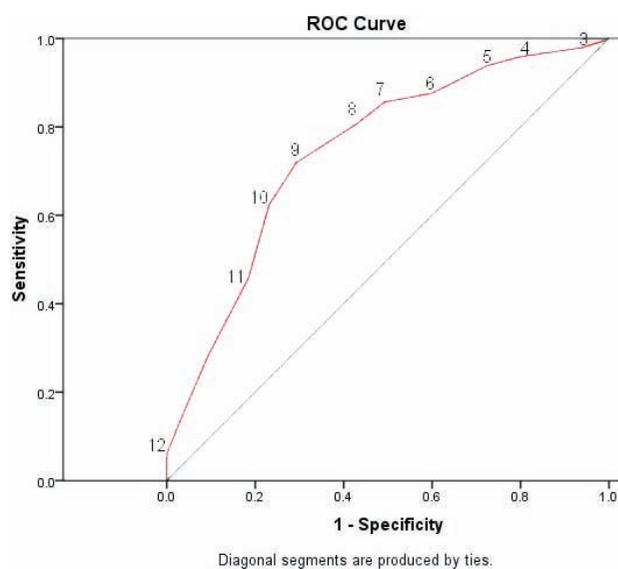
S Dian,<sup>1</sup> A R Ganiem,<sup>2</sup> L Chaidir,<sup>1</sup> Ida Parwati,<sup>2</sup> R Van Crevel.<sup>3</sup> <sup>1</sup>Medical Faculty, Universitas Padjadjaran, Bandung, <sup>2</sup>Neurology, Hasan Sadikin Hospital, Bandung, Indonesia; <sup>3</sup>Internal Medicine, Radboud University Nijmegen Medical Center, Nijmegen, Netherlands. e-mail: sofiatidian@gmail.com

**Background:** TB meningitis (TBM) is the most severe form of TB. Diagnosis is difficult. Recently, a uniform case definition has been developed for diagnosis of TBM, which incorporates clinical and CSF criteria, cerebral imaging, and evidence of TB elsewhere

(Marais et al., Lancet Infect Dis 2010; 10: 803–812). There is a maximum score of 22 (with cerebral imaging) or 16 (if no imaging is available). We evaluated this scoring system in a hospital setting in Indonesia, comparing it with a very sensitive PCR performed on CSF samples.

**Design/methods:** Marais' scoring system was used in a prospective cohort of adult meningitis suspects in Hasan Sadikin Hospital Bandung Indonesia. IS6110 real-time PCR using 5–7 ml of CSF was used to define the predictive value of the scoring system and the optimal cut-off. This PCR has shown to be very specific and sensitive in previous studies (IUATLD 2011 Lille, OP 930-28). No cerebral imaging was available.

**Results:** 211 adult patients with subacute meningitis and available *M. tuberculosis* PCR data were included. According to Marais' algorithm, 20.8% had no TBM (score <6), 29.5% had possible TBM (score 6–9), and 49.7% probable TBM (score  $\geq 10$ ). TB PCR was positive in 69.2% of patients, patients with positive PCR had a median score of 10, compared with 6 for PCR-negative patients ( $P < 0.001$ ). Using PCR as gold standard, Marais' algorithm had a sensitivity of 87.7% and specificity of 40% when using the proposed score of 6 as cut-off. A cut-off score of 9 was more accurate (sensitivity 71.9%, specificity 70.8%, see ROC-curve). Cranial nerve palsy, lowered consciousness, systemic symptoms, CSF cells (10–500/ml) and low CSF glucose (<50% of plasma; or <2.2 mmol/L), and chest X-ray abnormalities had the highest positive predictive value for a positive PCR.



**Conclusion and recommendations:** The newly developed uniform case definition has a good predictive value for TBM and can help clinical management and research of TBM. Prospective studies like ours may help define the optimal cut-off in particular settings.

### PC-766-17 Towards improved tuberculosis treatment data outcomes in uMkhanyakude District, KwaZulu-Natal, South Africa: a monitoring and evaluation approach

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**Background:** South Africa ranks 3rd in highest TB burden countries list worldwide. Data management systems are recognized as core to evaluate TB program performance. The USA Agency for International Development (USAID) TB program run by University Research Corporation (URC) provides technical support to National Department of Health and TB control program at all levels of management. In Umkhanyakude, one of the project supported districts, interventions were prompted by the need to understand the drastic drop in favorable TB outcomes observed in Q2/2010.

**Methods:** The exercise was conducted the first month of the following quarter. A joint monitoring and evaluation visit was conducted to determine data accuracy, completeness, and timeliness. The sampling frame was the 64 consistently reporting health facilities out of which 38 were randomly selected. We conducted one-on-one interviews with the district TB coordinator, information officer and data capturers, and compared captured data for the 4 indicators under investigation with the filed paper trail. Findings revealed limited indicators understanding by data capturers, unclear and inconsistent data flow system, limited accountability, improper filing system of the collected data system, and weak data tracking system. One-on-one mentoring and coaching of data capturers and receivers were guided by the displayed knowledge gap.

**Results:** We assessed cure, treatment success, defaulter and death rates for new smear positive cases and



**Figure** Treatment outcomes for a USAID TB program supported district, Umkhanyakude, January–December 2010.

prospective data analysis showed that both favorable outcomes peaked, while a gap reduction occurred between cure and success rates, a marker of program quality improvement.

**Conclusion:** This study concludes that formal skill transfer is a key to achieving accurate and consistent quality results. Involvement of local information and facility staff is essential to produce sustainable results.

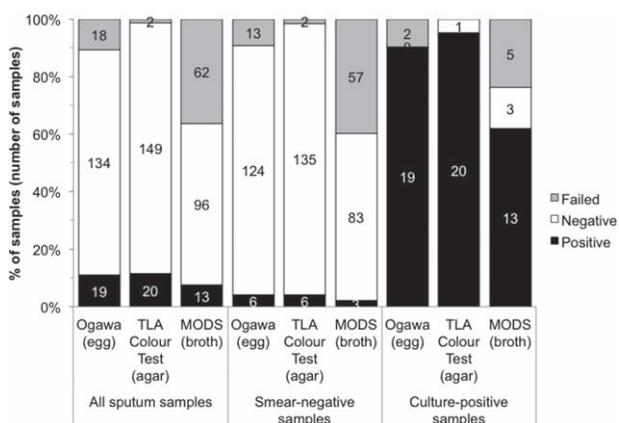
### PC-767-17 Field assessment of tuberculosis culture techniques in a resource-poor jungle setting

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**Background:** Sputum smear microscopy negative and drug resistant TB principally occur in resource-poor settings but research evaluating tests to diagnose them is usually done under optimized conditions. We therefore assessed the performance of 3 TB culture techniques for samples collected under operational conditions and tested in a basic TB laboratory in the Amazon compared with testing in a distant reference laboratory.

**Methods:** Sputum samples were collected from patients with suspected pulmonary TB and sent to the local laboratory. Sputum was tested immediately by: direct un-concentrated sputum smear microscopy; modified-Petroff decontamination and Ogawa culture; and the thin-layer agar (TLA) MDR/XDR-TB Colour Test technique. The residual sputum was then refrigerated and flown to a biosafety level-3 reference laboratory for broth culture testing with the MODS (Microscopic-Observation Drug-Susceptibility) technique.

**Results:** The established Ogawa culture and the newly implemented Colour Test culture had similar ease-of-use and performance (Figure). The broth MODS culture technique had a significantly higher failure rate



due to contamination, principally for samples for which un-refrigerated transport from remote jungle regions had delayed culture by more than 2 weeks. Consequently, MODS diagnosed significantly fewer patients than other tests, although it did so significantly more rapidly. The Colour Test and MODS provided concurrent MDR-TB testing results with 100% concordance.

**Conclusions:** This ongoing study has demonstrated that TB diagnostic test performance was strongly dependent upon delay until testing. For samples that had prolonged unrefrigerated transport, the optimal speed of broth culture was outweighed by frequent contamination. The MDR/XDR-TB Colour Test was successfully implemented in a basic field laboratory under operational conditions and provided significantly greater diagnostic yield than testing in a distant reference laboratory.

## TUBERCULOSIS MANAGEMENT: HEALTH SYSTEMS AND HUMAN RESOURCES

### PC-798-17 Engaging all care providers for estimation of tuberculosis disease burden in Pakistan

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**Background:** The health sector in Pakistan is diverse and mostly unregulated private sector. 70% of health expenditure is through out of pocket fee for service. Private sector is divided into private practitioner, not NGOs, Para-statal organisations. 96% of TB patients consult other care providers. The non-NTP providers do not follow the NTP guidelines recommended by NTP. There is a need to estimate the extent of under-reporting by these providers and find out missing cases.

**Design/methods:** A cross-sectional study was carried out from January to March 2012 in twelve districts selected on the basis of notification status, including Rawalpindi, Rajanpur, Lodhran, Khushab from Punjab, Buner, Batgram, Swat, from KPK, Lasbela, Wauhuk, Zhob from Balochistan. In selected districts all non-NTP private providers including private practitioners, informal hakims and homeopaths, private hospitals, polyclinics, university hospitals and from non-NTP public sector included public health facilities such as social security and public university hospitals engaged. The modified suspect and modified laboratory register distributed in engaged sites.

**Results:** Three data sources, i.e., non-NTP private, non-NTP public and NTP compared and record linkage done to see the extent of missing cases and under-reporting by these sites. The data was collected from January to March 2012, 3023 TB suspects identified

with varying referral and management of tuberculosis, mostly the practitioners prefer X-ray chest and smear microscopy with ESR for diagnosis.

**Conclusion and recommendations:** The study is a breakthrough for NTP Pakistan and complimentary with the results of disease prevalence survey recently completed to find out the incidence of TB (capture recapture analysis) and compare it with the disease prevalence.

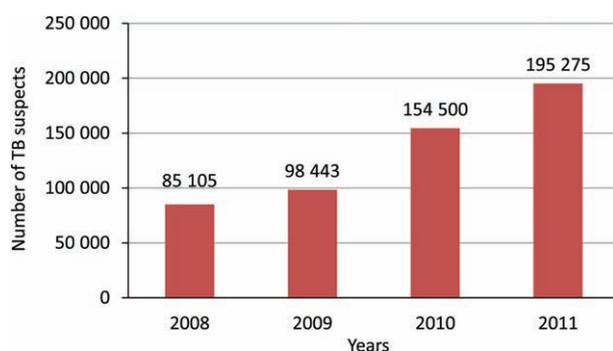
### PC-799-17 Identify the impact of standard operation procedure implementation on early tuberculosis case detection in Afghanistan

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**Background:** Since 2004, SOPs had not been revised and no health facility staff was trained in TB service delivery that resulted in delayed case detection, diagnosis and treatment. TB CARE I, USAID TB project, assisted NTP on SOP implementation. This study assessed to determine impact of SOPs implementation in TB screening and case detection.

**Intervention:** TB CAP and follow-on TB CARE I, assisted NTP through revision, printing and dissemination of SOPs for case detection to public clinics; training of 2072 health facility staff, distribution of diagnostic package (metal boxes), training package (SOPs and guidelines) and treatment packages (patient pack kits) to 1500 clinics and on-the-job training to staff. In January to February 2012, data for 2008–2011 of 637 health facilities was collected, reviewed and analyzed. The NTP's standard recording and reporting system was used in data collection.

**Results:** Triage and screening of attendees resulted in a steady increase in number of TB suspects screened from 2008 to 2011. TB suspect screening increased from 85 105 (2008) to 98 443 (2009), 154 400 (2010) and 195 275 (2011). This led to an increase in TB case notification, e.g., 7% increase in TB cases in 2010 and 5% in 2011 in TB CARE intervention areas. The



**Figure** Trend of TB suspect examined 2008–2011.

total TB cases notified in 2009, 2010, and 2011 were 26 258, 28 238 and 28 138 respectively. Interestingly, 90% of these achievements occurred in TB-CARE I/ USAID intervention areas.

**Conclusions:** The SOP implementation resulted in significant improvement in access to TB services, consequently, TB case detection in Afghanistan. Therefore, we recommend scale up and implementation in similar setting elsewhere.

### PC-800-17 Task shifting: an option for increasing tuberculosis case notification in Nigeria—a case study in Gombe State, Nigeria

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**Background:** Poor access to diagnostic centers and shortage of qualified laboratory personnel are among the major factors contributing to low case notifications in Gombe State TB program. The main objective of the study was to increase TB case notification within the piloted LGAs by at least 30% from 2010 figures through engagement of health workers (HW) at DOTS centers on sputum smearing by the end of 2011.

**Design/methods:** This was a prospective study carried out over a one year period (January to December 2011). Twelve DOTS centres within 3 LGAs (4 per LGA) with lowest case notification and the most difficult access to diagnostic services were purposefully selected. Health workers (HW) from 3 designated microscopic centres within the LGAs were trained on slide smearing, storage and transportation to the state reference laboratory.

**Results:** Of the 117 TB suspects seen at these facilities whose smeared sputum were examined, 28 were smear positive (23%). The contributions of the initiative to the case notification in the piloted LGAs by the end of 2011 were 42%, 33% and 20% in Dukku, Kwami and Yamaltu Deba, respectively. The external Quality report from the centers showed good quality smears by the HW as 89% of blinded rechecked slides were having normal sizes and thicknesses and 87% had normal staining.

**Conclusion and recommendations:** Task-shifting (smearing by HW) contributes to increase TB case notification and its adoption by TB programs will strengthen and expand health work-force to rapidly increase access to AFB microscopy services in an era of increasing dearth of human resources.

### PC-801-17 Impact of TBIC implementation on magnitude of tuberculosis infection among health care workers in ten hospitals in two Afghanistan provinces, 2011

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**Background:** USAID-supported TB CARE I program assisted the Afghan NTP in implementing TBIC measures (patient flow, triage, cough etiquette, renovation, and face mask usage). Measures are being implemented in 45 HFs. In November 2011, a team assessed the impact of TBIC among HCWs in ten hospitals of Kabul and Khost Provinces. Intervention TB CARE I and NTP team assessed 10 public hospitals. In total, 240 staff from high-risk areas (DOTS rooms, labs, OPDs, emergency rooms, internal medicine wards) was screened for TB. We used a WHO staff risk assessment log, documented sign and symptoms, HIV status, staff category, and offered X-rays and sputum examinations.

**Results:** Facilities with TBIC had less suspected and new TB SS+ cases than facilities without. 120 health care workers from facilities with TBIC screened for TB, of them 11% were identified as TB suspects. Three (27%) were diagnosed as new TB SS+. Out of 120 HCWs from facilities without TBIC, 18% were identified as TB suspects and seven (31%) were diagnosed as new TB SS+ cases. All suspected and SS+ cases tested HIV-negative. 41% of new TB SS+ cases were diagnosed among lab techs and 27% among OPD and DOTS staff; the TB incidence rate among the intervention group was 2500 per 100000 populations vs. 5833 among the control group without TBIC measures.

**Table** Staff screening results for TB infection in intervention and control areas

Variable	Intervention area (with TBIC measure application)	Control area (without TBIC measure application)
Sample size	120	120
Identified as TB suspects	13 (11%)	21 (18%)
Diagnosed as TB SS+	3 (27%)	7 (31%)
HIV status	Negative	Negative
Proportion of DOTS room staff affected by TB out of all staff categories	8%	19%
Proportion of lab techs affected by TB out of all categories of staff	12%	29%

**Conclusions:** TBIC implementation reduced the risk of TB infection for HCWs significantly. Therefore, as the TB rate is higher among health workers, we recommend the scaling up of TBIC implementation to additional HFs.

### PC-802-17 Role of mentoring in strengthening state tuberculosis programme performance in Nigeria. Is it useful?

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**Background:** Mentoring is most often defined as a professional relationship in which an experienced person (the mentor) assists another (the 'mentee') in developing specific skills and personal support. Despite the robust supervisory schedule in many TB programs, its effectiveness in solving program challenges is limited because supervisory systems are usually focused on performance of task; limited time; weak feedback and relationships are usually not personal. These were some of the reasons why specific challenged states were identified to be supported using the mentoring approach rather than supervision only.

**Intervention objective:** Describe the value of mentoring in strengthening TB programs.

**Methodology:** 9 states were selected from the 37 states in Nigeria, based on a 5 year's desk review of the program bothering on key performance indicators including states with low TB case notification rates; high default rates; high notification of retreatment cases; recurring data discrepancies and low DOTS coverage. All previous supervisory reports were also reviewed. Consequently a list of mentors was drawn up by the NTP and a one-day meeting was held with the identified mentors to discuss differences between mentoring and supervision, develop terms of reference, mentoring tool and reporting format and identify a mechanism for feedback.

**Results** Within a period of 6 months, 78% (7) of the 9 states had an average of 2 visits each by a team of 2 to 3 mentors. The results varied by states but most common benefit as mentioned by >80% of the state team members was on team building, office filing systems, analysis of program performance and defining next steps and practical tips on how to increase TB case detection. Office organizational skills were improved through support to develop organograms, clear job descriptions, creation of office board and files. Capacity for data analysis was also achieved.

**Conclusions:** Mentoring should be widely adopted at all levels to improve performance.

### PC-803-17 Factors associated with reporting low tuberculosis notification in Mutare District, Manicaland Province, Zimbabwe

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**Background and challenges to implementation:** In 2009, Mutare and Buhera Districts had TB notification

of 200/100 000 and 694/100 000/population/year, respectively. We conducted this study to determine factors contributing to low reporting of TB notification in Mutare District, Manicaland Province, Zimbabwe.

**Intervention or response:** Training of health care workers at health facilities on TB-HIV programme activities. Strengthening TB-HIV collaborative activities. Assurance of availability and supply of TB-HIV data collection tools and commodities at health facilities in Mutare District. Routine support and supervision of the health facilities by the District Health Executive.

**Results and lessons learnt:** Clinics with nurses not trained in HIV Testing and Counseling were 2.51 times more likely to report low TB notification (OR 2.51) (95%CI 0.64–10.54). None availabilities of the following: transport for sputum collection from clinics (OR 95.29) (95%CI 10.17–2246.06), ART guidelines (OR 58.00) (95%CI 6.50–1316.36), TB screening tools (OR 46.00) (95%CI 50–371.11), HIV laboratory registers (OR 46.00) (95%CI 50–371.11), ART attendance registers (OR 8.50) (95%CI 2.07–37.85) and TB suspect registers (OR 7.00) (95%CI 1.22–52.23) respectively were associated with reporting low TB notification. Fourteen (47%) clinics in Mutare District and 27 (90%) clinics in Buhera District reported sputum turn around time of less than seven days respectively. Buhera had 23 (77%) clinics and Mutare had one clinic (3%) with partner support respectively, ( $\chi^2$  30.63) ( $P < 0.0001$ ).

**Conclusions and key recommendations:** Transport of sputum from clinics, supply of missing TB-HIV data collecting tools, financial and material support may increase TB notification in Mutare District.

#### PC-804-17 Analysis of capacity building of tuberculosis prevention and control institutions in Guizhou Province

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**Objective:** To understand the capacity building status at all levels of tuberculosis prevention and control institutions in Guizhou Province.

**Methods:** TB prevention and control institutions at all levels were investigated by questionnaires from September to October in 2010.

**Results:** To build the TB prevention and control institutions at all levels, the professionals at prefecture, county levels were increased 51.6%–137.6%, respectively. The education and professional title of staffs were obviously improved. The infrastructure could meet the basic work need.

**Conclusions:** The capacity building of TB prevention and control institutions in Guizhou Province were acquired greatly achievement. But it is necessary

to improve the qualities and quantities of staffs, renew the equipments and further strengthen the laboratory building.

#### PC-805-17 Determinants of health system and patient related delay among tuberculosis cases in Western Australia

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**Background:** Early diagnosis and effective management of tuberculosis (TB) is the principal factor that determines the success of TB control programs. The current study was conducted in the WA TB Control Program aiming to describe patient and health system delay, and to identify factors contributing to this delay.

**Design/methods:** This study is a retrospective analysis of the WA TB notification data.

**Results:** Of 286 cases, 55% were males with mean age of 44 years, mean age for females was 41 years. The overall mean patient delay was 79 days, health system delay had a mean of 29 days. The 30–44 year age group had the longest patient delay average (93 days) while the longest health system delay average was observed for the 45–64 age group (37 days). Extra-pulmonary TB cases had longer delays compared to pulmonary cases: 8% longer patient delay and 54% longer health system delay ( $P = 0.02$ ). Time in Australia was a risk factor for patient delay with the longest average delay noted for those in the country from 11–25 years (90 days). Health system delay was the opposite with the longest delay (30 days) in patients in Australia from 1 to 5 years. No significant difference was seen between migrant and Australian born patients in patient delay, while migrants had on average a 34% longer health system delay ( $P = 0.01$ ). Among migrants, permanent residents had the longest patient delay (82 days), refugees had the longest health system delay (57 days). Patient from low risk TB countries had a 9% longer patient delay than those from high risk countries, while the health system delay for these two groups did not show any significant difference.

**Conclusion and recommendations:** The current analysis showed middle aged, extra-pulmonary TB, time in Australia since migration and being from low risk countries as risk factors for patient delay while extra-pulmonary TB, history of migration, and being a refugee as risk factors of health system delay.

### PC-806-17 Intensified case finding of tuberculosis in an HIV care clinic in Kenya: implementation and outcomes

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**Background and challenges to implementation:** Intensified case finding is the regular screening for evidence of tuberculosis in people infected with HIV. Though TB intensified case finding was introduced to HIV care clinics in Kenya two years ago, it has yet to become a routine aspect of HIV care and little is known on its outcomes in Kenya. The objective of this study was to document the implementation and outcomes of ICF in Makindu District Hospital HIV care clinic with 1956 patients (2011). Clinic attendance is scheduled one-two monthly.

**Intervention or response:** In March 2010, staffs at the HIV care clinic were trained on TB intensified case finding. A seven symptom item screening tool was administered on PLHIV during routine clinic attendance. A patient with any of the symptoms of cough, contact, weight loss, night sweats, fever, swelling, chest pain was recorded as TB suspect and investigations to confirm TB using the Kenya national guidelines were done. All cases diagnosed were initiated on TB treatment in the HIV care clinic. Data on number screenings conducted, number of suspects and number confirmed with TB in 2011 was collected at the end of each clinic and summarized monthly.

#### Results:

Type of patient	Q1 2011		Q2 2011		Q3 2011		Q4 2011	
	Pre-ART	On-ART	Pre-ART	On-ART	Pre-ART	On-ART	Pre-ART	On-ART
Number of screening events	1036	2990	1391	3020	1702	3763	1699	5522
Suspects	42	22	89	79	98	65	78	197
Confirmed cases	12	18	18	36	21	16	27	30
Number of screening events to realise one case	86	166	77	84	81	235	63	184

TB screening increased from quarter one to quarter four. Cumulatively 12.2% of all the HIV clinic attendees were diagnosed with TB in 2011.

**Conclusions and key recommendations:** ICF is feasible in routine program settings. However, pre-ART patients were at a higher risk of developing TB. The antiretroviral treatment guidelines should consider earlier ART initiation to prevent these patients (pre-ART) from developing TB disease.

### PC-807-17 Overcoming work climate challenges of human resource management in the delivery of quality procurement and supply management services: the Nigerian experience

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**Introduction:** In countries where personnel work largely under challenging or de-motivating conditions; compliance tends to be low while apathy and/or resistance rates gravitate on the high side. Dissatisfaction with pay, poor working environment, vested interests (religious, political or professional) are a few of the many factors that induce resistance. Until October 2010, the NTP supply system was highly destabilized as evidenced by high stock out rates expiration of drugs and wastages. This was largely attributed to resistance to implement the national logistics system perceived as adding more tasks.

**Objective:** To describe how personnel in de-motivating environments can be *influenced* to deliver optimal PSM services despite poor work climate.

**Methodology:** In July 2010, the entire pipeline was opened up for clear info visibility by updating a new database of all facilities and personnel details in NTP down to the DOTS sites: they were to be held accountable for individual performances. The pre-existing national LMIS was reviewed to introduce *strong but subtle* persuasive elements: e.g., quarterly performance profiles, PSM liabilities flagged in monetary values, etc to be use for strong peer reviews and feedback among managers. The new initiative was rolled out nationally in same quarter after the state control managers were trained to collect data which were fed into the database; analyses thereof were shared among stakeholders with emphases on any queries raised.

**Results:** By July 2011, the overall PSM indicators were shown to have improved dramatically: e.g., stock outs and pipeline leakages (down to near zero) and wastages < 9%. 25 of the 28 previously resistant state control managers had intensified self drive for optimal performances, apparently motivated by concerns to avoid indictment from colleagues and superiors.

**Conclusion:** Use of peer review, monitoring and feedback can influence performance even in difficult work setting.

### PC-808-17 The integrated pharmaceuticals logistics system reduces drug stock outs in Ethiopia's Amhara and Ormia Regions

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**Background:** Ethiopia's pharmaceuticals supply management system regularly experiences setbacks within their drug supply including lack of availability, poor storage, and irrational use. TB pharmaceutical management also faces the problem of frequent stock outs at health facilities. One mechanism to address this problem is through the implementation and use of the Integrated Pharmaceuticals Logistics System (IPLS). This study assessed the level of IPLS implementation in USAID's Help Ethiopia Address Low TB (Heal TB)-supported health facilities and the contribution of IPLS in improving stock outs in these facilities.

**Design:** This cross-sectional study was performed between November 2011 and January 2012. The study evaluated 687 public health facilities.

**Result:** IPLS has been implemented in 229 facilities (33.33%). About 21.5% of the health facilities reported anti-TB drug stock outs during the three months preceding the assessment. Facilities using IPLS had a mean stock out rate of 17.03%, while those that had not implemented IPLS had a mean stock-out rate of 23.7%. Health facilities that had not implemented IPLS had 1.5 times higher stock out days than health facilities implementing IPLS [OR = 1.53 (95%CI 1.01–2.3)].

**Conclusion:** Health facilities implementing IPLS experienced lower stock out than those health facilities not implementing IPLS. These results reflect a need for different parties to scale up IPLS implementation.

### PC-809-17 A case for decentralisation: health centres surpass hospitals in tuberculosis outcomes within two Ethiopian regions

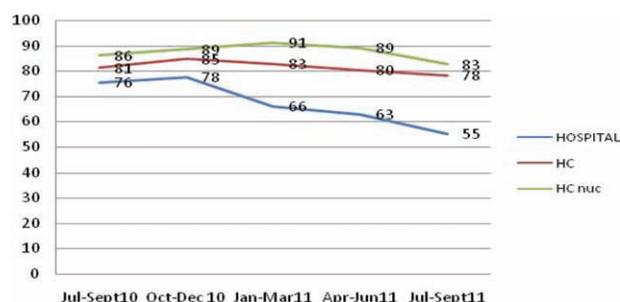
M Melese,<sup>1</sup> B Girma,<sup>1</sup> Y Kassie,<sup>1</sup> T Benyam,<sup>1</sup> A Hadgu,<sup>1</sup> F Mikru,<sup>1</sup> P G Suarez.<sup>2</sup> <sup>1</sup>Heal TB Project, MSH/HEAL TB, Addis Ababa, Ethiopia; <sup>2</sup>Center for Health Services, Management Sciences for Health, Arlington, VA, USA. e-mail: mmelese@msh.org

**Background:** Ethiopia remains among countries with the highest tuberculosis (TB) burden, although the overall TB treatment outcomes are approaching the global target. Ethiopia is struggling to keep pace with this progress and it is crucial to identify the weak points in the health care system and to take corrective action.

**Methods:** From October 2011 through January 2012, USAID's Help Ethiopia Address Low TB (HEAL TB) project conducted a baseline assessment of the exist-

ing TB service conditions in 596 health facilities. A clinical mentoring team reviewed the case performance and patient treatment outcomes from five quarters preceding the assessment.

**Results:** The treatment success rate (TSR) in hospitals ranged between 55% and 78%, while a TSR of 78%–91% was documented in the health centers. The transfer-out rate ranged between 7% and 17% in hospitals, while health centers had a transfer out rate of 1%–5%. Hospitals had a higher default rate (9.3%) than health centers (3.8%). The overall treatment success rate increased from 70% to 80% when transfer-out cases were removed from the denominator.



**Figure** Treatment success rate by category of health facilities of patients evaluated during the specified periods.

**Conclusion/recommendations:** The hospitals' lower TRS in comparison to health centers is attributed to the hospitals' high transfer-out and default rates. These results indicate that decentralizing treatment to lower level health facilities, more accessible to patients improves treatment outcomes.

### PC-810-17 Evaluation of the effectiveness of health services in the diagnosis of tuberculosis at the triple border of Brazil, Paraguay and Argentina

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**Background:** Tuberculosis control involves organizing health services to perform diagnostic actions in an integrated and collaborative way. The study aimed to evaluate the effectiveness of different health services in the diagnosis of tuberculosis in the city of Foz do Iguaçu, Paraná.

**Methods:** A cross-sectional study was carried out with 101 patients who were diagnosed with tuberculosis from January to November 2009. Interviews were conducted by using an instrument based on the *Primary Care Assessment Tool* adapted for tuberculosis care. Data were analyzed using descriptive statistics (absolute and relative frequency). Effectiveness

was assessed by indicators built for three types of health facilities (primary care units, emergency services and specialized services). Proportions and respective 95% confidence intervals were calculated for observed results.

**Results:** The first health service visited with the highest percentage on tuberculosis suspicion (46%) was the specialized service. Sputum smear tests were requested for 50% of patients interviewed in the three types of health care services. The best result for X-ray request percentage was observed in the emergency services (30%). Primary care units referred patients (75%) mostly to the X-ray exam, showing a statistically significant association ( $P < 0.05$ ). In primary care units, 75% of patients had to return until five times the health service to attain diagnosis, more than other services. In specialized services, the time of the diagnosis was seven days (median), in emergency care ten days (median) and primary health care seventeen days (median).

**Conclusions:** The health services as the first option chosen by the patient were not effective in suspicion and diagnosis of tuberculosis, indicating barriers to the structure and process of controlling the disease. The most effective services to provide the diagnosis of tuberculosis were the specialized services.

#### **PC-811-17 A hard look at soft skills training assessment: developing and piloting a soft skills assessment tool for tuberculosis health care staff in Tamilnadu, India**

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**Background:** TB treatment involves several interactions of TB patients with health staff from point of entry of patients for diagnosis until completion of treatment, which necessitates soft skills training to health staff. The present abstract describes process of developing and piloting a soft skills assessment tool to understand usefulness of soft skills training given to health staff.

**Intervention or response:** Under Project Axshya, district health staff in government health centers (treatment supervisors, laboratory technicians, village health nurses, etc.) in districts of Tamilnadu, India, underwent soft skills' training. Subsequently a review was conducted with 272 trained health staff in groups of 15 to 20 after a period of 3 to 6 months using soft skills assessment tool.

**Results and lessons learnt:** Soft skills assessment tool consisted of 3 parts. Part 1 included 6 scenarios which assessed soft skills found most useful during health staff interactions with TB symptomatics, initial defaulters, patients starting TB treatment and those who 'perceived stigma', while 2 scenarios each assessed soft skills used most in their interaction with community and family. Part 2 elicited soft skills they

found useful or felt needed additional training. Part 3 presented 2 TB case studies to assess application of soft skills. Health staff perceived inter-personal communication skills and counselling skills as important in patient interaction while stress management was considered critical in community/family interaction.

**Conclusion and key recommendations:** The above results describe a first of its kind information on development of soft skills assessment tool for assessing these skills for health staff as there is no available set scale for measuring them. There is a need to develop such tools which would provide input for further refresher trainings and for possible policy implications to mandate such soft skills trainings for all health staff along with technical skills.

#### **PC-812-17 Do they know how to correctly categorise a tuberculosis patient? Findings from the effects of DOTS clinic staff training in Nigeria, West Africa**

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**Background:** Nigeria had about 3900 DOTS centers spread all over the country and the drive for DOTS expansion has necessitated the need for training of DOTS staff. However, the competencies of these staff need to be determined.

**Methods:** Data used was from the Training Impact Evaluation study of DOTS clinic staff conducted in each of the six geographical zones in Nigeria by the National Tuberculosis and Leprosy Control Program (NTBLCP) and major stake-holders in March, 2012. A total of 159 general health care workers (GHWs) who have been trained on DOTS strategy between July 2010 and December 2011 were randomly selected.

**Results:** At the bivariate level, analysis shows significant association between knowledge of TB symptoms and the ability of DOTS staff to correctly categorize and institute appropriate treatment regimen to registered TB patients; 32.9% ( $P < 0.01$ ). Also with knowledge of the main route of TB transmission; 33.3% ( $P < 0.02$ ). There is a positive relationship between those who understood all the criteria of treatment and how to correctly categorize a TB patient; 62.5% ( $P < 0.0001$ ). At the multivariate level, respondents who knew the criteria of treatment were 7.3 times more likely to categorize a TB patient correctly than those who do not have such knowledge (OR = 7.392, 95%CI 3.238–16.874,  $P < 0.0001$ ).

**Conclusions:** Training and mentoring of DOTs staff is fundamental to provide the skills needed for patient categorization and appropriate treatment regimen. This is essential for the delivery of quality TB treatment services.

## MEDICAL MANAGEMENT/ TUBERCULOSIS OUTBREAK AND CONTACT INVESTIGATION

### PC-843-17 Spatial statistics: a tool to guide active case finding of tuberculosis cases in the community

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**Background:** Distribution of tuberculosis cases takes place in foci following a cluster pattern. This study aimed at using spatial statistics to map and analyze the spatial relations between the cases within a GIS environment. The ultimate goal is to guide active case finding in the community.

**Design/methods:** The electronic surveillance system applied in Egypt was used to provide 2010 notification data for Alexandria governorate. The addresses of cases were geo-referenced, mapped and different spatial statistics tools were employed.

**Results:** 539 TB cases were registered during 2010. Of these, 365 (68%) were male and the rest female. 54% were in the age group 15–34 years of age. 73% were living in suburban and urban slums. Spatial analysis showed that the highest number of cases was in Al-Maemora District (22%) and the lower number in Karmouz District (5.3%). The central TB case was located in Al-Raml District and the mean case in Sidi Gaber District. 68% of the cases clustered around their mean center with a cluster radius of 3.1 km. Using nearest neighbor calculations indicated that >90% of TB cases occurred at distances < 571 m from their nearest reported case.

**Conclusion and recommendations:** Using this information, the national programme in Egypt will be able to carry out a targeted approach in the mapped areas with active case finding of TB cases within the mean cluster radius and with guided distance searches in the following year.

### PC-844-17 SF36v2 norms and discriminative properties among healthy households of tuberculosis patients in Malaysia

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**Background:** The aim of the study was to obtain norms of SF36v2 health survey and association of summary component scores with socio-demographic variables in healthy households of tuberculosis (TB) patients.

**Design:** All households (18 years and above; literate) of registered tuberculosis patients who came for contact tracing during 1st March 2010 until 28th February 2011 at respiratory clinic of Penang General Hospital were invited to complete SF36v2 health survey using the official translation of the questionnaire in Malay, Mandarin, Tamil and English. Scoring of questionnaire was done by scoring software version 4. Multivariate analysis was conducted to uncover the predictors of physical and mental health.

**Results:** A total of 525 respondents participated in the study. Internal consistencies met the minimum criteria (>0.7) for all scales except for vitality in Tamil version. Reliability coefficients of the scales were always less than their own reliability coefficients. Mean physical component summary (PCS) scale scores were equivalent to USA general population norms. However, difference was more than 3 norm based scoring points for mean mental component summary (MCS) scores indicating poor mental health. A notable proportion (31.4%) of the respondents were at the risk of depression. Age 75 years and above ( $P = 0.001$ ; OR 32.87), widow ( $P = 0.013$ ; OR 2.6) and postgraduates ( $P < 0.001$ ; OR 7.87) were predictors of poor physical health whereby, unemployment ( $P = 0.033$ ; OR 1.72) was the only predictor of poor mental health.

**Conclusion:** To best of our knowledge this study is first of its kind indicating mental stress in households of TB patients. Our findings may help health-care professionals to have an insight of the value of quality of life in households and thereby aid in the designing strategies to maintain or improve quality of life. Future studies should also investigate the impact of household quality of life on treatment success of TB patients.

### PC-845-17 Evaluation of tuberculosis case finding through systematic contact investigation, Chhattisgarh, India

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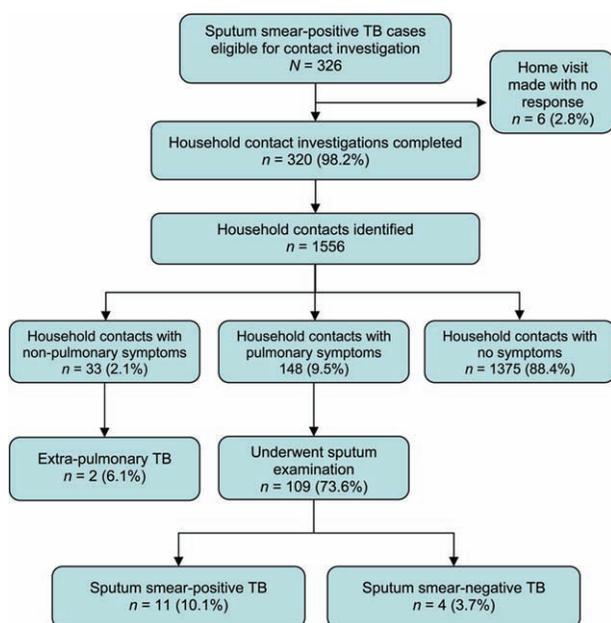
**Rationale:** Contact investigation is an established tool for early case detection of tuberculosis (TB). In

India, the lack of standard operational guidelines has limited the implementation of contact investigation, and the yield of contact investigation is not well described.

**Objective:** To determine the yield of evaluating household contacts of sputum smear-positive TB cases in Rajnandgaon District, Chhattisgarh, India.

**Methods:** Among 14 public healthcare facilities with sputum microscopy services, home visits were conducted to identify household contacts of all registered smear-positive TB cases. A standardized protocol assessed clinical symptoms suggestive of active TB with referral for additional clinical assessment with chest radiograph and sputum collection.

**Results:** From December 2010 to May 2011, 1556 household contacts of 312 sputum smear-positive TB cases were identified, of which 148 (9.5%) were symptomatic. Among these, 109 (73.6%) were evaluated by sputum examination resulting in 11 cases (10.1%) of sputum smear-positive TB and 4 cases (3.6%) of smear-negative TB. Among 233 contacts age <6 years identified, 148 (63.5%) initiated isoniazid chemoprophylaxis after thorough evaluation to rule-out active tuberculosis.



**Figure** Flow diagram depicting the outcome of household contact investigation, Rajnandgaon District of the State of Chhattisgarh, India, December 2010–May 2011.

**Conclusion:** A standard procedure for conducting household contact investigation identified additional TB cases in the community, and offered an opportunity to initiate isoniazid chemoprophylaxis among children.

### PC-846-17 Development of a tuberculosis contact investigation interviewing skills course

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**Background:** Contact investigation is a high priority for TB programs in the USA. To successfully conduct contact investigations, effective interviewing skills are necessary. Data from the U.S. National TB Indicators Project indicate poor performance in identifying and evaluating contacts. To improve contact investigation outcomes, the CDC Division of Tuberculosis Elimination and the Regional Training and Medical Consultation Centers developed the TB Contact Investigation Interviewing Skills Course.

**Intervention:** The course was developed using the systematic health education process. Materials were adapted from existing TB and STD interviewing courses. Discussions with field investigators and others helped identify key information and skills-building activities to include. Subject matter experts reviewed the materials.

**Results:** A 4-day curriculum emphasizing the development of interviewing skills to identify contacts was developed. Course materials include a facilitator guide, slide sets, exercises, and role-plays. Ten pilot test courses were conducted in 2011. Results show knowledge gained, with an average pretest score of 86% and an average posttest score of 94%. When asked whether their interviewing skills were enhanced as a result of the training, 97% of participants agreed.

**Conclusions:** Interviewing skills are necessary to successfully conduct contact investigations. Providing participants an opportunity to practice interviewing skills through role-plays is an effective method to build interviewing skills. Results indicate the course improved participants' knowledge and self-efficacy. Using the systematic health education process ensured the development of an effective course to meet the needs of the target audience. Final revisions to the course will be made after pilot testing is complete.

### PC-847-17 Reaching the unreachable: active case finding among SS+ tuberculosis patients' household contacts living in remote areas in five provinces of Afghanistan

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**Background and challenges to implementation:** Though TB patients household contacts in Afghanistan

are at high risk for developing TB and often suffer from poor access diagnostic services, contact management is very poor due to difficult terrain, seasonal constraints and high workload. Under a TB REACH wave 1 grant, ATA-AP/ACREOD initiated active case finding among household contacts of SS+ TB patients in 5 provinces of Afghanistan. Two health facility (HF) staff were tasked with visiting the SS+ TB patients' households, identify suspects living there, and collect and deliver the sputum samples to the respective HFs' laboratories. Staff received USD 15 for each trip and expected to visit the households of 3 index cases in each trip. This study analyzed one year data from 47 HFs during Q4, 2010 to Q3, 2011 and aimed to explore the magnitude of TB amongst SS+ TB patients' household contacts and document feasibility of this intervention.

**Results and lessons learnt:** In total, 7232 household members were screened for TB and 1480 suspects (20% of screened) were identified. Among the suspects, 136 were confirmed SS+. The data shows the prevalence of 2 SS+ cases among 100 household contacts.

**Conclusions and key recommendations:** Active contact tracing resulted in higher TB case notification among contacts and is a feasible solution for reaching the population who live in remote areas of Afghanistan. The prevalence of previously unreported TB among contacts in 5 provinces in Afghanistan was 2%. This kind of activity can improve case detection rates and may be implemented on a larger scale.

#### **PC-848-17 Integration of tuberculosis diagnosis and treatment into primary health care services: experience and lessons learnt from South Sudan**

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**Background and challenges to implementation:** Low DOTS coverage is one of the key challenges facing tuberculosis (TB) control in South Sudan. Only 6% (65/1147) of health facilities are providing TB services. In order to increase DOTS coverage, the Government of South Sudan has included TB in the Basic Health Package and is advocating for integration of TB into general health services. An assessment was conducted to determine which health facilities have minimum criteria to integrate TB diagnosis and treatment into general health care services.

**Intervention or response:** An integration framework including a rapid assessment tool and criteria for integration of TB services was developed by the National TB Program (NTP) and partners. The minimum criteria includes a functional health facility,

presence of at least 3 medical personnel, a general laboratory, the catchment population and its burden of TB and/or HIV/AIDS.

**Results and lessons learnt:** The assessment tool was piloted in 13 health facilities in April, 2011. Of the 13 health facilities, 4 (31%) were already providing TB services, 6 (46%) met the minimum criteria but did not provide TB services and 3 (23%) did not meet the minimum criteria. The feasibility of this assessment is based on the simplicity of the tool and the criteria to be measured.

**Conclusions and key recommendations:** Integration can rapidly expand TB DOTS services as many health facilities meet minimum criteria. Assessment should be carried-up throughout the country to involve more health facilities.

#### **PC-849-17 Improving quality of tuberculosis detection at the primary health care system in Bryansk and Saratov Oblasts, Russia**

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**Background and challenges to implementation:** In 2010, the percent of newly-detected TB patients with sputum smear positive microscopy results (SS+) at Primary Health Care System (PHCS) in Russia composed 18.1%. In Bryansk and Saratov Oblasts it composed 17.0% and 38.0% respectively.

**Intervention or response:** Analysis of the existing TB detection process at PHCS and causal link of key reasons in delayed TB detection were carried out based on quality improvement (QI) tools or 'Driver's Diagram'. Key barriers for TB detection were identified and grouped into 5 sections (see attached). A list of proposed changes for quality improvement of TB detection and indicators to assess their effectiveness were developed. A work plan of project activities was composed accordingly.

**Results and lessons learnt:** QI teams were formed in 5 pilot PHC facilities, which tested and implemented the following changes into TB detection practices: standardization of techniques and multiplicity of sputum collected; regular feedback between lab and clinical staff; algorithm for PHC workers to form patients' flow for microscopy. Activities of QI team from City Polyclinic #5 in Bryansk resulted in increase of patients covered with SS from 154 in 2010 up to 394 in 2011. Number of newly-detected TB patients with SS+ increased more than twice.

**Conclusions and key recommendations:** System analysis of PHCS and its interaction with TB services using the QI methodology makes it possible not only to identify key barriers for early TB detection, but to

develop and implement an effective set of activities that can be replicated in any PHC facilities in the short term. Active participation of healthcare stakeholders provides a consolidation of the best organizational changes and their scale up in the territory.

**Analysis of key reasons in delayed TB detection**

1. Secondary drivers depending on PATIENTS	Proposed changes	Micro-indicators
<ul style="list-style-type: none"> <li>Social status: low health priorities, drug/alcohol abuse, low educational level</li> <li>Lack of knowledge on TB symptoms</li> <li>Lack of knowledge on the services provided at PHC facilities</li> <li>Undervaluation of illness severity</li> <li>Lack of documentation (medical assurance, passport, etc)</li> <li>Self-stigmatization</li> <li>Self-treatment</li> </ul>	<ul style="list-style-type: none"> <li>Develop billboards, posters and other social ad</li> <li>Develop leaflets for patients:                             <ul style="list-style-type: none"> <li>With information on TB facility</li> <li>On TB</li> <li>On healthy lifestyle</li> </ul> </li> <li>Work with mass media</li> <li>Improve the preventive work with youth and their connections</li> <li>Spread information about possible pre-doctor examination without medical insurance</li> </ul>	<ul style="list-style-type: none"> <li>Number of publications in mass media (municipal, territorial)</li> <li>Number of leaflets spread among the patients</li> <li>Number of posters and leaflets placed in PCH facility in front of X-rays rooms and lab</li> </ul>
2. Secondary drivers depending on MEDICAL PROVIDERS	Proposed changes	Micro-indicators
<ul style="list-style-type: none"> <li>Poor personnel qualification (lack of experience, education, motivation)</li> <li>Low suspicion for TB</li> <li>Insufficient knowledge on TB symptoms and detection methods                             <ul style="list-style-type: none"> <li>Clinical «masks» of TB</li> </ul> </li> <li>Insufficient educative activities with patients</li> <li>Association of TB with high-risk groups</li> <li>Poor time management</li> <li>Insufficient knowledge on command and control instruments</li> <li>Lack of wish and demand in self-development</li> <li>Lack of quality control</li> <li>High workload</li> <li>Non-compliance with diagnostic minimum</li> <li>Definition of population, which shouldn't be screened on TB</li> <li>Work with TB contacts</li> </ul>	<ul style="list-style-type: none"> <li>Educate the specialists</li> <li>Introduce the rules on quality sputum collection to the job descriptions of nurses at PHC facilities</li> <li>Carry out the independent audit of medical documentation</li> <li>Include the quality algorithm implementation into the medical audit</li> <li>Develop algorithms and recommendations for doctors</li> <li>Establish rooms for pre-doctor examination</li> <li>Include TB discipline into postgraduate education for PHC specialists</li> </ul>	<ul style="list-style-type: none"> <li>Proportion of patients medical records with correctly filled doctor's algorithm to the total number of patients medical records</li> <li>Availability of instruction sheets and algorithms for the district doctors</li> <li>Number of polyclinics accepting patients without residence registration</li> <li>Proportion of sputum collected under the supervision of medical staff to the total number of sputum collected that proceed to the lab</li> </ul>
3. Secondary drivers depending on CARE ORGANIZATION	Proposed changes	Micro-indicators
<ul style="list-style-type: none"> <li>Lack of personnel (low salary rate, lack of housing)</li> <li>Poor system of continuing education for medical doctors and nurses</li> <li>Limitations in working hours of X-rays rooms</li> <li>No registration of X-rays screening at the reception or level of pre-doctor examination</li> <li>Poor administrative monitoring of quality of work performed</li> <li>Poor infection control measures</li> <li>Poor preventive work</li> <li>Insufficient quality of places for sputum collection (rooms, cabins)</li> <li>Poor work with TB contacts</li> <li>Inadequate budgeting and resource allocation TB</li> <li>Poor cooperation with TB services: education on TB, patients' referral, quality control</li> <li>Low level of access to high risk groups, immigrants, released prisoners</li> <li>Lack of understanding from the heads of PHC facilities</li> <li>TB screening among non-transportable patients</li> <li>Lack or impossibility to use transportable fluorographs</li> <li>Cooperation of PHC facilities and police departments</li> <li>Development of regulatory structure</li> <li>Allocation of priorities at PHC</li> </ul>	<p><b>To stakeholders at PHC facilities:</b></p> <ul style="list-style-type: none"> <li>Enhance the capacity of PHC personnel</li> <li>Establish the information exchange on X-rays screening within PHC specialists</li> <li>Educate specialists in IC, and develop IC plan for the facilities</li> <li>Equip the places for sputum collection with cabins, operating materials, inhalers, instructions</li> <li>Provide sufficient number of quality operating materials</li> </ul> <p><b>To regional government:</b></p> <ul style="list-style-type: none"> <li>Develop and approve regional TB preventive plan as a part of territory program – include all necessary technical components</li> <li>Form accurate priorities among regional stakeholders</li> <li>Organize the pre-doctor examination available for vulnerable groups</li> <li>Establish interagency cooperation                             <ul style="list-style-type: none"> <li>Committee on prevention of socially important diseases</li> <li>Joint plans</li> <li>Regular meetings to evaluate the results of previous decisions</li> <li>Joint monitoring and analysis</li> </ul> </li> <li>Lobby the interests of target groups and medical workers</li> <li>Influence the formation of accurate regulatory structure at the region</li> <li>Provide external control to the quality of lab examinations</li> </ul>	<ul style="list-style-type: none"> <li>Number of specialists trained in IC</li> <li>Availability of IC TB plan at the PHC facility</li> <li>Existence of special sputum collection rooms/cabins at PHC settings along with the qualified personnel and instruction how to collect sputum</li> <li>Number of PHC specialists trained in early TB detection (from the total number of specialists)</li> <li>Number of specialists trained in lab diagnostics (from the total number of specialists)</li> <li>Number of polyclinics where X-rays room has working hours from 8am to 8pm</li> <li>Proportion of patients referred to TB services within first 3 days after getting SS+TB results to the total number of TB suspects</li> <li>Proportion of referred patients, who came to TB services within first 3 days after getting SS+ TB result, to the total number of patients referred to TB services</li> </ul>

4. Secondary drivers depending on LABORATORY conditions	Proposed changes	Micro-indicators
<ul style="list-style-type: none"> <li>Low quality of diagnostic materials</li> <li>Low qualification of lab specialists</li> <li>Lack of operating supplies and equipment</li> <li>Low motivation</li> <li>Assuring the collection of the quality diagnostic material</li> <li>Low expectations from labs</li> <li>Lab workers don't provide detailed reports separately for each of the district</li> </ul>	<ul style="list-style-type: none"> <li>Control the quality of diagnostic materials</li> <li>Introduce the registration of sputum quality for microscopy test</li> <li>Educate the lab specialists</li> <li>Equip the laboratories</li> <li>Provide quality control of sputum smear microscopy</li> <li>Provide regular feedback from lab specialists to the doctors</li> </ul>	<ul style="list-style-type: none"> <li>Number of labs with the registration of sputum quality</li> <li>Number of sputum culled by lab for microscopy tests</li> <li>Number of labs fully equipped with operating supplies</li> </ul>
5. Secondary drivers depending on SOCIETY	Proposed changes	Micro-indicators
<ul style="list-style-type: none"> <li>Stigmatization in society, at work</li> <li>Low health priorities</li> <li>Lack of understanding in the society</li> <li>Problems associated with socially vulnerable population: poverty, homeless, jobless, drug abuse</li> <li>Poor involvement of business sector</li> <li>Low awareness on TB among population</li> <li>Low social responsibility among employers</li> <li>Climatic and geographical location</li> </ul>	<ul style="list-style-type: none"> <li>Work with mass media</li> <li>Lobby the interests of TB patients and healthy society</li> <li>Improve health education</li> <li>Involve the governmental social protection services through interagency committees, etc.</li> <li>Work with employers:                             <ul style="list-style-type: none"> <li>Reduction of stigma and discrimination towards TB patients;</li> <li>Timely preventive TB screening of employees;</li> <li>Help to families with TB patients;</li> <li>Assistance in work with TB contacts</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>Number of publications in mass media</li> <li>Proportion of patients receiving social support to the total number of patients in need</li> <li>MACRO: Social studies on stigmatization towards TB patients among the population</li> </ul>

**PC-850-17 Setting up tuberculosis treatment follow-up after release from prison**

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**Aim:** To ensure TB patients released from prison are continued treatment in the civilian TB facilities through joint efforts.

**Methods:** To strengthen treatment adherence among released TB patients a Memorandum of Understanding (MOU) was signed on March 2009 between Ministry of Health (MOH/NTP), Ministry of Justice (MOJ) and International Committee of the Red Cross (ICRC) on piloting follow-up of TB patients after release from prison. The parties implemented the following tasks: 1) Conducted educational sessions prior to release for patients and handed over from prison TB hospital to NTP. 2) Ensured patients are registered in civilian TB facilities and provided with adequate treatment. 3) Developed a standardized approach, monitored and provided a set of social support and incentives including food and hygienic parcels, transportation fees to ensure treatment adherence.

**Results:** The pilot project was successfully implemented and the process and support mechanisms (counselling, education, social networks, incentives) put in place and valuable experience were gained which later in 2011 was handed over to national NGO to continue. Since April 2009 up to December 2011, 42 MDR-TB patients were released from prison and 39 of them were provided with continuation of treatment.

**Conclusion:** Project shows significant success since the vast majority of the released TB patients can be followed-up in order to continue their treatment. Pilot project came to an end at the end of 2010. As a result of patient support program carried out jointly by

three parties and later by local NGO, treatment adherence among released TB patients was ensured 98%, while it was only 10% of treatment continuation in previous years.

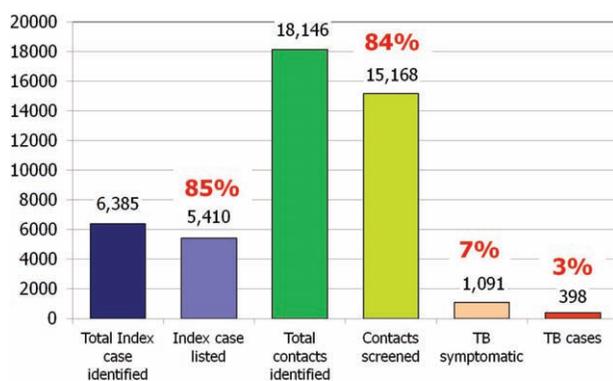
### PC-851-17 Feasibility and effectiveness of systematic tuberculosis household contact investigation: The Philippine experience

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**Background and challenges to implementation:** The CATCH project, supported by WHO-CIDA, aims to develop and test a set of policies and guidelines on systematic household contact investigation (CI) in selected DOTS facilities in Metro Manila as a strategy to increase case finding.

**Intervention or response:** Index TB patients were initially identified and listed together with their contacts—individuals who reside in the same house and share the same kitchen as the index patient. Household contacts of smear positive index cases registered were prioritized, but there were health centers that screened contacts of all registered index cases. Community volunteers helped in following-up those who did not report to health centers. Contacts were screened for TB symptoms, children among the household of 0–4 years were given a tuberculin skin test (TST). The NTP protocol was followed for identification of active TB disease among contacts. Quarterly monitoring and desk review were conducted.

**Results and lessons learnt:** From June 2010 to December 2011, there were 6385 index cases identified. 85% of them were listed together with their 18146 contacts (Figure). In all, 15168 (84%) contacts were screened of whom 1091 (7%) were TB symptomatic. 398 (3%) of the symptomatics were secondary TB cases with 76% children below 14 years of age.



**Figure** Summary of household CI, Metro Manila, Philippines, July 2010–December 2011.

Sixty-nine contacts were sputum smear positive. Identifying TB symptomatics and sputum smear positive contacts are strong predictors for getting secondary TB cases ( $P < 0.01$ ).

**Conclusions and key recommendations:** Household CI was feasible in these health centers. The procedure was able to detect possible source cases. To increase the yield the project will include CXR as screening tool in selected health center settings.

### PC-852-17 Features of tuberculous pleural effusion in HIV-infected patients

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**Background:** To study clinical and morphologic features and diagnostic standards of tuberculous pleurisy (TP) in HIV-infected patients.

**Design/methods:** We studied 270 patients with TP. All of them were new TB cases, and TP was the only site of TB affection by the disease onset. The average age was  $28.6 \pm 0.9$  years, 95.6% patients ( $n = 258$ ) were males, as much as 44.8% ( $n = 121$ ) patients were HIV-infected (HIV+). No one of the latter had obtained anti-retroviral treatment prior to admission. TB was confirmed with combination of clinical examination, X-ray, smears/cultures for *Mycobacterium tuberculosis* along with the results of thoracoscopy. Medical thoracoscopy with pleural biopsy were made in a routine fashion. Pathologic examination of biopsates, polymerase chain reaction (PCR) and cultures of the biopsy specimen and exudates for TB were carried out.

**Results:** HIV+ patients were more symptomatic than HIV negative (HIV–), with weight loss in 56.3% and 35.0% cases, night sweats in 41.4% and 25.2% cases, febrile temperature in 55.2% and 23.8% cases respectively ( $P < 0.05$ ). Thoracoscopy was carried out in 75 patients, 46.7% ( $n = 35$ ) of them were HIV+. No major complications occurred. Total dissemination of TB nodules upon the pleural surface was found in 14.3% of HIV+ cases, and in 7.5% HIV– patients. Nodules more than 1.0 cm in dimension were observed in 37.2% ( $n = 13$ ) HIV+ and in 10.0% ( $n = 4$ ) HIV– patients ( $P < 0.01$ ). Alternative TB inflammation was found in 37.2% pleural specimen from HIV+ patients, and in 20.0% samples in HIV– group, productive TP inflammation occurred in 25.7% ( $n = 9$ ) pleural samples from HIV+ and in 50.0% ( $n = 20$ ) specimen from HIV– patients ( $P < 0.01$ ). Cultures for TB were positive in 24.4% HIV+ and only in 5.4% specimen from HIV– patients. PCR was made in 87 HIV+ and 10 HIV– samples and was positive for TB in 66.7% ( $n = 58$ ) and 40.0% ( $n = 4$ ) cases, respectively. Thoracoscopy in

combination with pathology, PCR and cultures of the bioplates was 99.9% successful to confirm the TB origin of pleurisy.

**Conclusion and recommendations:** Tuberculous pleurisy in the patients with HIV co-infection presents with more defined inflammatory syndrome. Thoracoscopy with pleural biopsy remains a golden standard of diagnostics for TB pleurisy in HIV-infected patients.

### PC-853-17 Improving tuberculosis programme performance through championing selected health facilities in South Africa

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**Background:** South Africa ranks 3rd of high TB burden countries worldwide. The national program has achieved noticeable improvements, but some districts have performance challenges still. The USA Agency for International Development (USAID) TB project, run by the University Research Corporation (URC) provides technical support to National Department of Health and National TB Control Program at all levels of management. In 2009, jointly with districts management, we identified facilities with program challenges, and embarked into quality improvement interventions.

**Interventions:** In October 2009, we identified 28 health facilities in 9 districts; a baseline assessment was conducted and TB and HIV related challenges identified: data recording, clinical management and follow-up, defaulter and contact tracing and TB-HIV integration. Emphasis was put on TB suspicion and new pulmonary TB cases indicators. Sites were visited once to twice a month, jointly with facility management and staff; on-site mentoring consisted of staff capacity building (bedside coaching, assistance with data updates, need based trainings), regular data verification exercise—all following a quality improvement cycle—and provision of job aids, pamphlets and posters.

**Results:** Indicators were captured in an Excel database: aggregated data show a 2 years 1, 6.3, 6, 13 and 7% increases in case detection, treatment initiation, 3 months sputum conversion, cure treatment success rates respectively and an 8% average turnaround time increase; unfavorable initial interim and end of treatment outcomes (lack of microscopy, defaulter and death rates) decreased in a less significant way; cotrimoxazole, CD4 and ART uptakes increased by 10, 55 and 57%, respectively.

**Conclusion:** Over 2 years, districts/facilities/partners collaborations quality improvement interventions (supportive supervision, need based mentoring, coaching) in jointly identified sites led to significantly improved performance.

### PC-854-17 Sustained improvement in tuberculosis programme performance after partner's exit: Ilembe District, KwaZulu-Natal, South Africa

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**Background:** South Africa ranks 3rd in the TB highest burden countries list worldwide. TB treatment outcomes are keys to evaluate program performance and hence TB control. The USA Agency for International Development (USAID) TB project run by the University Research Corporation URC provides technical support to national department of health and TB control program. In 2004, Ilembe District was jointly identified for its performance challenges (42% cure rate in smear positive pulmonary TB). Jointly with the district we developed quality improvement interventions that were sustained after our exit from the area.

**Intervention:** We used the PDSA (Plan, Do, Study, Act) improvement cycle in the district, involving district and subdistricts management, facility staff, and community members. Contributing factors ranged from poor access to quality TB services, weak Directly Observed Therapy, Short course (DOTS) program and limited community involvement. Baseline need assessments were conducted at all management levels (facilities, sub districts and district), multidisciplinary plans focused actions plans developed and implemented at different levels of care (including data verification exercise, capacity building for managers and staff on TB management, improved community/DOT supporters TB awareness through dialogues), and post assessments conducted.

**Results:** Between 2004 and 2010, through the collaborative model, significant improvements in data quality and program performance at district and sub districts level were noted (42%, 30% increase in cure and treatment success, 11% decrease in defaulter rate). TB managers' involvement allowed quality sustainability after our exit in 2009.

**Conclusion:** Quality improvement interventions have been sustained in Ilembe district through the formation of multidisciplinary teams actively involved in all levels of care and management.

### PC-855-17 Comparison of immune recovery among HIV and TB-HIV co-infected patients on antiretroviral therapy in Nigeria

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**Background:** Effects of tuberculosis on CD4 cells contribute to the course of HIV infection in dually

infected patients. Using CD4 counts, we compared immunological response to antiretroviral therapy (ART) between HIV-positive patients and patients co-infected with HIV and TB.

**Design/methods:** Data used in the analysis were abstracted from patient records at 14 facilities. The patients were  $\geq 15$  years old, initiated on ART between April 2006 and September 2010, and on treatment for at least one year, with documented baseline CD4 count and at least three follow-up results. Using STATA, frequencies and proportions for baseline characteristics were computed and median changes in serial CD4 counts were compared using Mann-Whitney *U* test. Statistical significance was set at 5%.

**Results:** Total patient enrollment on ART within the period was 5338; 62.0% of the patients included in the study were female, and 5.7% of the patients were TB-HIV co-infected and on TB treatment. Mean age at registration was  $36.5 \pm 9.9$  years for TB-HIV co-infected patients and  $35.8 \pm 9.7$  years for HIV-infected patients ( $P = 0.03$ ). At baseline, median CD4 count was 126 cells/ $\mu$ l (IQR 57 to 201) for TB-HIV co-infected patients and 161 cells/ $\mu$ l (IQR 81 to 243) for HIV-infected patients ( $P = 0.0$ ). Median on treatment peak CD4 count was 517 cells/ $\mu$ l (IQR 369 to 733) and 532 cells/ $\mu$ l (IQR 373 to 728) for TB-HIV co-infected and HIV-infected patients respectively ( $P = 0.4$ ). Median difference in CD4 counts between baseline and peak was 364 cells/ $\mu$ l (IQR 186.5 to 571) ( $P = 0.5$ ).

**Conclusion and recommendations:** Immunological recovery in HIV-infected patients did not differ significantly from that found in TB-HIV co-infected patients studied.

#### PC-856-17 The mortality of patients with HIV-associated tuberculosis after prescription of antiretroviral therapy in different terms of anti-tuberculosis treatment

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The treatment of TB is the priority of the treatment of patients with HIV-associated tuberculosis. Antiretroviral therapy (ART) prescription is made in different terms of anti-TB treatment. Since 2010 in Ukraine has been applying the 'Clinical Protocol of antiretroviral therapy of HIV infection in adults and adolescents' #551, based on WHO recommendations.

The goal is to make comparative analysis of mortality TB-HIV patients after prescription ART in different terms of anti-TB treatment.

**Materials and methods:** 95 patients with HIV-associated tuberculosis and the low level of CD4 cells

( $\leq 350$  cells per cubic mm) have been examined. All patients received treatment of TB on the 1st category. Patients were divided into two groups. The 1st group included 19 patients (20%) who have been treated in 2009. ART was prescribed them after the intensive phase of treatment TB.

The 2nd group consisted of 76 (80%) patients, who have been treated in 2010. ART was prescribed them after achievement of satisfactory tolerance to anti-TB drugs (from 2 weeks to 2 months).

**Results:** 24 TB-HIV patients who used ART were dead: 9 (47.4%) patients were from the 1st group, 15 (19.7%) from the 2nd group.

**Conclusion:** Thus the early terms ART prescription allows decrease the mortality of TB-HIV patients in 2.4 times.

#### PC-857-17 Nécessité de la durabilité des acquis du Projet tuberculosis Reach dans les 6 districts à faible détection, cas du Kasai Occidental Ouest

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**Introduction :** La CPLT de KOO est parmi les 23 que compte le pays. Depuis le retrait des appuis de Partenaires, 6 districts sanitaires, à savoir Tshikapa, Mutena, Kalonda Ouest, Mikope, Kamonia et Kamwasha, ont connu une diminution de la détection dont la moyenne a atteint 58% en 2010. L'avènement du Projet TB Reach avec ses approches innovantes s'est avéré pertinente.

**Objectif :** Evaluer les acquis de ces approches sur la détection de cas de TB et les pérenniser pour consolidation la détection.

**Méthodes :** Formation de 136 prestataires de CS, de 76 anciens malades tuberculeux, sur ces approches à savoir l'investigation de cas contacts de TB, le transport des échantillons de suspects vers les centres de diagnostic, le dépistage actif de TB auprès de populations spéciales et la sensibilisation dans ces districts pendant la période d'Octobre 2010 à mars 2012.

**Résultats :** Un total de 1209 cas additionnels de TPM+ a été détecté dans ces 6 districts dont 347 de contacts, 44 des populations spéciales et 818 de transport des échantillons des suspects TB.

**Conclusion :** Cette innovation des stratégies de lutte a fait des preuves dans la détection de cas de TB dans les 6 districts et leur pérennisation à travers les appuis du round 9 du Fond mondial et du Projet TB 2015 va consolider et améliorer davantage la détection.

## TUBERCULOSIS: PUBLIC HEALTH PRACTICE

### PC-882-17 One-stop TB HIV services for healthy outcomes for uniformed services populations in metropolitan Nairobi

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**Background and challenges to implementation:** The needs of most-at-risk and key populations living and working in the congregate settings as the uniformed services need emphasis when addressing HIV and TB combined epidemics. Reducing the burden of TB among people living with HIV involves delivery of '5 Is' that includes Intensified case finding, Infection prevention control, INH prophylaxis, Integration and prompt Initiation of Anti-Retroviral drugs (ARVs). Staff at the Administration Police-Security of Government Buildings (AP-SGB) clinic noticed delay of initiating ARVs among referred patients to neighbouring facilities and poor adherence among those on both ARVs and TB drugs. Routine data to the Division of TB, Leprosy and Lung Disease (DLTD) showed ARVs uptake among TB patients at AP-SGB of 20-25%, lower than the 30-40% achieved by Kenya in the last 3 years.

**Intervention or response:** Operation AIDS Response In Forces in Uniform (Op-ARIFU) supported the initiation of the integrated TB and HIV services in this facility to offer care and treatment under one roof. This aimed at improving ARVs uptake and promoting adherence to treatment. Facility staff were trained and mentored on provision of this one-stop TB and HIV services while adhering to treatment protocols/guidelines. ARVs to co-infected patients were initiated during the first month of TB treatment based on WHO criteria. There was strict adherence to confidentiality, consent and continuous counseling despite increased recording workload.

**Results and lessons learnt:** Adherence to treatment improved to double-fold following this integration. Management of drug reactions and interactions was prompt. Increased workload led to documentation challenges of recording and reporting including incomplete registers, delayed registration and reporting.  
**Conclusions and key recommendations:** Integrated TB and HIV services promotes adherence to treatment. Challenges of documentation should be addressed.

### PC-883-17 Factors that could improve adherence to treatment among pulmonary tuberculosis patients: a qualitative study among tuberculosis patients in Tomsk, Russia

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**Background:** The goal of the study was to identify motivational factors that could influence adherence among TB patients with treatment interruptions.

**Methods:** 200 TB patients from the city of Tomsk and the Tomsk region were selected using an approximation model. Interruptions in TB treatment were reported for all of the patients. Specially-trained personnel from the local TB services and the Russian Red Cross conducted a survey with subsequent data analysis.

**Results:** Of the 200 patients interviewed, 64 were at the TB Hospital, 80 were treated as outpatients in the city of Tomsk and 56 were treated as outpatients in rural areas. Among all respondents, the leading factor in motivating patients to adhere to treatment was the daily delivery of food packages (68% of patients agreed). In addition, 51.5% of hospitalized patients and city outpatients believe that personalized attention from medical staff is an important stimulus for taking medications regularly. Furthermore, 46% of the city ambulatory patients suggested providing transportation tickets; 39% of the hospitalized patients and patients from the rural areas stated a need for clothing and footwear; and 48% of the surveyed patients find individual stories of other TB patients rather useful in improving their motivation to continue treatment.

**Conclusion:** TB patients often need more attention from medical personnel, require some social support and consultation from additional specialists, as well as encouragement from other TB patients who successfully completed treatment.

### PC-884-17 Detection of active tuberculosis among people living with HIV/AIDS and vulnerable population groups (commercial sex workers and injecting drug users)

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**Background:** Vulnerable groups (persons living with HIV/AIDS, migrants, homeless, commercial sex workers, and substance users) are at greater risk of developing TB, including MDR-TB, and are likely to have worse treatment outcomes. They experience

longer delays in seeking care, increased suffering from disease and higher risk of community transmission.

**Objectives:** To increase coverage of TB screening and assess incidence of TB among vulnerable groups in Tomsk, Russia.

**Methods:** During 2010 and 2011, a cohort of 1385 persons was identified as a risk group for TB. Screening was conducted twice a year and included basic evaluation of symptoms, PPD (DIASKIN-TEST) and chest fluorography. Evaluation involved qualitative interviews with suspects to detect chronic cough, weight loss, night sweats and hemoptysis and other symptoms of TB. Outreach workers of Tomsk-Anti-AIDS Foundation provided field counseling, TB and HIV education, phlebotomy, PPD with further referral to TB Services for medical evaluation. Nutritional support, hygiene packages and accompaniment used as incentives to complete screening.

**Results:** Out of 1385 people at risk screened for TB, 55 suspects were sent for medical examination to TB Services (4%). Out of them, 11 were diagnosed with active TB (20.0%), including 4 MDR-TB cases.

**Conclusion:** Screening and medical assessment of TB suspects from vulnerable population resulted in high incidence of active disease (794/100 000) in comparison with 78/100 000 in general population. There is a need to continue and expand coverage of preventive screening for the rest of risk group in Tomsk Oblast.

#### PC-885-17 Use of medication monitors to improve tuberculosis treatment adherence in China

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**Background:** We develop a medication monitor for use in a cluster randomized trial to determine whether its use can improve TB treatment adherence in China.

**Methods:** The medication monitor has 3 features which include storage function, reminding function and recording function. With the reminding function, medication monitor could be used to remind patients to take medication, return for refill and sputum smear examination, which is the key feature to improve TB treatment adherence. Patients were given the medication monitor at the start of treatment for new TB cases and were instructed to return every month for medication refill during which time data were downloaded into the computer.

**Results:** As of 23 March 2012, 2362 patients were given the medication monitor and there had been

10940 monthly follow-up visits. At enrolment only 2.7% of enrolled patients required help from family members with using the medication monitor. During follow-up, some problems with the medication monitor were reported in 859 (7.9%) visits, with battery or hardware problems most commonly reported (44% and 35%, respectively). Only 31 patients (1.3%) discontinued the use of the medication monitor.

**Conclusion:** The medication monitor is well accepted by patients as a means to monitor treatment adherence but quality of the medication monitor should be further improved.

#### PC-886-17 Tuberculosis among intravenous drug users in Georgia: The Global Fund Project

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**Background and challenges to implementation:** IDU is a widespread problem in Georgia and regardless of HIV status drug users are at an increased risk of developing active TB. It is necessary to conduct the screening and effectively address the TB cases among IDUs.

**Intervention or response:** From April 2008 to March 2011 IDUs were screened for TB symptoms using the special questionnaire at harm reduction and VCT sites to assess the prevalence of TB among IDUs through the screening program. TB suspect cases were referred to TB units for further investigation and diagnosis.

**Results and lessons learnt:** 6053 IDUs were screened for TB symptoms, 79 (1.3%) of them were female and 5974 (98.7%) male. Majority (53.6%) belonged to 30–39 age group. 103 (1.7%) from the screened IDUs were HIV-positive and 4031 (66.7%) were diagnosed to have hepatitis B or C. 538 (8.8%) were classified as TB suspects. 498 (92.6%) suspected TB cases were presented at TB units for further examination. TB was diagnosed in 285 (57.2%) cases. 189 (66.3%) had pulmonary TB and 96 (33.7%) had extra-pulmonary. The prevalence of TB among IDUs is 5030/100 000.

**Conclusions and key recommendations:** IDU and TB represent a public health problem in Georgia. Active case finding is one of the useful tools for addressing TB problem among this group.

### PC-887-17 Strengthening treatment adherence among tuberculosis patients after release from prison in the Republic of Azerbaijan

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**Aim:** To ensure the local NGO effective involvement in TB patients treatment follow up and strengthening their treatment adherence.

**Method:** Project has been implemented by 'Support to Health' (SH) NGO with the financial support of GF round 9 since March 2011 which covers both; drug sensitive (DS-TB) and drug resistant (DR-TB) TB cases. Patients were provided with adequate treatment and social support until treatment was completed.

**Result:** By end of 2011, 114 TB patients (70 DS-TB and 44 DR-TB) were discharged from prison and continued treatment in the civilian sector. Two of DS-TB patients re-imprisoned and continued treatment in prison; 51 of them finalised treatment with outcomes: 46 (90%) cured, 1 (2%) defaulted, 3 (6%) treatment failure and 1 (2%) died. Four of DR-TB re-imprisoned and continued treatment in prison; 17 of them finalised treatment with outcomes: 14 (82%) cured, 2 (12%) failure and 1 (6%) died. Moreover, 38 (87%) had MDR-TB, 1 (2%) XDR-TB, 5 (11%) PDR-TB. Co-infection and drug addiction rates were very high; 36 (82%) had hepatitis C, 6 (14%) HIV and drug addiction was in 57% of cases.

**Conclusion:** These patients' treatment adherence varied from original TB patients in civil sector, however, this problem has been successfully tackling through involvement of local NGO. Thus, the NGO managed to follow up 98% of released patients, while it was only 10% of treatment continuation in previous years. As a result of patient support program carried out by SH NGO with the support of Main Medical Department of Ministry of Justice and NTP, default rate is significantly reduced.

### PC-888-17 Role of tertiary level hospitals in detection of smear-negative, extra-pulmonary and child tuberculosis

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**Background and challenges to implementation:** Tuberculosis is a major public health problem in Bangladesh. BRAC an NGO has been collaborating with National Tuberculosis Control Program since 1994 for scale-up of community based DOTS in two-thirds

of the country. The program is integrated with general health services at different care levels to demonstrate sustainable results for TB control. The objective is to establish linkage with the health professionals at tertiary level hospitals to increase the detection of all types of tuberculosis cases through utilizing various diagnostic tools.

**Intervention or response:** BRAC in collaboration with NTP established DOTS corner at 24 tertiary level hospitals to enhance DOTS services. Specialized health personnel and different diagnostic tools are available in these facilities. Presumptive TB patients attending both in-door and out-door are referred for diagnosis utilizing appropriate tools. After diagnosis, patients residing closely to the hospital are registered and given DOT from the hospital. Medicines are also given to the admitted TB patients without registration. Patients who are not registered and discharged from hospitals, referred to the peripheral DOTS centers according to patients' convenience for treatment continuation. Proper counseling during referral is done so that patients can report at referral centre without any delay.

**Results and lessons learnt:** Of the 90 372 patients diagnosed in BRAC supported areas in 2011, 2904 smear positive (4% of total smear positive cases), 3159 smear negative (30% of total smear negative cases), 6286 extra pulmonary (48% of total extra pulmonary cases) and 953 child TB (40% of total child TB cases) cases were diagnosed from 24 tertiary hospitals.

**Conclusions and key recommendations:** Engaging hospitals and systematic involvement of health professionals in NTP will increase detection of all types of TB.

### PC-889-17 Challenges encountered in tuberculosis diagnosis and treatment of apparently healthy prospective migrants

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**Background:** Prospective migrants for several countries are requested to have a health assessment. People found to have abnormal chest X-rays are required to undergo further TB laboratory investigations. Most prospective migrants are apparently healthy people who find it hard to accept that they have TB. It is a challenge to convince such people to start and complete the WHO recommended Direct Observed Therapy (DOT) treatment for tuberculosis.

**Intervention:** All persons diagnosed to have tuberculosis who attended the IOM Health Assessment Centre between 2006 and 2011 were contacted by telephone. A structured questionnaire was used to identify the attitudes to the diagnosis of tuberculosis and the

number of patients who started and completed TB treatment. This information was used to justify the need for IOM Dhaka health assessment center to offer DOT services.

**Result:** 60% of the migrants found to have TB reported that they received treatment from a national tuberculosis control DOT facility. 22.5% of the migrants did not take treatment. 12.5% of the migrants discontinued treatment because they had some side effects and were not convinced of the diagnosis of TB. 5% of the cases were detected to be TB negative by the national TB control programmes and thus did not receive treatment for tuberculosis.

**Discussion and conclusion:** Unwillingness to TB treatment can be attributed to a lack of acceptance that an apparently health individual can have tuberculosis. IOM Dhaka Health assessment clinic now offer DOT to ensure that all of their patients have access to treatment.

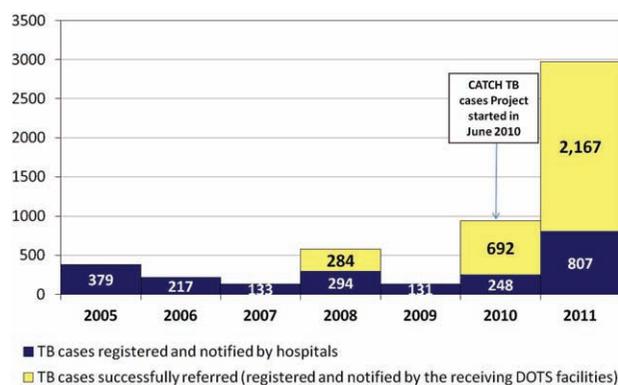
#### PC-890-17 A systems breakthrough: partnering with public hospitals for DOTS provision in the Philippines

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**Background:** To boost TB casefinding, the Philippine Department of Health (DOH) will engage 90% public and 60% private hospitals by 2016. In June 2010, the CATCH TB cases project of the NTP, supported by WHO-CIDA, pilot-tested an innovation in 14 big public hospitals in Metro Manila, which enhances TB two-way referral system within and outside the hospitals. Five of these hospitals have been existing as DOTS providing for five years or more, but case-finding did not focus on getting TB cases within the hospital. Four of the five hospitals were PPMD units. Of these, three have a two-way referral system to peripheral DOTS facilities, but this was not systematically done. This study evaluates the impact of the innovation in the five hospitals.

**Methods:** A descriptive study was done in February 2012. We reviewed the cases notified by the hospitals from 2005 to 2009, and compare it to year 2010 and 2011. Hospitals' contribution to NTP (the sum of cases notified by hospitals and the referrals to peripheral DOTS facilities with successful outcomes) was determined. Key informant interview was also done.

**Results:** From 2005 to 2009, the annual contribution of these hospitals ranged from 131 to 578 (median 217). In 2010 and 2011, this increased to 940 and 2974 cases respectively. Comparing the year 2011 contribution against 2008 at 578 cases, which was the highest prior to the project, a five-fold rise was noted (Figure). Hospital TB teams and management



**Figure** Trend of five DOTS-providing hospitals' contribution to NTP, 2005–2011, Metro Manila, Philippines.

appreciated the system and its outcome. An effective and comprehensive partnership between hospital TB teams and other hospital departments was developed, and linkage with peripheral DOTS facilities was enhanced.

**Conclusion and recommendations:** The innovation introduced in the five hospitals accounted for the substantial increase in their contribution to NTP. Recognizing this impact, NTP will scale-up the strategy by prioritizing the remaining TB-DOTS providing hospitals, including those installed under the PPMD initiative.

#### PC-891-17 Engaging large hospitals helps make substantial gain in tuberculosis case detection: lessons from Metro Manila, Philippines

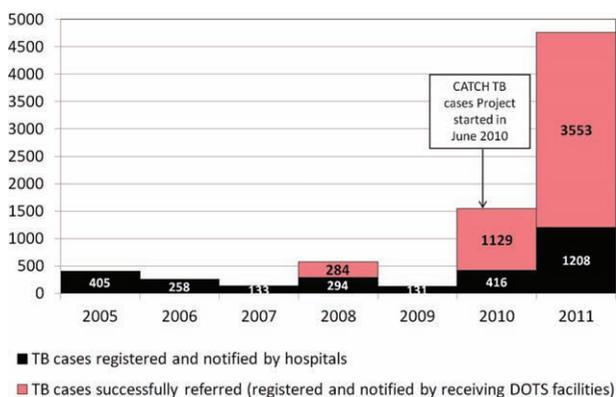
R Vianzon,<sup>1</sup> M Mantala,<sup>2</sup> M L Averilla,<sup>2</sup> A L Carillo,<sup>2</sup> A Medina,<sup>3</sup> W J Lew,<sup>2</sup> M Uplekar.<sup>4</sup> <sup>1</sup>Department of Health, National Center for Disease Prevention and Control, Manila, <sup>2</sup>Stop TB, World Health Organization, Manila, <sup>3</sup>Department of Health, Center for Health Development, Manila, Philippines; <sup>4</sup>Stop TB, World Health Organization, Geneva, Switzerland. e-mail: lhorsun@yahoo.com

**Background and challenges to implementation:** The Department of Health (DOH) estimated that 112 000 TB cases were undetected in the Philippines in 2009. A 2007 national survey found that 42% of TB suspects consulted hospitals where most are not adopting DOTS despite a national policy. CATCH TB project, supported by WHO-CIDA started in 2010 to help the NTP address this issue. The initiative is to ensure that TB cases seen by hospitals are managed and notified following NTP protocol.

**Intervention or response:** DOH engaged 14 public hospitals in Metro Manila in June 2010 with beds ranging from 150 to 4200. Eight are owned by DOH. Key activities were: advocated for stakeholders support; organized hospital TB teams; put in place logistics; established the internal and external TB two-way referral system and held regular meetings between hospitals and health centers. Results of the intervention

were monitored through an electronic information system and regular visits. Outcome of referrals were usually known through the returned referral slip, use of telephone and SMS, and review of manual and electronic TB registries.

**Results and lessons learnt:** From June 2010 to December 2011, TB clinics of the 14 hospitals detected 8921 TB cases from 12 085 referrals from wards and outpatient units. Of these, 1624 (18%) were registered and notified by hospital TB clinics, while 6861 (77%) were referred. Sixty-seven percent of these referrals were accepted and registered/notified by the peripheral DOTS facilities. This is a substantial increase from a baseline of 5% in 2008. The total no. of TB cases contributed to NTP (notified and successfully referred) by the hospitals rose from 578 in 2008 to 1545 and 4761 in 2010 and 2011, respectively (Figure).



**Figure** Trend of 14 hospitals' contribution to NTP, 2005–2011, CATCH TB cases project, Philippines.

**Conclusions and key recommendations:** Strengthening the referral system of hospitals led to the increased detection of TB cases. NTP intends to expand this strategy to the rest of the 1800 public and private hospitals.

### PC-892-17 Barriers to tuberculosis treatment access and adherence in Myanmar refugees in Malaysia

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It is estimated that Malaysia currently has approximately 171 000 refugees (USCRI 2009), but only 88 100 are registered with UNHCR. Of these, 93% (81 600) are from Myanmar. The prevalence of tuberculosis in Myanmar is estimated at 525 per 100 000 (WHO global report 2011). However, there is very limited information regarding tuberculosis (TB) in this vulnerable population of refugees, who have experienced conditions highly amenable to the spread

of tuberculosis during their flight and who face limited access to healthcare services, economic opportunities and education in the host country. Therefore, the aim of this study was to assess barriers to TB healthcare access and adherence to treatment among Myanmar refugees in Malaysia.

**Methods:** The study was conducted at Institut Perubatan Respiratori (IPR) TB clinic in Kuala Lumpur with the support of UNHCR Malaysia. A pilot-tested survey was administered to 50 refugee TB patients, with the help of treatment adherence counselors from the same community.

**Results:** The average age of the study population was 30.7 years and 78% were male. 70% were UNHCR documented. Most lived in households with multiple families and friends. The average household size was 9; one had 40. Adherence to treatment was quite high; 93% reported never having forgotten to take their treatment. 68% were unemployed and only 22% were employed full-time. 86% felt that they were more likely to lose their jobs because of their diagnosis of TB. It cost the patients an average of one-third of their monthly income to get medical treatment. 20% of respondents reported being robbed, attacked or sexually assaulted while traveling to receive TB treatment. Additionally, this study identified a large amount of social stigma associated with TB among the refugees.

**Conclusions:** Major barriers were language, misinformation, insecurity, and poor socio-economic conditions. Interventions such as health education and tuberculosis screening in this community are warranted.

### PC-893-17 Linking tuberculosis patients to welfare schemes increases treatment completion rates

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**Background and challenges to implementation:** One of the largest barriers to prevention and treatment of tuberculosis (TB) is defaulting on treatment. Treatment default contributes to higher transmission rates and drug resistance. Patients default on treatment primarily because of harsh drug side effects, because they feel healthy before they are cured, inconvenience of TB treatment, inability to work during TB treatment. The 2010 India TB report estimated that, on average, TB patients lose 3–4 months of work and 20–30% of annual household income.

**Intervention or response:** CARE India developed an innovative strategy for mitigating the financial burden TB and TB treatment causes. Through advocacy and partnership with local governments (Panchayat Raj Institutions) in West Bengal, CARE India facilitated the linkage of 6768 TB patients with various welfare

schemes provided by the government of India. Data was collected through TB registers in CARE districts of West Bengal. The risk of completing treatment for those who were linked to welfare schemes was compared to the risk of completing treatment for those who were not linked in two quarters of 2010.

**Results and lessons learnt:** Category II patients who were linked to welfare schemes were 28% more likely to complete treatment than those who were not linked to welfare schemes (RR = 1.28;  $P = 0.002$ ). There was no difference in treatment completion rates in Category I patients.

**Conclusions and key recommendations:** Linking TB patients to welfare schemes has the potential to reduce the treatment default rate by mitigating the financial burden TB treatment causes. Advocacy and linkage of TB patients to welfare schemes should be scaled up and evaluated across India and beyond.

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***Air partagé, air pur?***  
***Shared air, safe air?***  
***¿Aire compartido, aire puro?***



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