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ABSTRACT BOOK

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44th World Conference on Lung Health of the International Union Against Tuberculosis and Lung Disease (The Union)
Paris, France, 30 October–3 November 2013

PLENARY SESSIONS

FRIDAY, 1 NOVEMBER 2013

Are we winning the battle against HIV?

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It is difficult to argue that we are winning the battle against HIV when there are still 2.5 million new HIV infections and 1.7 million HIV related deaths annually. However, the case can be made that we have the knowledge to begin to end the HIV epidemic. This case is based on recent groundbreaking studies in HIV prevention that demonstrate adult male circumcision protects against HIV acquisition in men, that pre-exposure antiretroviral therapy prophylaxis (PREP) can reduce risk for HIV acquisition in both men and women and that antiretroviral therapy is extremely effective in reducing HIV transmission through sexual transmission and from mother to child.

Deploying interventions that reduce and even eliminate new HIV infections is a key component of ending the HIV epidemic. Expanding antiretroviral treatment, strategic use of PREP, and evidence-based measures tailored to specific populations such as clean needle exchange for injection drug users will all reduce new HIV infections. Mitigating HIV-related morbidity is a second goal that can be achieved by starting antiretroviral therapy earlier in the course of HIV disease and preserving immune function. Finally, we must reduce HIV-related deaths. This will require an HIV care cascade that identifies, treats and retains persons living with HIV into integrated, efficient and affordable health systems.

Winning the battle against HIV and winning the battle against tuberculosis are inextricably linked. How priority HIV interventions and health systems strengthening favorably impact and synergize with new and emerging TB control efforts will be the focus of this presentation. Needed scientific, political and community support and engagement to achieve aspirational goals for both diseases will also be discussed.

SATURDAY, 2 NOVEMBER 2013

Asthma: the neglected epidemic

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Asthma is a large and neglected worldwide problem. Those affected struggle to breathe, on occasions with little warning, need urgent medical attention, have hospital admissions, and there are occasional deaths. The direct costs of asthma are high; however, the indirect costs, which result in loss of productivity, are even higher, such as absenteeism from school (lost education) and work—for adult sufferers and parents of asthmatic children. Improved access to essential asthma medicines and effective health service delivery will reduce this burden.[1]

Asthma starts usually in young childhood, is the commonest chronic disease in children and an important non-communicable disease (NCD).[2] The International Study of Asthma and Allergies in Childhood (ISAAC http://isaac.auckland.ac.nz/) 1991–2012, by studying nearly 2 million children in 105 countries (80% of low- and middle-income countries [LMICs]) identified the global prevalence and severity of asthma in children, the changing patterns and potential risk and protective factors. In ISAAC centres, about 15% of children and adults in the world have asthma, with more severe symptoms in LMICs.

The high global burden of asthma necessitates continuation of the ISAAC work, by building on the ISAAC network and merging with work undertaken by The International Union Against Tuberculosis and Lung Disease. The Global Asthma Network (http://www.globalasthmanetwork.org/), established in 2012, will focus on LMICs to improve asthma care globally and improve access to quality-assured essential asthma medicines, currently unavailable to many asthmatics in LMICs. Targets include reducing by 50% by 2025 the severity of asthma, the proportion of symptomatic people not on inhaled corticosteroids, time off

work/school, unplanned urgent medical visits, hospital admissions, and asthma mortality. The Global Asthma Network will investigate the role of potential risk factors suggested by ISAAC including exposure to high intensity truck traffic and tobacco smoke, open fire cooking, damp homes, high fast food intake, low fresh fruit and vegetable intake, less breast feeding in non-affluent countries, and obesity. National asthma strategies and asthma guidelines will be promoted with enhancement of capacity in health service delivery for people with asthma.

1 The Global Asthma Report 2011, Paris, France: International Union Against Tuberculosis and Lung Disease, 2011.
2 Pearce N, Asher I, Billo N, et al. Asthma in the global NCD agenda: a neglected epidemic. Lancet Respiratory Medicine 2013; 1: 96–98.

Pneumonia in children: still a major challenge to child health globally

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Pneumonia remains the leading cause of mortality and a major cause of morbidity including hospitalisation in children under 5 years of age living in low- or middle-income countries. In the last decade, there have been several advances and new interventions against childhood pneumonia. These include more widespread implementation of protein-polysaccharide conjugate vaccines against *Haemophilus influenzae type b* and *Streptococcus pneumonia*, use of case management, and better prevention and treatment of HIV. In addition, general measures such as promotion of breast feeding, better nutrition, improvements in living conditions and reduction in exposure to indoor air pollutants may reduce pneumonia incidence and severity. As a result there has been a substantial reduction in pneumonia incidence and improved outcomes; however, pneumonia mortality in children is still currently estimated at approximately 1.3 million cases annually, with most deaths occurring in low-income countries. Most deaths are preventable using currently available tools; more widespread roll-out of pneumococcal conjugate vaccine globally, especially in the areas of highest pneumonia mortality remains a challenge.

Determining the aetiology of childhood pneumonia remains difficult in the absence of reliable diagnostic tests. Nevertheless data from vaccine-probe studies indicate that the predominant aetiological agent is *S. pneumoniae*, which is estimated to cause 18% of severe cases and 33% of deaths. Respiratory viruses also contribute considerably to the burden of childhood pneumonia. Severe pneumonia may reflect co-infection with multiple pathogens. With improved vaccine uptake, the importance of vaccine-targeted pathogens is anticipated to diminish, while a greater proportion of cases may occur due to *Staphylococcus aureus, Klebsiella pneumoniae* and *Mycobacterium tuberculosis* in TB-endemic areas.

Appropriate antibiotics and supportive care including oxygen remain the key elements of effective treatment. Use of the pneumonia case management strategy included in the WHO-IMCI program may reduce childhood mortality by approximately 20%, with even higher reductions in pneumonia-specific mortality. Community-based case management of childhood pneumonia is effective, reducing pneumonia mortality by up to 70%. Oral rather than intravenous antibiotics have been reported to be effective for treatment of severe pneumonia; community-based use of these may be a feasible and effective strategy for reducing mortality. However, widespread implementation of such effective preventative and management strategies for pneumonia still remains challenging in low- and middle-income countries.

SYMPOSIA: FRIDAY
1 NOVEMBER 2013

CRITICAL ISSUES AND CHALLENGES FOR MAXIMISING THE IMPACT OF XPERT® MTB/RIF

Strategic approach for Xpert® MTB/RIF implementation: results from Nigeria

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Introduction: With the adoption of Gene Xpert® MTB/RIF by WHO, countries need to pay careful consideration to existing laboratory network, infrastructure, human resource, capacity for MDR-TB enrollment and care, development of guidelines; establishment of Gene Xpert advisory team (C-GAT) and; effective coordination between TB and HIV for better impact on early access to treatment.

Methodology: Consisted of a desk review of Gene Xpert implementation plan, reports of activities of C-GAT; and quarterly statics and supervisory reports.

Results: Of 34 functional Gene Xpert machines in 24 states with support from different partners, 26 (76%) are within TB-HIV comprehensive sites. About 19 (56%) machines are located in secondary health facilities, while 14 (41%) are at the tertiary and only 1 (3%) in private health facility. Data from the 15 Gene Xpert sites supported by TB CARE I revealed that a total of 7267 sputa were tested from Q4, 2011–Q2, 2013; 52% (3779) of those tested men and only 15% (1086) of the clients were PLHIV TB suspects. Furthermore, *Mycobacterium tuberculosis* positivity rate was 31% (2246); proportion of Rif resistance among all tested was 7.6% (557) and 24.8% among *M. tuberculosis* positive cases. Higher proportions (63.7%) of RIF resistance were male. The *M. tuberculosis* positivity rate among PLHIV TB suspects was 17% (189) and RMP resistance of 1% (9).

Conclusion: In spite of the low utilization of the machines especially for PLHIV; poor maintenance system for the machines; and the inadequate capacity for good quantification, there is a need for a systematic approach and effective collaboration with HIV/AIDS program in the implementation and roll out of GeneXpert to ensure access to the diagnosis and early treatment.

Financing the introduction of new tuberculosis diagnostics and treatment: reflections from Rwanda and Uganda

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Background: Successful uptake of TB interventions will require viable financing strategies and mechanisms. The approach was developed to assess financing of new TB diagnosis and treatment interventions, and identify financing gaps and barriers to maintaining existing TB interventions and introducing new one.

Methods: We carried out case studies in Rwanda and Uganda from July to September 2012 to develop the assessment approach. A desk review of the National TB Program (NTP), MOH documents and budgets, and consultations with key stakeholders involved in TB control on decision-making and planning processes, resources requirements for diagnosis and treatment, introduction plans of new TB interventions, and challenges to TB financing were conducted.

Results: The Uganda national tuberculosis and leprosy program planned to roll out MDR-TB treatment and GeneXpert machines to reach 100 machines by financial year 2014. The incremental cost of implementing GeneXpert diagnostics is about US$29.65 per test and installing each GeneXpert machine is approximately US$45 400. The Rwanda national tuberculosis program planned to roll out the GeneXpert in 2 phases and reach 16 machines in the country by financial year 2014. The National technical working group develops criteria of placement of the machines and a budget for 2012–2017 was developed and submits for funding through the TB National strategic plan. The cost of implementing and installing each GeneXpert GX4 machine is approximately US$48 070.

Conclusion: Determining and ensuring adequate financing for TB diagnostics and treatment interventions 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. In both countries, GF represented a significant source of funding for their TB programs. Estimating financing requirements and financing gaps is not part of routine.
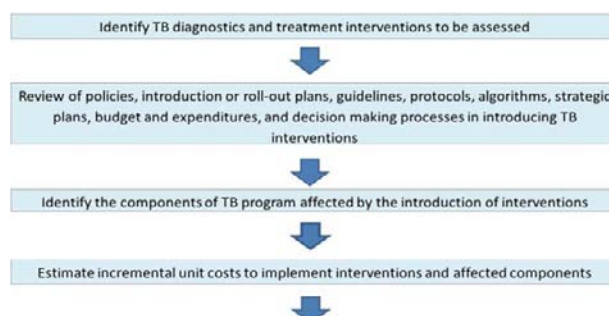
Global evidence, tools and revised WHO guidance for Xpert® MTB/RIF

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Background: WHO first recommended the Xpert® MTB/RIF assay in December 2010, with subsequent policy guidance and an accompanying Rapid Implementation document describing technical and operational 'How-to' issued in May 2011. WHO policy documents on TB diagnostics are reviewed every 3–5 years, and updated based on new evidence available.

Methods: Systematic reviews were commissioned by WHO in early 2013 to collect and analyze the most up-to-date body of evidence on the diagnostic accuracy of Xpert MTB/RIF for the detection of pulmonary TB and associated rifampicin resistance, for the detection of extrapulmonary TB (stratified by biological specimen type), for the detection of TB and associated rifampicin resistance in children; and on the affordability, cost-effectiveness and resource implications of diagnostic and screening algorithms for scaling-up use of Xpert MTB/RIF. An Expert Group meeting was convened by WHO in May 2013 to synthesize and evaluate the evidence using the GRADE process. Draft recommendations were developed by the Expert Group and approved by the WHO Strategic and Technical Advisory Group for TB.

Results: Refined WHO policy guidance and an associated manual describing practical and operational considerations will be issued in Q3 2013. In 2013 WHO has also issued a revised edition of its Definitions and Reporting Framework, prompted largely by the introduction of Xpert MTB/RIF. A WHO TB laboratory biosafety manual has also been published in several languages and features a risk-based approach that guides the essential biosafety measures required for performing different technical procedures, including Xpert MTB/RIF. A training package on Xpert MTB/RIF is under development by GLI partners, combining and updating existing materials developed by FIND, KNCV and Cepheid.

Conclusions: WHO policy guidance and associated tools based on the most up-to-date evidence provide a solid foundation for countries to effectively adopt and implement Xpert MTB/RIF.

PREVENTING HIV-RELATED TUBERCULOSIS AT THE COMMUNITY LEVEL: A SYNTHESIS OF THE CREATE STUDIES

Preventing tuberculosis in high HIV prevalence areas: outcomes of the Thibela tuberculosis and THRio studies

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Background: TB case notifications in South African gold mines are extremely high (>4%/year), due to a high prevalence of HIV (~30% in 2000) and silicosis. The 'Thibela TB' study evaluated the impact of community-wide IPT at a population and individual level.

Methods: Cluster randomised trial with clusters (8 intervention, 7 control) comprising all mine workers at a mine shaft and associated hostels. The intervention included community mobilization, TB screening (symptoms and chest radiograph), and 9 months of IPT after excluding active TB. The primary outcome was TB incidence at cluster level over a 12 month period, starting 9 months after enrolment ended, or equivalent for control clusters.

Results: Among 78 744 miners (37 763 intervention, 40 981 control clusters), 95.9% were male, median age 41 years. In the intervention arm, 27 126 (66.2%) miners participated, and 23 659 (87.0%) started IPT. Community-wide IPT did not reduce TB incidence in the intervention arm (intervention 3.02/100 py vs. control 2.95/100 py, adjusted incidence rate ratio [IRR] 0.96 [95%CI 0.76–1.21]. At the individual level, among 10 909 miners IPT reduced TB incidence during the 9 month intended treatment period by 58%, (2.91 vs. 1.10/100 py for control and isoniazid cohorts, respectively, aIRR 0.42 [95%CI 0.20–0.88]), but protection was subsequently lost rapidly.

Conclusion: Community-wide IPT did not reduce TB incidence at a population level, despite substantially reducing TB incidence while taking IPT. Improving TB control in this setting will require more potent and durable interventions to reduce TB transmission, and also interventions to address susceptibility.

The CREATE legacy: taking study results to the next level

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The convergence of HIV and tuberculosis has led to unprecedented rises in tuberculosis rates in many countries and presents one of the major challenges to tuberculosis control. CREATE is a consortium

of academics; policy-makers at local, national, and international levels; health services and communities that have worked over the past decade to develop, implement and assess new approaches to address these challenges. The results of CREATE's three major community-randomised trials have contributed to changes in policies both locally and internationally. The capacity built for large scale intervention research, with strong community engagement and enhanced laboratory, epidemiological and social science teams in several sites is now being used for further studies of HIV and tuberculosis prevention, diagnosis and care.

TUBERCULOSIS REINFECTION: IMPACT ON TUBERCULOSIS CONTROL

The prevalence and impact of tuberculosis reinfection in China

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Whether the development of post-primary active tuberculosis (TB) represents an episode of endogenous reactivation or exogenous reinfection has been debated for decades. Until the 1990s, by using of genotyping techniques, it has been possible to demonstrate that exogenous reinfection can occur. However, the prevalence of exogenous reinfection, and its role in maintaining the circulation of tuberculosis in community and its contribution to the tuberculosis incidence, have not been fully understood yet, especially in tuberculosis high-burden settings—where the majority of cases are found today. Based on a study of molecular epidemiology of tuberculosis in five different provinces in China, we have demonstrated several findings to possible data on the extent which tuberculosis is attributable to reinfection. Firstly, it is

generally assumed that the proportion of clustered isolates in a population reflects the amount of recent transmission of *M. tuberculosis*. The proportion was found to be 30% overall. The frequency of cluster isolates among patients with treatment history was also determined to be 32%, at least indicating the occurrence of exogenous reinfection. Secondly, among recurrent tuberculosis patients with paired isolates available, comparing the DNA genotypes of bacilli isolated during the initial episode with those of bacilli isolated during the subsequential episode revealed that nearly half (49%) of them had unmatched DNA genotypes and were categorized as reinfection. Thirdly, tuberculosis patients simultaneously infected with multiple strains of *M. tuberculosis* provide further evidence of the occurrence of exogenous reinfection. The prevalence of multiple infections was found to be 5%–11% in these settings in China. In all, these findings emphasized that the reinfection is widespread in China and its impact on TB control is a concern.

Implications of tuberculosis reinfection on LTBI treatment

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One third of the world's population is infected with tuberculosis (TB). People with HIV have a greatly increased risk of TB disease, which can be reduced by treatment of latent TB infection (LTBI). Isoniazid preventive therapy (IPT) in the pre-HIV era was shown to durably reduce the risk of TB in settings with declining or low TB transmission. A recent meta-analysis showed that 6 months of IPT reduced the risk of TB in HIV-infected, TB infected adults by 64%. In high TB transmission settings in the pre ART era the durability of IPT was less than 2 years. In the ART era, the durability of 6 months of IPT was shown to be about 6 months in Botswana. In high TB transmission settings (Botswana and South Africa), continuous IPT reduced the risk of TB while taking it, but TB rates increased soon after stopping IPT. Among South African gold miners, IPT for 9 months reduced the risk of TB disease at an individual level by 58% while taking it, but the protective effect was subsequently lost rapidly, and community-wide IPT did not improve TB control. TB after IPT may be due to reactivation of inadequately treated LTBI or reinfection. In high transmission settings the annual risk of infection ranges from 4–20% and reinfection may limit the durability of IPT. Mathematical modelling suggests that continuous IPT combined with scaling up antiretroviral therapy, case finding with a more sensitive tool (e.g., GeneXpert) and doing the basics better, may substantially improve TB control.

The implications of tuberculosis reinfection on modeling the epidemic

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Molecular studies have confirmed that humans can be repeatedly infected with *M. tuberculosis*. In this talk, we will use insights from mathematical and simulation models to highlight the ways in which reinfection may influence the behavior of TB epidemics. Reinfection acts to reduce competition between strains of *M. tuberculosis*; models with reinfection thus support greater long-term diversity than models without reinfection. Reinfection resulting in mixed infection can also affect treatment outcomes and modify the expected impact of interventions, particularly when individuals may harbor both drug-resistant and -susceptible strains. We will suggest important open questions that must be addressed to improve our understanding of how reinfection influences the trajectory of epidemics and the effectiveness of control measures.

IMPROVED TUBERCULOSIS DIAGNOSTICS ADDING NEW DYNAMICS TO TUBERCULOSIS CONTROL

Technology transfer and implementation of new diagnostics within UNITAID-funded EXPAND-TB project

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Background: EXPAND-TB, a UNITAID-supported six-year project implemented as a collaboration with WHO and FIND, focuses on accelerating access to rapid WHO-endorsed diagnostic technologies for patients at risk of MDR-TB in 27 countries around the globe. We describe the project outcomes and a transitioning model that will allow the project to be effectively phased-out while maintaining laboratories operations beyond 2014.

Methods: Throughout the project we have assured political commitment and policy review; upgraded laboratory facilities; delivered commodities for liquid culture and drug susceptibility testing (DST), line probe assay (LPA), and rapid speciation; and initiated a capacity building and mentoring program for laboratory staff in collaboration with partners. At present we are developing a transitioning strategy to ensure that this level of operations is maintained beyond the project, including a set of tools that will

allow governments and local/international partners to provide the needed support.

Results: By the Q1-2013, 44325 MDR-TB cases were detected in 65 laboratories in 25/27 countries (38% of the global target). Technologies have been integrated into the national diagnostic algorithms but continued support is required to ensure their rational use. Costly infrastructure and biosafety upgrades, inadequate and turnover of staff, complex importation regulations and poor sample transportation systems are amongst the major limitations to improved laboratory diagnosis of MDR-TB.

Conclusion: The EXPAND-TB project has successfully supported TB laboratory work in 27 countries, contributing to narrowing the diagnosis gap for MDR-TB cases. Obstacles faced at the project start up directly relate to the challenges of technology transfer, complex nature of diagnostic technologies and set up of laboratories. We currently focus on continuous improvement while developing a transitioning strategy to ensure long-term sustainability of the achievements made.

Uptake of new tuberculosis diagnostics and diagnostic algorithms in the Republic of Moldova

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Background: Moldova has one of the highest burdens of TB drug resistance TB in the world. Multidrug-resistant TB (MDR-TB) was found in 23.7% of new and 62.8% of previously treated culture-positive cases in 2012; 98.6% of rifampicin-resistant cases were MDR. Xpert® MTB/RIF technology was introduced in March 2012, with the support of TB-REACH grant.

Settings: Twenty-five Xpert instruments were placed at district level TB units (56% population coverage), reference laboratories, penitentiary facilities and AIDS centers. Xpert is used as primary diagnostic test for TB, parallel to smear microscopy. Xpert tests are performed in TB suspects during their first visit to a TB facility; no sputum transportation is used.

Objective: To assess the effectiveness of Xpert MTB/RIF use at peripheral TB service delivery level.

Results: A total of 13433 Xpert tests were performed between April 2012–March 2013. The time for a patient to receive results is 0–1 days. Failed tests amounted to 5.6% of total tests. A total of 2293 tests were positive for MTB with the overall positivity rate 18.1% of all valid tests. Among all Xpert MTB-positive cases, 56.0% were smear positive by microscopy and 44.0%—smear negative. Resistance to rifampicin was found in 796 cases (34.7% of all MTB-positive cases, new and retreatment).

Among 2199 MTB-positive cases with HIV test results, 277 (12.6%) were HIV-positive.

Conclusions: Xpert MTB/RIF is effective as an initial diagnostic test in the high MDR-TB setting, reducing time to diagnosis and allowing for early detection of drug resistance. Xpert renders a very high (over 40%) yield in bacteriological confirmation compared to smear microscopy. The level of rifampicin resistance is very high, similar to that identified by routine drug susceptibility testing. The test proved sensitive in HIV-infected individuals. Further efforts are required to integrate Xpert in routine diagnostic and treatment pathways countrywide.

Role of new rapid tuberculosis diagnostic tools in strengthening TB-HIV interventions in Swaziland

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Background: Swaziland has an overall HIV prevalence of 19%, which increases to 26% among the age group 15–49 years, and a TB incidence of 1320 cases per 100 000 population and an HIV co-infection rate among TB patients of 80%. The proportion with multi-drug resistant TB among new cases of TB and previously treated cases is 7.7% and 33.8%, respectively. In 2012 the Swaziland Health Laboratory Service introduced Gene-Xpert machines in various facilities in the country, aimed at enhancing sensitivity of TB detection in smear negative, culture positive patients, early recognition of Drug Resistant-TB cases, and finding an additional pool of drug sensitive and resistant TB cases.

Method: Mapping of priority health facilities for Xpert implementation was conducted in 2012 and a laboratory algorithm that incorporates new rapid diagnostics into the Swaziland Health Laboratory service was agreed upon by stakeholders. Retrospective data abstraction was done for two quarters between January 2012 (before Xpert rollout) and January to June 2013 to measure diagnostic yield and impact of Xpert treatment enrolment.

Results: In Swaziland, Xpert increased diagnostic yield by about 13%. The proportion of bacteriological confirmed cases enrolled into treatment tested for TB was 59% (511/873) for January–March 2012 and 43% (520/876) for April to June 2012, while for the same period in 2013, it was 70% (622/900) and 73% (749/1035) respectively. Gene-Xpert was able to detect TB in one out of 8 tests done 18% (409/2250) in January to March 2013 and 12.9% (153/1182) in April to June 2013 of tests done were MTB+.

Conclusion: The introduction of GeneXpert machines

has increased diagnostic yield for MTB+ and case detection in Swaziland TB case detection and DR-TB diagnosis and treatment enrolment. Hence contributing significantly to improved TB case finding and treatment enrolment.

HOW CAN TOBACCO CONTROL STRATEGIES IMPROVE HIV AND TUBERCULOSIS PATIENT OUTCOMES?

Smoking and mortality among HIV-infected individuals: findings from a nationwide population-base

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Objective: To assess mortality attributable to smoking among HIV patients.

Methods: We estimated mortality rates (MR), mortality rate ratios (MRR), life expectancies, life years lost and population attributable risk of death associated with smoking and with HIV among current and non-smoking individuals from a population-based, nationwide HIV cohort and a cohort of age- and gender matched HIV negative individuals.

Results: 2921 HIV patients and 10 642 population controls were followed 14 281 and 45 122 person-years, respectively. All-cause mortality and risk of non-AIDS-related death was substantially increased among current compared to non-smoking HIV patients MRR 4.4 (95%CI 3.0–6.7) and 5.3 (95%CI 3.2–8.8), respectively. Excess MR/1000 person-years among current versus non-smokers was 17.6 (95%CI 13.3–21.9) for HIV patients and 4.8 (95%CI 3.2–6.4) for controls. A 35-year-old HIV patient had a
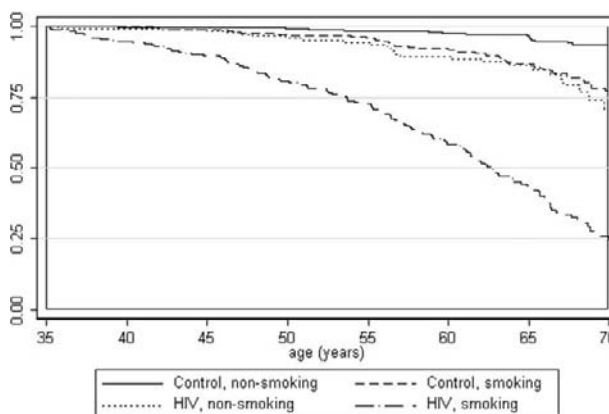
median life expectancy of 62.6 years (95%CI 59.9–64.6) for current and 78.4 years (95%CI 70.8–84.0) for non-smokers; the numbers of life years lost in association with smoking and HIV were 12.3 (95%CI 8.1–16.4) and 5.1 (95%CI 1.6–8.5), respectively. The population attributable risk of death associated with smoking was 61.5% among HIV patients and 34.2% among population controls.

Conclusion: In a setting where HIV care is well organized and antiretroviral therapy is available free of charge, HIV infected smokers with long-term engagement in care lose more life years to smoking than to HIV. The excess mortality of smokers is tripled and the population attributable risk of death associated with smoking is doubled among HIV patients in Denmark compared to the background population.

Tobacco control strategies with HIV and tuberculosis patients in Africa: impact, opportunities and challenges

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Sub-Saharan Africa remains one of the regions of the world most affected by HIV and tuberculosis. With nearly one in 20 adults (4.9%) living with HIV, representing 69% of people living with HIV worldwide and more than 260 cases per 100 000 inhabitants in 2011 for tuberculosis. For both diseases, smoking remains a major risk factor. However one of the major challenges of tobacco control in Africa is weak resources and limited involvement of health professionals for its development. Meeting the challenge of tobacco control opens a major opportunity to improve TB prevention and treatment/outcomes of tuberculosis and HIV. Indeed, in many African countries, TB and HIV have a well organized structure and major reach into communities which can enable good reach of tobacco prevention strategies. These structures have the advantage of the resources both in the form of government grants or from international partners such as the Global Fund. This is a good opportunity to exploit these resources for the benefit also of tobacco control, which is less well-funded, but has a major influence on millions of TB-HIV patients and their families. Despite the convergence between HIV and TB with smoking and the important number of people in African countries with TB-HIV, there is a lack of integration of tobacco control in national strategies and plans against TB and HIV in many of these countries. One of the major challenges is the lack of communication and collaboration between stakeholders and programs. For this reason, it is important to involve stakeholders in national tobacco control in the development process elaboration or review of national strategic plans to fight against TB and HIV for inclusion of tobacco control in these plans. Budget must be allocated for tobacco control.

Sessions on cessation of tobacco use, education about the dangers, monitoring levels of smoking among patients, creating non-smoking spaces in hospitals, clinics and homes of patients are all examples that can be integrated into strategies against tuberculosis and HIV.

How is tobacco control in Bangladesh doing to benefit people with tuberculosis and HIV?

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Background: In Bangladesh, production and consumption of tobacco are high. Here, 43% of adults use some form of tobacco and 23% are tobacco smokers. 75.7% non-smokers are exposed to second-hand smoke at workplaces. Tobacco smoking is an important risk factor for developing TB. In May 2011, BRAC started smoking cessation initiative among TB patients. The aim of the intervention is to improve the treatment outcome of TB patients by reducing tobacco consumption.

Intervention: BRAC supported 17 Dhaka peri-urban TB centers were selected for the pilot intervention. TB programme staff were 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 guideline "Smoking cessation and smoke-free environments for tuberculosis patients" by The Union. The tools and contents of the guideline were translated in Bengali. Counseling is given to patients for smoking cessation during the initiation of treatment and subsequent visits to TB centre. A brief counseling is done by Shasthya Shebika (Frontline Community Health Worker) during DOT.

Results: All the 17 centers were declared as smoke-free and 'No smoking' signage is placed at the entrance of these centers. From May 2011 to April 2013, a total of 6782 TB patients were enrolled at these centers. Of them, 1471 (22%) were smokers and 2139 (32%) patients were identified who were exposed inside the home. Of the patients who initiated TB treatment between April 2011 to March 2012, 75% (419) quit smoking at the end of treatment; the cure rate increased to 94% in 2011 which was 89% in 2010. The default rate is also 1% reduced in the same period which was 3% before intervention.

Conclusion: Smoking cessation intervention among TB patients found to be effective through counseling. It helps improving TB patient's lung condition as well as treatment outcome. The intervention is recommended to expand other areas.

CLIMATIC CHANGE AND ENVIRONMENTAL AIR POLLUTION: OUR RIGHTFUL CONCERN

Cook stoves and use of solid fuels: a policy maker's perspective

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Setting: More than 2 billion people still use traditional stoves with biomass as fuel for cooking. This causes a range of adverse health effects because of indoor air pollution (IAP)—women and small children being the worst affected. IAP is an important risk factor for many diseases of the lung including asthma and TB, which disproportionately affect the poor. Women spend a lot of time in collecting firewood and cooking.
Objective: Complete coverage of all rural households with improved efficient cook-stoves must become a sustainable development goal for 2030.
Design: Such stoves with 5 year lifespan may cost between US$30–50. Poorest cannot afford. Would require some subsidies. CER prices between Euro 7–8 could have easily funded millions of stoves but carbon market has crashed. Financing options require creation of a premium voluntary carbon market and a niche fund from the proposed International Climate Fund. Nations must create eco-system—standardised manufacturing of components; regional testing and technical support centres; designing stoves as per consumer preferences through pilot projects and conducting large scale awareness drives.
Result: Improved cook-stoves will greatly reduce IAP and improve quality of life of the poor and poorest rural women and households.

Emerging future threats to chronic respiratory diseases due to climatic change and urbanisation factors

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Climatic change strikes population health directly and indirectly. Its outcome is extreme and leads to massive population movements and social interlinked changes. Human cost of climatic change is enormous; it is beyond the economical consequence, the offputting impact on the eco-system and infrastructure, it threatens human population health and depletes the people as a capital and a major development pillar. Health related effects/chronic respiratory diseases (CRDs) of climatic change and urbanization should be well tackled as a justice issue. Developing world has little hand on this change yet it is the foremost sufferer, being pushed more into poverty, and disease —poverty vicious cycle, making them more prone and vulnerable. Enacting science and evidence in a

multidisciplinary partnership, is our path and template so as to perform a global insurance regulations with more focus on poor world. We should all be incharge advocating theme of 'Climatic Change is a fundamental Threat to Human Capital'. Assisting countries in a manner that bridges science with health services; strengthening the health system and health players as main front line players in adapting to, and reducing health impacts and vulnerability to climatic change and urbanization is crucial. Supporting the integration of health effects and climate change at national, regional and international level should be our mandate.

TUBERCULOSIS AND ENVIRONMENTAL MIGRANTS: PREPAREDNESS AND RESPONSE TO MIGRATION IN DISASTERS

Japan: Fukushima triple disaster responses to ensure tuberculosis care

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Background: East Japan was severely hit by earthquake and tsunami on 11 March 2011, with a death toll of more than 18 000. In addition it damaged nuclear power plants in Fukushima, resulting in high radioactive release, which led to temporary or permanent evacuation of local residents.
Objective: To evaluate tuberculosis (TB) programme of public health centre (PHC) at the time of combined disaster.
Method: Information on case finding and case holding were collected through the author's visit to Fukushima and conduct of cohort analysis of TB patients with public health nurses of PHC.
Results: Examples of case finding: A person became bedridden at his house in semi-evacuation area. Mobile medical team found him. But he died of TB 3 days later. Delay of diagnosis of a smear positive PTB in a shelter caused infection to several persons. Case holding: In two PHC areas affected by radioactive release, 41 TB patients were on treatment at the time of disaster. Two patients were taken away by tsunami. Conditions of all other patients were reported to the PHC by staff of other PHCs, medical facilities, or family members who took care of patients during temporary evacuation. All these patients resumed treatment by the end of March.
Conclusions: At the time of the disaster, health staff themselves also suffered and were busy with emergency services at shelters and radiation screening. Delay of TB diagnosis occurred in such circumstances. However communication network functioned well

between TB patients, medical facilities and PHCs which had been established through efforts of routine programme.

Indonesia: tsunami crisis response and tuberculosis control in Aceh

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Setting: The Tsunami disaster (December 2004) resulted in enormous human suffering and material destruction. Several key TB-Leprosy (TB-L) program staff died and critical resources including drug stocks, laboratory equipment, vehicles, computers, and surveillance registers washed away or were completely destroyed. This caused complete collapse of the TB-L control program in 11 of the 21 districts of Aceh province in Indonesia. Due to its long and strong relation with the national TB program, the Ministry of Health requested KNCV Tuberculosis Foundation and NLR to assist the National Program in rebuilding the combined TB-L program in Aceh as quickly as possible. Support aimed at re-establishing coordination capacity of the provincial and district CDC offices, restoring the diagnostic and treatment capacity for TB control, and rebuilding the surveillance functions at provincial and district CDC level.
Results: Due to the concerted efforts from local health services in close collaboration with KNCV, NLR (financial support from Dutch Emergency Funding, SHO and USAID), TB and Leprosy control services could be resumed to a level almost equal to the situation before the tsunami within a period of 6 months. Notification of new TB patients in the year following the disaster even increased compared to TB notification in 2004. Treatment success rate (TSR) of the 2004 patient cohort was similar to that of the previous year's cohort (82%). Although the treatment of 23% of patients who started in Q3 2004 was interrupted by the direct impact of the tsunami, TSR increased further during 2005 (to 89%).
Conclusion: Close collaboration with local health authorities and intensified external (technical and financial) assistance were crucial for a successful re-establishment of TB-L services in Aceh in a relatively short time frame after the tsunami. This support was critical to minimize the interruption of diagnostic and treatment services for TB and leprosy patients.

Kiribati: rising ocean, disappearing country

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Setting: The Pacific Ocean and potential of disappearing islands as a consequence of climate change.
Objective: To present what the potential migration responses might be to climate change in the Pacific and how this might be reflected in TB migration policy.

Design: A literature review on the effects of climate change and migratory responses as a consequence of this. Additionally an analysis of potential whole of government response will be presented.
Results: Climate change is already being experienced by a number of Pacific Islands including Kiribati and Tuvalu. However there is a common assumption that this may lead to increased permanent migration. Studies indicate this response may be less pronounced than first thought. Current migratory patterns between Australia and the Pacific are overwhelmingly temporary with a strong pattern of circularity. There is little evidence that this is likely to change.
Conclusions: Climate change impact on Pacific islands is already being felt including increased frequency of natural disasters, disruption of agriculture and rising sea levels. There is less evidence on what the health impacts may be although it is postulated that this may affect disease patterns and spread, as well as accessibility to health care. The long term large scale displacement of people expected to occur due to climate change will potentially require development of whole of government and regional policy response to assist people in need of relocation. These potential increased flows and corresponding impacts upon TB transmission would be considered within these calculations but it is believed that the present TB migratory regulations would be able to accommodate any potential shifts in migration flows.

Pakistan: flooding emergency—challenges and solutions to tuberculosis control

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Background: In 2010, flood brought an enormous destruction and misery for Pakistani people, in all 17 flood affected Districts of Sindh about 7.27 million people were displaced, 100 000 houses, 350 health facilities were destroyed and this resulted in about 2800 TB cases discontinuing their TB treatment.
Objectives: 1) To identify TB patients living in the camp, who had discontinued their anti-TB treatment due to displacement; 2) to detect and register new TB cases among residents of camp.
Design/methods: The intervention was conducted at flood relief camp 13 kilometers away from city Karachi. In camp 8509 men, women and children of different parts of province Sindh affected by flooding were placed. The TB clinic established in Razzak abad camp was managed by a team of five comprised of two physicians, two paramedics and one laboratory technician, paramedics made announcement on a daily basis and visited families to inform them about availability of TB clinic and delivered educational messages about TB.

Results: A total of 411 clients attended the camp's TB clinic during 42 days, out of which 18 TB patients were identified who had discontinued their treatment due to displacement. Total 40 TB suspects were identified, among them 3 were diagnosed for TB, all 21 cases were registered for treatment during their stay in the camp and referred back to nearest TB DOTs centre on return to their homes for continuation of treatment.

Conclusion: Through above innovative approach we were able to find 18 TB patients who had discontinued treatment due to displacement and re-started their treatment and found 3 new cases. This public private partnership in TB provides evidence that similar type of work can be repeated at any place in any disaster situation to identify TB cases to prevent transmission of TB infection in displaced population and prevent drug resistance and other consequences.

REDUCING SECOND-HAND SMOKE EXPOSURE IN THE HOME

Measuring exposure to second-hand smoke in the home and car: UK, Ireland and Malaysia

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Background: Second-hand smoke (SHS) exposure in the private spaces of homes and cars continues to be common even in countries with comprehensive smoke-free laws. There is little data available on the concentrations of SHS experienced within these micro-environments.

Methods: Linked studies to measure concentrations of fine particulate ($PM_{2.5}$) as a marker for SHS within homes in Scotland, Ireland and Malaysia, and in cars in Scotland and England, were carried out. Sidepak AM510 Personal Aerosol Monitors or Dylos DC1700 devices were used to gather real-time data on $PM_{2.5}$ in smokers' homes and cars. $PM_{2.5}$ concentrations were compared to the World Health Organisation limit of 25 $\mu g/m^3$.

Results: The mean $PM_{2.5}$ concentration measured from more than 3800 hours of data collected from 107 smoking households across all three countries were 76 $\mu g/m^3$ (range 1–499). The average 1-minute peak level recorded was 507 $\mu g/m^3$ (range 9–4767). In cars the mean journey concentration of $PM_{2.5}$ was 85 $\mu g/m^3$ (range 16–331) in journeys where smoking took place ($n = 49$) compared to 7 $\mu g/m^3$ (range 0.4–29) during non-smoking journeys ($n = 34$).

Conclusions: Concentrations of SHS in home and cars can be considerable with the average smoking home exceeding the 24 h World Health Organisation limit

for $PM_{2.5}$ by a factor of 3: the respiratory and cardio-vascular health effects of daily exposure to these levels is likely to be substantial. Feedback of this air quality information may be a useful way of encouraging smokers to think about changing their behaviour to protect their family from the harmful effects of SHS.

Reducing children's exposure to second-hand in the home: the REFRESH project (Scotland)

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Background: Exposure to secondhand smoke (SHS) is associated with a number of illnesses in children. Children from disadvantaged homes are particularly at risk, having higher rates of parental smoking and fewer restrictions on smoking in the home. There is little evidence of effective home-based interventions to reduce children's SHS exposure.

Objective: To pilot an intervention (REFRESH) aimed at reducing children's exposure to SHS in homes in deprived areas of Aberdeen (Scotland).

Design: A randomised feasibility study design involving 54 smoking mothers with at least one child under 6. The study involved four home visits over one month. Visits included measurement of home air quality ($PM_{2.5}$) and a motivational interview on changes to reduce child SHS exposure. The enhanced group received their air quality data at the start of the intervention; the control group at the last visit.

Results: Both groups experienced reductions in $PM_{2.5}$. The reduction was greater for the enhanced group. There was a significant difference ($P < 0.05$) between visit 2 and visit 4 values for maximum $PM_{2.5}$ ($P = 0.006$) and for percentage of time over recommended concentration of 35 $\mu g/m^3$ ($P = 0.017$). Mothers understood the data they were shown and reported 'shock' at the levels in their home. They appreciated having personalised data and were motivated to protect their children from the knowledge they had gained.

Conclusions: Providing mothers who smoke with personalised information about the air quality in their home along with a motivational interview is feasible and improves measures of air quality after one month. Participants found the intervention understandable and acceptable.

Reducing second-hand smoke exposure in the home: involving mosques (England and Pakistan)

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Objective: To establish evidence on the effectiveness of a Smoke Free Homes (SFH) intervention delivered

through mosques, in England and Pakistan. The intervention is designed to encourage families to implement smoking restrictions in their homes and reduce their exposure to second-hand smoke (SHS).

Methods: Household exposures to SHS were assessed in Pakistan and England. The SFH intervention was pilot tested in community settings in both countries. The imams participating in the pilot, requested for a SFH educational resource that could be used in mosques. A dedicated resource was subsequently developed and implemented in five mosques in England. We also embarked on a cluster-RCT (pilot) titled 'Muslim Communities Learning About Second-hand Smoke' (MCLASS), to further establish the effectiveness of SFH delivered through mosques.

Results: In Pakistan 90.8% (167/184) of non-smokers who live in households with a smoker, are exposed to SHS. In contrast, 42% (73/173) of such non-smokers living in an inner city deprived area in England are exposed to SHS. We found that a multifaceted SFH intervention has the potential to influence adult smoking behaviour in households; the proportion of smoke-free homes increased from 43% to 85% in Pakistan and from 35% to 68% in England, after the intervention. Findings also suggest that mosques are an acceptable and feasible setting for promoting SFH. The MCLASS trial, which will report its findings in summer 2014, is testing this approach. So far, 14 mosques and 150 households have been recruited. According to the trial's baseline data, 62.5% (90/144) of non-smokers of south Asian-origin living in households with at least one smoker are exposed to SHS.

Conclusion: Majority of the non-smokers in Pakistan and those of south Asian-origin in England, who live in households with smokers, are exposed to SHS. The influence of mosques offers an opportunity to change smoking behaviours and reduce this exposure.

Figure   An imam speaking in Lahore to a congregation about the harms of second-hand smoke.

Reducing exposure to second-hand smoke in the home—involving schools (Bangladesh)

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Background: Second-hand smoke (SHS) is a major threat to the health of children in Bangladesh. To contribute towards national efforts to reduce children's exposure to SHS, we conducted a cluster RCT to evaluate a school-based 'Smoke Free Homes' (SFH) intervention. The intervention is designed to encourage families to implement smoking restrictions in homes and reduce their exposure to SHS.

Methodology: The study was conducted in primary schools in Dhaka, Bangladesh. Year 5 pupils (9–11 years) were recruited and baseline data were collected. A total of 24 schools were randomly allocated to three trial arms; eight schools each. Arm A schools received teacher's training session (half-day), and two school-based activities for pupils (45 minutes each, delivered over two days); Arm B received the above and another four school-based refresher sessions (15 minutes each, delivered in subsequent weeks); and arm C received no intervention. Our primary outcome is self-reported smoking restrictions and visibility in homes. Secondary outcomes included a reduction in the number of households with at least one smoker. This was assessed through pupils' surveys repeated at the end of week 1 (post-intervention in Arm A), week 12 (post-intervention in Arm B), week 27 and week 52.

Results: A total of 781 pupils were recruited in the trial. A preliminary analysis suggests that overall 36% of the pupils noticed adult smoking without any restrictions at the baseline, which reduced to 30.7% in 52nd week. However, this reduction was more remarkable in the intervention arms: smoking without any restrictions reduced from 47% to 20.4% in arm A, and from 33% to 16% in arm B. After one year, the proportion of pupils with at least one smoker at home declined from 58% to 28% in arm A, 45% to 24.5% in arm B, and 41% to 34% in arm C.

Conclusion: Preliminary findings suggest that the school-based SFH intervention was successful in implementing smoking restrictions and reducing smoking visibility.

CHILD PNEUMONIA: NEW EVIDENCE AND NEW POSSIBILITIES TO REDUCE CHILD MORTALITY

Bacteria and tuberculosis as causes of pneumonia in severely malnourished children

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Pneumonia and malnutrition are two of the major causes of deaths in young children globally. Severe malnutrition is a risk factor for child pneumonia and is associated with a poor outcome. The range of pathogens causing pneumonia in children with severe malnutrition is different from those causing pneumonia in well-nourished children. However, etiological data are limited from high mortality settings and the role of *Mycobacterium tuberculosis* is uncertain. This presentation will provide data from a systematic review of the causes and outcome of pneumonia in young children with severe malnutrition. The presentation will also include original data from a recent study of 405 children (<5 years) with severe malnutrition and radiological pneumonia admitted to the Dhaka Hospital of icddr,b in a 15 month period in 2011–2. Investigations included blood culture, and sputum for smear microscopy, mycobacterial culture and Xpert® MTB/RIF assay. Case-fatality rate overall was high—16.5%—with half of the deaths occurring within 3 months post-discharge. Bacteria were isolated from blood 4.4% of children and 72% of these were Gram negative pathogens. Tuberculosis was confirmed by culture and/or Xpert in 7% of study children. There were an additional 16% of children with clinically diagnosed pulmonary tuberculosis, not microbiologically confirmed. Compared to culture, the sensitivity and specificity of Xpert MTB/RIF were 67% (95%CI 24–94) and 92% (95%CI 87–95) respectively. Tuberculosis may be more common than is generally recognized in children presenting with severe malnutrition and pneumonia in a tuberculosis endemic setting.

Antibiotics for severe pneumonia: from injectable to oral?

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Guideline development has evolved in recent years with increasing demand for evidence-driven processes across many major health care institutions. The Grad-ing of Recommendations Assessment, Development and Evaluation (GRADE) system in particular has been used extensively including in low income settings like Kenya where it was adapted for the revision of the national paediatric guidelines in 2010. In addition to evidence, GRADE acknowledges the importance of contextual factors in the development of recommendations. During the Kenyan exercise the guideline development panel was presented with evidence for the proposed use of oral amoxicillin in place of injectable benzyl penicillin for severe childhood pneumonia. Despite high quality evidence from large RCTs suggesting equivalence between the two treatments, a majority of the panel members rejected the proposed amendment, based largely on concerns over the generalisability of the findings. The debate on the appropriate treatment for severe pneumonia in children has been reignited following the recent launch of the second edition of the WHO Pocketbook of Hospital Care for Children—which was developed using GRADE. These revised guidelines support the use of amoxicillin over previously recommended penicillin, based on the same evidence reviewed by the Kenyan panel. We conducted a pragmatic, non-inferiority trial to address policy maker concerns, enrolling participants from six Kenyan hospitals to establish the primary and comparative clinical effectiveness of penicillin versus amoxicillin. As recruitment approaches conclusion, it is anticipated that the findings of this study will help define treatment of pneumonia for Kenyan children and contribute to the debate in Africa more widely. However, the absence of funding for capacity to undertake clinical research on childhood pneumonia in Africa, threatens the development of evidence-based guidelines for this leading cause of childhood death in this region.

MDR-TB IN CHILDREN AND ADOLESCENT TUBERCULOSIS ISSUES

Burden of paediatric DR-TB in four South African provinces

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Background: In 2011, more than 490 000 children worldwide fell ill with tuberculosis (TB) disease. The prevalence of drug-resistant TB (DR-TB) among children globally and in South Africa is unknown. Based upon data from Western Cape and Johannesburg, there is regional variation in treatment outcomes

among children with multi-drug resistant tuberculosis (MDR-TB); however little is known about childhood DR-TB outside of these regions.

Methods: We conducted a retrospective review of children (0–12 years) and adolescents (13–17 years) with DR-TB receiving care at five MDR-TB hospitals in four South African provinces and five academic hospitals in Gauteng, from January 2005 through June 2010.

Results: Of 968 children and adolescents with DR-TB, 48% were diagnosed in KwaZuzlu-Natal, 33% in Gauteng, 17% in Eastern Cape, and 2% in Limpopo. In Gauteng, 53% of the 320 patients received care from academic hospitals. Of 813 patients with DR-TB and known HIV status, 58% (n = 470) had HIV, ranging from 34–60% across the provinces. The most resistant profile for the majority of patients was MDR-TB (n = 363, 42%), while 7% had extensively DR-TB. Just over half of patients were cured or completed treatment (n = 373, 53%), although 24% died (provincial range 15–36%). Factors associated with an increased risk of death on treatment were male gender ($P < 0.01$), being 0–4 years of age ($P = 0.04$), living with HIV ($P < 0.01$), a history of poor weight gain ($P = 0.03$), or receiving care at an academic hospital ($P < 0.01$).

Conclusion: Nearly one-quarter of South African children and adolescents with DR-TB in four provinces died while receiving TB treatment and only half had good TB treatment outcomes. Interventions to reduce DR-TB mortality should focus on children with factors associated with an increased risk of death.

Effectiveness, tolerability and adherence to a 3-drug MDR preventive therapy regimen

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Background: There is limited evidence to guide the management of children exposed to multidrug-resistant tuberculosis. We aimed to study the tolerability and toxicity of a standard preventive therapy regimen, given to children exposed to infectious multidrug-resistant tuberculosis, and explore risk factors for poor outcome.

Methods: Prospective cohort study: Western Cape, South Africa. Children <5 years old, or HIV-positive children <15, were recruited from May 2010 through April 2011 if they had been exposed to an ofloxacin-susceptible, multidrug-resistant tuberculosis source case. Children were started on a preventive therapy regimen as per local guidance: ofloxacin, ethambutol and high-dose isoniazid for six months. Standardized measures of adherence and adverse events were recorded; poor outcome was defined as incident tuberculosis or death from any cause.

Results: 186 children were included, median age 34 months (inter-quartile range: 14–47). Of 179 children tested for HIV, 9 (5.0%) were positive. Adherence was good in 141 (75.8%) children. Only 7 (3.7%) children developed Grade 3 adverse events. One child (0.5%) died and six (3.2%) developed incident tuberculosis during 219 patient-years of observation time. Factors associated with poor patient outcome were: age <1 year (rate ratio 10.1; 95%CI 1.65–105.8; $P = 0.009$), HIV-positive status (rate ratio 10.6; 95%CI 1.01–64.9; $P = 0.049$) and poor adherence (rate ratio 7.50; 95%CI 1.23–78.7; $P = 0.026$).

Conclusions: This three-drug preventive therapy regimen was well tolerated and few children developed tuberculosis or died if adherent to therapy. The provision of preventive therapy to vulnerable children following exposure to multidrug-resistant tuberculosis should be considered.

Pharmacokinetics of fluoroquinolones in children

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The fluoroquinolone antibiotics have demonstrated potent activity against *Mycobacterium tuberculosis*. They are the most important drug in current treatment regimens for drug-resistant (DR) tuberculosis (TB), and are likely to be key components of future regimens for the treatment and prophylaxis of drug-susceptible and DR-TB in adults and children. Concerns about arthropathy in juvenile animals have historically limited the use of fluoroquinolones in children. There are few child-friendly formulations and limited data on their pharmacokinetics in children, particularly in children with TB and latent TB infection. Though cumulative clinical experience has shown them to be safe in children for short term use, there is little paediatric data on fluoroquinolone safety and tolerability for prolonged courses required for DR-TB treatment, including on their known potential to prolong the QT interval. An ongoing study in Cape Town, South Africa is evaluating the pharmacokinetics and safety of multiple second-line anti-tuberculosis drugs in HIV-infected and uninfected

children. We present preliminary data from this study on the pharmacokinetics of ofloxacin and levofloxacin in children for the treatment and prophylaxis of DR-TB, and discuss these results in the context of previously published paediatric and adult data. We further present data on the cardiotoxicity of ofloxacin and levofloxacin, and review existing data on the long-term safety of ofloxacin. We discuss the implications of this data for the use of fluoroquinolones in children with DR-TB, review ongoing studies of the fluoroquinolones in children with TB, and highlight important questions for future research.

A framework for evaluating novel MDR-TB regimens in children

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A novel approach for accelerating access to new TB drugs and regimens in infants and young children was presented last year. It involves a paradigm shift, whereby all pediatric age groups are studied simultaneously (instead of the classical sequential age-de-escalation approach), as soon as adequate safety and efficacy have been established in adults. The evidence base for safety in each age group of infants and children is built not on safety data collected in older children, but on safety data collected in single-dose PK studies conducted simultaneously in those age groups (initial dose selection based on adult PK data and modeling), followed by multiple-dose PK studies (with dose selection based on single-dose PK and safety results in each age group) and studies of longer-term dosing in each age group to rapidly establish an adequate safety database to inform more widespread use. This year we will discuss particular aspects of this approach relevant to the development of novel MDR regimens: 1) Are single-dose PK studies in children ethical? 2) Should infants be studied simultaneously with older children or sequentially? 3) To what extent can children with DS- and MDR-TB be studied interchangeably? 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.

TOWARDS SAFER AIR: DIFFERING APPROACHES TO REDUCING THE RISK OF TUBERCULOSIS TRANSMISSION IN HIV CLINICAL SETTINGS

Tools for engaging nursing associations and civil society for tuberculosis infection control implementation

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With case detection rates for tuberculosis (TB) continuing to be below target and the circuitous route that patients often end up taking through various health services before being diagnosed with TB, it is essential that we consider TB infection control and prevention (TBICP) way beyond the National TB Programme. While TBICP must continue to be strengthened in all areas providing diagnostic and treatment services for TB, providers of wider health care services in hospitals and communities need to understand the important contribution they can make. Indeed it is arguably the people who do not yet have an inkling that they might be suffering with TB who may pose the greatest risk to the people around them. Involving professional associations and civil society organisations who may not see themselves as having a role in TB control has the potential of reaching much a broader audience and developing greater capacity to spread important messages throughout civilian as well as health care communities. National nurses associations and organisations have a responsibility to ensure the safety and welfare of their members, regulators want to ensure that patients are not put at risk through unnecessary exposure to a harmful environment when seeking care. Civil society organisations are focused on informing and empowering communities on issues affecting their health and well-being. Reinforcing messages about early diagnosis and general cough etiquette with regard to all respiratory infections could improve both administrative and environmental controls of TB. A number of practical examples will be presented and suggestions made regarding requirements for expanding successful interventions.

Scale-up of tuberculosis infection control in Botswana ART clinics

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Botswana has been increasing its focus on facility TB infection control, with special emphasis on locations with high proportions of HIV-infected persons. In February 2012, the MOH partnered with the US and Botswana Centers for Disease Control and Prevention to implement a training of healthcare workers

from 10 facilities. Following the training, each facility was evaluated using a facility risk assessment tool. Each facility developed an implementation plan and was re-evaluated at 6-months. In the interim, supportive supervision was provided on a regular basis. At follow-up, performance on key indicators had improved, specifically in the areas of cough triage and use of natural ventilation. All but one facility had implemented a healthcare worker screening program at follow-up. The training package with supportive supervision led to improvements in TB infection control implementation at the 10 facilities evaluated. Scale-up of TB infection control is ongoing and has been included in the Botswana Ministry of Health, National Tuberculosis Control Program, Strategic Plan, 2013–2017 with a particular emphasis on providing training and mentorship in additional districts as well as improving capacity in building design and maintenance.

Implementing HCW tuberculosis screening in ART clinics in Ndola, Zambia

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Background: Health care workers (HCW) are at higher risk of contracting TB. According to WHO/ILO guidelines they should get priority access to care for TB, and TB among HCW should be monitored.
Objective: To assess feasibility of a program on TB and HIV screening and monitoring among HCW.
Methods: 13 government supported clinics (together 700 staff members) and 2 hospitals (together 900 staff members) in 1 district agreed to participate. HCW were screened in their own facility by an entrusted person. The agreed screening algorithm for HCW included annual symptom screening, with sputum smear, priority access to culture and chest X-ray performed for those suspected of TB. Only aggregated data were collected to ensure confidentiality. Only priority diagnostics and data collection were funded, but not staff time, to encourage sustainability.
Results: All stakeholders showed commitment to the HCW screening process and the HCW were eager to be screened. Local ethical and administrative clearances took over a year. Screening started in April 2013 and within two months 12 clinics have screened 110 HCWs for TB. Two thirds of them were also screened for HIV. Eight (7%) were suspected of TB and one of them was diagnosed with sputum positive TB while one HCW was already on TB treatment (1.8%). Challenges encountered were consensus on and delayed access to priority diagnostics at referral facilities, re-sensitization on protocol due to a staff rotation process, few HCW not showing up for

screening, and clinicians assigned to perform screening had limited time. One hospital delayed start of screening but covered 120 HCW in one month.
Conclusions: It is feasible to conduct screening for TB and HIV among HCW in clinics. Advocacy is needed to target managers, clinicians and other HCW on the protocol and the chosen screening algorithm. Practical solutions and resources should be found for ensuring priority access to diagnostics, logistics and confidential registration.

TRANSLATING *MYCOBACTERIUM TUBERCULOSIS* MOLECULAR DIAGNOSTICS INTO CLINICAL MANAGEMENT

Performance characteristics needed for molecular diagnostics to replace growth-based DST

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Molecular resistance assays have the advantage of speed, limited biosafety requirements, reproducibility and the potential of including resistance targets for multiple first- and second-line drugs. In order to be useful for clinical management they need to have high sensitivity as well as high specificity. High sensitivity for detecting *Mycobacterium tuberculosis* tuberculosis is important since this will allow application directly on sputum and obviate the need for a culture step; it will depend mainly on the assay platform. High sensitivity for identifying drug resistance is needed to avoid false-negative results (high negative predictive value). It will depend mainly on the number of different genes and mutations involved in resistance and on the proportion of these that have been included in the assay. The distribution of mutations responsible for resistance to a particular drug, and therefore test sensitivity, may vary between geographic regions. High specificity for identifying drug resistance is needed to avoid false-positive results (high positive predictive value, PPV). The specificity will depend on platform characteristics and on the type of targets used. Because of silent mutations wild-type targets may have lower specificity than specific mutation targets. Wild-type targets may be needed when resistance is encoded by multiple mutations in long base pair sequences, such as for pyrazinamide. High PPV is important because of the high cost, long duration and high level of toxicity of second-line treatment. The PPV however also depends on, and declines with, the prevalence of resistance in the patient population that is tested. For low resistance prevalence, such as for multidrug resistance in new

patients in most countries, the PPV can be well below 50% even with high specificity. Then confirmation testing may be needed by conventional DST or molecular testing, using an assay for which the specificity is independent of that of the initial test.

Sensitivity and specificity of mutations for predicting global XDR-TB phenotypes

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Background: Molecular diagnostics based on detection of mutations conferring resistance are promising technologies for rapidly detecting multi/extensively drug-resistant TB (M/XDR-TB), but large studies of mutations as predictors of phenotypic resistance are rare. A large multinational sample of *M. tuberculosis* isolates with high prevalence of drug resistance was analyzed by the Global Consortium for Drug-resistant TB Diagnostics (GCDD) to determine the sensitivity and specificity of mutations for predicting M/XDR-TB phenotypes and to inform development of rapid diagnostics.
Methods: We collected >450 M/XDR-TB clinical TB isolates from regions of high TB burden in India, Moldova, Philippines and South Africa. Isolates underwent phenotypic drug susceptibility testing (DST) to isoniazid (INH), rifampin (RMP), moxifloxacin (MOX), ofloxacin (OFX), amikacin (AMK), kanamycin (KAN) and capreomycin (CAP) using MGIT 960 and WHO critical concentrations. Genes *kat*G, *inh*A, *rpo*B, *gyr*A, *gyr*B, *rrs, eis* and *tly*A were sequenced with Sanger sequencing, and observed single nucleotide polymorphisms (SNPs) were evaluated in the context of phenotypic resistance.
Results: 416 TB isolates were evaluated. 370 were INH resistant (INH-R), 356 RMP-R, 292 MOX/OFX-R, 230 AMK-R, 219 CAP-R and 286 KAN-R. SNPs in *kat*G/*inh*A had combined sensitivity of 96% and 97–100% specificity for detection of INH-R. 11 SNPs in *rpo*B had combined sensitivity of 98% for RMP-R. SNPs in *gyr*A88-94 had sensitivity of 90% for MOX/OFX-R. The rrs 1401/1484 SNPs had 89–90% sensitivity for detecting AMK/CAP-R, but only 71% sensitivity for KAN-R. Adding eis promoter SNPs increased sensitivity for detecting KAN-R to 91%.
Conclusions: <30 SNPs in six genes predicted clinically relevant M/XDR-TB phenotypes with 90–98% sensitivity and almost 100% specificity. Given that less than 20% of MDR-TB cases are currently being diagnosed with phenotypic DST alone, there is a clear clinical role for rapid molecular diagnostics.

Clinical molecular diversity of tuberculosis on a genome-wide scale: lessons learnt for molecular diagnostics

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Background: Using Whole Genome Sequencing (WGS), we are beginning to understand the genetic diversity of *Mycobacterium tuberculosis* on a genomic scale and its consequences for treatment of tuberculosis (TB). The Global Consortium for Drug-resistant TB Diagnostics (GCDD), a large multinational study of TB isolates with high prevalence of drug resistance, conducted genome scale variant analyses of 366 *M. tuberculosis* genomes (mostly MDR/XDR) to inform development of rapid diagnostics.
Methods: Drug susceptibility of 366 clinical TB isolates from India, Moldova, Philippines and South Africa to isoniazid, rifampin, moxifloxacin/ofloxacin, amikacin, kanamycin and capreomycin was determined using MGIT 960 and WHO critical concentrations. Isolates were sequenced using PacBio RS WGS platform. Genome-wide variant analysis was conducted using an in-house pipeline (PacDAP) for identifying single nucleotide polymorphisms (SNPs).
Results: PacDAP analysis revealed 28 963 unstable loci in the genome where genetic mutations can occur. On average 99.1% of the genome had sufficient coverage for base and variant calling. On average, ~2000 SNPs were detected for each isolate. SNPs were stratified into functional groups: those with potential to confer resistance, increase fitness, serve as molecular clock, serve as markers for an outbreak, and serve for high-resolution lineages differentiation.
Conclusions: WGS has significant consequences for TB treatment, due to its ability to observe diversity at a much finer scale. TB treatment outcomes depend on the combination of resistance causing mutations, fitness and heterogeneity of the pathogenic population, emergence of resistance (evolution) or reinfection during the course of treatment. The combination of groups of markers identified by PacDAP can detect all of the above conditions and inform the clinician in a timely manner. For instance, lineage and outbreak markers can help in contact tracing, and distinction between reinfection and evolution.

Whole genomic sequencing for drug resistance determination: the new era

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Introduction: The World Health Organization (WHO) endorsed molecular test have advantages of speed and reproducibility but are limited by the genetic markers included in the diagnostic test. The increasing availability and reducing costs associated with sequencing have the potential to accelerate the early detection of drug resistance and provide more accurate and comprehensive resistance determination for multiple genetic targets. We evaluated the MiSeq platform (Illumina, UK) for drug resistance determination of first and second line resistance using a whole genome sequencing (WGS) approach.

Methods: A total of 24 *Mycobacterium tuberculosis* isolates with known phenotypic resistance were used. Sequencing was performed on the MiSeq Platform (Illumina, UK) and analyzed on the CLC Genomics Workbench V6.0.1. Genomes were assembled using *M. tuberculosis* H37Rv (Sanger Institute) as the reference genome and quality-based variant detection analysis was performed to determine any changes in the genes of interest compared to the reference. Mutations were interpreted using the TBDREAM database and correlated to MGIT phenotypic testing. Resistance determination was performed for rifampicin, isoniazid, fluoroquinilones, aminoglycosides and pyrazinimide.

Results and conclusion: Samples sequenced had an average depth of 40× coverage, Q-scores averaging 30 and achieved more than 99% coverage in most cases. Correlation between the phenotype and WGS approach was excellent. The use of MiSeq for the detection of drug resistance using a WGS approach was simple to perform, suited laboratory work flows and the consumable costs were below $80 per whole genome. Additional information on compensatory mutations and strain typing are added benefits using the WGS approach.

Integrated molecular diagnosis of TB-HIV and drug resistance at point of care: SATURN model

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The Hlabisa health sub-district in northern KwaZulu-Natal, South Africa, is a rural area with high dual burden of HIV and TB. Levels of drug-resistant TB and acquired antiretroviral resistance are equally high. HIV and TB services are provided at primary health care clinic level while management of drug-resistant TB is currently decentralised to district hospital level as per Department of Health policy guidelines. We have developed and successfully implemented, in this rural sub-district, the Southern African Treatment and Resistance Network (SATURN) model for HIV treatment failure management, which involves an affordable, open access antiretroviral resistance genotyping method. An infectious disease specialist interprets and provides management recommendations, remotely, which facilitates comprehensive patient management at primary health care clinic level. As many of our patients are co-infected with TB, an integrated HIV-TB resistance genotyping and management approach is warranted. Furthermore, given that up to 50% of MDR-TB strains harbour additional resistance to second-line drugs, there is an urgent need for rapid and affordable diagnostic methods that can identify the full TB resistance profile and inform selection of the optimal treatment regimen. We, therefore, will adapt our genomic tests and bioinformatics databases to include TB resistance genotyping. We have now developed a model for detection of TB drug resistance through DNA sequencing directly from sputum, which is being validated against phenotypic drug susceptibility testing (DST). The aim is to replicate the HIV model with specialist interpretation and advice to facilitate management of drug-resistant TB at remote primary health care clinics.

Translating molecular knowledge into clinical findings: M/XDR-TB case studies

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Introduction: Until recently, the standard system for establishing the diagnosis of *Mycobacterium tuberculosis* infection and drug sensitivity was microscopy and culture. The former test does not detect tuberculosis (TB) well in paucibacillary disease common in the HIV-infected population. The time taken to get the results and thus to decide on correct patient management may result in continued transmission of a possibly resistant organism as well as on-going morbidity and mortality. A number of new molecular-based tests have now entered routine practice globally. TB health care workers need to have a working knowledge of these tests: their advantages and limitations.

Method: A case study method will be used to teach the advantages and limitations of
- GeneXpert MTB/RIF
- GenoType® MTBDR*plus* version 1 and 2
- GenoType® MTBDR*sl*
- Urinary antigen detection by LAM (lipoarabinomanin)

The latest data will be presented at the end of each case study to enforce the teaching method.

Outcome: After the session, attendees will be able to interpret tests using the latest molecular tests. The specificity and sensitivity, positive and negative predictive value will be discussed in the HIV infected and non-infected patient.

'MAN DOES NOT LIVE BY BREAD ALONE'. EFFECTS OF NUTRITIONAL SUPPORT FOR TUBERCULOSIS PATIENTS IN TUBERCULOSIS TREATMENT OUTCOMES

Food by prescription: experiences from food supplements in TB-HIV treatment in Temeke

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Setting: Temeke region hospital, Dar es Salaam Tanzania with well developed food by prescription programme but unreliable supply of food supplements and no immediate solution to this problem.

Objective: To highlight the importance of nutrition assessment and indicators for food and to share experiences regarding to various nutritional entry points for TB-HIV patients for food supplements.

Design: Selection of 60 TB-HIV patients who were nutritional assessed and meet eligibility criteria for food supplement and being provided for three consecutive visit.

Results: Shows that there is an increase of 2.5 to 3.8 kg of their body weight.

Conclusion: Also, referring to Temeke experience food supplement improves adherence for care and treatment for TB patients, support treatment, minimize and mitigate drug side effect together with improvement of treatment.

An egg today is better than a chicken tomorrow. Training in better utilisation of local food items

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Background: Good nutrition is very crucial for those who are sick. Having TB makes consuming a nutritious diet even more important. The more knowledge people have about how to utilise traditional locally-available food, the better equipped they are to make wise choices in relation to their dietary needs. For a long time a lot of people in Malawi ignored many of our own traditional locally-available foods in our diets. Reminding ourselves and understanding ways of preparation and utilisation of these traditional locally-available foods is therefore important.

Objectives: To demonstrate better ways of utilizing traditional locally-available foods based on experiences from Malawi.

Methods/approach: Experiences from Former TB Patients (FTBP) and People Living with HIV (PLWHIV) will be used to demonstrate and discuss the best approaches to utilising traditional locally-available foods. The FTBP and the PLWHIV are from Paradiso TB Patient Trust in Malawi.

Results: It is expected that through the training, participants will learn more on how to group traditional locally-available foods in order to have a balanced diet. Further, the training will provide space for participants to share knowledge on how best to utilise local foods and how to set up backyard gardens to produce different varieties of local vegetables. It is also envisaged that participants will see the need to empower support groups to run nutritional support activities and the importance of taking stock of their daily dietary intake.

Conclusion: Choosing traditional locally-available foods is one way to promote healthier food choices as well as the health of the environment. There is therefore need to promote the use of traditionally locally-available food.

The role of nutrition during MDR-TB patients' treatment

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Background: Tuberculosis 'consumption disease' and nutrition are interdependent. TB causes under-nutrition, and under-nutrition (low body mass index) increases the risk of activating TB infection to disease.

Aim: To describe the role of nutrition to hospitalized MDR-TB patients during intensive phase of treatment at Kibong'oto Centre of excellence for MDR-TB management in Tanzania.

Method: Patient medical charts were reviewed retrospectively from November 2009 to December 2010. Under programmatic management patients were provided with locally available food putting into consideration of achieving balance diet. Patients were routinely tested for HIV, if positive CD4 count were measured. Height was measured at baseline only while weight and hemoglobin (Hb) levels were also monitored monthly. Interim treatment outcome was established at the end of intensive phase (6–8 months of injectable). Analysis was done using SPSS version 20.

Results: Of 46 admitted MDR-TB admitted for second-line therapy intensive phase, 35 (76%) were male with mean age of 46 years (SD 14). Forty-five (98%) had prior TB treatment and 21 (46%) were treated more than twice. Forty-two (92%) were discharged for continuation phase remained 4, (50%) died and defaulted. Mean baseline BMI was 19 kg/m² (SD 3) while that at month 6 was 21 kg/m² (SD 4). Twenty-five (54.3%) had baseline normal BMI ($\geqslant$18) and at month six, 37 (80%) had normal BMI. Mean increase of BMI was 2.1 kg/m², 95%CI (1.5–2.7) ($P < 0.0001$). BMI was related to interim treatment outcome; two (100%) of patients who died had severe thinness (BMI < 16) and those who defaulted

2 (100%) had normal BMI. Mean increase of Hb was 2.1 g/dl while mean Hb at month 6 was 14 g/dl ($P <$ 0.0001).

Conclusion: Nutritional supplement to MDR TB patient played a significant role in improving interim treatment outcome during intensive phase treatment at Kibong'oto.

Food parcel distribution to reduce tuberculosis incidence and improve adherence in HIV-positive prisoners

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Setting: The Arkhangelsk TB Program in the North-West of Russia has over the years established a strong partnership with the prison system. A unified approach to treatment and diagnosis has been established both for the civil and penitentiary systems. As a result, the TB mortality in the prison reduced almost 6-fold, TB incidence almost 8-fold. The major challenges of the TB Program at present are MDR-TB, XDR-TB and HIV-TB co-infection. In the North-West of Russia, in the last decade the HIV-TB incidence increased 6-fold.

Objective: To ensure treatment adherence to preventive TB therapy among HIV-infected prisoners through distribution of food parcels.

Design: As of March 2013, in the penal facilities of the Arkhangelsk Region there were 376 HIV-infected prisoners. In May 2013, they were interviewed to assess motivation factors for preventive TB therapy. The two main factors for rejecting preventive TB therapy reported were 'not feeling sick with TB' and 'loss of salary'. According to internal prison regulations, when started on treatment patients are not allowed to work and hence lose salary. 180 HIV-infected prisoners gave written informed consent on preventive therapy (6 months with izoniazid). They receive a food package (cost approx. US$10) once every 2 weeks if they adhere to treatment well. Food packages are meant to compensate for salary loss and improve treatment adherence.

Results: The project is expected to yield 80% treatment adherence rate in the project group. It is estimated that the number of HIV-TB co-infection cases will decrease in the next several years by 50%.

Conclusion: The project aims to demonstrate how TB prevention and treatment adherence improves in settings where patients receive food support. This is a highly cost-effective intervention, since the cost of TB treatment many times exceeds the cost of preventive TB therapy and food support.

Skills development training can improve nutritional status among MDR-TB patients in Nepal

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Setting: Morang district of Nepal has a well-developed TB program including a hostel facility for DR-TB patients, but lack of sufficient nutritional support for those patients during their treatment.

Objective: To improve the nutritional status of DR-TB patients by enhancing their skills on different income generating activities.

Design: This was a descriptive qualitative survey using purposive sampling methods. Primary data were collected by using semi-structured questionnaires and in-depth-interviews were used to assess the training needs of the DR-TB patients its impact in their daily life. FGD methods used for qualitative purpose.

Results: Since 2009 to 2012, 38 DR patients participated in skill development activities. After completion they started a business and earned extra money in average NPR 5000/person/month and used that money to buy nutritious foods. The conversion rate was more than 90% among the skilled patients and cure rate was 85%. Based on health worker monthly result monitoring report, 2 kg weight gained per person/month was recorded. The nutritious foods helped them to fight with DR-TB.

Conclusion: Adequate nutrition during treatment is a major aspect to fight against DR-TB. The skill development training enhances the income generating capacity of DR-TB patient enabling them to afford nutritious foods during and after treatment duration. Therefore, skill development approach is a very efficient way to help improve the nutritional status of DR-TB patients.

TUBERCULOSIS CONTROL IN PRISONS: SAFER ENVIRONMENTS FOR INCARCERATED POPULATIONS

Early and effective tuberculosis case finding in the Azerbaijan penitentiary system

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Background and challenges: Join Global Fund and Ministry of Justice of Azerbaijan TB control program in prisons has successfully implemented TB case identification among prisoners by combination of different case finding (CF) tools. The optimal set of these means was a challenge to achieve early and effective detection of TB cases.

Intervention: Case finding, screening medical and lab records have been retrospectively analyzed against task schedules, timing, reporting and means used for CF in 2012. Health care givers used standardized for the penitentiary system CF algorithm. More than 17 300 inmates passed TB CF procedures: X-rays (16 431), questionnaire (11 584), simple smearing (5396), culturing (6006) and PCR GenExpert (1608). Ministry of Justice emphasizes and prioritizes clinical (background diseases), HIV associated and occupational risk groups among them.

Results: From 2011 to 2012 year regular examination coverage for tuberculosis according to the standardized CF procedures increased from 74% to 94%. Nearly 1.9% of the general prison population have been identified as TB cases (2012). Culture positive cases (SS−/C+) significantly exceeded the number of simple smear positive (SS+/C+) ones. PCR (Xpert MTB/RIF) tool has obtained a special place in the standardized TB CF algorithm in the Penitentiary Sector.

Conclusions: This investigation confirmed a good practice of the early CF. Significantly higher number of SS−/C+ cases compared to SS+/C+ indicates an early detection and epidemiologically is quite distinctive. Advancing identification procedures allows more suspects to be reached and early TB detection recorded. Moderate MMR and GenExpert use shall be deployed at the Primary health care level for prioritized groups within the MARP's in prison settings.

Isoniazid preventive therapy in congregate settings

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Background: Isoniazid preventive therapy (IPT) is an effective TB control intervention. Limited data exists about IPT implementation in congregate settings. We aimed to investigate the treatment completion rate and safety of IPT in a cohort of patients attending a substance misuse treatment centre (SMTC) in Malaysia.

Methods: The SMTC offers housing and in-house rehabilitation programme for up to 3 months for voluntarily enrolled individuals. Attendees of the centre between January–April 2012 who were enrolled in the methadone (MMT) programme and with positive tuberculin skin test (TST) were approached to participate in the study. Subjects with or suspected of having active TB were excluded from the study. Consented participants were prescribed daily isoniazid (5 mg/kg) for 6 months. Hepatic function was assessed at baseline, two weeks after IPT initiation and as required thereafter. Symptoms referring to active TB or to adverse events (AE) were assessed on a monthly basis. No incentives were offered to participants.

Results: Of the 177 individuals who fulfilled the inclusion criteria, 112 subjects were enrolled in the study. The majority of recruited subjects were men (92%), older than 35-year old (62.5%), previously injected drugs (71.4%) and had a history of an entry into a correctional institution (95.5%). Eight (7.1%) and 82 (73.2%) subjects were HIV and hepatitis C infected, respectively. Only half ($n = 57$, 50.9%) of the enrolled participants completed 180 doses of IPT. Half of the participants who stopped taking IPT cited work commitments or AE as reasons for stopping. Documented AE were responsible for stopping IPT in 9.82% of participants. Non-completers were more likely to default MMT after leaving the facility (OR 5.91, 95%CI 2.36–14.75).

Conclusions: The study revealed a low IPT completion rate in this sample, mostly due to participants' self-stopping of treatment. Interventions to improve adherence to IPT regimen need to be explored in similar settings.

Tuberculosis infection control measures in Indonesia's correctional system

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Background: Indonesia is a TB high burden and concentrated HIV epidemic country. In overcrowded prisons, HIV and TB were the first two causes of death among inmates in 2011. The Directorate General for Correction (DGC) has been collaborating with NTP and NAP to implement TB-HIV control in prisons since 2007. However, the national TB-IC guideline and self-assessment for prisons were developed and implemented in 2012.

Interventions: The best strategy of IC is early detection and treatment of TB among inmates. Adding to screening all new inmates for TB, the DGC conducted annual TB screening and treatment for all inmates since 2011. Some prisons conducted cough surveillance to detect TB. MDR-TB suspects were screened by Xpert MTB/Rif and DST and DR-TB received treatment in 5 sites in prison system with isolated cells. The prisons conducted IC assessment and improved IC emphasizing administrative measures. Triage and separation of suspects and TB patients were implemented in some prisons with distribution of masks, cough etiquette training and installation of sputum collection booths. Some prisons provided isolated cells for active TB patients.

Results: Among 434 prisons, 200 are implementing DOTS with the GF's support. In 2013 (January–June); 277 active TB were detected and treated from 1455 suspects. In 33 prisons, 65 MDR-TB suspects were detected and 12 were confirmed and 10 were treated. Among 89 prisons oriented on IC guideline, 25 of

them conducted IC assessment, developed safe sputum collection system with open space waiting areas and gave masks to coughing inmates. Among those, 18 prisons assigned isolated cells for TB patients and 12 prisons separated active TB from HIV inmates.

Conclusion: TB-IC in the prisons could be implemented with commitment and support from DGC. The strong collaboration with MoH's NTP is crucially needed as well as financial support from GF and technical assistance from the partners. It should be an integral part of TB control in prisons.

Tuberculosis in prisons: health systems strengthening for sustainability

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High rates of tuberculosis and other diseases like HIV in prisons are increasingly being recognized as both a violation of inmates' human rights as well as a broader threat to public health. In most low- and middle-income countries, however, recognition of the problem of rising disease rates has not been matched by high levels of success in controlling those problems despite known curative regimens and a captive population. Why is this so? This presentation will discuss current and alternative frameworks for thinking about prison health systems with the aim of demonstrating new ways of approaching the traditionally clinically defined problem of disease control in these settings. It will argue that successful and sustained control of TB and other infectious and non-communicable diseases in prisons will ultimately rely on a more holistic approach to health service delivery that requires application of 'systems-thinking' approach.

HEALTHY LUNGS, HEALTHY CHILDREN: USING ADVOCACY TO IMPROVE CHILD LUNG HEALTH

Child lung health advocacy: challenges and opportunities

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Lung disease is the commonest cause of morbidity and mortality in children worldwide. There is a very wide range of causes including infections and non-communicable diseases such as asthma. Pneumonia is the single biggest killer of children worldwide responsible for more than 1 million deaths each year. Tuberculosis is increasingly recognised as a common cause of child morbidity and mortality in TB endemic

countries. Lung disease is the major co-morbidity for children living with HIV. Yet, these diseases are being neglected in the global public health arena and by current research funding. A major practical challenge is that it is often difficult to confirm the cause of acute or chronic respiratory disease in young children where the greatest disease burden exists. However, data that better defines disease burden and mortality are greatly needed and are critical for effective advocacy to attract greater attention and investment. A renewed focus on child survival post-2015 that many low- and middle-income countries regard as a major health priority is an opportunity to increase and improve research and implementation strategies. Operational research that does not necessarily require sophisticated diagnostic technology, but rather employs the tools we have, has huge potential to inform improved management of lung disease in children. This presentation will provide an overview illustrated by examples of implementation strategies and the data required to support advocacy.

EDUCATIONAL AND BEHAVIOUR CHANGE APPROACHES TOWARDS TOBACCO CONTROL: A GROWING NEED

The behaviour change approach: an experience from the field in India

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Behavioral frameworks help identify determinants of desired and undesired behavior. Behavioral change involves four elements:

1 Information/education/knowledge: The education has to be based on information needs of target population to determine exactly what would make a difference. Plus other determinants of behavior are needed. All material should be easy to understand, realistic/credible, and perceived beneficial by the target population. It has to be solution-oriented and broad-based. The source of education has to be credible.

2 Motivation for action: Motivation comes from gains that individuals can expect. For educational strategy to be motivational, it must include compelling statistics.

3 Skill, the ability to act: Life skills are vital. Skills are defined as psychosocial competencies to deal with themselves and others in a pro-active and constructive way to succeed in wider society. These are: decision-making, critical thinking, communication, self-awareness and coping with stress and emotions. Some of the methods used are group discussion.

4 Enabling environments are needed to sustain new behavior.

Using the behaviour change approach in Scotland: lessons learnt

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Smoking remains the single most important preventable cause of death and inequalities in health in Scotland. However, the number of deaths is now declining. This reflects the considerable success in Scotland in recent years in reducing both smoking uptake in young people and smoking prevalence in adults. Among 15 year olds, regular cigarette smoking declined from 30% in 1996 to 13% in 2010. This presentation will critically review the action that has been taken to achieve this decline in youth smoking. Through the lens of behaviour change, it will consider the key determinants of youth smoking uptake and highlight that action was needed not only at the individual level (to reduce the desirability and acceptability of smoking among young people) but also at the family and community levels to change social norms around smoking. In addition it will consider the crucial role of changing the attitudes and behaviours of a range of key stakeholders including politicians and health professionals to enable policy action to reduce the accessibility, availability and affordability of tobacco and cigarettes for young people. This involved reducing tobacco companies ability to target children and young people with their products and marketing strategies. In conclusion, achieving behavioural change at the individual level requires action directed not only at the individual (e.g., education) but also behavioural change approaches that engage with a range of key stakeholders from the community to the national level.

Helping smokers to quit and protecting others from smoke through behavioural support

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Individual smokers and populations differ in how difficult they find it to stop smoking. In countries with high prevalence of smoking, a substantial proportion of smokers are usually not aware of the health risks of smoking and simple information and advice can generate large effects. In countries with long-running health promotion campaigns where the prevalence of smoking is now low and the remaining smokers are well aware of health risks of smoking, those still smoking tend to be people who found quitting difficult and who can benefit from more intensive treatments. The profile of the smoking population can change within the same country and this necessitates changes in treatment approaches and priorities. The presentation will illustrate these points on the examples of changes in approaches to help smokers quit in the UK over the past 40 years. It will also discuss behavioral approaches likely to be useful with smokers showing different degree of dependence, and with populations at different points of the tobacco prevalence trajectory.

The role of nurses in developing and implementing behaviour change models in tobacco control

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Since 2003, specific short training (80 hours) in tabacology has been developed in Belgium for all the health professionals. As of 1 January 2013, 292 professionals were qualified included 55 nurses and 25 midwifes. They are working in a very wide range of places (hospitals, schools, prevention area, etc.). An introduction to motivational interviewing (MI) is included in the tabacology training, we encourage all the tabagologist to be fully trained in MI. The nurses trained in tabacology have to mains activities areas: hospitals and prevention ground (i.e., schools). In hospitals specializing in tabacology nurses are directly involved for hospitalized patients in the 5A/5R application regarding tobacco control (5A: Ask, Advise, Assess, Assist, and Arrange) (5 R: Relevance, Risk, Rewards, Roadblocks, Repetition). They help smokers to stop smoking or to avoid craving symptoms when they are hospitalized and do not want to stop smoking. It is really a main 'new' function. Ambulatory consultations (with a social security paying) offer assistance to smokers, too. Moreover the tabacologist nurses are involved in training of other health professionals and help their colleagues to play this rule. A lot of decision-making algorithms were developed to organize and structure the nursing interventions; it includes 'confided (entrusted) act' for Nicotine Replacement Therapy using. In prevention areas (i.e., schools) the activities are less developed and concern, mainly, group activities regarding addictions and specially smoking. Motivational interviewing is directly used for 'all to face' communication.

ZOONOTIC TUBERCULOSIS: STILL A PUBLIC HEALTH CHALLENGE

Zoonotic tuberculosis: its challenges on diagnostics and public health in Zambia

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Introduction: Zambia has an estimated incidence of 433/100 000 of all forms of TB according to the 2013 WHO report. In Namwala, a pastoral district located in the southern province in Zambia, humans live in

direct contact with animals infected with *Mycobacterium bovis* and the consumption of unpasteurised milk and dairy products is practiced, hence increasing the risk of humans infections by *M. bovis*. In Zambia, TB diagnosis is routinely done through microscopy, a method that does not discriminate among the various members of *M. tuberculosis* complex species.

Objective: Molecular identification of members of the *M. tuberculosis* complex from pulmonary TB patients.

Design: A cross section survey was conducted in which sputum samples were collected and submitted to the laboratory for culture and molecular identification from 100 suspected pulmonary TB patients.

Results: Thirty-six of the isolates belonged to the *M. tuberculosis* complex and of these 2 were confirmed as *M. bovis* belonging to the SB 0120 Spoligotype. The other 34 were found to be *M. tuberculosis*.

Conclusion: This study highlights the public health significance of *M. bovis* isolated from sputum samples in TB patients in pastoral areas of Zambia. The need for new strategies to better prevent, diagnose, and control *M. bovis* infection in humans should be instituted. The study also highlights the importance of differentiating the causal agent of TB as part of routine diagnosis in high risk regions in order to apply a targeted treatment for those human patients suffering from zoonotic TB.

Control of zoonotic tuberculosis in Ghana within the One Health, One Medicine perspective

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Tuberculosis is a major public health problem in Ghana with annual new cases estimated to be over 52 000. It is not known what proportion of this problem is contributed through contaminated meat and milk, in which prevalence of TB by the comparative tuberculin skin test of cattle on the coastal plains alone ranges between 11.3–19.0%. Some studies done in the country also suggests 3% of human pulmonary TB cases to be due to *Mycobacterium bovis*, the causative agent of bovine TB, an infectious disease that affects cattle, man and many other domestic and wild animals. It is an important zoonotic disease with public health importance due to its transmission to humans through consumption of contaminated meat and raw milk and occasionally through inhalation. The disease has also serious economic implications due to carcass condemnation, weight loss, and loss in international trade in milk and meat products and live animals and reduction in work output of draught animals. It also leads to loss of profit due to death of animals at an early stage and lower growth rate. The disease is detected in Ghana mainly by active search—tuberculin skin test and passive search—meat inspection. With the One Health approach, the disease is being controlled by strong intersectoral collaboration between medical and veterinary professions such as joint meat inspection, extensive veterinary and health educational campaigns, screening of cattle, butchers, herdsmen and food vendors for TB, restriction of animal movement from infected areas, precautions at frontiers and strict quarantine measures.

Zoonotic tuberculosis at the human-elephant interface in the USA

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Fifty-six documented cases of *Mycobacterium tuberculosis* infection have been confirmed by culture in captive elephants in the United States since 1994. The few reported outbreak investigations have shown that humans associated with these facilities suggest both possible and documented interspecies infection occurs. Two outbreaks demonstrated skin-test conversions among the animal handlers while in one case *M. tuberculosis* strains isolated from an animal handler and 4 infected elephants were genotypically indistinguishable, although direction of transmission could not be proven. A significant risk for human exposure was found to be associated with use of high pressure spraying in the barn of an infected elephant. Between 1997 and 2013, genotyping of *M. tuberculosis* isolates from 42 elephants has been performed at the National Veterinary Services Laboratory. In all but 2 cases where successive isolates were made from the same elephant, the genotypes matched, indicating recrudescence rather than re-infection. Although elephants with shared exposure histories tended to share the same genotype of *M. tuberculosis*, some animals had rare or novel strains. There have been at least 3 confirmed drug-resistant strains of *M. tuberculosis* from elephants at initial isolation, which presents increased public health concerns. Serologic tests, which have been demonstrated to accurately diagnose infection in animals, suggest that elephants can be infected for up to 9 years prior to diagnosis by culture. These findings highlight knowledge gaps necessary to understand the risks of zoonotic TB transmission between elephants and humans.

Mycobacterium bovis infection in bovines and humans in India

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Setting: In India, tuberculosis (TB) is one of the most important zoonotic diseases, adding 1 500 000 new human cases every year and ranked amongst top ten TB burdened countries in the world by the World Health Organization (WHO). Besides, increase in number of *Mycobacterium bovis* infection over the years among human immunodeficiency virus (HIV) patients and presence of *M. tuberculosis* in animals, including wildlife is a cause of concern. However, a comprehensive study on status of bovine tuberculosis and its impact on animal and human health is lacking in India.

Objective: To define a paradigm of reemerging zoonoses of bovine tuberculosis in human-animal interface and its status in India.

Design: Techniques used include both conventional including tuberculin test, cultural isolation followed by biochemical characterization, and molecular techniques for identification of mycobacteria.

Results: Prevalence of *M. bovis* infection in human exhibiting clinical evidence of tuberculosis and that of bovine tuberculosis in healthy animals with 95% confidence intervals (CI) were 17% (13.11–20.65%), and 13% (8.13–18.15%), respectively. Further, tuberculin testing in organized farms revealed lower prevalence of TB in indigenous breeds compared to crossbred or exotic animals.

Conclusions: Control of TB in both human and animal population is required for successful eradication of tuberculosis in India. Methods like Revised National TB Control Program (RNTCP) to revitalize the human TB control is underway adopting internationally recommended DOTS strategy. On the contrary, susceptibility of animal to bovine TB due to implementation of crossbreeding programme in cattle and buffaloes is posing a huge challenge for its control. Hence, to make the national TB control programme more successful, there is an urgent need to include animal population in one-health approach.

Zoonotic tuberculosis: experience from a wildlife veterinarian in South Africa

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Bovine tuberculosis (caused by *Mycobacterium bovis*) was first recorded in Kruger National Park (KNP) in July 1990 near the south-western boundary in a diseased buffalo (Syncerus caffer). Organism typing and retrospective analyses of State Veterinary records suggest the disease entered the KNP in the late 1950s or early 1960s from a dairy herd located on the outside of the park. Regular monitoring surveys recorded increases in both incidence and prevalence of infected buffalo herds as the disease spread northwards. By 2005, the disease was detected in buffalo in the far-north of the park indicating that it had spread ± 400 km from the initial point of entry. During this period, bovine tuberculosis was detected in 11 other wildlife species; lions being the most concern important from a conservation perspective. In 2006, large sections of the fence separating KNP from the Limpopo National Park (LNP) in Mozambique were removed to allow the unrestricted movement of game between these two parks. This has raised concerns of re-exporting the disease out of KNP as a large number of rural people and their domestic stock still live a largely unchanged traditional lifestyle within LNP. The possibility of disease transfer from wildlife to domestic stock and people is increased by limited seasonal water sources utilized by cattle, goats and wildlife, and shared grazing areas. The potential for zoonotic disease transfer is also influenced by poor sanitary measures, inadequate education, limited resources for disease management, uncontrolled movements and consumption of animal products, and the HIV/AIDS epidemic in sub-Saharan Africa.

SYMPOSIA: SATURDAY 2 NOVEMBER 2013

RECENT PROGRESS IN TUBERCULOSIS CLINICAL TRIALS

Results of the Rifaquin trial

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Aim: Rifaquin is a randomised controlled trial to assess if moxifloxacin and rifapentine given intermittently in the continuation phase of a 4 or 6 month regimen is not inferior to standard treatment.

Methods: Patients with new smear-positive pulmonary tuberculosis were randomly allocated to:

1 Control regimen: 2 months daily ethambutol, isoniazid, rifampicin, and pyrazinamide followed by 4 months daily isoniazid and rifampicin.
2 4-month regimen: Isoniazid replaced by moxifloxacin in the intensive phase and 2 months of twice weekly moxifloxacin and 900 mg rifapentine.
3 6-month regimen: Isoniazid replaced by moxifloxacin in the intensive phase and 4 months of once weekly moxifloxacin and 1200 mg rifapentine.

HIV-infected patients not on ART were eligible if CD4 < 150/mm^3. Follow-up was monthly for 12 months and then 3-monthly to 18 months. The primary efficacy outcome is unfavourable status during follow-up. The primary safety outcome is occurrence of grade 3 or 4 adverse events on treatment.

Results: From August 2008 to August 2011, 827 patients were enrolled in South Africa (464), Zimbabwe (292), Botswana (56) and Zambia (15). 233 (28%) were HIV-positive, with a median CD4 count of 312/mm^3, 509 (62%) were male and median weight was 53 kg. 39 (5%) patients with initial drug resistance were excluded from both efficacy analyses. The increase in proportion unfavourable between the 4-month regimen and control was 11.8% (95%CI 3.8–19.8) in the ITT and 12.6% (95%CI 5.9–19.2) in the PP analysis. The difference between the 6-month regimen and control was −1.10% (95%CI −8.0–5.7) in the ITT and −1.0% (95%CI −5.1–3.1) in the PP analysis. 45 grade 3 or 4 adverse events were reported in 38 patients (16 on control, 12 and 17 on study regimens). Six events were hepatic.

Conclusions: The 6-month regimen with weekly 1200 mg rifapentine and moxifloxacin in the continuation phase was non-inferior to control, even at the 95% level, safe and well tolerated. The 4-month regimen was inferior to control.

The TBTC Studies 29/29X: a phase 2 evaluation of high dose rifapentine

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A major obstacle to TB control is the long treatment duration—at least 6 months—required for cure of drug-susceptible pulmonary TB. Potent TB regimens of shorter duration would facilitate treatment completion and improve individual and public health. Strategies for increasing regimen potency include the development of new drugs as well as the optimization of existing drugs. Of the drugs in current use, the rifamycins hold the most promise for treatment shortening through pharmacodynamic optimization. Rifapentine is a ring-substituted rifamycin. Compared with rifampin, rifapentine has a longer half-life and lower (more advantageous) minimum inhibitory concentration against *M. tuberculosis*. Preclinical studies using the mouse model of TB chemotherapy have shown that regimens containing daily rifapentine can achieve durable cure after only 3 months of treatment. The Tuberculosis Trials Consortium of the US Centers for Disease Control and Prevention recently has conducted a series of phase 1 and 2 clinical trials to determine the safety, tolerability, and antimicrobial activity of rifapentine, with the end goal of shortening the duration of treatment required for cure of drug-susceptible pulmonary TB. The findings from these phase 1 and 2 trials of rifapentine will be discussed and put into context.

OPTIMISING TUBERCULOSIS CONTROL IN HIGH HIV PREVALENCE SETTINGS

Introduction

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Modelling is a unique tool that can contribute to global health planning and implementation, but it requires that clear questions be asked and credible data used to build the models. While models will not provide right or wrong answers, they can provide a structure for policymakers, program managers and funders to prioritize the limited resources faced at every level of the global health architecture. To date, TB modelling has lacked co-ordination and a focus on support for country-level decision-making.

The TB Modelling and Analysis Consortium (TB MAC, www.tb-mac.org) was formed in June 2012 and aims to improve global TB control by coordinating and promoting mathematical modelling and other

quantitative research activities to provide scientific support for policy decisions and implementation. Its objectives are to: 1) identify research questions concerning TB control that require input from mathematical modelling or other quantitative research, 2) facilitate sharing of data, information and expertise to achieve consensus on knowledge gaps, standards and current best practice, 3) fund analytical/modelling research projects, and 4) disseminate results/tools to key stakeholders.

To date TB MAC has held three meetings on high priority issues: the first concerned the focus of this symposium—TB control in high HIV prevalence settings, held in Johannesburg in September 2012; the second was on the impact and cost-effectiveness of current and future diagnostics for TB, held in Amsterdam in April 2013; and the third was on the rational introduction of new drugs and drug regimens held in Beijing in September 2013.

In high HIV-burdened settings, there have been steep increases in TB incidence and standard approaches for TB control have been inadequate. Novel strategies are urgently needed. In this session, we will describe the TB-HIV Modelling Research Agenda from the first TB MAC meeting, as well as recent key modelling research projects in this area.

Tuberculosis spectrum: a model for country-level TB-HIV estimates and projections

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Objective(s): The Spectrum suite of policy tools is widely used to support national planning for HIV programs. Futures Institute has joined forces with the TB Modelling and Analysis Consortium (TB MAC), the WHO Global TB Programme, The STOP TB Partnership, UNAIDS and other partners in the TB community, to develop a similar model for TB.
Design: The model comprises two parts: the Spectrum TB Estimates (STBE) model which projects key TB indicators using cubic-spline regression techniques, and the Spectrum TB Impact (STBI) model which is a transmission model for *M. tuberculosis* infection and TB disease. Both models are integrated into Spectrum and pull in existing demographical and HIV related data from more than 150 countries.
Methods: STBE imports the existing Global TB Programme TB incidence estimates and breaks these down by HIV status. It further estimates TB mortality through the application of case-fatality ratios stratified by TB notification and HIV/ART status. STBI follows a standard TB compartmental model structure and captures primary infection, reactivation, reinfection and progression to TB disease (low and high infectiousness).

Results: The Spectrum TB Estimates (STBE) model was used successfully in 2013 to fit TB and HIV data from more than 150 countries. The results will be published in GTB and UNAIDS reports. STBI is scheduled to be available in early 2015 and will be introduced for use by representatives from National TB Programmes during workshops organised by WHO's Global TB Programme (GTB) and bi-annual regional UNAIDS workshops.
Conclusions: These Spectrum tools will provide TB professionals with the tools to project the short term course of key TB indicators, study the cost and impact of TB as well as joint HIV-TB interventions, and help improve national TB strategies with the aim of improving country TB care and control planning.

Does tuberculosis preventive therapy cure latent *M. tuberculosis* infection in HIV-infected individuals in high-burden settings? A modelling approach

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Introduction: Recent trials of isoniazid preventive therapy (IPT) for people living with HIV in southern Africa show high rates of tuberculosis (TB) disease immediately after cessation of preventive therapy. This could be due to reactivation of pre-existing infections, or reinfection followed by rapid progression to disease. We use a modelling approach to estimate the degree to which preventive therapies cure latent *M. tuberculosis* infection in HIV-infected individuals in high tuberculosis burden settings.
Methods and findings: We identified randomised controlled trials that compared IPT to placebo or alternative regimens, in HIV positive, tuberculin skin test positive study groups. A model describing tuberculosis transmission in a closed cohort of HIV-positive, *M. tuberculosis* infected individuals not taking antiretroviral therapy was fitted to post-preventive therapy TB rates to estimate the annual risk of *M. tuberculosis* reinfection and the proportion of individuals whose latent infection was cured after TB preventive therapy. Three trials met our inclusion criteria. Estimated annual risks of reinfection ranged between 3.3 and 4.5%. Our results suggest six months of isoniazid cured in a small proportion of the population (estimated proportion cured = 6.5% (0–35.4%) while three month regimens containing rifampicin or rifapentine had much higher cure rates (63%–100%.)
Conclusions: To provide long-term protection in settings with high rates of infection, continuous IPT should be integrated with other HIV care. Where reinfection rates are lower and reactivation of pre-existing infections make up a significant proportion of cases, preventive regimens with better curative potential would be advantageous for both individuals and populations.

The potential impact and cost-effectiveness of new tuberculosis vaccines

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Cost-effectiveness studies of future vaccine technologies can be used to inform candidate vaccine decisions and aid clinical trial design. Here, the impact and cost-effectiveness of different tuberculosis (TB) vaccine profiles in all low and middle-income countries was explored. An age-structured transmission model was used incorporating TB and HIV. The countries were modelled and calibrated individually, and the results aggregated by income group. The novel vaccines were assumed to prevent active disease, have 1–20 yrs or lifetime duration of protection and 20–80% efficacy. In the 'vaccine' scenario, two strategies were modelled starting in 2024: a) 'Infant': annually targeting 6 month olds, or b) 'Adolescent/ Adult': annually targeting 10-year-olds plus mass vaccination of the 11+ year olds every 10 years. Outcomes were TB cases, deaths and discounted Disability Adjusted Life Years (DALYs) averted between 2024 and 2050. Plausible ranges for TB vaccine prices at which the vaccine would be considered cost-effective were created based on uncertainty in disease burden, treatment costs and multi-drug resistant TB prevalence assumptions. Preliminary results from the 22 high burden countries suggest that, over 2024–50, 94 (71–115) million cases of TB disease and 13 (8–19) million TB deaths may occur. Even if protection were lifelong, over 2024–50 an 'Infant' vaccine may prevent less than 8% (3–10) of this burden, whilst an 'Adolescent/Adult' vaccine may prevent up to 71% (56–72). Over 2024–50, an 'Adolescent/Adult' vaccine would be cost-effective at higher vaccine prices than an 'Infant' vaccine in all scenarios. In contrast to a novel, 'Infant' TB vaccine with limited duration of protection, over 2024–50 the introduction of an 'Adolescent/Adult' vaccine may be cost-effective even at relatively high vaccine prices and could alleviate a substantial burden of disease in high burden countries before 2050.

The economics of Xpert® MTB/RIF for tuberculosis control in HIV-prevalent settings

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Background: In 2011, South Africa announced that it would roll out Xpert® MTB/RIF country-wide. This provided the basis to evaluate the impact and cost-effectiveness of Xpert MTB/RIF in a real-world setting (the XTEND study).

Methods: A model to predict Xpert MTB/RIF costs was developed to inform the treasury in planning the financing of roll-out. This modelled costs and resource requirements over a five year period from a health service perspective, using a decision analytic model previously developed to assess the cost-effectiveness of Xpert MTB/RIF introduction globally.

Findings: We identified several key economic considerations and knowledge gaps that are important to address in the economic evaluation of the scale up of Xpert MTB/RIF at the country level. These included; obtaining accurate test costs from a sufficient number of sites to better understand economies of scale during roll-out; understanding the financial impact of complementary policies, such as intensified case detection amongst those with HIV; gaining an understanding of the pathways that undiagnosed TB cases follow; the inclusion of patient costs associated with an incorrect or lack of diagnosis of TB; and finally, obtaining accurate MDR-TB treatment costs. The economic component of the XTEND study was then designed to collect data on and assess these issues. This included a comprehensive data collection process at 22 laboratories, a large patient costing effort and a broad TB-HIV health service costing. A Markov model was then developed using this empirical data to both estimate cost-effectiveness and better understand the implications of both demand side and health systems constraints on both costs and impact.

Conclusion: The economics of Xpert MTB/RIF for TB control in HIV-prevalent settings can be informed by modelling, but needs to take account of 'real world' constraints, in particular the impact on patient costs and broader health system factors.

ACCELERATING SCALE-UP: RAPID AMPLIFICATION OF PMDT CAPACITY

Kazakhstan: universal access to MDR diagnosis and treatment

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Introduction: The control over tuberculosis in Kazakhstan is one of the priority goals in the activity of Ministry of Health and it is implemented in accordance with the State Programme 'Salamatty Kazakhstan'. It is due to the high prevalence of multidrug-resistant tuberculosis (MDR-TB). Thus, in 2011 rate of MDR-TB constituted 19.1% while percentage of the acquired resistance was 53.3%.

Materials and methods: There were implemented the high specific molecular genetic methods BACTEC

MGIT-960, Hain-test, GXpert in the country that impact greatly on increase in number of newly detected patients with MDR-TB. In 2011 there were covered with drug sensibility testing 98.2% of new TB cases and 98.9% of TB relapses. In all regions practice of social support and incentives for TB patients is realized. Jointly with penitentiary system mechanism of transferring TB prisoners to the civil sector at discharge is elaborated.

Results: Through joint activity of anti-TB service, primary health care, AIDS Centers and penitentiary system main indicators of TB incidence and TB mortality were decreased in 2012 compared with 2011. TB incidence decrease constituted 9.1% (86.0 versus 94.6 per 100 000). Decrease of TB mortality constituted 14.0% (7.4 in 2012 versus 8.6 in 2011 per 100 000).

Conclusion: Strong political support of TB services is the primordial condition to realize the anti TB policies. Joint activity of all Departments participating in the detection, treatment, medical and social support to TB patients will lead to reduce TB infection pull in the country.

Moldova: great solutions in a small country

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Setting: Penitentiary system of Republic of Moldova including 18 institutions with the capacity of 7980 places, annual average population of 17 500 inmates.

Objective: Evaluation of the TB control and prophylaxis programme in prisons of Moldova (2006–2012)

Method: Retrospective data analysis of the National TB Monitoring and Evaluation system.

Results: TB has decreased in the penitentiary system at a much faster pace than in the civil sector (11% annually over the last 5 years in PS vs −2.6% in the CS). This is on the one hand due to the decrease in the number of people incarcerated (−26% since 2004), but certainly also the result of successful TB control interventions by the Medical Division of the Department of Penitentiary Institutions (DPI) supported by the National TB programme and national and international NGOs.

Conclusions: Since the initiation of the first DOTS project in the country, Moldovan Prison Authorities continuously demonstrated high commitment for building a comprehensive strategy for TB control by ensuring: active screening and rapid methods for TB diagnosis of 99.5% of prison population, universal access to TB treatment (DOTS and DOTS+ treatment), multidisciplinary approach of the TB case management (providing incentives, psychological

counseling, follow-up of released prisoners), infection control measures and functionality of the Integrated TB Evaluation and Monitoring system. Integration into the National TB Programme and openness for collaboration with NGOs made possible the achievement of the actual results.

Mobilising stakeholder coalitions for integrated supply planning and quantification of tuberculosis medicine

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Background: Effective drug supply and management system is listed among the first component of the Stop TB strategy. There is an expectation for a reliable system of procurement and distribution of essential anti-TB drugs including a functional recording and reporting system designed to provide the information needed to plan, procure, distribute and maintain adequate stock of drugs. Yet, documented experiences on the operational processes and challenges overcome are scant. Failure to have timely planning, identification of financial gap, resource mobilization, procurement and distribution of commodities will affect country's TB treatment objectives.

Aim: Describe the annual quantification, financial mobilization and procurement planning process as critical processes to ensure uninterrupted supply of TB commodities.

Design: Step 1: Identification and notification of the key partners who form the DLTLD commodity security committee. Step 2: One day pre-quantification meeting with various stakeholders to build key assumptions for quantification. Step 3: Three days quantification and report finalization exercise. Both morbidity and consumption data was utilized in establishing the requirements of the TB commodities.

Results: 2011–2013 quantification report done and the financial gap identified. About 88% ($13 million) of funding needed was committed from the government and development partners with 11.8% ($1.6 million) funding gap realized. The DLTLD procured TB medicines and buffer for the FY 2013–15. In 2012, the government used the quantification report to obtain a loan of US$3.8 million from the World Bank (KHSSP) which was used to procure first and second line TB medicines buffer stocks for 2013–15.

Conclusion: Establishment of a commodity security committee led to a timely quantification and procurement planning. However, to secure financial resources timely notification of the key partners and follow-up of partners' financial commitments was needed.

Supply chain challenges in scaling-up a decentralised MDR-TB programme

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Background: In Tanzania 1.1% of the new cases and 3.1% of retreatment cases were notified MDR-TB. MDR-TB management was inaugurated in November 2009 at Kibong'oto National TB Hospital (KNTH). The management protocol follows a 18–24 months treatment course. The intensive phase of about 8 months is at KNTH and the continuation phase of about 12 months takes place in the respective DOT facilities close to the patient's home. The procurement of MDR-TB medicines is funded by the government and partners through the Medical Stores Department (MSD) and the consignment delivered directly to KNTH.

Objective: To describe challenges in the design and implementation of supply chain of decentralized MDR-TB program in a resource-constrained setting.

Methods: Review of secondary data from MDR-TB quarterly and cohort reports; and medicines management reports from facilities managing MDR-TB cases.

Results: The total number of MDR-TB cases remains small (Figure), however, there has been a steady increase of cases treated each year and are spread all over 21 regions of Tanzania. Once cases are discharged to their respective DOT treatment facilities for continuation phase, KNTH is responsible for the distribution of MDR-TB medicines using aggregated orders received from districts. Unlike the distribution from MSD to KNHT, there is no allocated budget to cover the cost of distribution from KNTH to districts. KNTH staff use public transport to deliver medicine during supportive supervision. The knowledge and skills of staffs on MDR-TB treatment guideline and commodity management is not adequate resulting in poor inventory reports and inadequate quantities delivered to DOT centers.

Conclusion: The assured supply of MDR-TB medicines is important to avoid any interruption to treatment. For the decentralized MDR-TB management to be successful, KNHT need to be well funded to manage and support districts on all areas of supply and commodities management.

Figure Trend of patients received/receiving MDR-TB treatment, 2009–2012, Tanzania.

ROLLING-OUT LED FLUORESCENCE MICROSCOPY: YIELD AND CHALLENGES

The problem of a gold standard when few tuberculosis bacilli are present

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Two years after the WHO endorsement of LED-fluorescence microscopy (FM) (2009), only 2% of microscopy laboratories are using LED-FM (2012 WHO global TB report) despite its increased sensitivity and decreased workload, as compared to the light Ziehl-Neelsen microscopy. One of the reasons that could explain the slow introduction is the lack of confidence in the LED-FM technique due to the risk of false positive results.

Thanks to the fluorescence and the larger screening of the smear, the LED-FM is able to detect very low positive results (scanty) that would not be detected by Ziehl-Neelsen microscopy, which explains the 10% average gain of sensitivity. However, the specificity results of the LED-FM are discordant across the studies and a large multicentric trial has shown a reduction of specificity of 5% (94.1%, 95%CI 86.4–88.1) as compared to Ziehl-Neelsen microscopy (98.4%, 95%CI 98–98.7). Some 'false positive' results might be wrongly classified due to the imperfect *Mycobacterium tuberculosis* culture Gold standard (GS) used in most studies. Indeed, the killing effect of sample decontamination during specimen processing may lead to false negative culture results, particularly for very paucibacillary samples.

Through a review of published and unpublished studies of the performance of the LED-FM, we try to identify the factors that may explain the variation of specificity across studies with a particular focus on the GS used in the different studies and the approaches used by the researchers to overcome the problem of imperfect GS. We also discuss different ways to address the limitation of the culture GS for paucibacillary specimens, such as the use of a composite GS, the external review of discordant results and the statistical correction methods for imperfect GS.

A new quantification scale for fluorescence AFB microscopy

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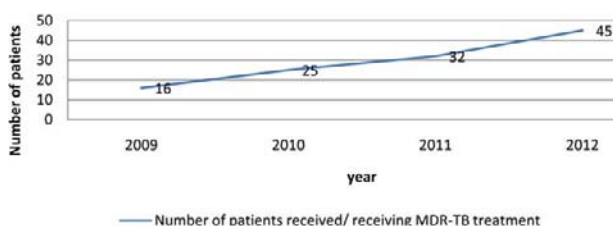
Grading systems for AFB microscopy serve a number of key functions in modern tuberculosis programs, including quantifying sputum bacillary load for clinical and programmatic risk stratification and facilitating quality control. Standardization of grading scales ensures diagnostic accuracy and reproducibility across the population of patients being evaluated for TB. The recent introduction of low-cost LED fluorescence microscopes and WHO's endorsement of their use offers the potential to transform the speed and sensitivity of sputum smear microscopy in high-burden settings, but the use of non-traditional magnification objectives ($20\times$ and $40\times$, instead of the traditional $25\times$) demands an update to the traditional grading scale, which the Union has recently provided. We will discuss the scientific basis of this new grading scale and review its particulars.

Studies on LED FM staining variations and shelf life

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We compared the two best documented LED fluorescence microscopes, Zeiss Primostar iLED and Olympus CX21™/FRAEN FluoLED, differing considerably in background luminosity and possibly technician acceptance, together with staining variations. The multicentric study was performed by Damien Foundation Bangladesh. The first phases used blinded reading on both instruments in 8 routine laboratories, the last phase comparing destaining/counterstaining techniques was performed in 30 laboratories on one instrument. Reference laboratory rechecking of restained discordant series provided the gold standard. Shelf life was checked for new working solutions from $10\times$ concentrated auramine stock in alcohol or alcohol/phenol prepared 3-monthly at the reference laboratory, with staining of positive control smears monthly to quarterly. Exactly 9.6% AFB-positives and the same error rates were registered for both instruments on almost 65 000 smears read in duplicate. The stronger 0.3% auramine-O formulation did not perform better, while Thiazine red counterstaining resulted in non-significantly more false positive and false negative results. Combined destaining/counterstaining was significantly less good, but destaining with 1% HCl/10% alcohol in water showed equivalent results. More than half the instruments of both brands broke down at least once. Auramine stocks kept in the dark at ambient temperature retained full activity for more than 12 months. We conclude that auramine staining variations are not better than standard technique, but 10% alcohol is enough for destaining. The policy to bring down prices and quality of the microscopes must be abandoned.

AIRBORNE DATA: OPPORTUNITIES FOR ELECTRONIC HEALTH TO IMPROVE TUBERCULOSIS CARE AND LUNG HEALTH

Bringing treatment results faster to patients with drug-resistant tuberculosis (Cameroon and Nepal)

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Setting: In Nepal, a TB REACH funded project being run in eastern Nepal by the International Organization for Migration using Xpert® MTB/RIF tests. Through the Cameroon EXPAND-TB Project, WHO funded an open-source web-based application running on Ubuntu for rapid transfer of MDR-TB patient results to diagnostic centres.

Objective: To reduce the time taken to transfer test results to patients, caregivers, and program managers and ease reporting of TB and MDR-TB cases.

Methods: In Nepal, software (XpertSMS) was set up to automatically harvest results from GeneXpert machines and transfer them to a central server over the Internet or SMS. XpertSMS allowed results to be transferred on test completion and also retrospective transfer for older test results. The data included details of the machine, module, and cartridge used to perform the test, as well as error codes. In Cameroon, software was developed based on the standard laboratory request form. Results are entered and validated in the lab and immediately viewable at diagnostic and treatment centres, and NTP. The results include direct examination, line probe assay, Xpert MTB/RIF, culture and drug susceptibility testing.

Results: In Nepal between March and June 2013, XpertSMS has been deployed at all nine sites for the project. 1560 test results collected of which 20 were rifampicin resistant. XpertSMS enabled providers to start patients on treatment within a day. The software helped monitor GeneXpert sites remotely. In Cameroon, after training and 2 months trial, the software is running in 3 regions. During quarter 2, 1656 patients were tested and 49 were detected MDR.

Conclusion: The two technologies can be utilised effectively to bring test results faster to TB and DR-TB patients in low-resource settings. The use of such software will allow faster reporting of test results, expected to lead to a reduced time to treatment. Future evaluation of these efforts will be useful to help improve their performance.

Use of smart phones for supportive tuberculosis supervision: collaboration for rapid scale-up

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Background: Based on in-country consultations, capacity to provide high-quality TB and TB-HIV 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: To 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 proposed a pilot 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 unto 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 h per facility using the smart phones compared to 4 h 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 2011 to 85% in 2012 reporting year, for cases registered in the previous year.
Conclusions: NTP through support of other partners should adopt and scale up the use of smart phones for supervision nationwide.

Mobile technology in asthma care: the potential of incorporating a set of long-term impact indicators and short-term sustainability strategies

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The potential of mobile technology is evident from the growing worldwide momentum and enthusiasm to capitalise on improvements in telecommunications and rapid uptake of mobile technologies to strengthen health care systems. Mobile Health (mHealth) applications promise to revolutionise health services in developed as well as developing countries. While Africa reports the least activity, there are notable examples on the uses of mobile technologies for emergency and disaster situations, health call centres for specific diseases, SMS and voice mail for treatment compliance and health promotion. This paper reports on an asthma follow-up system being developed at Epi-Lab as part of a pilot asthma management system in Gezera State. The pilot was started following a situation analysis that found asthma to be the third most common cause for hospitalisation in Sudan after malaria and pneumonia. The aim of the mHealth application is two-fold. First, to provide real-time data collection and analysis capabilities to the existing asthma management system that uses register book and telephone call as means for follow-up; and second to assess the effectiveness of the system in terms of health outcomes and cost, as well as the appropriateness of m-solutions in local context. While commonly used evaluation criteria and dissemination methods for public health interventions are defined for this project, a set of 'long-term' indicators and 'short-term' sustainability strategies are incorporated in the project design. The author argues that in the absence of an empowered civil society and weakness of basic services, sustainability of proven-solutions in developing (and autocratic) countries may need to consider community-led, small-scale and self-sustaining project design strategies; to include indicators of impact on local economic activity, human labour and skills; and to find ways of assimilating the project's service within the existing social networks and grass-roots mobilisation.

Where are the tuberculosis cases? Electronic notification and geospatial data analysis in high burden settings

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New tools to collect and analyze spatial data offer exciting opportunities to leverage information about the geographic locations of TB patients to more precisely target control efforts and to focus studies within areas of particular concern. Here, we present several recent examples of how we have used information about the spatial distribution of TB patients to address questions related to the emergence, transmission, and control of MDR-TB. We conclude by offering a perspective on how investing in electronic notification of TB (with location information) can help tuberculosis control programs meet short- and long-term goals.

MEASURING THE CONTRIBUTION OF ACSM TO INCREASED TUBERCULOSIS CASE DETECTION AND IMPROVED TREATMENT OUTCOMES

Gap analysis of major barriers to effective tuberculosis diagnosis and treatment

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Success in TB diagnosis and treatment requires specific behaviors from the patient and health care providers, as well as a supportive environment. There are many reasons (barriers) which influence these behaviors and, thus, contribute to delays in diagnosis and starting or completing TB treatment. From Cough-to-Cure: A Path of Ideal Behaviors in Tuberculosis Control (developed by AED) helps identify specific barriers, and, therefore, informs the design of ACSM interventions to address them. It is important not to make assumptions but to assess available data, and when necessary, to conduct qualitative and quantitative research, to determine specific barriers and identify target audiences to address them.

PATH incorporated the Cough-to-Cure tool and developed the following model for designing effective ACSM interventions to increase case detection and improve treatment outcomes:

1 Analyse national TB programme objectives and targets and compare with TB programme data. Identify priority TB control challenges to address through ACSM.
2 Link selected TB control challenges with appropriate NTP goal and objective.
3 Use the Cough-to-Cure Pathway and conduct ACSM needs assessment to identify and prioritise barriers to be addressed with ACSM activities.
4 Develop a SMART ACSM objective.
5 Identify ACSM intervention(s) that will help to eliminate barrier(s).
6 Determine indicators to measure success and develop an M&E plan.
7 Implement and monitor ACSM activities.
8 Conduct an evaluation.
9 Plan for the next phase of activities based on evaluation results.

Linking ACSM activities with TB control challenges, barriers, and NTP goals and specific objectives helps assess the outcomes of ACSM activities and their contribution to TB diagnosis and treatment targets, applying results to improve ACSM interventions.

Developing ACSM monitoring and evaluation plans

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The successful use of monitoring and evaluation (M&E) to demonstrate the contribution of ACSM to TB programmes depends on the development of comprehensive M&E plans based on sound analysis of programmatic gaps. M&E activities are a critical component of ACSM planning and implementation because they help identify what is working well, unexpected results, and areas that may need further investment or support in order to accomplish goals. The presentation will demonstrate links between gap analysis results, strategies and action plans to support ACSM and set the stage for practical examples of ACSM planning and use of M&E data to support ACSM activities. It will cover key components of M&E planning to support ACSM activities, with a focus on M&E frameworks, indicators and the overall structure of the M&E plan. The discussion of M&E frameworks will include an overview of inputs, processes, outputs, outcomes and impact and how these components can be used to highlight the contribution of ACSM to National TB Programme goals and objectives. The presenter will demonstrate how different types of indicators can be used to track both implementation of ACSM activities and key results and summarise issues to be considered when choosing indicators, including the need to identify routine data sources and ensure validity and reliability of measurement.

The ACSM monitoring and evaluation toolkit and telling your ACSM story

S Okromeshko. HIV/AIDS & TB Global Program, PATH, Washington, DC, USA

Advocacy, communication, and social mobilisation (ACSM) includes a set of cross-cutting activities that are relevant to all aspects of the Stop TB Strategy. ACSM activities should be integrated into the national TB programme (NTP) strategic plans and proposals to reinforce the idea that advocacy, communication, and social mobilisation are not an end in themselves, but tools to achieve specific NTP objectives. The focus should be on measuring the impact resulting from the activities, such as additional cases detected or additional cases cured.

Stakeholders, including NTP managers, ACSM coordinators, M&E officers, technical partners, Global Fund recipients, civil society organisations at all levels, and donors, need to know how ACSM is contributing to desired prevention, detection, and treatment outcomes so they can refine strategies and activities, effectively allocate resources, and build an evidence base for ACSM best practices. Conducting better M&E of ACSM interventions has been identified as a key need of the global TB community.

With funding from the US Agency for International Development, and in collaboration with the Stop TB Partnership and other partners, PATH developed the

following new ACSM M&E tools endorsed by the Stop TB Partnership for global use:

- The *Guide to Monitoring and Evaluation of Advocacy, Communication, and Social Mobilization to Support Tuberculosis Prevention and Care* to help strengthen routine M&E of ACSM activities.
- An accompanying five-day training curriculum, *Monitoring and Evaluation of Advocacy, Communication and Social Mobilization Interventions to Support TB Prevention and Care* to build capacity for rigorous monitoring and evaluation of ACSM activities.

To download all of PATH's ACSM tools, please visit us at www.path.org.

Tanzania: monitoring and evaluation of community-based efforts to support HIV/TB integration

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Background: Engaging communities is important for improving health outcomes and the performance of health systems. Involving communities in the fight against TB has the potential to increase awareness and reduce stigma so people are more likely to access facilities for TB diagnosis. With support from the United States Agency for International Development (USAID), PATH piloted strategies to engage community members in support of TB control.

Methods: In collaboration with the National TB and Leprosy Program, PATH worked with Council Health Management Teams (CHMTs) in Kisarawe District to identify community members, such as traditional healers, former TB patients, and private drug sellers to help create community awareness on TB and TB/HIV through theatre and dance, screening for TB symptoms, referrals to people with presumptive TB, and sputum fixing and transport. In total, 397 people were trained to support the work. We conducted routine monitoring to determine the progress of ongoing community interventions and an evaluation of effectiveness of work in Kisarawe.

Results: From 2009 to 2011, there was an increase of TB cases in Kisarawe district while TB case notification nationally decreased. These results prompted scale-up of community interventions to 35 districts in PATH-supported regions. Data indicate that the results of the six month period after scale-up are comparable to the full year prior: nearly the same results were achieved in half the time.

Conclusion: Community stakeholders can help the national program expand TB prevention care and control. Advocacy in terms of sensitization of the CHMT district leadership is important for gaining support for community-based interventions.

India: monitoring and evaluation of chemist identification and referral of possible tuberculosis cases

S Kaipilyawar. PATH, New Delhi, India

Background: India has the highest TB burden in the world, accounting for one-fifth of all new TB cases and two-thirds of the cases in South and South-East Asia. Involvement of the private sector in case detection, TB awareness and prevention, and promotion of safe and effective TB treatment practices is vital to the continued success of India's Revised National TB Control Programme.

Description: The chemist pilot project was carried out from July 2010 through March 2011 in the state of Andhra Pradesh in collaboration with the State TB Office, the Prakasam District TB Control Office, and the Ongole Chemists and Druggists Association. Its purpose was to:

- Actively involve private chemists to identify those presumed to have TB and refer them to government Designated Microscopy Centers (DMCs) for diagnosis and treatment.
- Train participating chemists to promote community-level awareness about TB prevention.
- Reduce the sale of TB drugs without a prescription.

PATH assessed the pilot in April 2011, using interviews with chemists, knowledge assessments of trained and untrained chemists, and recorded reviews at chemist shops and DMCs.

Results: Of the 60 chemists and druggists trained, 32 (53 percent) referred at least one client. The average number of referrals for the chemists and druggists who were referring was four, with a range from 1 to 28. One hundred and seventeen TB suspects were referred by chemists, and 104 (89 percent) actually went to and were served at a DMC. Six cases of TB were detected from these 104 referrals, an increase of 2.4 percent in case detection for 3 DMCs.

Recommendations: Interventions should be tailored to the education level of those involved. While the pilot indicated that chemists could make a notable contribution, a greater understanding of treatment-seeking behavior is required to determine whether the involvement of chemists will be beneficial in a particular site.

Mexico: monitoring and evaluation of integrated ACSM and public-private mix activities

J A Martinez. Consultant, Queretaro, Mexico

Background: Tuberculosis, particularly drug-resistant TB, remains a serious health challenge in Mexico. Many private providers, who manage nearly 35% of TB cases, do not adequately screen for TB or routinely refer patients or follow national guidelines for diagnosis, which has resulted in low case detection

and diagnostic delays. Varying levels of commitment to PPM means that mobilizing diverse private providers in support of NTP objectives is an urgent need.

Description: A gap analysis was conducted in 12 priority states to identify specific barriers which prevent private providers from routine screening and timely referral of those presumed to have TB for diagnosis and treatment. Based on the gap analysis, action plans (including M&E plans) were developed and key indicators monitored. ACSM was identified as an efficient way to establish PPM partnerships which involved bringing together diverse providers in each state, documenting their commitment to DOTS, and providing training on implementation of quality DOTS.

Results: Between 2010 and 2012, providers receiving PPM support, on average conducted 39.3% more sputum examinations for people with respiratory symptoms. The number of positive TB cases detected by supported facilities increased by an average of 28% over the same time period. By the second year of the project, referrals of those presumed to have TB to NTP facilities increased from 40% to 95% among PPM network facilities (hospital to primary health care).

Recommendations: A gap analysis should be undertaken to develop tailored ACSM objectives, action plans, outputs, outcomes, and indicators that support PPM contributions to NTP objectives. Providers should be encouraged to generate information that increases demand for health services, and results should be used to inform and expand future PPM and ACSM activities.

FEASIBILITY OF SUPPLY-SIDE MEASURE FOR TOBACCO'S ENDGAME

Industry arguments against endgames

B Bellew, A Jones. Tobacco Control, The Union, Edinburgh, UK

The core supply reduction provisions in the WHO FCTC are contained in the Articles 15 through 17. These provisions cover the following domains:
- Illicit trade in tobacco products;
- Sales to and by minors; and,
- Provision of support for economically viable alternative activities.

This presentation will bring the audience up to date regarding:
1 Problems we currently face around the world with respect to the three domains identified
2 Recent work and progress in progressing the implementation of the WHO FCTC Articles 15 through 17.

The presentation will conclude with a feasibility assessment of the 'tobacco endgame' taking account of the update.

Subsidising the tobacco industry

P Lal. The Union South-East Asia Office, International Union Against Tuberculosis and Lung Disease, New Delhi, India

Tobacco and tobacco products are extremely affordable and widely accessible to all developing countries. The entire lifecycle of tobacco products is heavily subsidised—with low minimum wages for workers, heavy subsidies on input materials, access to public finance, and tax waivers for manufacturers. These incentives by the government keep production costs of tobacco products low, making them highly affordable to its users and profitable to its manufacturers. Such incentives are perverse as they fail to account for the full economic, social and environmental costs. These factors driving the lifecycle of tobacco and facilitating its production also limit the effectiveness of demand-side strategies to combat the prevalence of tobacco use. Increasing taxes, in particular, fails to induce any perceptible changes on retail prices of tobacco products. As input and manufacturing costs are kept artificially low, even significant tax increases do not translate into corresponding price increases and cuts to manufacturers' profits are nil or negligible. At the same time, governments are often reluctant to increase taxes drastically as it appears unethical to benefit from sin taxes. Additionally, tobacco industry has easy access to public funds and no restrictions which prevent capital flight.

Using India as a case in point, this presentation makes the argument that taxes will be effective only if several corrections are made across the supply side of the product lifecycle. It will analyse the political economy of the smoked and chewed tobacco products and suggest potential strategies to make demand-side strategies more effective. Three potential interventions are proposed to reduce tobacco industry's financial clout. First, eliminate all subsidies and bring in price corrections; two, eliminate access to public funds; and three, prevent capital flight of all tobacco companies from within a country, and across domains.

Gutkha Ban in India: a first step towards an endgame for tobacco in India?

R Kumar. Tobacco Control Unit, The Union South-East Asia, New Delhi, India

Background: Smokeless tobacco (including gutkha) use is a big menace in India. The number of users of smokeless tobacco products (25.6%) is more than double the number of smokers in India. Food Safety and Standards regulations 2011 became a new weapon to eliminate gutkha, pan masala with nicotine and such other tobacco products.

Interventions: Gutkha was considered a food product. Madhya Pradesh became the first state in India to ban the gutkha on April 1, 2012. The FSSA regulations put a ban on manufacturing, trade, sale and use

of gutkha. Now ban is imposed by all other 28 states in India.

Results: Gutkha industries imposed several litigations across different courts of law including apex court of India, but failed. The implementation of the ban is variable across states. Enforcement is suboptimal and lacks planning. Industry is adopting new tactics to carry on the business. Gutkha is virtually available in another name or package; hence defying purpose of the ban.

Conclusions and recommendations: The gutka ban imposed by Indian states can be considered as India's first step towards tobacco endgame. However, ban must be covering all form of smokeless tobacco. Strict enforcement for law implementation must be ensured Indian judiciary's active pro-active stand for protecting people from tobacco harms must be tapped. There is a need of developing multi-sectoral partnerships to plan for the tobacco endgame, where health departments can take the lead.

How can countries use international treaties to protect their citizens from tobacco industry tact

A Jacob. International Union Against Tuberculosis and Lung Disease, New Delhi, Delhi, India

The fight against tobacco is essentially the fight for protecting the rights of individuals to lead a healthy life with human dignity. This is enshrined in various treaties and international human rights conventions, committed to by the comity of nations. Including but not limited to these conventions, sovereign states are provided sufficient 'flexibilities' to so exercise their right to protect their people.

Nevertheless, a number of pressures operate upon sovereign states to engage in a 'race to the bottom' to attract foreign capital. States have resorted to reducing non-tariff barriers, engaging in structural adjustment programmes, rationalizing health expenditures to signal their openness to capital, but at the expense of the health of their citizens. In this context, the tobacco industry remains an influential actor in OECD political systems and has the capacity to influence the agenda of free trade agreements, bilateral investment treaties and so on to retain market access to the growth markets of the South.

Recent international litigation throws light on the nature of the instruments that states can draw upon to ensure that they retain their right to legislate in the public interest notwithstanding commitments made under bilateral, regional or multilateral treaties. Doing so requires creative extensions of provisions of existing international law and fair and transparent legislative processes at the domestic level. Mini case studies of recent events will illuminate this contention and thereby encourage states to utilize existing provisions for legitimate public health needs.

DIAGNOSTIC AND THERAPEUTIC CHALLENGES FOR LATENT TUBERCULOSIS INFECTION

The predictive value of interferon-gamma release assay conversions

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Given the present lack of effective vaccines against tuberculosis (TB), the accuracy of screening tests for determining or excluding latent TB infection (LTBI) is a cornerstone of effective TB control. In a recent meta-analysis, prospective cohort studies were investigated with respect to the positive and the negative predictive value (PPV and NPV) from a test-determined LTBI state for progression to active TB of interferon-gamma release assays (IGRAs) and the tuberculin skin test (TST).

The PPV and NPV for progression of commercial and 'in-house' IGRAs and the TST for persons not receiving preventive treatment (PT) in the context of the respective IGRA studies were pooled and weighted rates were calculated for all study populations and for groups at high risk of TB development solely.

The pooled PPV for progression for all studies using commercial IGRAs was 2.7% [95%CI 2.3–3.2] compared with 1.5% [95%CI 1.2–1.7] for the TST [$P < 0.0001$]. The PPV showed a modest increase to 6.8% [95%CI 5.6–8.3] and 2.4% [95%CI 1.9–2.9] for the IGRAs and the TST respectively when only high-risk groups were considered [$P < 0.0001$].

In contrast, pooled values of NPV for progression for both IGRAs and the TST were very high at 99.7% [95%CI 99.5–99.8] and 99.4% [95%CI 99.2–99.5], although significantly higher for IGRAs [$P < 0.01$].

In conclusion, commercial IGRAs have a higher PPV and NPV for progression to active TB compared to those of the TST, especially when performed in high-risk persons. However, none of the currently available tests for LTBI can accurately predict who will develop active TB.

A new approach to preventive therapy provision: results of a cluster randomised trial in Kenya

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Setting: Kenya, where the dual burden of TB and HIV is high. Uptake of IPT in this setting has been low.

Background: People living with HIV are at increased risk of TB disease. Isoniazid given for not less than six months has been documented to reduce the risk of TB in PLHIV, however for a variety of reasons the uptake of IPT has been low. We set out to determine if it was feasible and safe to implement a household based targeted TB screening and provision of IPT in the setting of a national TB control program in Kenya, a low income country with a high burden of TB-HIV.

Methods: This was a pragmatic clinical trial. New smear-positive HIV infected patients were enrolled from a total of 18 facilities (9 intervention and 9 control sites), across Kenya. In the intervention sites new smear-positive HIV-infected PTB patients were recruited and followed by lay community health care workers to their homes. Household contacts of these index patients were enumerated and screened for TB using a symptom questionnaire. Contacts without symptoms of TB were provided with IPT and monitored for the development of TB, adverse events and adherence. In the control sites current policy recommendations were adopted in which household contacts were requested via the index cases to report for TB screening and IPT provision. One month after recruitment of the index case, contacts were visited at their homes and, as in the intervention group, enumerated and followed up monthly for observation of TB symptoms. All contacts were also offered HIV testing.

Results: A total of 359 index cases were recruited leading to the identification of a total 1259 contacts of whom 613 were in the intervention and 646 in the control group. Of the 646 contacts in the intervention group, 641 (99%) started IPT as opposed to 53 (8.6%) of 613 contacts in the control group ($P < 0.0001$). The IPT completion rate was in excess of 92% in both groups. There were 10 cases of TB in the control group as opposed to 1 case in the intervention group. There were no serious adverse events reported.

Conclusion: The provision of IPT at the household level using lay community health care workers is feasible and safe and should be included in the package of care constituting the management of contacts of HIV infected PTB patients.

ENGAGING PHARMACISTS FOR TUBERCULOSIS CONTROL: RHETORIC OR REALITY?

Pharmacy involvement in tuberculosis control: the journey made and milestones to be accomplished

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Background: The Stop TB Strategy's "Engage all care providers" component underscores the importance of involving a wide variety of private sector providers, including pharmacists and pharmacy associations. In recognition of the role of pharmacists in TB prevention and care, the WHO and the International Pharmaceutical Federation's joint statement in September 2011 provided impetus for engagement with a country's pharmacy-based stakeholders. However, the extent to which the intent of pharmacy engagement has been translated into a country's policy and programmatic interventions is unclear.

Methods: We undertook a systematic review of the peer-reviewed literature indexed in PubMed and grey-literature using Google Scholar search. Our search expanded to include 1) PPM sub-group meeting minutes, reports and documentation, 2) past Union conference abstract books, 3) WHO annual TB reports, 4) strategy documents/action plans from the 22 high-burden countries and 5) relevant WHO/Stop TB high-level meetings and reports.

Interim findings: We found studies from only three countries in the peer-reviewed literature, clearly documenting the impact of pharmacy engagement on TB case detection and referral. There are several publications that examine the sale of anti-TB medicines but interpretation of data is limited to recommendations of private pharmacy engagement or regulatory policy options to limit dispensing. From past Union conferences, there are a number of abstracts from various countries that provide results of interventions from private pharmacies. We find that engagement of private pharmacies as part of the country's overall PPM strategy has gained traction in the last three years. Regulatory policy options to limit the sale of non-prescription anti-TB medicines must complement PPM strategies. Synthesis and content analysis of various documents found in our search is ongoing. Key findings with recommendations will be presented in the symposium.

Engaging the retail pharmacies and accredited drug outlets for tuberculosis case detection in Tanzania

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Background: The Tanzania National TB and Leprosy Program 2009–2015 strategic plan identifies as a priority private sector provider's engagement to improve TB case finding through innovative approaches to shorten delays in TB treatment initiation and improve treatment outcomes.

Objectives: A study was conducted to characterise accredited drug dispensing outlets (ADDOs) and pharmacies dispenser's level of TB awareness and assess

the availability of first and second-line TB treatment. The study was the first step in the design of the intervention to engage the retail pharmaceutical sector.

Design: A cross-sectional descriptive study design that involved administration of the questionnaire to drug dispensers in randomly selected 122 pharmacies and 173 ADDOs in Dar es Salaam and Morogoro region respectively.

Results: About 95% of dispensers knew that persistent cough is a TB symptom and only 30% knew about drug-resistant TB. Both pharmacies and ADDOs stocked first line anti-TB medicines (none was in fixed-dose combination) which are legally restricted to be sold at retail outlets. Only 1% of dispensers had received any TB related training in the past three years. The majority (63%) of dispensers in both pharmacies and ADDOs reported to come across with clients presenting with TB symptoms. In addition, pharmacies and ADDOs dispensers were trained and received communication materials with TB messages.

Conclusion: Retail pharmaceutical outlets can potentially contribute to TB case detection and treatment, but a coordinated effort is needed to train dispensers and put appropriate TB suspect referral procedures in place. Preliminary results indicate increased referral and TB cases detected. NTLP is currently undertaking a final evaluation to disseminate and if successful scale up nationwide.

Harnessing the popularity of chemists in high-burden tuberculosis settings in Pakistan's four urban areas

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Background: An estimated 70% of people in Pakistan seek health care from private facilities. While successful PPM interventions already exist with general practitioners, NGO hospitals, and other private clinics, there has been a lack of engagement with retail chemists. However, the NTP views the engagement of chemists as critical, particularly as it seeks regulatory action to ban the over the counter sale of TB medicines by chemists.

Objectives: To engage retail chemists in early identification of clients with TB-like symptoms and referral to TB diagnostic centers for adequate treatment. To enhance the skillset of chemists to ensure that provision of treatment is in accordance with NTP guidelines when presented with a prescription.

Design: Cross-sectional baseline study using a questionnaire to assess provider's knowledge on TB and availability of TB medicine for 150 retail chemists in Islamabad, Rawalpindi, Peshawar and Lahore.

Findings and next steps: The most frequently available TB medicines were in fixed-dose combination (Figure). However, only 22% of providers have ever heard of NTP and only 2% have received any kind of training on TB in the past two years. The NTP designed an innovative approach to training and established referral linkages between retail chemists and TB DOT centers to improve case detection and appropriate dispensing of TB medicines. The limited availability of educational material and insufficient record-keeping will be addressed. Evidence on the extent to which a pharmacy-centric model contributes to enhanced TB case detection will be generated.
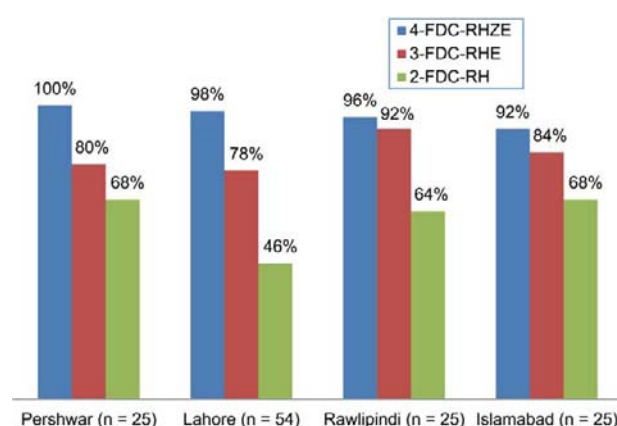
Figure Availability of fixed-dose combination first-line TB medicines in chemists in four cities in Pakistan.

Conclusion: The majority of the population in Pakistan purchases their TB medicines from private chemists; however the depth of knowledge of these providers about TB and its management is limited. The findings permitted broader stakeholder consultation and consensus on the interventions including the development of an innovative training approach for the private sector.

Why are profit-driven pharmacies motivated to contribute to tuberculosis case detection and treatment?

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Objective: IPA's objective was to develop public private partnership engaging retail pharmacists in the national health programme, Revised National TB Control Program (RNTCP).

Design: IPA initiated the work, funded by Eli Lilly, in and around Mumbai in year 2010 and the pharmacists were trained for their role in case detection, patient counseling, DOTS medicine provision and community awareness. More than 400 pharmacists have been trained by now in state of Maharashtra

and pharmacists continue to play their role and are partners with the local TB programme. Focused persistent advocacy efforts were made to communicate the results of Mumbai project to the policy makers. Realizing the potential for pharmacists role, National TB Programme took decision to spread the pharmacists model to pan India. Pharmacists are as such not given any monetary incentives. It was important to find out what are the incentives for the pharmacists to volunteer for the TB control efforts. Focused group discussions (FGD) with the participant pharmacists revealed many interesting facts.

Result: For the national scale up, Memorandum of Understanding (MoU) was signed first in April 2012 between Ministry of Health and IPA and other stakeholders. This MoU was renewed for 2 more years in May, 2013 IPA has started training pharmacists in other states and first such training was conducted in state of Gujarath in May 2013. FGD revealed that pharmacists work mainly with the non-financial incentives and with social attitude to serve the TB patients. Satisfaction of curing the TB patients, partnering with the government, recognition of the work were some of the other reasons for the pharmacists to continue working for this cause. Many of them opined that financial incentives may bring in more number of pharmacists in this partnership.

Conclusion: Public private partnership involving pharmacists can be a sustainable low cost model to strengthen the National TB Control Programme.

Engaging Cameroon pharmacists for early tuberculosis case finding and rational use of tuberculosis medicines

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Background: In 2009 Cameroon's tuberculosis case notification and treatment success rates were reported at 62% and 77% respectively. However, the emergence of drug resistance in the West and Central regions underscores the need to use multidisciplinary teams to support early identification of cases and promote rational use and adherence to anti-TB medicines. Led by the Cameroon Pharmaceutical Society (CPS), this intervention aimed to first characterize healthcare worker perceptions of pharmacists' role in TB care and to describe the experience of patients in accessing anti-TB medicines. The findings were then used to develop strategies to improve TB case finding and treatment.

Setting: National Leprosy and Tuberculosis Program (NTLP), two hospitals and nine private community pharmacies in the Central, West and South regions of Cameroon.

Method: Doctors, nurses, pharmacists, and patients from the public and private sectors were interviewed to assess their perceptions of the role of pharmacists in TB care. Patients were asked how and from where they collected their medicines after hospitalization and the challenges they faced. The information gathered from interviews was complemented by a desk review of the Cameroon NTLP Guidelines.

Preliminary results: The CPS and NTLP have used the findings to map the roles and develop strategies that address the needs of community pharmacies. Patient education materials were developed and will be distributed from community pharmacies. Nine community pharmacy TOTs have been trained and a pharmaceutical care protocol and standardized checklist for case finding and referral have been developed. The protocol will also address rational use of medicines and management of drug side effects or interactions.

Conclusion: Stakeholders identified pharmacists' roles in TB case management and developed priority action steps to improve and build upon these roles. Implementation is underway and results will be shared after final evaluation.

CAN NEW DIAGNOSTIC TOOLS REDUCE THE TIME TO APPROPRIATE TUBERCULOSIS TREATMENT INITIATION?

LPA implementation in the civil sector and penitentiary system in Arkhangelsk, Russia

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Setting: The rate of MDR-TB in Archangelsk region of Russia amongst new and retreatment cases is the highest in the world. In 2012, 33.5% and 70.0% of new cases and relapses, respectively, had MDR-TB. The line probe assay (LPA) is used as a rapid diagnostic tool for defining MDR-TB in this setting.

Objectives: To evaluate the influence of LPA on time from first sputum sample collection for initiation of the MDR treatment and preliminary outcome after 12 months of treatment in the civil sector and penitentiary system.

Methods: Two cohorts of patients with pulmonary MDR-TB were selected: current cohort (251 patients), for whom MDR-TB was diagnosed by LPA, Bactec MGIT, and Löwenstein-Jensen method and historic cohort (283 patients) diagnosed with MDR-TB by BACT/ALERT. The data of current cohort was compared with historical cohort. Time difference between result of LPA and MGIT, BACT/ALERT for civil sector and LJ in penitentiary system was calculated and preliminary outcome after 12 months of treatment in civil sector was evaluated.

Results: LPA introduction in civil sector led to a median decrease in time to initiation of MDR-TB treatment of 21.5 days for smear positive patients and 11.5 for smear negative patients ($P < 0.005$). In penitentiary system median decrease was 14.5 and 14.0 days for smear-positives and smear-negatives accordingly ($P < 0.005$). In historical cohort time to treatment initiation was 50 days and was more than that in current cohort ($P < 0.05$). Results after 12 months of treatment showed that the number of patients still on treatment after 12 months was higher ($P < 0.05$) in concurrent cohort (79%), compared to historical cohort (64.5%), all-cause mortality and default rate was higher ($P < 0.05$) in historical cohort (10.8% and 22.2%, respectively) compared to concurrent cohort (5.4% and 10.2%, respectively).
Conclusion: LPA speeds up MDR-TB treatment initiation cases compared to culture based DST. It is also an important factor that contributes to improvement of treatment outcomes.

Health systems evaluation of implementation and scale-up of LPA and Xpert® MTB/RIF in Cape Town

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A PROVE-IT (Policy Relevant Outcomes from Validating Evidence on ImpacT) research study was implemented in Cape Town, South Africa as part of the TREAT TB (Technology, Research, Education and Technical Assistance for Tuberculosis) initiative. The study aimed to assess the impact of new molecular diagnostics on tuberculosis (TB) diagnosis and treatment.

In January 2008 the health department implemented Hain MDRTB*plus*® line probe assay (LPA) as a replacement for conventional drug sensitivity tests for high MDR-risk cases. Between 2011 and 2013 Xpert MTB/RIF (Xpert) was implemented, replacing smear microscopy for all TB suspects. These are referred to as the 'Targeted' and 'Universal' algorithms respectively.

This study, done in Cape Town, South Africa, compared the LPA-based 'Targeted' algorithm to the Xpert-based 'Universal' algorithm focusing on the magnitude and range of benefits for patients and their care and the inputs required to implement molecular diagnostics as part of a TB diagnostic algorithm in a routine operational setting. The evaluation was undertaken from both a health system and a patient perspective.

Data will be presented for a range of impact measures including: TB treatment commencement times; diagnostic yield; laboratory costs per sample tested and per valid test result; patient costs and impact on household income; and patient's perspectives of their diagnostic pathway.

The benefits and limitations of this operational evaluation will be discussed. Recommendations include the need to address both health system and patient factors to optimise the impact of new molecular TB diagnostics.

Going to scale: assessing health system requirements and impact using virtual implementation

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Introduction: Randomised controlled trials if well designed can provide strong evidence on the most appropriate diagnostic tools for tuberculosis (TB), particularly for the settings in which the trials are conducted. Virtual Implementation is a modelling approach that has the potential to widen the evidence from such trials to other contexts and algorithms. It can be used to project impacts on patients and the health system to provide comprehensive and detailed evidence to support policy on scale-up. This presentation will show how the approach is being applied to the Prove-It studies in Brazil and South Africa.
Methods: Flexible simulation models using packaged software have been developed that model the patient and sputum sample pathways for TB and MDR-TB diagnosis and treatment. The models are then configured to represent different epidemiological contexts, frontline TB diagnostic tools, diagnostic algorithms, treatment regimen, and central TB laboratory facilities. This enables a virtual implementation of new diagnostic tools and algorithms to be tested and impacts projected over many simulated years. A visual display of the operation is produced so that non-modellers can engage and validate the model. Data is input via spreadsheets so the sensitivity of the projected impacts to key parameters can be determined.
Summary: The presentation will demonstrate how virtual implementation is being used to study the impact
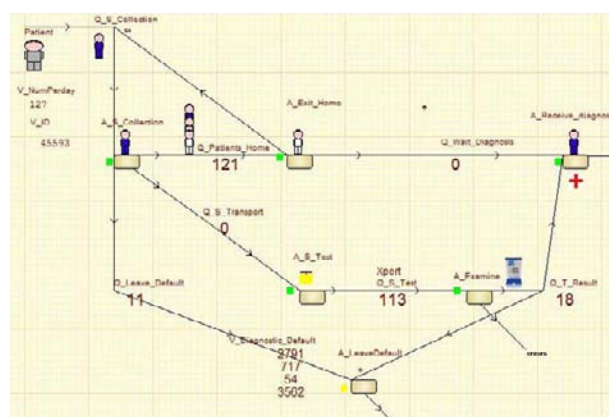
of frontline Xpert scale-up in Brazil alongside the different options for drug sensitivity testing in the central laboratories that are part of the Prove-It trial (i.e., Löwenstein-Jensen, MGIT, Line Probe Assay, or Xpert).

RATIONAL DRUG USE FOR MDR-TB: START SAFE, STAY SAFE, BREATHE SAFE

MDR-TB drug utilisation review programmes: tool to ensure rational use of second-line anti-tuberculosis drugs

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Background: National TB Programmes in resource-limited settings do not systematically monitor the appropriate use of medicines for MDR-TB treatment. When medicines used to treat MDR-TB are misused or patient care is mismanaged, the patient's disease may worsen, the patient may stop taking medicines because of adverse drug reactions (ADRs), MDR-TB may spread, or further resistance (extensively drug-resistant [XDR-TB]) can develop.
Approach: SIAPS offers a systematic ongoing, indicator-based process designed to maintain the appropriate and effective use of medicines for MDR-TB treatment. The approach includes detailed guidelines describing the process for implementing an MDR-TB Drug Use Review (DUR) programme; evidence-based, published criteria for monitoring appropriate medicine use and ADR management; sample data collection forms; improvement strategy suggestions; and accompanying resources (e.g., a list of oto-, nephro-, and neurotoxic drugs, potentially overlapping toxicities of anti-retrovirals and anti-tuberculosis agents).
Accomplishments: MDR-TB DUR programmes are being implemented in Kenya and South Africa. Data has been collected on the use of five individual drugs (Cm, Cs, Km, Lfx, Pto) administered to 100 MDR-TB patients treated in Kenya. Data will be analysed to identify, resolve, and prevent any problems related to the use of the drugs reviewed. Data collection on a standardised MDR-TB regimen administered to at least 90 patients is anticipated to begin before the end of 2013 in South Africa.
The way forward: MDR-TB DURs contribute to preventing drug resistant TB development, optimising patient treatment outcomes, and ensuring patient safety through better management of ADRs and co-morbidities. Strengthening the capacity to ensure patients are receiving treatment and are managed according to international standards by implementing an MDR-TB DUR programme could save many lives and reduce the development of new infections.

Role of adherence to tuberculosis treatment guidelines to prevent the development of drug resistance

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Background: To prevent development of drug resistance the use of tuberculosis (TB) treatment guidelines is promoted. We performed a meta-analysis and systematic reviews to assess: 1) whether multidrug resistance develops more frequently after TB treatment not following treatment guidelines; 2) the knowledge of health workers (HCW) of TB treatment regimens recommended by the guidelines; and 3) the frequency of inappropriate TB treatment prescription.
Methods: MEDLINE, EMBASE and other databases were searched for relevant articles in January 2011. For each study different search terms were used and respectively cohort studies including TB patients who received treatment or observational studies published from 2000 that assessed HCW knowledge or included TB patients receiving treatment were selected. A treatment regimen was considered inappropriate if it was not recommended by the World Health Organization.
Results: The meta-analysis included two studies and showed that the risk of developing MDR-TB in patients who failed treatment and used an inappropriate treatment regimen was increased 27-fold (RR 26.7, 95%CI 5.0–141.7) when compared with individuals who received an appropriate treatment regimen. The first systematic review included 31 studies. In all studies, HCWs with inappropriate knowledge of treatment regimens (8–100%) were observed. The second systematic review included 37 studies. Inappropriate treatment regimens were prescribed in 67% of studies. The percentage of patients receiving inappropriate regimens varied between 0.4% and 100%.
Conclusions: The studies show that knowledge of HCWs of TB treatment guidelines is insufficient and many TB patients receive inadequate treatment. Although only two studies provided data for the meta-analysis the association between inadequate treatment and the development of MDR-TB was strong. Thus adherence to tuberculosis treatment guidelines to prevent the development of drug resistance is important.

WHAT DO WE KNOW ABOUT THE TUBERCULOSIS BURDEN IN GLOBALLY MOBILE POPULATIONS? THE LATEST GLOBAL EVIDENCE

Twenty-first century migration

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Over 200 million people live in a country that is not their country of birth but incidence rates for some diseases are often similar to rates in their birth country; such diseases include tuberculosis, which infects one-third of the world and claims nearly 2 million deaths yearly. Immigration patterns have changed over the past few decades. In the United States, there have been shifts from European to Hispanic and now Asian immigrants. US refugee resettlements have also transitioned from European to African and now Asian and Middle Eastern populations. There are similar trends in immigrant and refugee arrivals to other Western countries. The top immigration source countries are also some of the highest burden countries for tuberculosis, including India, China, Philippines, and Vietnam. Consequently, 62% of tuberculosis cases diagnosed in the United States are among foreign-born persons. To help address these challenges, in 2007, the United States began implementing updated tuberculosis screening for the 450 000 overseas immigrant applicants and 50–70 000 refugees annually; screening requires mycobacterial cultures and treatment to cure using directly observed therapy (DOT). Worldwide, screening physicians are diagnosing >1100 cases yearly, 60% of which are smear-negative but culture-positive. The increase in diagnosis and treatment overseas has led to decreases in diagnosis after arrival among persons suspected of having tuberculosis overseas. Overseas diagnosis and treatment have contributed to reductions in foreign-born tuberculosis cases and associated costs of illness averted for US health departments, which perform the majority of treatment. In addition, implementation has led to >20 new laboratories performing liquid cultures and drug susceptibility testing and additional DOT capacity worldwide. In the globally mobile world, tuberculosis control strategies must include control in mobile populations in order to achieve elimination targets.

Tuberculosis burden among globally migrant groups: findings from the International Organization for Migration

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Migration as a social determinant of health increases TB-related morbidity and mortality among migrants and surrounding communities. IOM contributes to international TB prevention and control by screening migrants for active TB, according to requirements of and with support from partner countries, prior to migration. In 2011, IOM conducted about 270 000 migration health assessments in over 60 countries. This presentation will provide an overview of detection rates of active TB among refugees and immigrants served by IOM from 2010 to 2012, as published in annual Migration Health Reports. Data gathered and reported to partner countries during migration health assessments, are managed using a centralized IOM data management system. Descriptive quantitative analysis of this data was conducted using STATA 10, and detection rates are presented per 100 000 population, by year, region of origin, age group and sex; also showing comparison with respective WHO reported TB estimates and limitations of such comparisons. Active TB cases for the purpose of this analysis are those referred for TB treatment based on either microbiological confirmation or clinical findings, per respective partner country protocols. Preliminary analysis shows, for example, overall detection rate of 280 active TB cases per 100 000 migrants in 2011; with a higher prevalence among refugees [466 per 100 000] as compared to immigrants [176 per 100 000]. Among refugees, active TB case detection in 2011 was 840 and 225 cases per 100 000 for Asia and Africa, respectively. Similarly, drug susceptibility testing, which was done for about 97% of all cases with positive sputum culture results showed that about 14% of all cases were resistant to one or more TB drugs, and 2% were multi-drug resistant. Active TB screening of migrants contributes to the global detection of TB, and can be an important tool in TB control, benefiting migrants and their families, sending and receiving countries.

Linking tuberculosis burden and its geographic distribution among Mexican immigrants to the United States

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Setting: Immigrants from Mexico represent the largest proportion of foreign-born individuals in the United States (US) population. Mexican immigrants in the US represent the largest share of active tuberculosis (TB) cases detected in the foreign-born population. With leadership from the US Public Health Service, panel physicians worldwide implemented guidelines that required the use of culture and directly observed therapy on immigrants found to have TB disease prior to emigrating to the US.

Objective: To link the geographic distribution of TB burden in Mexican immigrants to resettlement communities in the US and to inform interventions within the US and overseas targeted migrant populations.

Design: Between October 2007 and December 2012, US designated panel physicians in Mexico detected 214 cases of active pulmonary TB in a population of Mexican immigrants moving from Mexico to the US. The place of origin in their home country (Mexico) was identified as well as their intended and eventual destination in the United States.

Results: These case studies further strengthen the cause for orderly, controlled migration and how public health measures identifying, diagnosing, treating and controlling the spread of TB disease have a great impact on TB control in communities where new immigrants are a fact of life.

Conclusions: Overseas medical evaluation for TB among migrants is a particularly high yield intervention for persons emigrating from a higher incidence region of the world to another region that has a lower incidence and can have a significant impact on health promotion and disease prevention.

What is the burden of tuberculosis among prospective Ethiopian immigrants?

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Background: US-bound prospective immigrants from countries with a World Health Organization (WHO)-estimated TB incidence rate of over 20 cases per 100 000 population are required to undergo screening for tuberculosis. According to 2009 WHO statistics, the national TB prevalence in Ethiopia was 258 per 100 000.

Objective: To determine the prevalence of TB among prospective Ethiopian immigrants who were screened at Saint Yared General Hospital in Addis Ababa, Ethiopia.

Methods: During the period 2009–2012, 13 136 applicants across all ages were screened for TB. About 54% were females. The majority (78.6%) were adults 15 years or older. Children under 2 years represent 6.7% of all screened; 14.7% were in the age 2–14 years. The 2009 CDC Technical Instruction was used to screen patients. Univariate statistical method was employed to test for any associations between the prevalence of pulmonary TB and patients' age, sex and year of screening.

Results: The period (2009–2012) prevalence of sputum-confirmed pulmonary TB was 0.14%. The prevalence of sputum-confirmed pulmonary TB during the study period increased by over fourfold from 0.05% in 2009 to 0.22% in 2012, but not significantly ($P = 0.110$). There appears to be an increase in the prevalence of sputum-confirmed pulmonary TB with age although the difference was not statistically significant—from almost nil among the under 2 children to 0.10% and 0.16%, respectively, among 2–14 and 15 or older age groups. There was also no significant variation by sex.

Table   Prevalence of sputum confirmed TB cases by year of screening, sex and age, Saint Yared Hospital, Addis Ababa, Ethiopia, 2009–2012

Sputum confirmed TB cases	Year				Total	Test statistic
	2009	2010	2011	2012		
Total screened population, 2009–2012	2117	2816	3631	4572	13,136	$Chi^2(3) = 6.03$ P value = 0.110
Sputum confirmed TB cases	1	1	7	10	19	
%	0.05	0.04	0.19	0.22	0.14	
Sex						
Male	972	1410	1660	2075	6117	$Chi^2(3) = 1.93$ P value = 0.603
Sputum confirmed TB cases	1	0	2	3	6	
%	0.10	0.00	0.12	0.14	0.10	
Female	1145	1406	1971	2497	7019	$Chi^2(3) = 4.84$ P value = 0.193
Sputum confirmed TB cases	0	1	5	7	13	
%	0.00	0.07	0.25	0.28	0.19	
Age group						
<2	42	41	225	579	887	**NA**
Sputum confirmed TB cases	0	0	0	0	0	
%	0.00	0.00	0.00	0.00	0.00	
2–14	220	254	551	904	1,929	$Chi^2(3) = 0.82$ P value = 1.000
Sputum confirmed TB cases	0	0	1	1	2	
%	0.00	0.00	0.18	0.11	0.10	
15+	1855	2521	2855	3089	10,320	$Chi^2(3) = 7.15$ P value=0.064
Sputum confirmed TB cases	1	1	6	9	17	
%	0.05	0.04	0.21	0.29	0.16	

Conclusions: The prevalence of TB in the studied population is consistent with the WHO estimated national prevalence for Ethiopia.

STRATEGIES FOR SOCIAL SUPPORT: NAVIGATING THROUGH THE COMPLEXITY OF CARE TO TUBERCULOSIS PATIENTS

Social support for tuberculosis care: evidences from academia research to health services practice

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Scenario: In Brazil, the incidence rate the tuberculosis (TB), in 2012, was 36.1 per 100 000 inhabitants.

Objectives: To provide scientific evidence in relation to the relevance of social support in coping with some determinants of the TB.

Methods: It was possible to conduct a survey along with the families of TB patients who were monitored by the health services of a priority municipality for control, in Brazil, and with a population of 605 000 inhabitants. The authors validate an instrument composed of 65 items and divided into four constructs. The instrument proved to be valid after the psychometric testing and also sensitive to the study's population. The sampling was a probabilistic kind, totaled a minimum sample of 110 subjects.

Results: In relation to the sample, 85 subjects (77.3%) were women and aged between 39 and 59 years old. It was identified the relationship of the social variable education (OR = 4.39, 95%CI 1.11–17.35); watching television (OR = 3.99, 95%CI 1.20–13.26) and

internet access (OR = 5.01, 95%CI 1.29–19.38) with knowledge about TB, but the DOT was not associated with it, yet. It was also observed that less educated families tend to suffer more with the stigma, and this interferes in providing support for TB patients. The importance given by the families to the DOT was associated with the quality of user-professional interaction, to the support given for them during the treatment and the very age of the participants.

Conclusion: The families' knowledge about TB was related to contextual variables; however, there is no evidence that the DOT contributed to this process. The social stigma interfered with the relationships network and social support of TB patients. The social support, in an intersectionality perspective, should be the strategic action launched in order to improve the quality of life and well-being of patients and families affected by the TB.

Social support for patients with tuberculosis: experiences from London

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One in six of the 3500 new tuberculosis (TB) patients diagnosed annually in London have complex needs, characterised by homelessness, drug/alcohol dependence, destitution and imprisonment. These same patients are at higher risk of delayed presentation, drug resistant disease, onward transmission and death. The Find&Treat team use mobile digital chest radiography to screen almost 10 000 vulnerable and socially excluded people each year and support the onward care of all new cases detected through mobile screening and around 200 others referred by treatment services locally and nationally. This talk will collate the experience of developing and delivering an integrated package of health and psychosocial care to people with active TB whose social circumstances put them at high risk of delayed diagnosis and poor treatment outcomes. The talk is structured in four parts:

1 TB and ?—describes the social profile and complexity of the Find&Treat caseload;
2 Defining cure—challenges the biomedical model of treatment success and highlights the importance of addressing the social determinants of TB as imperative to restoring health and reducing future risk of disease;
3 Solutio Intus—highlights the importance of involving patients as peers in the design and delivery of care;
4 Moving forward—summarises the structural and professional barriers to implementing integrated health and social care within the UK context and further a field.

Financial and social support to internal migrant tuberculosis patients in Shanghai: an intervention study

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Background: Financial issues are major barriers for rural-to-urban migrants accessing tuberculosis (TB) care in China. This paper discusses the effectiveness of providing financial incentives to migrant TB patients (with a focus on poor migrants), the effect of financial incentives in terms of reducing the TB patient cost, and the incremental cost-effectiveness ratio of the intervention.

Methods: Each migrant TB patient received a monthly transportation incentive of RMB10 (US$1.6) in the intervention district. Those who were classified as 'poor' were allocated a financial subsidiary of RMB1000 (US$157) at intervals throughout treatment. A comparable control district was selected where no financial incentives were provided to migrant TB patients.

Results: Ninety and ninety-three 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 only a 3% increase (from 73% to 76%) in the control district ($P = 0.03$). Default rates significantly decreased by 11% (from 22% to 11%) in the intervention district, compared with 1% (from 24% to 23%) in the control district ($P = 0.03$). In the intervention district, the financial subsidy (RMB 1080/US$170) accounted for 13% of the average patient direct cost (RMB 8416/US$1332). Each percent increase in treatment completion costs required an additional RMB 6550 (US$1301) and each percent reduction in defaults costs required an additional RMB 5240 (US$825) in the intervention district.

Conclusions: Overall, financial incentives proved to be effective in improving treatment completion and reducing default rates among migrant TB patients in Shanghai. The results suggest that financial incentives can be effectively utilized as a strategy to enhance case management among migrant TB patients in large cities in China, and this strategy may be applicable to similar international settings.

Collaborative work of nurses and social workers to support tuberculosis treatment among homeless in Japan

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Setting: Japanese law requires all infectious TB patients to be hospitalized. Local public health centers support treatment of discharged TB patients, so healthcare providers at TB hospitals and public health nurses cooperate in planning continued support. Financial support is provided to patients who cannot afford treatment.
Objective: To evaluate a case that successfully completed the TB treatment requiring a multi-disciplinary effort, and to clarify how local health and welfare departments can collaborate in supporting TB patients.
Design: Case report.
Results: A 36-year-old TB patient traveled all over Japan, continuing his TB treatment intermittently. Non-compliant phase (five years): The patient repeatedly self-discharged from a hospital as soon as he received life-support funds from local welfare departments. Treatment-compliant phase: The patient, social workers, and public health nurses discussed and agreed that life-support funds from the welfare department were to be provided on an incentive or physical basis. After being discharged, he went to see a public health nurse at a local public health center for DOTS every day and received monetary support in person from the local welfare department on his way home. Throughout the course of treatment, public health nurses supported the patient and provided life-style and nutrition consultation along with DOTS.
Conclusions: The key to the successful completion of his treatment was comprehensive support provided by welfare and health departments, including financial and health-promoting support. After evaluating the support for this case, we concluded that the approaches below would help ensure better TB patient care in the community.
- Educational sessions on TB should be provided to welfare department officers to promote understanding of TB patients in need of welfare.
- Support flexibility is needed for those in unstable living conditions.
- Departments must cooperate in support for TB patients.

Is social support improving case detection and treatment outcomes? BRAC experience in Bangladesh

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Background: BRAC begins its journey in controlling TB in 1984. It is the major partner of National Tuberculosis Control Program and providing TB services to 93 million populations. To improve case notification and overcome unfavorable treatment outcome, it introduced social support under TB program.
Intervention: In early 1990s, BRAC addressed compliance and adherence with prolonged treatment as emerging issues which possess unsatisfactory treatment outcome. It introduced incentive system for the Shasthya Shebikas (Frontline Community Health Worker) who mobilize community, identify suspect and provide DOT to TB patients. Diagnosis of smear negative (SN), extra-pulmonary (EP) and child TB are difficult, costly and many poor people remain undiagnosed and untreated. To prevail over the situation, BRAC starts to provide social support in 12 districts in April 2012 and in rest of the areas in January 2013. The poor TB symptomatic get diagnostic and transport support. All MDR-TB and TB-HIV co-infected patients get nutritional and investigation support.
Results: During April 2012 to June 2013, a total of 97 023 TB symptomatic, 178 TB-HIV co-infected, 1237 MDR-TB and 793 ultra-poor TB patients got support from BRAC. In BRAC supported areas, notification of all forms of TB cases increased to 111 in 2012 which was 99 in 2011. Treatment success rate was 93% in 2011, which remain the same as previous years, though higher numbers of TB patients were detected. In 2011, a total of 10 608 SN and 13 011 EP cases were identified; which were 13 481 and 15 209 in 2012, were 18 649 and 11 145 up to June 2013 respectively. This proves that detection of SN and EP cases in 2013 would exceed the number of detected cases in 2012.
Conclusion: Introducing social protection scheme by providing diagnostic support to poor TB symptomatic surely increase the case notification with high treatment success rate and also reduce the burden of TB among the people with TB symptom.

ECONOMIC BURDEN OF TUBERCULOSIS: STUDY CASES AND POLICY IMPLEMENTATION

Economic burden of tuberculosis at household level: highlight of the research and policy gaps

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Objectives: To document the state of knowledge on the financial burden of tuberculosis (TB) care to patients and households in low- and middle-income countries, and to highlight the research and policy gaps in the work conducted to date.

Methods: We systematically searched for published articles in English between January 2002 and May 2013 in eight databases. Broad search terms were used. Only studies that reported costs of TB care for patients/households using the "WHO/StopTB tool to estimate patient costs" were retained in order to allow for a pooled analysis. All costs were converted to 2012 US dollars (USD) in accordance with WHO cost analysis guidelines.

Results: Overall eight articles that surveyed 1512 tuberculosis patients living in rural and urban areas from 11 countries met the inclusion criteria. All the studies had high quality reporting of study population and cost data. Pooled mean pre-diagnosis costs were US$420 and the mean post-diagnosis cost was US$226. Furthermore, pooled mean direct costs of TB care were US$155 and the indirect costs were US$491. Transportation (31%), hospitalization (24%), feeding (%), and non-TB drugs (9%) account for most of the direct cost expenditures. Also, total mean expenditure for TB care was equivalent to 16% of annual household income. Household income fell by 25% to 100% following the onset of TB.

Conclusion: Patient and household costs for TB care in low- and middle-income countries are substantial and must be reduced. This may be through a mix of financial and social protection interventions for TB patients. There is need to adapt the 'tool estimate patient costs' in quantifying the economic burden of care for TB patients with diabetes mellitus, drug-resistant TB and other co-morbidities in order to provide evidence base for future interventions.

Case studies from Benin and Burkina Faso: direct and indirect economic burden of tuberculosis

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Background: A pilot research protocol has been adapted from Burkina Faso to Benin—whose results were published in February 2013 in PLOS ONE. The study located in Benin involved six health districts from urban and rural areas covering a population of 1 348 700 inhabitants. The aim was to measure economic burden of tuberculosis care pathway.

Methods: A retrospective cross-sectional study reviewed all smear-positive tuberculosis patients treated under the national strategy from August 2008 to February 2009 in the selected districts. Out-of-pocket payments associated with tuberculosis and care-seeking pattern and opportunity costs were exhaustively collected from onset of symptoms to end of treatment. Household income was also investigated to report on financial burden.

Findings: Population pattern and outcomes data were reported for the 245 tuberculosis patients interviewed. The mean age was 35 years; 60% (146) were male and median overall direct cost was US$163 per patient. Patient, provider, and treatment delays were reported. Pre-diagnosis stage was the most critical; corresponding to a median of 38% of the overall direct cost. Self-medication, travel and food expenditures contributed largely to this cost-burden. Patients also reported opportunity costs and the median of direct economic burden achieved 2 months of their household income and represented 17% of the annual household income.

Interpretation: The study showed particular financial and organisational barriers that need to be tackled during critical stages. The most critical stage was pre-diagnosis followed by intensive treatment stage; whereas in Burkina Faso those were likely diagnosis process, treatment initiation and pre-diagnosis in decreasing order of importance. Out-of-pocket payments for TB in Benin remain prohibitive and are much higher than payments observed in rural Burkina Faso. However, direct economic burden appeared slightly lower than in rural Burkina Faso.

Case study: catastrophic health expenditure associated with tuberculosis in Bangladesh

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Background: Tuberculosis (TB) is a principal cause of mortality and morbidity among the adult population of low income countries. With a prevalence of 411 per 100 000 populations, Bangladesh ranked the 6th highest for the burden of TB among 22 high-burden countries. Under the National TB Program (NTP), directly observed treatment (DOTS) services are provided from more than 500 government-run

centers and NGO clinics in all upazilas, districts and city corporations. Although there is a high burden of TB in Bangladesh, little has been done to estimate TB-related medical expenses and financial consequences.
Objective: To investigate the medical expenses and catastrophic health expenditure (CHE) due to TB among Bangladeshi people.
Methods: The nationally representative Household Income and Expenditure Survey (HIES) 2010 data was used in this study. The survey reported 10 931 symptoms and diseases suffered by household member in the past 30 days of the survey. Among those, 23 TB cases were found. CHE are defined as medical expenditures exceeding 10% of total household expenditure. Multiple logistic regression analyses were used to estimate the association between incidence of CHE and TB.
Findings: Average medical expenditure due to TB in last 30 days was 1428.5 BDT (US$19) with spending on medicine (746.7 BDT), transportation (270.7 BDT) and consultation (202.8 BDT) being the major drivers. CHE was experienced by 30.4% (95%CI 11.2%–49.7%) of the participants who suffered TB in past 30 days. Participants who had TB were 4.8 times (OR 4.798, 95%CI 1.89–12.19) more likely to experience CHE than those who observed fever symptom.
Conclusion: This study shows that although TB diagnosis and treatment services are free under the NTP program, patients face difficulties affording services through high out-of-pocket payment. To address the negative financial impacts of TB, innovative healthcare financing mechanisms are needed in Bangladesh.

Free tuberculosis care: too expensive for people to afford

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Background: Despite TB treatment being ostensibly free in Peru, hidden costs may worsen poverty and increase adverse TB treatment outcomes. We aimed to measure these hidden costs and evaluate their effect on treatment outcomes.
Methods: From 2002–9, 876 TB patients were recruited to a prospective cohort study and interviewed prior to treatment and every 2–4 weeks throughout treatment with a questionnaire detailing TB costs. Total household costs were defined as out-of-pocket direct expenses plus indirect expenses (lost income). These total household costs were then calculated as a percentage of annual income for that household.

Adverse outcome was defined as TB treatment failure or default, death during treatment, or TB recurrence within two years of completing treatment.
Results: Household costs were higher pre-treatment than during treatment (24% vs. 17%, $P = 0.05$), intensive phase (7.7%, $P < 0.0001$) or maintenance phase (9.0%, $P = 0.0016$). Although poorer households had lower out-of-pocket direct expenses than less poor households (355 vs. 433 Peruvian Soles, $P < 0.02$), their household costs were two-fold higher (54% vs. 27%, $P = 0.003$). 93 (11%) patients had multi-drug resistant (MDR)-TB. Households with MDR-TB patients incurred 1.5-fold higher household costs than non-MDR-TB (62% vs. 38%, $P = 0.002$). TB-associated costs greater than 20% of the household annual income were defined as catastrophic because this threshold best predicted an adverse outcome (55% vs. 34%, $P < 0.0001$). Households with MDR-TB patients were more likely to incur catastrophic costs than non-MDR-TB households (54% vs. 38%, $P < 0.003$) regardless of the patient's treatment outcome (Figure).
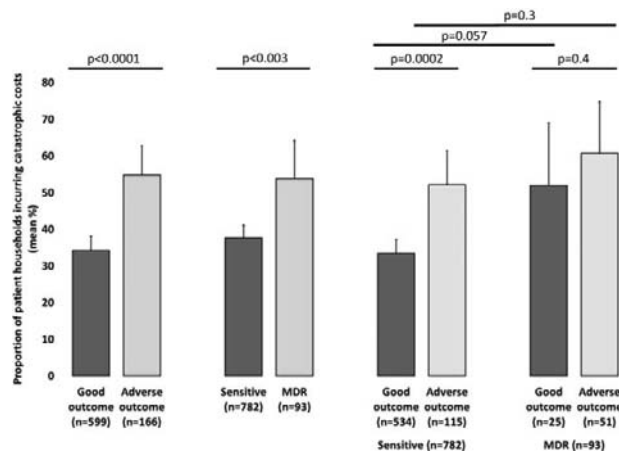
Figure Patient households incurring catastrophic costs by TB resistance profile and treatment outcome. Error bars represent confidence intervals. *P* values represent association in univariate logistic regression.

Conclusion: Free TB care was expensive for poor TB patients to access. MDR-TB patients had the most catastrophic costs and the worst treatment outcomes. Socioeconomic support may be needed for TB and particularly MDR-TB patients to be able to afford free TB care and avoid TB causing greater impoverishment.

Burden and determinants of catastrophic household payments for tuberculosis in Nigeria: policy implications

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Objective: To assess the burden and determinants of catastrophic payments that households incur on services which are supposedly free-of-charge, using the example of tuberculosis care in rural Nigeria.

Methods: We assessed patient/household direct costs and income from a survey of 452 pulmonary tuberculosis patients sampled from three rural health facilities in Ebonyi State, Nigeria. We analysed the incidence of household catastrophic payments using as thresholds the traditional >10% of household income and ⩾40% of non-food income, as recommended by World Health Organization. We used logistic regression analysis to identify the determinants of catastrophic payments.

Results: Using the threshold of household costs of TB care ⩾40% of non-food income, the incidence catastrophic payment was 44%; with 69% and 15% of the poorest and richest household income-quartile experiencing catastrophe respectively. Using the traditional threshold of costs >10% of household income, the incidence of catastrophic payments was 65%. Independent determinants of catastrophic payments based on the recommended WHO threshold for catastrophe were: age >40 years (adjusted Odds Ratio [aOR] 3.9), male sex (aOR 3.0), urban residence (aOR 3.8), formal education (aOR 4.7), care at a private facility (aOR 2.9), poor household (aOR 6.7), household where patient is primary earner (aOR 3.8), and HIV co-infection (aOR 3.1).

Conclusion: Current cost-lowering strategies are not enough to prevent households from incurring catastrophic out-of-pocket payments for tuberculosis care. Financial and social protection interventions are needed for identified at-risk groups. These observations should inform the post-2015 tuberculosis control strategies.

TUBERCULOSIS IN THE MINING SECTOR: POLITICS, POLICY AND PRACTICE

Tuberculosis and HIV summit action plans

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Introduction: The Department of Mineral Resources in South Africa is responsible for regulating the Mining Industry through the Mine Health and Safety Act (MHSA) as amended in 2008. The MHSA provides for the establishment of the Mine Health and Safety Inspectorate, which is to ensure compliance by the industry to Mine Health and Safety matters. The Mine Health and Safety Council State Owned Entity through which several tripartite Advisory Committees to the Minister of Mineral Resources are established. These committees engage in research and innovation, regulation review promotion of occupational health and safety in the mining industry as well as TB and HIV related programs in the sector.

Discussion: In November 2011 Mine Health and Safety as well as the TB-HIV summits were held where commitments on TB and HIV were signed by all Tripartite Stakeholder Principals.

The commitments were formulated into action plans post signing. The advisory committee on HIV and TB is working on project that emanated from the action plans.

The summit action plans are divided into four categories.
• Prevention,
• Treatment, Care and Support,
• Research Monitoring and Surveillance, and
• Human Rights.

Below are a few of the summit action plans that were agreed upon, otherwise there are 22 of them in total.
• The TB HIV Reporting form has been developed for the use by mines to report on programs available for their workers.
• Develop an integrated policy for the management and reporting of TB, HIV and AIDS, TB and Silicosis (HATS) in line with DMR, DOH, DoL and SANAC policies, norms and standards.
• Explore policy options to reduce negative impact of migration of mine workers. (Mining industry to align its migration programs to the National policy, employee awareness on the mining charter, including housing and living conditions, annual progress reports on compliance with the mining charter and social labour plans.)
• Recommend to DoH to revise IPT Policy to include individuals with Silicosis. (DoH to revise the IPT Policy.)
• Integrating TB and HIV/AIDS programmes in mining sector with other sectors including trucking and commercial sex workers. (A guideline for development and implementation of an integrated programme.)

Conclusion: The industry has acknowledged the need to continuously improve the health and safety of mine workers. The projects that are to be implemented are not only limited to South Africa but reach out to all labour sending countries of SADC. All the summit action plans are to prevent adverse health effects to mine workers and to ensure that the industry complies with best practice on health and safety of mineworkers.

Cross border and multi-sector: sustaining action to combat tuberculosis in the mining sector

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The South African gold mines have on average 3 times higher incidence rates of TB more than those of the South African national average. Compared to all other industries, the mines report 90% of occupational lung diseases. The key risk factors that contribute to this are higher rates of silica dust exposure, which results in silicosis, the prevalence of HIV and AIDS epidemic amongst miners, and the generally poor communal living conditions in single-sex mine residences and increasing number of crowded, unhealthy and inhumane informal settlements mushrooming around mines.

There are a number of international and national plans, including strategies and commitments that guide intervention to decrease TB in the mining sector. These include the 2011 South Africa Mining Summit which called for rigorous commitments on TB-HIV surveillance system; increased TB case finding amongst miners; integrated referral systems; and community access to promotion and prevention of TB-HIV. The SADC technical committee, in collaboration with the STOP TB Partnership, World Bank, the governments of South Africa, Lesotho and Swaziland as well as ministries of Labour and Minerals in the region, thus called for regional action to ensure that TB in the mines is a priority in the Regional Agenda. This process led to the signing of the SADC declaration on TB in the Mines by 15 SADC Heads of State in November 2012.

Intensified tuberculosis case finding in mining affected communities in South Africa

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Among South African gold mines TB case notification rates are extremely high ($>3\%$/year), due to a high prevalence of HIV ($\sim30\%$ in 2000) and silicosis, and the prevalence of undiagnosed TB is high (2.5%). Chest radiographic screening for TB has been used in the mining industry for more than 50 years. Radiological screening in the pre-HIV era detected 70% of TB cases, which declined to 30% in the HIV era, due to rapid progression of TB in HIV-infected persons. The prevalence of radiologically detected TB has however remained stable. Increasing the frequency of radiological screening from annual to biannual detects more TB suspects and reduces TB specific mortality. Adding radiological to symptom screening more than doubles the number of TB cases detected, particularly of smear negative TB. Active case finding using Xpert® MTB/RIF detects substantially more TB than screen-

ing with symptoms and chest radiography. Modeling suggest that screening with a sensitive tool such as Xpert will have a substantial impact on TB control among miners. Among former miners the prevalence of undiagnosed TB remains high but access to diagnostic and treatment services is limited. TB case notification rates among peri-mining communities is high. Household contact tracing of index patients working in the mines detects undiagnosed TB cases. In conclusion, the prevalence of undiagnosed TB among current and former miners and mining communities is high. Active case finding and contact tracing detects a substantial yield of TB and contributes to TB control within the mines and surrounding communities.

CATALYSING THE PEDIATRIC TUBERCULOSIS DRUG MARKET: A CALL TO ACTION

Market research: new information on the dynamics of the pediatric tuberculosis market for drugs and diagnostics

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Recent initiatives at global level on TB drug and diagnostics research and TB surveillance are leading to more insights and information on the dynamics of the Paediatric TB market. Under the STEP-TB project being implemented by the Global Alliance for TB Drug Development and partners, WHO, with UNITAID support, efforts are underway to analyse disaggregated paediatric tuberculosis surveillance data from National Programs which would lead to more accurate quantification of the paediatric TB market size. Another approach has been to study trends in the past and current supply and utilization of paediatric TB drugs in countries and understand patterns in demand and access. A number of on-going and planned studies by global partners will throw light on the pharmacokinetics, safety and efficacy of new drugs, new drug combinations which include first line drugs, and of second line drugs in children, including in infants. Clinical studies in children lag the progress of such studies in adults and there are efforts to reduce this lag period by addressing regulatory mechanisms for drugs prior to market entry.

Quality care: identifying and treating children with first-line tuberculosis drugs

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Background: Nigeria is one of the 22 countries with high burden of tuberculosis (TB) with an estimated incidence of 118/100 000 population (WHO global

report 2012). However preliminary results of the National Prevalence Survey conducted 2012 indicated higher estimates. The proportion of childhood TB among all notified cases increased steadily from < 1.5% in 2008 to 9.5% in 2012, but access to quality diagnosis and care still remains a challenge.

Objectives: To describe steps developed to improve access to quality childhood TB care at all levels.

Methodology: A simple checklist was developed and incorporated into the mid term evaluation tools of the National TB Strategic Plan conducted in 2012.

Results: National TB guidelines addresses childhood TB management, but its availability and use by medical officers and pediatricians is sub-optimal. Other challenges include: diagnosis is mainly done by physicians; non-uniformity in the application of the criteria for diagnosis; minimal implementation of contact tracing, screening and isoniazid prophylaxis therapy; weak referral linkages between staff at peripheral units and physicians which is, usually, not documented; recording and reporting of cases diagnosed and treated by physicians have been sub-optimal.

Way forward: In collaboration with other stakeholders, the Programme designed steps to improve case detection and effective management in children. A roadmap and policy documents were developed focusing on increasing awareness, advocacy and training. The childhood TB guidelines were revised; a desk guide was also developed to standardize the management of TB in children. The guidelines for drugs and dosages in children were revised in line with the new global recommendations. Task-shifting to nurses and other category of staff was adopted as a strategy.

Conclusion: Plans to re-direct the implementation of TB control in children have been put in place in line with the present global demand and best practices.

New formulations: overcoming challenges to come to market with new first-line dispersibles

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As of today, the non-availability of the paediatric fixed dose combination for tuberculosis with dosage recommended by WHO is a major issue. Paediatric drugs require to be dispensed in a manner which is easy for administration and has a good acceptance by children. Water dispersible tablets especially for fixed dose combinations are very challenging for manufacturer. One of the solution is to have bilayer water dispersible tablets in order to separate active ingredients leading to better handling of stability and possible interactions. It also allows the use of layers of each active ingredient as parts of lego® and allow rapid assembly of different doses of active ingredients, or add or remove a component.

Access equation: what can be done to ensure pediatric formulations reach children in need?

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This presentation will explore how more children can be identified and treated for TB. The TB Alliance has conducted two studies to better understand where children with TB are currently being treated. In collaboration with the Global Drug Facility, the TB Alliance has analyzed distribution of pediatric medications to National TB Programs of the 22 high TB burden countries. These data will inform approximately how many pediatric cases are being treated with quality approved drugs. Additionally, to gain a better understanding where children are being diagnosed and treated outside of the NTP sector, the TB Alliance has conducted rapid assessments. Data from Pakistan, Indonesia and Nigeria will be presented. Based on the findings, suggestions of how and where pediatric treatment can be made more accessible will be proposed.

SYMPOSIA: SUNDAY 3 NOVEMBER 2013

HIV, TUBERCULOSIS AND HUMAN RIGHTS AND THE LAW

Screening of a video of tuberculosis survivors detained in Kenyan prisons

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Setting: Uasin Gishu and Embu Counties. Kenya has a large and rising TB disease burden and is ranked 12th among the 22 countries that collectively share about 80 percent of the world's TB cases. Kenya in 2010 adopted a constitution that has one of the most expansive and progressive bill of rights. The public health act has a provision that allows for the isolation of patients with infectious conditions. This provision has been utilised severally by public health offices to detaining defaulting TB patients in prisons.
Objective: To share the experience of Kenya on how to use the law and court process to protect the rights of TB patients.
Design: KELIN provided legal intervention in three cases involving TB patients who had been jailed for defaulting on their treatment in three separate counties in Kenya. These cases were brought to the attention of KELIN by the media and partner organisations. In partnership with NEPHAK, KELIN identified the clients; provided legal advice and representation before courts to challenge their imprisonment on the basis of allegedly defaulting on treatment.
Results: Success in two cases where the high court reversed the decision of the magistrate's court and released the patients back to the community noting that prison is not the right place for confinement.
Conclusion: The courts can be utilized to safeguard the rights of TB patients. In doing so the community and all stakeholders working on TB issues need to understand their rights and responsibilities to ensure that TB interventions are administered in a manner that respects human rights. Laws and polices dealing with provision of TB services must be reviewed and amended to reflect the human rights principles that are internationally recognised.

The role of the state in ensuring prisoners are tuberculosis free: case study

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A seminal judgment from the South African Constitutional Court in the case Dudley Lee v Minister of Correctional Services makes clear that the South African government has a duty to develop and implement a TB control programme in prisons. Simultaneously, new science is emerging to suggest that the secret to tipping the scales in the battle against TB more broadly may be to focus on bringing down transmission rates in prisons. We also saw more concentrated, strategic social activism catalyse around the Dudley Lee case in 2012 than the TB scene in South Africa has known in many years. Between the legal, scientific and social developments, South Africa is perched in a moment of contingency; calls for change in South Africa's prisons may sound louder than ever and may, at last, reach the right ears to bring about reform.

Dudley Lee spent over 4 years awaiting trial in Cape Town's Pollsmoor prison, the same prison that many believe was responsible for causing former president Nelson Mandela's TB infection. A study of the prison revealed that the risk of TB transmission in Pollsmoor may be as high as 90% per annum. The Constitutional Court found that the state had failed to take measures to prevent the spread of TB. The judgment sends a strong message about the state's duty in this regard.

At the same time, the state has recently indicated its intent to defend cases presenting almost the exact same facts as Dudley Lee's—a surprising development given the strong condemnation of such action from the Constitutional Court. Moreover, recent guidelines intended to address the crisis of TB in prisons were woefully inadequate.

These experiences give rise to questions about the efficacy of litigation and activism in the context of intransigent state actors and limited public funds. This case study examines the possibilities and limits of realizing the right to health through the strategic combination of the use of the law and social mobilization.

The use of human rights literacy as strategy to empower community members to use the law

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Background: ARASA is a partnership of over 70 human rights, TB and HIV organisations working together in southern and eastern Africa to promote a rights-based response to HIV and TB. To further this goal, a critical area of work for ARASA is the use of human rights literacy as part of a strategy to increase community and civil society capacities in promoting enabling legal and policy environments. This work includes advocating for the removal of legal and policy barriers, which hinder access to TB treatment, care and support. Protective legislation and policy as well as 'know your rights' literacy campaigns are essential components of an effective rights-based national HIV and TB responses. A human rights-based approach to TB prevention, treatment and care includes addressing

the legal, structural and social barriers to quality TB prevention, diagnosis, treatment and care services.

Description: Human rights based approaches ensure that patients who require TB treatment receive them and that patients understand their own rights to be free from discrimination (including in health care settings) and from coerced treatment. In environments where non-adherence is met with arbitrary arrests and incarceration, the training ensures that patients are able to articulate their rights and that bills which are counter-productive to the rights of the patients; are revised. The draconian provisions in the previous Public Health Act of Botswana, criminalized non-adherence of TB medication—thus the public were not confident to access services. Through BONELA, an ARASA partner from Botswana's human rights literacy interventions, the Act has since been revised.

Lessons learnt: ARASA has trained over 177 human rights advocates since 2008 in the SADC region. This training has increased the knowledge of civil society in the SADC region. Human rights and treatment literacy has affirmed that in order to achieve optimal uptake of prevention, testing, treatment and care services, it is necessary to reduce stigma and discrimination. This in turn will increase the use of health services without fear of discrimination, reprisal or forced treatment and isolation.

CONTACT INVESTIGATION: OPERATIONAL RESEARCH TO INCREASE CASE DETECTION AND IMPROVE THE SAFETY OF SHARED AIR

Results of a prospective study of child and adult household contacts to MDR-TB in South Africa

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Background: Despite intensive efforts over more than a decade, most countries in Asia and Africa continue to fall short of the World Health Organization goal of detecting and treating at least 70% of all smear-positive TB cases. Contact investigation has the potential to be an important means of boosting TB case detection rates, particularly in settings with high HIV prevalence and in settings where access to health care facilities may be challenging. However, TB contact investigation can be time consuming and expensive, and the yield needs to be carefully evaluated to determine when it is most effective. In a previous programme, among 3029 contacts ≥5 years, 93 (3.1%) started TB treatment: 19 (20.4%) were smear positive and 71 (76.3%) were culture positive. Among

361 (10.6%) who were <5 years of age, 34 (9.4%) started TB treatment. We are conducting a new prospective study with the aim to compare yield of TB from drug sensitive TB patients and rifampicin resistant patients.

Methods: Rifampicin resistant and drug senstive TB index patients identified at laboratories are contacted and permission is requested to visit their households. Contacts are investigated for TB using symptomatic screening, followed by Xpert testing, microscopy and culture of sputum. In addition, contacts are tested for HIV. We aim to recruit 200 rifampicin resistant and 400 drug susceptible index patients matched by age band and location.

Results: During the pilot phase of the study, we recruited 10 rifampicin resistant and 20 drug susceptible patients. We then traced 68 contacts, 8 (12%) known HIV positive. 32 contacts were symptomatic for TB and one case of TB has so far been identified. Early results of this study will be presented. Logistic issues and lessons learnt will be ellaborated on.

Discussion: The study will allow us to compare the yield of TB from drug resistant index patients with that of drug susceptible patients.

A, C, G, TB: INSIGHTS INTO TUBERCULOSIS EPIDEMIOLOGY AND EVOLUTION FROM WHOLE GENOME SEQUENCING

Overview of the *Mycobacterium tuberculosis* genome

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The human-adapted *Mycobacterium tuberculosis* complex (MTBC) exhibits a strong phylogeographic population structure. However, the evolutionary forces that shape global MTBC variation are not well understood. We have been using a combination of comparative whole-genome sequencing of MTBC clinical strains and molecular epidemiology to study the association between different phylogenetic lineages of MTBC with particular human populations around the world. Our population genomic analyses support an ancient African origin for human-adapted MTBC, and suggest that the global success of MTBC was partially driven by increases in human population densities during the Neolithic Demographic Transition. Moreover, our molecular epidemiological findings suggest that HIV co-infection perturbs the tight phylogeographic association between MTBC genotypes and their respective sympatric human host populations, further supporting a long co-evolutionary history between MTBC and anatomically modern humans.

Reconstructing outbreaks with tuberculosis genomics

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TB outbreak investigations typically include two components: contact tracing and molecular epidemiology. However, only a proportion of outbreaks can be "solved" using these approaches—field investigation may provide incomplete or uninformative contact data, while the low resolution of molecular typing techniques may incorrectly rule-in cases as belonging to a cluster and is often insufficient to reliably identify person-to-person transmission events.

With the advent of next-generation DNA sequencing technology, it has now become feasible to sequence the entire genome of every TB isolate from an outbreak. This provides an extremely high-resolution alternative to molecular typing, with individual mutations arising over the course of an outbreak acting as informative markers of transmission. For the first time, we can accurately reconstruct outbreaks and identify—with confidence—individual transmission events. By applying this technique to multiple outbreaks across different demographic and geographic settings, we can start to draw inferences about the natural transmission dynamics of TB—information that in turn can guide outbreak management and prevention strategies.

In this talk, I will introduce the basic principles behind the emerging field of genomic epidemiology and discuss that challenges associated with applying this technique to an organism like TB, where outbreak reconstructions are complicated by chronic infection, infection with multiple lineages, and latency.

Reconstructing regional transmission dynamics with tuberculosis genomics

T M Walker. University of Oxford, Oxford, UK

A number of recent studies have demonstrated the increased resolution of whole genome sequencing over established typing methods and have detailed the potential advantages to public health in detecting and managing individual outbreaks. How this new, more accurate technology might impact on public health policy at a regional level still needs to be investigated. We have sequenced at least one isolate from every patient with culture positive tuberculosis in Oxfordshire (UK) between 2007 and 2012, and from every patient in Birmingham (UK) between 2009 and 2013 to assess the regional transmission dynamics in these low and medium incidence settings respectively. I will present the preliminary results of these studies and discuss how the findings could inform bespoke, locally designed public health responses.

Benefits and challenges of rapid whole-genome sequencing for tuberculosis diagnostics

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Rapid whole-genome sequencing (WGS) directly from positive liquid mycobacterial cultures will likely become the standard of care in well-resourced countries, as illustrated by our recent investigation of a case of extensively-drug resistant (XDR) TB. WGS not only provides the ultimate molecular resolution for TB outbreak investigations, but is also theoretically capable of detecting resistance to all anti-tuberculosis drugs simultaneously. In order to harness the full potential of this technology, we will need to develop strategies to determine the genetic basis of antibiotic resistance in a timely manner. This could, for example, be achieved by mandating the elucidation of resistance mechanisms (as part of the approval process for new anti-tuberculosis agents) but the intellectual property issues relating to resistance mechanisms will have to be addressed. Finally, the analysis of WGS data will need to become automated and genetic information shared in an open access format before sequencing can become a routine diagnostic test.

Transmission of NTM reconstructed with genomics

J Parkhill. The Sanger Institute, Cambridge, UK

Mycobacterium abscessus, an opportunistic pathogen, is increasingly being isolated from cystic fibrosis patients worldwide. This multi-drug resistant organism is particularly difficult to treat, leading to chronic infection and an accelerated decline in lung function. Prior evidence suggests acquisition is primarily from the environment with an absence of patient-patient transmission. Whole genome sequencing was carried out on 168 samples collected from 31 CF patients attending Papworth hospital over a 4-year period. The phylogeny identified three sub-species of *M. abcessus* present in the patient group. Within each subgroup, different patients had acquired highly diverse strains indicating independent acquisition from the environment. Some clustering of strains between patients was evident, and two levels could be discerned; highly-related clusters with different patient samples identical or near-identical; and more distantly-related clusters with patient samples differing by approximately 50–200 single nucleotide polymorphisms. Epidemiological links consistent with recent transmission were identified in the first but not the second. We conclude that this data provides the first convincing evidence for both recent transmission within the CF centre, and the presence of two clones circulating in the wider population. The exact mechanism of transmission is

yet to be determined, however the strict infection-control procedures imposed in the hospital and our epidemiological analysis suggests that it is indirect.

EFFECTIVE TUBERCULOSIS EDUCATION AND COMMUNICATION INTERVENTIONS FOR PROVIDERS AND PATIENTS

Why work on communication skills?

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Background: Improving communication skills for health professionals is being advocated for and implemented as a way of strengthening provider-patient communication. Understanding the benefits of such improved communication skills is important for formulation and effective communication practices and policies for enhancement of disease management and control.

Objective: To document lessons learnt from a six months training of trainers in effective health communication for health care professionals working within the field of tuberculosis (TB).

Design: This is based on the participation in the six months training of health professionals from six different countries. The training focuses on strengthening communication skills and providing ways to deal with emotions and reaching goals. Observation of own communication and the effect it has on others is a major component in the training, and it builds on experiential learning.

Results: The observer-communicator concept employed in the training and the experiential learning exposed some hidden characteristics which usually bars effective communication, e.g., observation made it possible to notice the non-verbal signals one was passing to the other which in normal circumstances is forgotten but likely to send wrong messeges. The process stimulated the communicator to be present in the moment during the communication process and the end result is respect and relationship building with the possibility of influencing the right actions and avoiding unnecessary mistakes.

Conclusion: Being an observer-communicator helps one to be uptime. Practicing the skills changes your approach to communication both on personal and work-related issues.

Why work on communication skills?

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Setting: In the last decades, the Arkhangelsk TB Program (in the North-West of Russia) has made great achievements in TB control, with the incidence rate decreasing two-fold and mortality four-fold. Nevertheless, tuberculosis still remains a highly stigmatized disease. Care providers deal with patients suffering from emotional reactions (fear, shame, anger) and report fear of getting infected with tuberculosis which hinders effective communication. While official TB care is supportive of this dimension of patient care, they are more focused on the treatment, diagnosis and case finding and civil society organizations are getting more involved in stigma alleviation and patient empowerment.

Objective: To reduce stigma and improve the quality of the psychosocial support of TB patients.

Design: LHL International health communication methodology which includes processes of improving self-awareness, communication and motivation has been piloted in the context of TB control services in Arkhangelsk Region.

Results: Health care providers who have received training in health communication report increased job satisfaction and better relationship with colleagues, patients and family members. They report that they deal better with fear and anger. Before training the tendency was to categorize patients as the problem, and they were unaware of how negative emotions affect communication. After training they see that that it is the communication between care providers and patients that is the problem and not the patient himself.

Conclusion: Training in health communication is beneficial for all care providers dealing with tuberculosis. Health care providers embrace and recognize it as a tool to perform better in their work as well as being more satisfied with their work situation. Health communication relates very well to the WHO STOP TB strategy from 2006 where patient empowerment and engagement of all care providers are an indispensable part of TB control services.

Health communication: what, how, why and who?

H Amdal, M Drage. LHL International Tuberculosis Foundation, Oslo, Norway

Background: We have the technical skills and the medication to cure tuberculosis, but we still face challenges with case detection and default. How can we ensure that patients seek early diagnosis and stay on treatment? Based on years of experience working within TB control LHL International has developed a health communication concept to overcome these challenges.

Objective: Presenting a health communication concept and its effect on different stakeholders—health professionals, treatment supporters and patients.

Methodology: The concept is two-fold, where one part is the development of patient centered booklets

and the other part is training care providers in communication skills.

Results: Today a pool of trainers in several countries train care providers in their own setting, and the feedback is unison: this training should be mandatory for all working within health. Trained health-professionals report change in attitude and behavior towards patients, increased awareness of own communication, taking responsibility for solving problems, better relationships with patients and colleagues, improved self-esteem and improvement in anger-management. When involving patients in development of information material we meet their needs and empower them. The patients are able to open up and share information. Increased dialogue about TB in the community increases knowledge and decreases stigma. Knowledgeable patients can help identify new cases and encourage treatment adherence that leads to better treatment outcomes. These booklets are important tools of communication, and reinforces the TB knowledge and job-satisfaction of health professionals and treatment supporters.

Conclusion: The ability to communicate well with patients suffering from fear, stigma and misconception about TB is important when striving for better treatment outcomes. The health communication concept is a tool that is locally adaptable and empowers the different stakeholders in TB control.

'Now we are confident!': experiences of being trained and training others in effective health communities

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Fighting TB is a priority in Sudan, nevertheless several challenges have risen such as unsatisfactory case detection and high rates of loss to follow up. The potential of health communication in improving disease prevention and promoting health is substantial. Utilization of effective health communication is a crucial step that can be embedded in all aspects of curbing TB.

With an anticipation to rectify the situation, systematic-stepwise health communication workshops are conducted via a North-South partnership 'LHL, Epi-Lab and STPA'. These workshops are merely about building front-line health workers and volunteers' capacity in health communication and positive psychology aspects. It was a participatory ownership driven approach based on Sudan's context and needs. A qualitative evaluation/exploration of the short term outcomes was done. Many positive feedbacks were reported. It has shown momentous effect on trainees as human capital for TB care, such as self-actualization, satisfaction and reinforcing of confidence. Trainees have flagged that they can now handle stressful conditions, support patients throughout treatment, im-

prove their personal life, and practice new positive modes.

When I was in the trainees situation I gained confidence in this intervention, and as a facilitator I am much convinced that positive outcomes could be reached. 'Health Communication course should be a mandate for every health worker at every level. Under this light, this training could be a building block supported by a strong evaluation strategy and research element, so as to demonstrate its authenticity in TB prevention and control.

Evaluating tuberculosis behaviour: change communication campaigns

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Background: In Azerbaijan knowledge about TB transmission, the importance of early detection and treatment adherence is low, contributing to a high number of defaulters and high MDR-TB rates. A national-scale communication campaign to contribute to TB detection and treatment and fight stigma was conducted in 2010–2011. This was a very first comprehensive Advocacy, Communication and Social Mobilization activity in Azerbaijan to target both patients and healthy population.

Interventions: Six types of print and video materials for various audiences were developed. Research and partner consultations helped to form key messages for the 'TB is not shameful. Get treated' campaign. Behaviour change communication and entertainment-education approaches were employed to produce two public service announcements (PSAs) and an educational documentary broadcast on national and regional TV in November–December 2010 (950 showings).

Results: An omnibus survey and focus group discussions were used to evaluate the project outcomes. The first wave of the survey was conducted in June 2010, prior to the campaign and accounted for non-readers/viewers. Four FGDs with 20 participants demonstrated that those who read/viewed project materials received comprehensive information regarding TB symptoms, the importance of early detection and treatment by TB specialist. Viewers/readers reported that they would seek immediate health care if symptoms of TB arose. Omnibus survey results found that 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.

Conclusions: Communication interventions are vital in the struggle to overcome TB-related stigma as well as to raise awareness about TB. The use of television proved to be effective in reaching big audiences. Innovative entertainment-education approaches provided an appropriate and appealing way to deliver complex messages.

Using text messages as a cue to action for tuberculosis patients

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Background: Effective tuberculosis (TB) care requires adherence to a long course of medication and frequent clinic appointments. With the increased mobile phone penetration opportunities abound for improving TB case finding, linkage, treatment and retention in care. Support to adherence to anti-retroviral therapy using text messaging improves outcomes in resource-poor settings. We report on a pilot program to determine the feasibility of reminder texts in enhancing clinic attendance among TB patients at Moi Teaching and Referral Hospital (MTRH) TB clinic in western Kenya.

Methods: The 185 TB patients with mobile phones at MTRH TB clinic were informed that reminder texts will be sent to them in Ki-Swahili one day prior to their scheduled clinic appointments using the software FrontlineSMS (v1.6.1, kiwanja.net initiative) between April–May 2011. Rates of clinic attendance on scheduled days were recorded and compared between those receiving and not receiving the text reminders. Relative risks were used to measure strength of associations, χ^2 to compare proportions and t-test for continuous variables. Level of confidence (CI) was set at 95%. Each patient was analyzed only once when the text was delivered.

Results: Text program patients had a mean age of 31 years, 42% were female, 28% HIV infected, 8% re-treatment TB cases. Those who received and did not receive texts were not statistically different in the above characteristics. 144 (78%) patients received at least one text; 41 did not. Delivery of reminder texts led to an overall 43% increased chance (95% CI 1.03–1.98, $P = 0.016$) in adherence to scheduled clinic visits. The average cost of sending one text was US$0.19.

Conclusions: Text messaging is a potentially effective method to enhance adherence to TB clinic appointments. Carefully designed larger studies involving the community, providers and programs can enumerate the full potential of this and similar technologies in improving TB care and outcomes.

CHILDHOOD TUBERCULOSIS DIAGNOSTICS: WE HAVE MADE PROGRESS, BUT ARE WE THERE YET?

Diagnostic methods for childhood tuberculosis: an update from the TB CHILD study

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Background: Diagnosis of tuberculosis in children remains a major challenge. The lack of appropriate diagnostic tests impedes assessment of disease burden, development of new treatment and vaccination strategies and effective control of childhood TB.

Methods: The TB CHILD project evaluated 10 new diagnostic platforms in adults (pulmonary TB cases, $n = 178$; controls, $n = 124$) and in symptomatic children ($n = 493$). Results from 3 diagnostic approaches will be presented: Xpert® MTB/RIF in sputum, IP-10 in blood and urine, and T-cell activation marker-interferon gamma release assay (TAM-IGRA) in blood.

Results: Xpert MTB/RIF detected 67.5% of the culture-confirmed paediatric tuberculosis cases with a specificity of 100%. Only 1 out of 52 highly probable and 2 out of 62 probable TB cases were additionally tested Xpert positive. Preliminary results show that urine and blood IP-10 are associated with active TB in adults and children compared to healthy subjects independently of HIV status. However, IP-10 has only a moderate discriminatory capacity to distinguish active TB from 'no active TB' (i.e., respiratory disease other than TB). Data from the TAM-IGRA study suggest that down-regulation of CD27 on MTB-specific CD4 T cell is associated with active TB and that the assay allows the differentiation between latent and active TB in the vast majority of symptomatic children.

Conclusions: The Xpert MTB/RIF test identified—similar to previous studies—the majority of children with culture-confirmed pulmonary tuberculosis with excellent specificity. The finding that IP-10 can be detected in children's urine with lung diseases can open new strategies to define biomarkers of inflammation in compartments different from blood.

TAM-IGRA, a novel immune-based test with diagnostic turn-around time of 24 h, has great potential to improve diagnosis of paediatric TB in future.

Feasibility, tolerability and performance of alternative specimen collection methods for tuberculosis diagnosis in HIV-infected children using Xpert® MTB/RIF

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Background: Diagnosis of tuberculosis (TB) is challenging in HIV-infected children, due to the paucibacillary nature of the disease, and poor specificity of clinical and radiological features, in a situation of very high morbidity and mortality, and major therapeutic issues. We assessed feasibility, tolerability and performance of alternative specimen collection methods for the diagnosis of TB in HIV-infected children using the Xpert® MTB/RIF assay.

Methods: HIV-infected children aged ⩽13 years with a suspicion of intra-thoracic TB were enrolled after parental informed consent in pediatric HIV clinics in Burkina Faso, Cambodia, Cameroon, and Viet Nam. Children underwent 2 gastric aspirates (GA) or 3 sputum samples (SS) if aged ⩽ 10, and alternative specimen consisting of 1 nasopharyngeal aspirate (NPA), 1 stools sample (Sto), and 1 string test (ST) if aged ⩽ 4. To evaluate tolerability of GA, ST, and NPA, discomfort and pain were assessed by nurses using the FLACC behavioral scale (worse score = 10). All samples were tested using Xpert and culture.

Results: 174 children—mean age 7.2 ± 3.5 years, 83 (47.7%) female—were enrolled. Specimens were obtained from 171 children: 333 GA, 100 SS, 169 (98.8%) NPA, 164 (95.9%) Sto, and 105 (78.4%) ST in 134 children ⩽4 years. The mean FLACC scale score during collection was 4.6 ± 2.9 for GA, 4.7 ± 2.8 for NPA, 1.5 ± 2.0 for ST. TB was confirmed by culture in 20/171 (11.7%) children. Sensitivity of Xpert for the diagnosis of TB was 90.0% (18/20) and specificity was 98.7% (149/151). Xpert yield when performed on the combination of NPA+Sto+ST was similar to when performed on GA or SS (19 cases).

Conclusion: The combination of NPA, ST, and Sto is a promising and well tolerated alternative to collection methods usually recommended by national programs. Xpert MTB/RIF performed on respiratory and stools samples enables rapid confirmation of TB diagnosis in HIV-infected children.

Specimen collection and sampling strategies to diagnose tuberculosis in children

M Bonnet. Epicentre, Paris, France

In high burden and limited resource countries, the diagnosis of pulmonary tuberculosis in children is rarely confirmed. It is based on a combination of a history of tuberculosis exposure, presence of suggestive clinical symptoms and radiological findings. However, this is expected to change with increased access to the Xpert® MTB/RIF assay but the paucibacillary form and the difficulty to collect respiratory specimens in children, especially in the ambulatory setting, may limit the benefit of this new tool.

This presentation reviews the most recent published and unpublished research, which pertain to respiratory specimen collection methods and include the use of sputum induction, gastric aspirate, nasopharyngeal aspiration, string test and stools. The tuberculosis detection yield using the mycobacterium culture and the XpertMTB/RIF assay, in addition to the operational aspects of the different specimen collection methods in term of feasibility, acceptability and tolerability are discussed.

The use of different sampling strategies to increase the detection yield of the tuberculosis culture and the XpertMTB/RIF assay with a good feasibility and acceptability, especially for outpatient facilities, is addressed. These strategies include the concomitant collection of different types of specimens, the number of specimens to be collected and the pooling of specimens. Finally, optimising specimen processing methods for induced sputum and gastric aspirate in order to improve the tuberculosis culture detection yield is also discussed.

Validation of the NIH consensus case definitions for evaluation of diagnostic tests for childhood tuberculosis

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Background: Consensus international case definitions were recently proposed for use in paediatric tuberculosis diagnostic research. The relevance of these definitions to contact tracing studies is unknown.

Methods: We developed a standard case definition for use in a community-based household contact tracing diagnostic study, which assessed the diagnostic utility of Interferon-Gamma Release Assays for the detection of *M. tuberculosis* infection and disease, in Cape Town, South Africa. We compared the certainty of disease using the consensus case definition and protocol-defined case definition (which excluded tests of infection), and describe the disease spectrum and severity using a standard approach.

Results: There were 111 possible disease episodes in

109 children (21% HIV-infected) of 1093 total children enrolled. Based on consensus definitions, there were 8 episodes of confirmed, 12 probable, 17 possible, 3 unlikely and 2 of not tuberculosis. Using the protocol case definition there were 23 episodes of confirmed, 36 probable, 27 possible, 0 unlikely and 21 of not tuberculosis. Of the 111 possible episodes, 69 were unclassifiable using the consensus definition while 4 were unclassifiable using the protocol definition. Agreement between the definitions was fair (kappa: 0.30, 95%CI 0.23; 0.38, $P < 0.0001$). There were 24 (28%) episodes of severe and 62 episodes (72%) of nonsevere disease.

Conclusions: The consensus case definition has limited applicability to household contact diagnostic studies, where a surprisingly wide spectrum of disease was observed in this high-burden setting. Further research is needed to adapt these definitions to different epidemiological settings, to capture the wide spectrum of paediatric tuberculosis.

Diagnosis of pulmonary tuberculosis in children: assessment of the accuracy of the NIH expert consensus criteria

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Background: Accurate clinical diagnosis of PTB in children remains challenging. The NIH therefore convened a meeting of experts, who developed a consensus document of proposed standardised clinical case definitions and diagnostic categories for TB diagnostic studies, based on clinical, radiological and microbiological criteria.

Aim: To investigate the accuracy of the NIH criteria for different diagnostic categories.

Methods: Consecutive children hospitalised with suspected PTB in Cape Town, South Africa from February 2009 to June 2012, enrolled in a TB diagnostic study, were extensively investigated for PTB. Multiple specimens, including 2 induced sputa and 2 nasopharyngeal aspirates and if clinically indicated and feasible, extrapulmonary specimens, gastric lavage, tracheal aspirate or bronchoalveolar lavage were obtained for culture confirmation. Signs, symptoms and exposure history were carefully recorded; all children had a tuberculin skin test. HIV testing was done when the child's HIV status was unknown. Children were categorised as definite TB (culture positive), probable TB (signs or symptoms and a chest X-ray suggestive of TB), possible (signs or symptoms, but chest X-ray not suggestive) or NOT TB (not treated for TB and improved at 1 and 3 month follow-up). We compared the proportion of children diagnosed in these categories with the NIH categories and criteria.

Results: 914 children were included of whom 207 (22.7%) were HIV-infected. The median (IQR) age was 25.1 (12.7–61.0) months; 485 (53%) were male. Of these, 165 (18%) were classified as definite TB, 134 (15%) as probable, 310 (34%) as possible and 305 (33%) as NOT TB. Applying the NIH criteria, 306/914 (34%) were unclassifiable including 17 (6%) with definite PTB. Of these, 135/306 (44%) did not meet the NIH symptom inclusion criteria, 45 (15%) were lost to follow-up, 28 (9%) did not have a chest X-ray reading and the remainder improved without TB therapy but had no immunological evidence of TB or of exposure. Of the 135 who did not meet the NIH symptom criteria, 93 (69%) had cough less than 14 days, 59 (42%) had recent weight loss and 50 (37%) had fever less than 7 days. Of the 608 children who could be classified using the NIH criteria, 148 (24%) were classified as definite TB, 116 (19%) as probable, 315 (52%) as possible TB, 29 (5%) as NOT TB. Amongst these, there was good agreement for the definite, probable and possible TB groups but poor agreement between those classified in the NOT TB groups. Of the 147 classified as NOT TB in the prospective study, 21 (14%) were classified as probable, 99 (67%) as possible TB, 27 (18%) as TB infection and only 2 (0.3%) as NOT TB by the NIH criteria.

Conclusion: The NIH criteria for signs and symptoms lack sensitivity as they do not include children with acute symptoms. Conversely, the criteria have inadequate specificity leading to overdiagnosis of possible or probable TB and under diagnosis of children without TB. Improvement without TB therapy should be considered as a criterion for the NOT TB category.

Keeping pace with evolving evidence: a process to optimise the NIH consensus case definitions for tuberculosis diagnostics research in children

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Establishing a diagnosis of TB in children is challenging due to the paucibacillary nature of the disease, the nonspecific clinical manifestations and the difficulty in accessing specimen. This results in a lack of an appropriate reference standard that poses challenge for evaluation of TB diagnostics in children. Clinical case definitions represent the best option for classification of TB in diagnostic studies in children but require standardization and validation for optimal reproducibility and use in research. Several childhood TB case definitions for use in clinical care exist but suffer from lack of agreement and significant variations between them. A consensus case definition for research use generated by an international expert

panel was published recently in an attempt to use standardized terminology and definitions and constitutes an encouraging step in the field. This presentation discusses additional steps needed to insure validation, maximize reproducibility and promote broad adoption of these consensus case definitions.

CONTROVERSIES IN TUBERCULOSIS: SHORT COURSE CHEMOTHERAPY FOR ALL AS A STRATEGY TO ELIMINATE TUBERCULOSIS IN A SOUTH PACIFIC ISLAND

For: rationale for mass population treatment

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The elimination of TB globally by 2050 is an internationally agreed target. TB elimination is defined as an annual incidence rate of less than one new case per million population, a rate which is expected to prevent sustained transmission of *Mycobacterium tuberculosis*. However, this is clearly unrealistic without new tools and approaches. There are no current attempts to eliminate TB from a population. Attempts to eliminate malaria from populations have been reported since the 1930s, and global malaria eradication is targeted, even in the absence of a highly effective vaccine, and despite the need for a vector control component and multiple rounds of mass treatment. Mass prophylactic treatment against TB has been attempted, after active case finding and treatment of symptomatic disease. This approach reduces the incidence of TB dramatically, but does not reach the elimination threshold. This failure to eliminate TB may relate to the fact that current diagnostic tests cannot adequately distinguish those who are not infected from those who are infected with *M. tuberculosis*, or those who are latently infected from those who are diseased. Therefore, we propose a mass treatment approach that administers a full TB treatment course to the whole population: those with overt and occult disease are effectively treated, as are those with latent infection. In addition, those without infection are prevented from getting infected. Adopting a true TB elimination mind-set should involve consideration of a mass treatment approach. This will lead to robust debate and a new research agenda, such as trials of shorter regimens in those with asymptomatic disease. An effective treatment course of only a few weeks' duration in the future would change the landscape in favour of mass treatment dramatically. A mass treatment approach is of relevance to a restricted number of populations and countries at present, but may well become increasingly applicable as advances in treatment are made.

TOBACCO CESSATION AND SMOKE-FREE ENVIRONMENT FOR TUBERCULOSIS PATIENTS IN LOW-INCOME COUNTRIES

The Union working group on tobacco cessation and smoke-free environment for tuberculosis patients

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Introduction: The Union Lung Health Scientific Section established a working group in December 2009 to research a simple, cost-effective approach to smoking cessation for TB patients. This group's efforts led to the development of the ABC approach outlined in The Union guide Smoking Cessation and Smokefree Environments for Tuberculosis Patients published in 2010. The ABC (A = ask, B = brief advice, C = cessation support) approach was initially piloted in Bangladesh, China, India and Indonesia.
Objectives: To share the outcomes and lessons learnt from implementing The Union's Guide Smoking cessation and smokefree environments for tuberculosis patients.
Methods: Key approaches are; establish TB services 100% tobacco-free, presents ABC for identifying TB patients who smoke, helping them quit, and promoting smokefree homes for patients and families. It is delivered systematically within routine programme and can be done within 5–7 minutes.
Results: The Union ABC approach has demonstrated encouraging smoking quit rates at the end of 6 month TB treatment. In Bangladesh, of the 615 current smokers, 75.4% reported they quitted smoking. In India, of the 1333 current tobacco users, 67.3% remained quitters. In China, of the 233 current smokers, 59.7% quit smoking. In Indonesia, of the 582 current smokers, 66.8% quitted smoking successfully.
Conclusion: The results were self-reporting but it indicates that smoking cessation intervention is feasible and doable at the DOTS clinic.

Tobacco cessation and smoke-free environments for tuberculosis patients in Bangladesh

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Background: Bangladesh is one of the 14 countries of the world facing heavy tobacco burden. Tobacco smoking is an important risk factor for TB. BRAC started a pilot intervention for TB patients in May 2011. The aims of the initiative are to identify current

smokers among TB patients, support them to quit smoke and enhance smoke-free environment.

Intervention: BRAC supported 17 peri-urban TB centers of Dhaka with 2.8 million populations were selected for intervention. TB programme staff were trained on tobacco control with particular focus on harmfulness of smoking, second-hand smoking and its impact on TB, introduce counseling methods and documentations. All the tools were based on the guideline 'Smoking Cessation and Smokefree Environment for TB patients' by the Union. The tools were translated in Bengali. Counseling is given to patients for smoking cessation during initiation of treatment and subsequent visits to TB centre. A brief counseling is done by Shasthya Shebika (Frontline Community Health Worker) during DOT.

Results: All the 17 health centers were declared as smoke-free and 'No smoking' signage is placed at the entrance of these centers. From May 2011 to April 2013, a total of 6782 TB patients were enrolled in those areas. Among them, 22% patients were smokers where 40% were male and 1% female. In the same period, a total of 2139 patients were identified who were exposed inside home, of them 59% female. During April 2011 to March 2012, out of 556 identified smokers among enrolled TB patients, 75% quitted smoking, 12% were still smokers, 3% were relapsed smokers, 2% lost to follow-up and 3% died at the end of TB treatment. In the same period, about half of the patients (52%) who exposed inside home remain exposed to smoking even at the end of treatment.

Conclusion: Smoking cessation among TB patients is found to be effective through regular counseling. Hence the intervention will be recommended to expand to other areas.

Tobacco cessation and smoke-free environment for tuberculosis patients in Indonesia

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Introduction: The Union guide Smoking Cessation and Smokefree Environments for Tuberculosis Patients was piloted in 17 health centres in Bogor city in 2011. The Guide presents ABC (A = ask, B = brief advice, C = cessation support) approach for smoking cessation and smoke-free environments for tuberculosis patients.

Objectives: To describe the results of smoking cessation and lessons learnt in Bogor city in Indonesia.

Methods: Key approaches are: establish TB services 100% tobacco-free, present 'ABC for identifying TB patients who smoke, helping them quit, and promoting smokefree homes for patients and families. It is delivered systematically within routine programme; can be done within 5–10 minutes; includes personalized

and general advice. Cessation support also includes offering No Smoking signs and posters on health impacts of smoking. Patients' close family members were asked to confirm whether the patients quit smoking for the last two weeks at least.

Results: Between January 2011 and December 2012, 750 new TB patients were diagnosed, of whom 582 (77.6%) were current smokers. All health care (about 380) services in Bogor city declared tobacco free. Of the 750 patients, 84% of them created their home 100% smoke-free. Of the 582 patients, 66.8% quit smoking.

Conclusion: Brief advice of 5–10 minutes with minimum cessation support at every visit of TB patients resulted in high quit rates and higher awareness of health impacts of secondhand smoke exposure, which led patients to make smoke-free homes and health providers to make tobacco free health-care.

Smoking cessation interventions among tuberculosis patients in Nepal: lessons learnt from PAL

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Background: NTP Nepal has been implementing Practical Approach to Lung Health (PAL), since 2011. One of the components of the PAL is smoking cessation. However, the PAL does not provide educate guidance and materials on smoking cessation. Hence, in collaboration with NTP, we developed a behavioural support intervention to help people to quit tobacco. The intervention is being implemented in Kathmandu and Rupandehi districts.

Intervention: Action research was used with patients and health workers and included: qualitative interviews; focus groups with health workers; evidence and theory review of tobacco behaviour change interventions. In the first phase, communication materials were developed, field tested and used. Key challenges in designing the intervention were: health worker's limited time, knowledge of tobacco-related harms and lack of familiarity with behaviour change techniques; low literacy levels among patients as perceived by health workers. The evidence base and 'Stages of Change' theory point to the effectiveness of focusing interventions on those motivated to quit. This allowed more prudent use of health worker time as brief advice alone was given to those not motivated to set a quit date. Health workers were trained on behaviour change techniques and these were integrated within patient education materials, which were assessed during action research cycles. NTP staff were involved throughout to enable appropriate design of intervention and scale up.

Lessons: Using research evidence and qualitative work allowed the development of an appropriate intervention integrated within routine care. Working through PAL has maximised potential for sustainability of the approach and its potential scale up.

Conclusions: Using evidence and theory, behaviour change techniques and involving patients and health workers in the design of a tobacco cessation intervention increases appropriateness and sustainability. Final data will be presented in the conference.

SHARED AIR, BUT NOT NECESSARILY SAFE AIR: TUBERCULOSIS INFECTION CONTROL IN OUT-PATIENT AND CONGREGATE SETTINGS

Tuberculosis infection control in the community setting

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Background: Two TB IC implementation tools were developed to increase attention and action to TB infection control issues at the community level. The global community had developed facility level tuberculosis infection control training curriculum with limited community level focus.

Methods: The USAID supported Tuberculosis Control Assistance Program (TB CAP) led by FHI360 developed a Simplified Checklist for TB infection Control in 2010. Consultants in infection control participated in this process and eleven sub-Saharan African country representatives. The three part checklist was designed with a goal to increase attention and action related to TB IC issues at community level, to reduce the risk of TB transmission from clients to community health workers (CHW) and to reduce household and community transmission. Following agreement to use the checklist as a training tool, a TB infection control at the community level training handbook was developed in 2011 with information from the three checklists. Trainings and supervision of community volunteers trained have been done in a number of countries, including Zambia.

Results: Two hundred sixty-two (262) community volunteers were trained in Zambia from February 2012 to July 2013 (150 women and 112 men) including 50 traditional healers who are first points of contact in most communities in Zambia. The other community volunteers trained provide community level implementation of TB and HIV control activities including patient treatment support and tracing of TB contacts. Training of Trainers of program man-agers and supervisors followed by cascade trainings have also been held in Ethiopia, Cambodia, Mozambique and Zimbabwe, led by the FHI 360 community consultant.

Conclusions: Community level TB infection control measures have been introduced to key community stakeholders in a number of countries that have a high TB and/or HIV burden as a component of comprehensive TB infection control.

A case study of tuberculosis infection control in Integrated HIV Care out-patient departments in Mandalay, Myanmar

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As transmission of tuberculosis (TB) to PLHA is a global issue, Myanmar is one of the 41 high TB/HIV burden countries and it has also estimated that 60–80% of AIDS patients have TB, meaning that TB is the leading opportunistic infection among PLHA. Integrated HIV Care (IHC) for PLHA has been implemented by International Union Against Tuberculosis and Lung Disease (The Union) with good collaboration of National AIDS Program (NAP) and National Tuberculosis Program (NTP) providing Antiretroviral Therapy (ART) and other opportunistic infections (OIs) treatment since 2005. And currently IHC out-patient departments in Mandalay General Hospital are serving for more than 3000 enrolled PLHA and opening 6 OPDs per week. To reduce the transmission of TB among PLHA, TB infection control measures have been practicing in IHC clinic. Therefore my presentation will discuss a variety of TB control interventions in congregated IHC clinic site, a resource constraint setting, Mandalay, Myanmar. It will also discuss about the challenges in implementing each TB infection control measure and their effectiveness by analyzing the TB prevalence among PLHA.

SMOKE-FREE ENVIRONMENTS: USING COMPLIANCE TESTING AS A TOOL TO IMPROVING POPULATION LUNG HEALTH OVERALL

Use of smoke-free compliance studies in India at local and national level

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Background: Smoke-free initiatives have gained significant momentum since India enacted comprehensive smoke-free legislation in October 2008. Many compliance surveys were conducted across the country to assess the degree to which smoke free law is being obeyed and implemented in public places as

defined under the Indian tobacco control legislation. They also provided answers to another question, whether compliance improves with successive waves of enforcement? The findings that emerged were used to document compliance rates; and to identify types of venues and demo-geographic regions where fresh waves of enforcement efforts are needed.

Intervention: The smoke-free law requires compliance with a number of measures, and the presence/absence of these was used as criteria for determining the level of compliance. A survey protocol was used to assess the simple 'measures' such as the presence of signage, observation of active smoking and the presence of smoking aids such as ashtrays, lighters and matchboxes in buildings. The survey also incorporated observation of signs of smoking in the recent past (e.g., the presence of cigarette/bidi butts or smell of tobacco smoke) as indicators of non-compliance of a site.

Results: More than 70 smoke-free compliance surveys have been conducted since 2009 and the compliance to various provisions of legislation varied from 35 to 100% in jurisdictions across India which included cities, districts and states. The jurisdictions with high levels compliance were declared smoke-free by their government authorities and corrective measures were taken where low compliance was observed.

Conclusions: Compliance assessment surveys are a simple and cost-effective monitoring tool for validating progress in the enforcement of smokefree policies. Capacities need to be strengthened among local research organizations and a common protocol must be adopted to ensure standardization of study methods which can offer comparison across jurisdictions.

Smoke free compliance: opportunities in Africa?

D Adam. Tobacco Control/The Union Africa, Ndjamena, Chad

The tobacco epidemic in the world is a serious threat to the health of populations. Countries in Africa are being aggressively targeted by the tobacco industry. Recognizing this threat, most African governments are strongly committed to the fight against this scourge through several actions including the ratification of the Framework Convention on Tobacco Control (FCTC), the adoption of smoke-free laws and implementing regulations including a ban on smoking in public places. Despite this political commitment, governments find it difficult to enforce the ban on smoking in workplaces and public places. Compliance testing on smoke free in public places can be useful tools for implementing smoke free regulations. They are significant opportunities for the authorities to ensure the application of the law and regulations on smoke free. The approach to the study conducted in Mauritius is based on the analysis of data collected by the monitoring bodies of the Ministry of Health

in 300 public places. The main objective of this exercise was to create more awareness on the part of venues on the ground to ensure strict compliance of the regulation but also to collect data via questionnaire vital information in order to assess the level of compliance. The second compliance study conducted in Nairobi, Kenya is similar in assessing the level of compliance in public places using a questionnaire. The third study is conducted in public places and Chad which combines awareness of responsible public places to ensure compliance assessment by using a questionnaire and an Air Quality Monitoring (AQM). The AQM use Dylos DC1700 a practice material for secondhand smoke (SHS) measurement. The results of this compliance are useful for educating the owners, policy makers, employees and/or the general public about the existence of anti-smoking laws and compliance.

Compliance monitoring and the role of the tobacco industy: lessons from the Philippines

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Measuring a jurisdiction's compliance with laws and ordinances for smoke-free environments represents an important tool and opportunity to improve population lung health overall as well as cardiac health. This presentation will discuss recent compliance monitoring activity undertaken in the Philippines by The Union and Roswell Park Cancer Institute. The role of the tobacco industry regarding tobacco control overall and smoke-free ordinances in particular will be described, providing an important 'back story' to our efforts.

Lessons from the Philippines will be elucidated, referring mainly to

1 WHO FCTC Article 5.3 Guidelines;
2 Efforts in the country to implement this important Article; and
3 The Union's latest technical package to support implementation of Article 5.3.

How compliance studies helped develop smoke-free policy at local level in Indonesia

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Introduction: Two-thirds (67.4%) of males, 4.5% of females and 36.1% of overall adults (61.4 million) currently use tobacco. More than 97 million nonsmokers are regularly exposed to secondhand smoke (SHS). 78% of youth (age 13–15) are exposed to SHS in public place, and 69% of youth are exposed to SHS at home. Some 70% of all children less than 15 years of age are regularly exposed to

SHS. Government implementation regulation no. 109/2012 of the Health Law 2009 has a provision of smoke-free environment to be implemented by local government. Local governments are required to make local bylaws on smoke-free spaces. A sub-national smoke-free initiative is on progress. Monitoring compliance to smoke-free policy is critical to strengthen enforcement and to demonstrate evidences that smoke-free policy can be implemented and expanded.

Objectives: To describe compliance monitoring of smoke-free local laws in Jakarta and Bogor and share the lessons learnt to strengthen smoke-free policy.

Methods: A standard compliance tool was developed as per the local smoke-free policy. Compliance monitoring is conducted every four month. Results are presented to senior policy makers, enforcement agencies and media.

Results: Compliance to smoke-free Bogor law was significantly increased to 76.5% in March 2013 from 26% in March 2011. Similarly compliance to smoke-free Jakarta regulation is improving. Policy brief of compliance monitoring contributed to strengthen local regulation on enforcement in both cities. Compliance results from these cities demonstrated strong evidences that 100% smoke-free policy can be implemented. The data also contributes to counter TI's argument. Smoke-free is on progress to more than 80 sub-national jurisdictions and a comprehensive smoke-free policy is available in 20 cities.

Conclusion: A regular compliance monitoring is needed to strengthen smoke-free enforcement and to expand the smoke-free policy at sub-national level.

How can air quality monitoring equipment enhance compliance monitoring? And when should it be used?

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This presentation will provide a summary of the work to measure second-hand smoke levels in bars in Scotland, England and Wales to evaluate the impact of smoke-free legislation implemented there in 2006/7. The role of air quality monitoring in communicating the benefits of smoke-free legislation to the public, workers, media and policy makers will be explored with a description of how the data can be used to explain the effect of legislation on indoor venue air quality. A review of the equipment used for this work and some of the equipment now available for future work will also be given together with some discussion about carrying out educational and advocacy work to improve enforcement and compliance in countries with existing, but poorly implemented, smoke-free laws.

BEST PRACTICES IN IMPLEMENTING TB-HIV COLLABORATIVE ACTIVITIES IN MATERNAL AND CHILD HEALTH SETTINGS

Operational experience with providing isoniazid preventive therapy for pregnant women with HIV in Kenya

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Background: The World Health Organization recommends routine tuberculosis (TB) screening of HIV-infected pregnant women and provision of isoniazid preventive therapy (IPT) to those without active TB disease. We describe data on provision of IPT for pregnant HIV-infected women at Eastern Deanery AIDS Relief Program (EDARP) health-facilities.

Methods: We reviewed EDARP's electronic medical record on TB screening and IPT outcomes among pregnant HIV-infected women enrolled between January 2011 and December 2012. IPT was offered to pregnant women who had no TB symptoms following standardized TB screening.

Results: Eighty-six percent of 2429 pregnant HIV-infected women enrolled into prevention of mother to child transmission program PMTCT were screened for TB; 232 reported TB symptoms and 53 of them were diagnosed with TB. Among 1847 women with no TB symptoms, 269 (14.6%) received IPT. Pregnancy was the most common reason (41%) that clinicians gave for deferring IPT. Among women receiving IPT, median age was 28 years [Interquartile range (IQR) 25–33 years], median gestation at start of IPT was −7 weeks (IQR −16–1 weeks). Two hundred women (71%) completed IPT while 15 (0.5%) discontinued IPT due to adverse events.

Conclusion: Although majority of HIV-infected pregnant women were eligible for IPT, clinician discomfort with IPT provision was a major barrier to provision of prophylactic therapy. Longer term follow-up is needed to determine the impact of deferred IPT on TB incidence among women and their children.

Integrating isoniazid preventive therapy into routine care of children and families with HIV in Swaziland

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Background: Having the world's highest incidence of TB (1317/100 000) and an adult HIV-TB co-infection

rate of 77%, Swaziland's health system is extensively strained by this dual epidemic.

Setting: Baylor-Swaziland Centers of Excellence for pediatric HIV-TB care, where a family-centered approach for service delivery is embraced.

Aim: From 2008 to 2010, our Centers piloted the integration of isoniazid preventive therapy (IPT) into our comprehensive pediatric TB-HIV care. Informed by this pilot and in conjunction with expansion of national services, the program was replicated in our satellite clinics thereby offering IPT to 70% of HIV-infected children in Swaziland.

Results: From 2008 to date, over 550 HIV-infected children have initiated IPT through our programs. Program successes included seamless integration of IPT into HIV services, effective use of pediatric isoniazid (INH) formulations, and low incidence of INH side effect. Common obstacles arose among health care workers (reluctance to provide IPT, fear of IPT induced drug-resistance), caregivers (lack of an adult caregiver, inability to return for monthly refills) and the health system (INH and pyridoxine stock outs).

Conclusions: IPT can be delivered at the primary health level within a family centered program providing integrated HIV and TB services. This pilot program informed and enhanced the Swaziland national IPT program roll-out through identification of common barriers to successful IPT delivery.

INNOVATIVE APPROACHES TO BRINGING NEW TUBERCULOSIS DIAGNOSTICS TO THE PRIVATE SECTOR

Expanded access for lung health in Bangladesh through private laboratories

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Background: A large proportion of patients initially seek care from private healthcare providers for symptoms related to lung diseases. In Bangladesh, private laboratories (PLs) act as a hub for medical care where they house private medical practitioners and chest consultants in addition to their regular diagnostic services. PLs serve a large proportion of tuberculosis (TB) suspects, are often not linked to the National TB Control Program (NTP).

Methods: Sputum smear microscopy, chest X-ray (CXR) and GeneXpert (GXP) were used as part of a large active case finding strategy targeting towards four high volume PLs in Dhaka city through a well designed diagnostic algorithm from January 2012 to March 2013. Single, good quality sputum specimen was collected from suspects after providing sputum submission instruction and CXR was performed at the same time. The gateway to the GXP was TB suspects whose smear results were negative but the CXR shadow was in line with TB and/or suspects with previous history of anti-TB treatment for more than a month. All the identified TB patients were enrolled for treatment through the NTP or their consulting physicians in the private sector. However, both the groups were followed up by the project staff during their treatment maintaining the standard formats and were reported back to NTP quarterly.

Results: A total of 215 811 individuals were verbally screened for symptoms of TB. Sputum specimens from 6347 (3% of total screened) suspects were collected. During the intervention period, 807 (13% of 6347) TB patients were identified. Two hundred forty seven (31%) cases detected on smear microscopy, 342 (42%) on GXP and the remaining 218 (27%) on the ground of clinical decision based on their abnormal CXR shadow and related clinical signs.

Conclusions: Innovative approaches engaging the private laboratories and use of GXP are effective in improving access to TB diagnosis and management thereby strengthening public private mix initiative.

Tuberculosis diagnosis: market shortcomings in the private sector

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In many high TB-burden countries, the private sector is often the first point of contact with the healthcare system. There are many shortcomings in the private sector market. Poor quality of laboratories and tests and unclear regulatory landscape; high cost of quality tests and poor access to WHO-endorsed tests in private sector; insufficient engagement of the private sector with National TB Programs; poor adherence to standards and guidelines and low quality of care; perverse incentives to use inappropriate tests and widespread empiric treatment that is not supported by any diagnostics. Lastly, patients are not able to separate good from bad tests in the private market; despite free diagnosis in the public sector, patients still prefer private care; patients delay seeking care and/or move from one provider to another. Innovative business models and technologies are needed to overcome these market shortcomings.

COMMUNITIES WITH A HEAVY BURDEN OF TUBERCULOSIS IMPOSED BY POVERTY AND MARGINALISATION

A systematic review of indigenous burden of tuberculosis globally

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Background: The burden of tuberculosis (TB) in the estimated 370 million indigenous peoples worldwide is unknown.
Objective: To conduct a literature review 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.
Methods: A systematic literature review identified articles published between January 1990 and November 2011 quantifying TB disease burden in indigenous populations worldwide.
Results: Among the 91 articles from 19 countries included in the review, 56 were from outside Australia, Canada, New Zealand and the United States. The majority of the studies showed higher TB rates among indigenous groups than non-indigenous groups. Studies from the Amazon generally reported the highest TB prevalence and incidence, but select populations from South-East Asia and Africa were found to have similarly high rates of TB. In North America, the Inuit had the highest reported TB incidence (156/100 000), whereas the Metis of Canada and American Indians/Alaska Natives experienced rates of <10/100 000. New Zealand's Maori and Pacific Islanders had higher TB incidence rates than Australian Aborigines, but all were at greater risk of developing TB than non-indigenous groups.
Conclusion: Where data exist, indigenous peoples were generally found to have higher rates of TB disease than non-indigenous peoples; however, this burden varied greatly. The paucity of published information on TB burden among indigenous peoples highlights the need to implement and improve TB surveillance to better measure and understand global disparities in TB rates.

Case finding project in response to rising rates of tuberculosis in Nunavut Inuit of Northern Canada

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Background: The incidence rate of active TB disease in Nunavut has shown a rising trend over the past 10 years and in 2010 was 304 per 100 000 compared to the Canadian rate of 4.6 during the same year. The Taima (which means stop in Inuktitut) TB study aimed to implement and evaluate a public health campaign to enhance the existing TB preventative efforts in Nunavut.
Methods: A TB awareness campaign followed by a door-to-door campaign was carried out in Iqaluit, Nunavut. The aim of the campaign was to raise awareness about TB and provide in-home screening and treatment for people living in residential areas at high risk for TB. Screening was based on geographic location not on individual risk factors. Community involvement occurred at all levels including the introduction, design and delivery of the program.
Interpretation/conclusion: To be presented at the conference.

GETTING TO ZERO: A ROADMAP FOR ELIMINATING CHILDHOOD TUBERCULOSIS

Getting to Zero: a roadmap for childhood tuberculosis

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Tuberculosis is an important cause of morbidity and mortality in children living in TB endemic settings. Increasing attention over the last decade provides an important opportunity to improve the prevention and management of tuberculosis in children. National TB Control Programmes and the Global TB Programme are increasingly including children in TB control activities as the strategy expands towards a goal of elimination, engaging the wider health sector and focussing on integrated community-based care and prevention. The usual setting for diagnosis and care is not the tertiary hospital but rather the primary and secondary care settings including those that provide maternal and child health care, HIV care, or nutritional rehabilitation support as well as outpatient and inpatient facilities that care for sick children or adults with TB. Many children with TB and child TB contacts could be managed at the community level of care as part of a family-based approach likely to be

highly cost-effective by not requiring a major increase in resources. The Roadmap for Childhood TB was launched on October 1, 2013, and is available on WHO website. This initiative was a collaboration between the WHO Stop TB Partnership and Global TB Programme, The Union, US Centers for Disease Control, Treatment Action Group and UNICEF. This presentation will describe the important steps that the Roadmap has charted as a way of addressing the wide policy-practice gap that currently exists in childhood TB, taking the opportunity of the recent increase in political will at national and international level.

Creating and implementing childhood tuberculosis guidelines in Tanzania: a shared responsibility

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Background: Globally, paediatric TB is under-diagnosed, leading to unnecessary preventable childhood deaths. In most countries, TB case detection and management has focused mainly on adults. In Tanzania, paediatric TB (under 15 years) contributes 8.6% (NTLP report 2012). The number of children suffering from TB may be in greater than what is reported annually due to diagnostic challenges. Lack of paediatric TB guidelines and inadequate capacity of health workers to diagnose TB are amongst the reasons many children go misdiagnosed. With accurate diagnosis and a proper recording and reporting system, childhood TB may contribute 15–20% of all cases notified. It is in this regard; the Ministry has released the first guideline on management of TB in children in 2012 and started its operationalization.
Methods: A needs assessment on TB diagnosis and management in children was conducted and the findings were used to develop new national guidelines for paediatric TB in line with WHO guidelines. Data collection tools were also revised to capture age groupings for children. All partners were involved in the development of the guidelines and the rolling out of the training which started in July 2012. Data on peadiatric TB notifications from 11 regions from September 2012–June 2013 were analyzed and compared with similar data reported in the 2012 annual report for the same regions.
Results: Increase in number of children diagnosed with TB from 9% in 4th quarter, 2012 to 15% in 1st quarter, 2013 and 13% in 2nd quarter, 2013. The annual peaditric TB notification for 2012 was 8.6%
Conclusions: Increase in childhood TB notifications following the implementation of pediatric TB guide-

lines. The Ministry of health should incorporate paediatric TB management in pre-service training curriculum especially in resource limited countries for sustainability.
Challenges: Lack of adequate funds to train and supervise health care workers and printing of guideline.

What can a low-burden tuberculosis setting contribute to global childhood tuberculosis care and prevention?

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Many countries that historically had high burdens of tuberculosis have managed to substantially reduce the burden of childhood tuberculosis. While availability of resources is an important factor, the key factor has been organization of and emphasis on mostly low cost interventions that have been available for 50 to 100 years, such as: rapid reporting of suspected cases of infectious tuberculosis; performing timely contact investigations of infectious cases; providing isoniazid preventive therapy for both exposure and infection, especially for children <5 years of age; use of directly observed therapy; and, in some countries, use of BCG vaccines. In the U.S. in the 1960s, a family-centered approach was first developed to protect children and prevent their progression through the cascade of tuberculosis pathogenesis. the concept of a 'high-risk person' is augmented by the concept of a 'high-risk household'. A historical review of the steps and missteps that have been utilized will be presented. The biggest problem has been adherence to therapy, and several strategies to address this problem will be presented.

UNSAFE AIR: WHERE DOES IT HAPPEN, HOW SHOULD IT BE MANAGED AND WHAT ARE THE ETHICAL IMPLICATIONS?

Passive smoking and lung health

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Background: Second-hand tobacco smoke (SHS) is one of the important causes of indoor air pollution worldwide leading to passive smoking or involuntary smoking among non-smokers. It is composed of side-stream smoke (the smoke released from the burning end of a cigarette) and exhaled mainstream smoke (the smoke exhaled by the smoker). SHS contains more than 7000 chemicals. Hundreds are toxic and about 70 can cause cancer. This presentation would examine the situations where SHS pollution can cause lung disease and further discuss how these settings can be managed, with a focus on the ethical issues like freedom and personal choice.

Methodology: The literature related to harms of tobacco smoke since 1964 was reviewed for understanding health hazards attributed to second-hand smoke also called Environmental Tobacco Smoke (ETS).

Results: Passive smoking causes numerous health problems in infants, children and adults including deleterious effects on lung health. Non-smokers who are exposed to second-hand smoke at home or at work increase their risk of developing lung cancer by 20–30%.

Conclusions and recommendations: There is no risk-free level of exposure to second-hand smoke and even brief exposure is damaging. Millions of people globally continue to be exposed to second-hand smoke and infants and children are at special risk of suffering from its harms. Second-hand smoke exposure in the home has been consistently linked to a significant increase in both heart disease and lung cancer risk among adult non-smokers. Separating smokers from non-smokers, cleaning the air, and ventilating buildings cannot eliminate exposure of non-smokers to second-hand smoke. A smoke-free environment is the only way to fully protect non-smokers from the dangers of SHS.

IMPROVING TUBERCULOSIS CASE DETECTION IN SUB-SAHARAN AFRICAN HEALTH SYSTEMS: FROM COMMUNITIES TO TERTIARY HOSPITALS

Improving tuberculosis diagnosis and treatment initiation in Zimbabwe: role of The Union

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Background: Zimbabwe is a TB high burden country with an estimated annual incidence of 600/100 000, fuelled by HIV and only half of which are diagnosed.

Intervention: The Union support, through TBCAP/TB CARE I, began in 2008—a time of severe economic and health care decline. The support strategy is: strengthening national level management capacity, human resource capacity at implementation levels and TB-HIV collaboration implementation level support started in Midlands province, expanding to all 8 provinces and urban areas in 5 years technical areas covered are: universal access to TB diagnosis and treatment, laboratory services, infection control, programmatic management of drug resistant tuberculosis, TB-HIV, health systems strengthening and M&E/operations research.

Activities: National level support mainly involves development of management, training and M&E tools. At implementation level focus is on: training health workers on TB and TB-HIV epidemiology, diagnosis, treatment, case holding, MDR-TB, recording and reporting; data-driven support supervision; performance monitoring; recording and reporting. 10 Xpert® MTB/RIF units were installed. A sample/results transport system was introduced in main cities. Integrated TB-HIV care was introduced in 23 clinics in 17 urban areas.

Results: Midlands

Increased TB suspects/100 000: 83 in 2008 to 386 in 2011; Notification rates/100 000: 59 in 2008 to 88 in 2010; Treatment success rate: 53% in 2008 to 81% by 2010; CPT for TB/HIV patients: 52% in 2008 to 90% by 2010; ART for co-infected patients: 29% in 2008 to 65% by 2010. Reduced PTB without sputum result: 33% in 2008 to 9% by 2011; Defaulter rate: 19% in 2008 to 5% by 2010; Death rate: 13% in 2008 to 8% by 2010.

Lessons learned:

Competing priorities often override TB at implementation levels

Effective sputum management strengthens confidence in the health system

Data-driven approach is critical for effective support supervision

Provinces need support to access project funds.

ABSTRACT PRESENTATIONS FRIDAY 1 NOVEMBER 2013

ORAL PRESENTATION SESSIONS

IMPLEMENTATION OF GENEXPERT® MTB/RIF

OP-101-01   Assessment of diagnostic algorithms including Xpert® MTB/RIF for pulmonary tuberculosis in Cambodian settings

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Objectives: To assess diagnostic algorithms including Xpert® MTB/RIF (Xpert) for pulmonary tuberculosis in low MDR prevalent settings like Cambodia.

Methods: For subjects who visited National Center for Tuberculosis and Leprosy Control (CENAT), chest radiography (CXR), smear microscopy (SM), culture by solid media, identification test by Capilia and Xpert test were performed. Based on the results, the following five diagnostic algorithms were assessed: (I) Start with SM, followed by CXR for smear-negative (S−) subjects, and lastly Xpert test for only subjects with abnormal CXR. (II) Start with SM, followed by Xpert test for S− subjects, and lastly CXR for subjects with negative Xpert for diagnosing S- TB. (III) Start with CXR for screening purpose (normal/abnormal), followed by SM for subjects with abnormal CXR, and lastly Xpert test for only S− subjects. (IV) Start with CXR for active TB suspect, followed by SM for subjects with CXR suggestive or suspect of active TB, and lastly Xpert test for S− subjects. (V) Start with

Algorithm	(I) Smear→ CXR →Xpert	(II) Smear→ Xpert → CXR	(III) CXR(L)→ Smear →Xpert	(IV) CXR(2) → Smear →Xpert	(V) Xpert→ Smear or CXR
Number of smear-positive TB to be diagnosed	136	136	134	132	124
Number of smear-negative TB to be diagnosed	329 (47 X−)	331 (48 X−)	329 (47 X−)	326 (44 X−)	340 (48 X−)
Number of undiagnosed cases	4 cases (1 X−) 3 X-C−)	3 cases (3 S-X-C−)	5 cases (2 X−, 2X-C−) 3 S-X C−)	9 cases (4 S-X−, 2 S−X−, 2 S C−) mixed)	5 cases (3 S-C−, 2 S-C−)
Number of Xpert tests	430	630	430	326	766
Number of CXR exams	630	582	766	766	594
Total cost for Xpert and CXR	$6,820	$8,628	$7,364	$6,324	$10,036

S: Smear, CXR: Chest radiography, X: Xpert, C: Culture, +: positive result, −: negative result

Xpert test, followed by CXR for Xpert-negative subjects for diagnosing active TB, and SM for subjects with positive Xpert for categorization. The assessment was made based on the number of smear-positive (S+) TB and S− TB to be able to be diagnosed including TB suspects by CXR, the number of undiagnosed TB cases with either positive smear, positive culture or positive Xpert, and the amount of cost for testing, e.g., 10 USD per Xpert test and 4 USD per CXR.

Results: Out of 800 subjects having visited CENAT between 4th June and 25th Sept 2012, 766 subjects with the results of both CXR and Xpert test were analyzed. As Xpert test showed a higher sensitivity with 172 positive cases (126% to SM), most of which were *Mycobacterium tuberculosis* complex, compared to 136 S+ cases or 126 culture-positive cases, Xpert test is a very useful diagnostic tool for TB in developing countries. There was no great difference in the number of undiagnosed cases except algorithm (V) for diagnosing S+ TB and algorithm (IV) for diagnosing S− TB. Algorithms (I) and (IV) which perform SM and CXR examination prior to Xpert test were less costly than any other algorithm.

Conclusions: By combining Xpert test with CXR and SM, the necessary cost for testing and its performance of TB diagnosis varies greatly. Further studies are needed because the assessment of diagnostic algorithms depends on the quality of both CXR and culture examination.

OP-102-01   GeneXpert® MTB/RIF does not reliably identify sub-populations of MDR-TB in samples with mixed *M. tuberculosis* strains

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Background: The emergence and spread of multidrug-resistant tuberculosis (MDR-TB) poses significant challenges to patient care and disease control. Aimed to decrease the time-to-diagnosis and treatment initiation, the recently introduced Xpert® MTB/RIF assay (Cepheid, Sunnyvale, CA) detects the presence of *Mycobacterium tuberculosis* DNA and its susceptibility to rifampin (RMP) in a single reaction. As resistance to RIF rarely occurs alone, it is used as surrogate marker for MDR-TB. Until recently, patients with tuberculosis (TB) were thought to have disease caused by a single, clonal *M. tuberculosis* strain. However, molecular-based studies have demonstrated that within a patient TB disease may be caused by multiple strains, and exogenous reinfection is a common cause of recurrence. Moreover, some studies have reported that up to 60% of TB patients from high-burden TB settings have mixed *M. tuberculosis*

infections. The Xpert assay is based on a hemi-nested real-time PCR (RT-PCR) that targets the *rpo*B gene. Any deviation from the wild-type sequence resulting in a delay in the appearance of the signal exceeding a predetermined ΔCT value (>3.5), between the earliest and latest cycle threshold values, is reported as RIF resistant. This study aimed to determine the performance of Xpert MTB/RIF assay when testing samples with mixed (concurrent) MDR and pan-sensitive isolates.

Methods: Four MDR-TB cultures and an H37RV control pan-sensitive TB strain with known sensitivity were used. Dilutions with 10^8, 10^6, 10^4, and 10^2 CFU per ml solution of each isolate were prepared and mixed and indicated in the Figure. Each sample was tested by triplicate with Xpert MTB/RIF following the manufacturer instructions.

Results: The results of the testing of each of the mixed *M. tuberculosis* isolates are shown in the Figure. The results of the three tests were fully consistent on all cases.
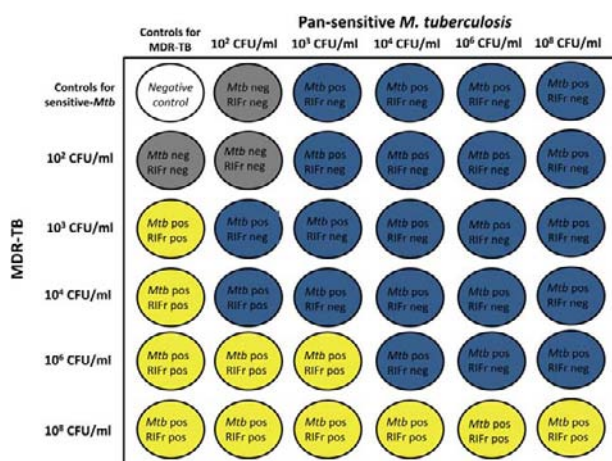
Conclusion: Xpert MTB/RIF is not a reliable tool for the identification of subpopulations of RIF-resistant *M. tuberculosis* in the presence of mixed *M. tuberculosis* isolates containing RIF-susceptible strains. As MDR-TB prevalence increases in high-burden settings, clinicians and public health officials must be aware of this limitation of the test. Following up the result of drug-susceptibility testing is still recommended in high-burden settings.

OP-103-01   Costs of Xpert® MTB/RIF from the patient's perspective in Manaus, Northern Brazil

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Background: The new automated polymerase chain reaction-based method Xpert® MTB/RIF has been progressively incorporated into the Brazilian National Health System since December 2012, as a replacement for two sputum smears for the diagnosis of sensitive pulmonary tuberculosis (TB) in primary care units. Although TB diagnosis and treatment in Brazil are free of charge, costs for patients during the diagnosis process may represent important barriers to access appropriate care. We estimated the non-medical direct and indirect costs of implementing Xpert for TB diagnosis from the patients' perspective.

Design/methods: The study was conducted in Manaus, the city with the fourth incidence rate in the country (86.3/100 000 population), where a pilot implementation study was carried out by the NTP. A random sample of 133 patients diagnosed with TB in primary care units answered a questionnaire which included information on costs for transportation, food and indirect costs, such as time spent during the diagnostic process as well as information on sociodemographic data, including monthly income. Costs with time spent were calculated based on the national minimum wage, considering a 44 weekly hour contract. Median costs were compared using the Mann Whitney test. Factors associated with costs were analyzed in a multivariate model.

Results: Out of 133 respondents, 71 (53%) were patients diagnosed by Xpert and 62 (47%) by smear. Their median age was 42 (30–56) and 33 (26–47) years ($P = 0.179$); their median income was US$350 (325–650) and US$400 (325–600, $P = 0.470$), respectively. Direct non-medical costs were similar using Xpert and smears (US$13 vs. US$14, $P = 0.111$), but the indirect costs were significantly lower with the new technology (US$11.50 vs. US$38.40, $P < 0.000$), due to less visits needed (2 vs. 3, $P < 0.000$) and the total time per visit (3 vs. 7 hours, $P < 0.000$). We did not identify factors significantly associated with costs, besides the type of test.

Conclusion: From the patient's perspective, Xpert is less costly than smears for pulmonary TB diagnosis in Manaus. These results complement the pilot implementation study which showed that the Xpert test increases confirmed TB notification, is cost-effective for the National Health System. It reinforces the recommendation of broad implementation of this technology in the country.

OP-104-01   Impact of up-front testing of tuberculosis suspects with Xpert® MTB/RIF on pulmonary tuberculosis case detection

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Background: India's Revised National Tuberculosis Control Programme (RNTCP) uses sputum smear microscopy as the primary diagnostic tool for pulmonary Tuberculosis(TB). Since 2012 a feasibility study of using Xpert® MTB/RIF (Xpert) is underway 'the RNTCP/FIND/WHO project'. In this project Amravati Corporation district (0.65 million population) is undertaking up-front testing of each TB suspect with Xpert. Sputum specimens provided by TB suspects from all the 7 Designated Microscopy Centres (DMCs) are transported to a central laboratory in district. All are subjected to smear microscopy for AFB as well as Xpert. We compared the pulmonary TB case detection in these DMCs following the use of Xpert with baseline values.

Design/methods: We reviewed the laboratory registers, TB register and referral for treatment register to identify the diagnosed pulmonary TB cases among TB suspects examined in the DMCs during the period of three months in 2011 and 2012. The Xpert diagnostic facility was added for TB suspects in 2012. We compared the case detection of pulmonary TB cases for these two periods. We also compared this for DMCs having availability of X-ray chest diagnostic facility with those with out.

Table Impact of up-front testing of TB suspects with Xpert MTB/RIF on pulmonary case detection in designated microscopy centres segregated based on X-ray facility

Particulars	DMC with X-ray facility		DMC without X-ray facility	
	2011 (sputum smear ± radiology)	2012 (+CBNAAT)	2011 (sputum smear ± radiology)	2012 (+CBNAAT)
TB suspects examined	803	800	666	648
Sm+ve cases detected	65	66	34	38
% Change		2%		12%
Sm−ve cases detected	63	81	3	25
% Change		29%		733%
Total pulmonary cases detected	128	147	37	63
% Change		15%		70%
	2011	2012	% change	
MDR-TB suspects specimen sent/ examined for drug susceptibility	34	93	174%	
Out of the above, number diagnosed as rifampicin resistant	3	9	200%	

TB = tuberculosis.

Results: Of 1469 pulmonary TB suspects, 165 pulmonary TB cases (99 smear positive and 66 smear negative) TB cases were detected in Oct–Dec 2011. In the same settings in Oct–Dec 2012, using Xpert, 210 pulmonary TB cases were detected in 1448 TB suspects using Xpert. 27% additional cases detected with up-front testing of TB suspects with Xpert. The increase in pulmonary TB cases was 70% in DMCs with no X-ray facilities available as compared to 15% increase in DMCs with X-ray facility. 7 TB suspects are required to be screened by Xpert for getting a pulmonary TB case. Multi-drug resistance TB suspects examined increased from 34 to 93 (174%).

Conclusion: Upfront testing of TB suspects with Xpert detects more pulmonary TB cases. It is much more useful in the setting which does not have X-ray facilities. Diagnosis of pulmonary TB cases can be ensured by sputum specimen collection and transportation to district level laboratory for Xpert instead of referring TB suspect for X-ray chest. TB control program should emphasize upfront testing of TB suspects where DMCs does not have radiological examination facility. Availability of Xpert at district level improves diagnosis of MDR-TB.

OP-105-01   Impact of molecular diagnostic tests in the referral of MDR-TB patients with HIV at Kibong'oto Infectious Disease Hospital, Tanzania

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Background: The prevention, diagnosis, and treatment of drug resistant TB is complicated by delays in diagnosis and appropriate treatment initiation with resultant high mortality and ongoing transmission. Conventional drug sensitivity testing (DST) necessitates a lengthy turnaround time, delaying diagnosis and initiation of MDR-TB treatment. Molecular diagnostic tests (MTBDR*plus*® and MTB/RIF®) were rolled out programmatically in Tanzania in 2011 enabling early recognition of drug resistant TB.

Aim: To describe the impact of programmatic implementation of molecular diagnostic tests in identifying HIV-MDR-TB patients for referral to Kibong'oto Infectious Disease Hospital for treatment initiation.

Method: Consecutive medical charts from patients referred for MDR-TB treatment to Kibong'oto MDR-TB treatment center from December 2011 to April 2013 were reviewed. Data abstracted included DST method leading to treatment referral, referring district, gender, HIV sero status, CD4 count and discharge status. Data were analyzed using SPSS statistical software.

Results: After scaling up rapid molecular diagnostic test for MDR-TB diagnosis from 2011, 13 (43%) regions of Tanzania referred 63 patients to Kibong'oto

for initiation of second-line anti TB treatment. Forty-four (71%) were diagnosed by a molecular test the majority, 35 (80%), by MTBDRplus. Dar es Salaam referred 33 (53%), Mwanza 12 (19%) Tanga 4 (7%) while other regions each contributed less than 3%. The mean duration between diagnosis and referral for treatment following molecular diagnostic test and conventional culture and DST were 59 days, 95%CI (30–89) and 230 days 95%CI (141–320) respectively. Forty (65%) were male, HIV positive were 26 (41%) of which 23 (88%) had CD4 count levels documented. Mean CD4 count was 254, while 10 (44%) had CD4 count less than 200 cell/μl. Forty-four (73%) had >2 prior TB treatment episodes of which 16(36%) were HIV positive. Twenty-seven (44%) were discharged for continuation phase of treatment while 4 (7%) died. The 4 deaths occurred had a median of 18 days (IQR 0–25) following hospital admission and 3 (75%) were HIV positive with median CD4 of 23 cells/μl, (IQR 22–118).

Conclusion: Molecular diagnostic tests increased the referral of HIV/MDR-TB cases and significantly minimized the total time delay between diagnosis and treatment.

OP-106-01   Did the introduction of Xpert® MTB/RIF reduce MDR-TB treatment commencement times in Cape Town, South Africa?

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Background: Cape Town has a high multi-drug resistant tuberculosis (MDR-TB) burden with 945 cases registered in 2011. Xpert® MTB/RIF (Xpert) was introduced as a screening test for TB in 2011. This study aims to evaluate whether the introduction of Xpert reduced MDR-TB treatment commencement times (TCT) in a routine operational setting in Cape Town.

Setting: Free TB diagnostic services are provided at 142 primary health care facilities with TB testing undertaken at a central laboratory. In 2008, Genotype MTBDRplus Line Probe Assay replaced conventional drug sensitivity tests for high MDR-risk TB suspects ('Targeted' algorithm). During 2011–2012 Xpert was sequentially introduced in sub-districts as a screening test for all TB suspects, replacing smear microscopy ('Universal' algorithm).

The last 3 years has seen a move towards decentralised care: from 2011, the 101 PHC facilities offering TB-treatment also initiated MDR-TB treatment.

Methods: This observational study was undertaken in 9 randomly selected high-TB burden clinics. New MDR-PTB cases diagnosed or on treatment at these clinics between January 2008 and December 2012 were identified from the laboratory database and clinic records. Clinical folders were reviewed and data recorded on case-report forms, quality checked and dual entered into a Microsoft SQL database.

Laboratory turn-around-times (TAT) (sputum taken to result available in the laboratory) and MDR-TB TCT (sputum taken to treatment commencement) were compared for cases diagnosed in the 'Targeted' and 'Universal' algorithms as facilities transitioned between these. Kaplan Meier time-to-event analysis was undertaken.

Results: In the 'Targeted' algorithm ($n = 314$) (Table) the median laboratory TAT was 25 days (95%CI 23–25 days) and median MDR-TB TCT was 42 days (95%CI 39–45 days). In the 'Universal' algorithm ($n = 108$) (Table) the median laboratory TAT was 1 day (95%CI <1–2 days) and median MDR-TB TCT was 20 days (95%CI 14–23 days). When corrected for clustering, the difference in MDR-TCT was maintained.

Table Comparison of cases tested in the 'targeted' and 'universal' algorithms

	'Targeted' algorithm (2008–2012)	'Universal' algorithm (2011–2012)
Number of cases commenced MDR-TB treatment	314	108
Mean age, years (SD)	36 (11)	35 (10)
Median laboratory TAT (p25–p75)	25 days (18–34 days)	1 (<1–20 days)
Median MDR-TB TCT (p25–p75)	42 days (30–64 days)	20 days (8–37 days)
Number female, %	137 (44%)	44 (41%)
Median TCT female	42 days	22 days
Median TCT male	43 days	16 days
Number HIV-infected, %	176 (57%)	64 (60%)
Median TCT HIV-negative	42 days	17 days
Median TCT HIV-infected	42 days	22 days
Number with high MDR risk (previous TB)	190 (63%)	57 (53%)
Median TCT—Low MDR-risk profile (no previous TB)	42 days	14 days
Median TCT—High MDR-risk profile (previous TB)	44 days	21 days

Conclusion: The introduction of Xpert MTB/RIF resulted in reduced MDR-TB TCT due to reduced laboratory TAT. Post-laboratory delays remain unchanged. In part, this reflects operational inefficiencies that need to be addressed to optimise the benefits of Xpert.

OP-107-01   Prioritising Xpert: people or places?

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Background: The World Health Organization recommends Xpert® MTB/RIF (Xpert) as the initial diagnostic for individuals suspected of MDR-TB or HIV-associated TB or as a follow-on test to microscopy. We hypothesize that the Xpert assay could be highly valuable, independent of patient characteristics, when used at point-of-care (POC) in areas with disproportionately poor access to TB diagnostics.
Objective: To assess the impact of Xpert implementation on patient care in a rural, sparsely populated area with poor access to laboratory and radiology.
Methods: One-module Xpert instruments were installed in three primary care facilities in the Karoo, Western Cape, South Africa. Facilities were selected for their remoteness from laboratory and X-ray services. A clinic nurse was trained in performing the assay. We conducted a before-after analysis of routinely collected data to determine the impact on time to treatment and bacteriological confirmation (by smear, culture, or Xpert) of TB.
Results: At the 3 sites combined, 946 people were assessed for TB during 1010 observation days, 571 by smear microscopy and 375 by Xpert. The number of patients assessed for TB was 9%, 31% and 51% lower after vs. before Xpert implementation, due to stricter adherence to criteria for defining a TB suspect. Despite this, the number of registered TB cases increased by 14%. Overall, only 26% of TB cases were HIV positive. Before Xpert, 87.0% were bacteriologically confirmed (62% smear microscopy, 25% culture), 3% were diagnosed based on X-ray and 10%

Figure   Time from first sputum collection to treatment.

were diagnosed empirically. After Xpert implementation, 100% were bacteriologically confirmed (98.7% by Xpert, 1.3% by culture). Only 1.4% were diagnosed with rifampicin resistance, both by Xpert. The proportion of confirmed TB cases initiating treatment increased from 89.6% to 98.8% ($P = 0.02$). The median time from collection of first sputum to initiation of treatment decreased from 12 days (interquartile range 6, 24) before to one day (IQR 0, 2) post Xpert implementation (Fig).
Conclusion: Xpert substantially improved the diagnosis of TB and patient care in an area with relatively low HIV co-infection rate but poor access to diagnostics, with a 14% increase in case detection, 13% increase in bacteriological confirmation, 9% increase in treatment initiation rate, and an 11-day reduction in delay between first sputum collection and start treatment.

OP-108-01   Evaluation on the roll out, scale-up and implementation of GeneXpert® MTB/RIF in three high-burden countries: South Africa, Kenya and India

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Background: Since the declaration of TB as a public health emergency by the World Health Organization in the 1990s,[1] the world has still not achieved a point of care (POC) tuberculosis (TB) diagnostic test. The new molecular TB diagnostic test GeneXpert® MTB/RIF (Xpert) is a positive step forward, particularly in diagnosing Rifampicin resistant strains of TB and TB in people living with HIV (PLHIV). In the face of fast following TB diagnostic technologies and the most effective roll out of Xpert, it is prudent that the role of civil society be enhanced for the adequate roll out of new TB diagnostic tools. Mapping the decision-making process for integration of new tools into country guidelines, policy, programs, and practice will allow activists to identify and advocate for streamlined decision-making processes. Subsequently, the advocacy strategies developed will accelerate access to the new tools, ameliorate the impact of new tools and facilitate the contribution of civil society actors in the implementation of new TB diagnostic tools. Tracking in-country operational research will identify gaps that create barriers to effective and efficient rollout of new tools, and ways to surmount these.
Intervention: In three high burden countries, South Africa, Kenya and India, TAG collaborated with in-country activists to collect the perceptions of TB advocates, donors, national TB programs, healthcare workers, lab personnel and opinion leaders on the gaps, barriers and lessons learnt in the roll out of GeneXpert. Through a review of the gathered perceptions, recommendations were accrued to address the
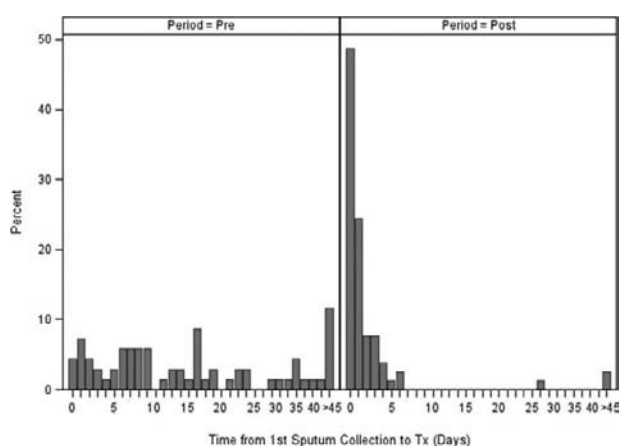
gaps in the roll out of Xpert; recommendations which could also be lent to newer TB diagnostic tools.

Results: Perceptions were documented of at least 20 key stakeholders in each country on the unique challenges and lessons learnt on the roll out of Gene-Xpert. Recommendations were then crystallized to improve the roll out of GeneXpert, and target the various stakeholders including civil society. In addition, we anticipate that these recommendations will be extrapolated for the roll out of new TB diagnostic tools in the near future.

Conclusions: So as to achieve zero, TB deaths, new TB infections and suffering, civil society must be part of the development and implementation of well-developed strategies on the roll out of new TB diagnostic tools. These strategies can be drawn from documenting the draw-backs and success during the roll out of Xpert (a new TB diagnostic tool). Documentation of perceptions from a variety of key stakeholders has resulted in recommendations and lessons learnt that have otherwise been missed out in earlier operational studies on the roll out of Xpert. For as long as developing countries do not substantially contribute in funding the roll out of new TB diagnostic tools; the rationale behind diagnostic tool placement will be based on the donor's agenda as opposed to disease burden. Implementing new TB diagnostic tools may reveal endemic issues within the public health system, such as competency of laboratory staff or Xpert result interpretation by healthcare workers, which will have to be addressed so as to reap the greatest impact of the diagnostic tool. Key stakeholders in especially HBC must adequately prepare now and keep abreast with real-time information in anticipation of newer TB diagnostic tools, in the near future.

1 http://www.who.int/tb/features_archive/mr_statement/en/

ADVANCES IN AFB MICROSCOPY AND RAPID CULTURE METHODS

OP-109-01   A cost-utility analysis of LED fluorescent microscopy for the diagnosis of sputum-positive tuberculosis in India

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Background: TB REACH is a project designed to update TB microscopy services in 200 identified medical colleges in India. Conventional ZN microscopy is phased out and replaced with LED fluorescent microscopy. This study aims to evaluate whether LED microscopy is cost effective compared to conventional Ziehl-Neelsen (ZN) within the project Medical Centres.

Design/methods: We constructed a decision tree model to inform the cost-utility analysis. The results of this cost-utility analysis are summarised using the Incremental Cost Effectiveness Ratio (ICER). Data from the 200 medical colleges was analysed to determine the number of sputum smear positive (SSP) and sputum smear negative (SSN) cases reported for quarter 3 in 2011. The following year, after LED roll out, the same medical colleges had their SSP and SSN cases identified in quarter 3. A full costings analysis taking an RNTCP perspective was carried out. Data was collected from a range of sources including local RNTCP testing centres. The costs of laboratory staff time and training, consumables, testing apparatus, solutions, maintenance, and building and overhead costs were obtained. Costs were presented as cost-per-slide on the basis each suspect had two slides examined. The analysis also included a one-way sensitivity analysis and a probabilistic sensitivity analysis to address uncertainty within the model and its parameters.

Results: The base-case analysis showed total costs for using LED microscopy are marginally higher but more DALYs were averted compared to Light Microscopy. The ICER for LED microscopy is $12.43 per DALY averted (Obtained by calculating the difference in total costs and DALYs averted between the novel and standard diagnostic). This result shows LED microscopy is very cost-effective within the willingness to pay threshold recommend by the WHO.

Conclusions: LED microscopy is cost effective for detecting TB cases in India. The results of this analysis support both the TB REACH initiative and the WHO in their recommendations for updating diagnostic equipment in India. Further research could incorporate comparisons of cost-effectiveness to other novel diagnostics such as rapid testing (GeneXpert) and extrapolate the data to a larger study population.

OP-110-01   End users' perception of LED fluorescent microscopy in comparison to bright field microscopy for tuberculosis diagnosis under routine programmatic conditions

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Background: Auramine based LED fluorescent microscopy has been recommended by WHO in 2009 for AFB detection in routine setting in low and middle income countries over Z-N microscopy. This is 8–10% more sensitive than Z-N Microscopy and having similar specificity and three times faster also. LED fluorescent microscopy services are introduced in 200 high workload laboratories in Indian NTP. Nearly 400 laboratory staffs were also trained from these

sites for the operation of services. A study was conducted to assess the insights of lab technician on LED fluorescent microscopy in routine RNTCP and record their voice on technical and operational challenges.

Design/methods: A cross-sectional nation-wide semi structured questionnaire based study was designed for laboratory technicians trained for operating LED FM. The questionnaire was sent to 400 lab technicians who are current users of the technique, out of which 116 replied. The questionnaire was focussed on handling of microscopes, reagent preparation, slide staining, reading and grading. Data was entered in Epidata 3.1, and was validated by double data entry technique. Data was analysed using Epidata analysis.

Results: Out of the 116 participating lab technicians, average laboratory experience was of 11.8 years and average duration of using of LED FM was 8 months. 72% rated 'excellent' in terms of handling, 88% agreed that it was less stressful to eyes. 88% do not face any problem in stain preparation and 41% agreed that fluorescent stains were easy on storage. Slide staining technique was easy for 89% but 70% said staining technique was time consuming. Slide reading and grading was easy for 96% and average time spent was 1.89 minutes per slide. 90% of respondent were willing to use the LED FM in future. However 6% were not willing to continue with it, as they were the only trained technician in the department and were not able to get leave for the same reason. 89% had perception that the technique helped them to detect additional cases.

Conclusion: In terms of handling, performance, efficiency and case detection it is one of the best interventions in medium and low resource settings. Also it has a high level of acceptance among the users under routine programmatic condition in India.

OP-111-01 LED fluorescent microscopy increases detection of smear positive pulmonary tuberculosis in medical colleges of India

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Background: Quality assured sputum smear microscopy facilities based on Bright Field Microscopy are available through more than 13 000 sputum smear microscopy laboratories facilitated by Revised National Tuberculosis Control Programme across the India. These Laboratories at District TB Centre, medical college, hospitals, etc. have a very high workload. In July 2012, Light-emitting diode fluorescent microscopy (LED-FM) replaced conventional light microscopy using Ziehl-Neilsen stain, for detecting sputum-positive pulmonary tuberculosis, in 190 microscopy centres of medical colleges operating under RNTCP to see the change in case detection in routine programmatic condition. The overall objective of study was to assess the performance of LED fluorescence microscopy with Bright field microscopy in routine programmatic condition in India.

Methods: Study population consisted of TB symptomatics who underwent sputum smear examination by ZN staining during July–December, 2011 and by LED-FM during July–December, 2012 in 190 medical colleges of India. The same months of 2011 and 2012 were chosen for comparison to minimize the effect of seasonal variation on the number of TB symptomatics examined and smear positive TB cases diagnosed. It is also assumed that the external factors were similar in these project sites. The data is collected from laboratory register on routine basis and verified by project staffs from centres on their field visits. The data is compiled at national level and compared to see the change in positivity rates for two year.

Results: In the period July–Dec 2011; 222 658 patients examined using Bright field microscopy and 28 042 (12.6%) were smear positive. Of 224 714 examined using LED-FM, 33 552 (14.9%) were smear positive during the July–Dec 2012. In relation to 2011, during 2012 the number of smear positive TB cases diagnosed and proportion smear positive rose by about 20% as against a marginal 1% rise in the number of TB symptomatics examined. Applying 12.6% positivity (observed in 2011) for the extra number of TB symptomatics examined in 2012, LED-FM services resulted in an additional yield of 5251 cases.

Table Performance of LED-FM (July–December, 2012) in comparison to conventional microscopy (July–December 2011) in 190 RNTCP designated microscopy centres in India

Period	Total TB symptomatics examined	Sputum Smear Positive TB Cases detected	Proportion found sputum positive
July–December 2011 (Conventional Microscopy)	2,22,658	28,042	12.6%
July–December 2012 (LED Fluorescent Microscopy)	2,24,714	33,552	14.9%
Absolute and incremental change between 2012 and 2011	+2,056 (1% increase)	+5,510 (20% increase)	+2.3% (18% increase)

Conclusion: The result highlights the success of LED-FM over conventional microscopy in India. This has led to an increase in the sputum positivity rate resulting in an increased number of TB cases, thus making a strong case for scaling up this technology to other high workload settings of India and other resource scase settings.

OP-112-01   Same-day microscopy to improve quality of tuberculosis evaluation in a low-income setting

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Introduction: Sputum smear microscopy is widely used for diagnosis of tuberculosis (TB) in high burden countries. However, the conventional approach requires patients to make multiple visits to health centers, resulting in loss to follow up prior to completing diagnostic evaluation. Same-day LED fluorescence microscopy (LED FM) may reduce this problem by facilitating collection and examination of two sputum specimens at a patient's initial health center visit. We sought to determine whether implementation of same-day LED FM could improve quality of TB evaluation at health centers in Uganda.

Methods: We conducted a quasi-experimental study from August 2011–March 2013 at six rural primary health centers in Uganda. These centers are part of an ongoing infectious disease surveillance network that collects quality-assured data on TB and malaria care. We provided a one week training course to staff at each health center to replace conventional light microscopy with same-day LED FM. We compared quality metrics of TB evaluation from the International Standards for Tuberculosis Care 6 months before and after introduction of the intervention using logistic regression models adjusted for age and sex and robust standard errors to account for clustering of outcomes within study sites.

Results: 1923 patients reporting cough of at least 2 weeks' duration presented to the six health centers during the study period. Of these, 907 (47.2%) were evaluated in the pre-intervention period, and 1016 (52.8%) in the post-intervention period. Median age (37 years vs. 39 years, $P = 0.07$), proportion female (46.2% vs. 49.7%, $P = 0.12$), and proportion smear-positive (9.9% vs. 7.8%, difference -2.1%, $P = 0.47$) were similar in the pre- and post-intervention periods. There was no change in the proportion referred for sputum examination (77.9% vs. 78.8%, difference $+1.0\%$, $P = 0.81$). However, the proportion completing sputum examination if referred increased from 75.2% to 96.3% (difference $+21.0\%$, $P = 0.02$), and the proportion initiating treatment if found to be smear-positive increased from 95.5% to 97.5% (difference $+2.0\%$, $P = 0.02$). Overall, the proportion of patients receiving ISTC-adherent care increased from 58.2% in the pre-intervention period to 75.7% in the post-intervention period (difference $+17.5\%$, $P = 0.04$).

Conclusion: Same-day LED FM was feasible and improved quality of TB evaluation at health centers in a low-income country. Further studies should evaluate impact and cost-effectiveness.

OP-113-01   Evaluation of sputum submission instructions for tuberculosis suspects to enhance diagnosis in Lusaka, Zambia

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Background: In 2009 WHO-estimated tuberculosis (TB) case detection rate in Zambia was 73% and only 40% of new pulmonary TB patients in Lusaka District were smear positive. Review of clinic processes suggested that patients were declining to submit sputum due to lack of guidance and understanding of the procedure, turn-around-time for sputum was lengthy, submitted sputum were often poor quality, and documentation of TB results were inadequate leading to high loss-to-follow-up. The objective of this evaluation was to determine if sputum submission instructions enhanced TB diagnosis.

Intervention: Lusaka District Health Office (DHO) and the Centre for Infectious Disease Research in Zambia (CIDRZ) implemented a pilot program at 3 clinics including a two-day training on sputum collection, submission and documentation for all clinic staff. After the training, CIDRZ staff monitored sputum collection activities daily and then semi-weekly to ensure that procedures were followed. We retrospectively abstracted data from the 3 clinics on TB diagnostic patients 6 months pre- and post-training from TB suspect and lab registers. We compared the proportion of patients found to be smear-positive using Mantel-Haenzel analysis stratified by clinic. Ethical approval was received by the University of Zambia and the University of North Carolina.

Results: This pilot program was implemented at 3 Lusaka clinics between March 2009 and July 2011. Overall, 162 of 1330 (12.2%) persons with suspected TB were identified as smear positive in the pre-implementation phase. In the six months post-implementation, 319 of 1535 (20.8%) were identified as smear-positive ($P < 0.0001$). This difference was observed consistently across all three clinics: Clinic A (11.0% vs. 17.8%, $P = 0.005$), Clinic B (15.5% vs. 20.9%, $P = 0.04$), and Clinic C (10.7% vs. 23.3%, $P < 0.001$).

Conclusions: An intensive two-day training of standardized instructions and supervision resulted in a

significant increase in smear positive patients, most likely due to patients producing better quality sputum. This simple, low-cost intervention has potential to increase the diagnostic capability of smear microscopy, identifying TB patients who otherwise would have been missed. These results suggest that similar interventions should be considered in countries using smear microscopy as their primary diagnostic tool. A limitation of the evaluation was the inability to assess quality or inter-rater reliability of lab technicians assessing sputum.

OP-114-01   Comparing same-day sputum microscopy with conventional sputum collection for the diagnosis of tuberculosis in Chhattisgarh, India

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Background: World Health Organization (WHO) now recommends same day sputum microscopy (spot-spot) in preference to conventional strategy (spot-morning) for the diagnosis of smear positive tuberculosis with the view that completing diagnosis on a single day may be more convenient to the patients and reduce pre-treatment losses to follow-up.
Methods: We conducted a cross-sectional study in seven selected district level hospitals of Chattisgarh State, India with a busy outpatient setting. During November 2012–March 2013, two sputum specimens (on-the-spot collection followed by early morning collection the next day) were collected from consecutively enrolled adult ($\geq$18 years) TB suspects as per current national guidelines. In addition, a second sample was collected (one hour after collection of first spot sample) from the same patients. All the samples received were processed and stained by acid fast Ziehl-Neelsen (ZN) stain. We compared the number (proportion) of sputum smear positive TB cases diagnosed through same day microscopy strategy with the conventional strategy. McNemar's test was used to compare statistical differences in the proportion smear positive between the two approaches (spot-spot vs. spot-morning).
Results: Of 2551 TB suspects, 92% were males. All patients provided the first spot specimen, 2361 (93%) provided the second spot specimen, and 2435 (96%) provided an early morning specimen. About 72% of specimens were mucopurulent in conventional strategy as compared to 60% in same day strategy. The proportion of smear-positive patients diagnosed by same day microscopy was 14.1%, as compared to 16.9% by the conventional method ($P < 0.001$). A

total of 73 (16.9) potential cases were missed by same day method compared to only 2 (0.5%) by the conventional method.
Conclusion: Same-day microscopy method missed a massive 17% of smear-positive cases and contrary to prior perception, did not even increase the proportion of suspects providing the second sample. These findings call for an urgent need to revisit the WHO recommendation of switching to same-day diagnosis over the current policy.

OP-115-01   Incremental yield in positivity and better preservation of sputum samples with the addition of 1% carbol fuchsin before transport to the microscopy centre, Gujarat, India

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Background and implementation challenges: Province of Gujarat initiated sputum collection centers (SCC) at 2/3rd of peripheral health centers to increase reach of microscopy. Examination rates increased by 30% over 5 years. But, samples reached microscopy centers (MC) with time delay causing putrefaction and foul smelling leading to displeasure of Laboratory Technicians for performing microscopy on these samples.
Intervention: To prevent drying, putrefaction and foul smelling of sputum samples we designed intervention to test feasibility of adding 1% Carbol Fuchsin (CF) in equal quantity to samples on collection before transportation in three stages. First at **Stage 1:** Addition of 1% CF to sputum samples discarded after routine microscopy at Reference Laboratory (RL) followed by repeat microscopy on day 0, 2, 4, 6, 8 and 10 by 2 independent Technicians, rechecked by Microbiologist. **Stage 2:** Addition of 1% CF to sputum samples discarded after routine microscopy at 2 randomly chosen District TB Centers (Dahod and Mehsana) followed by repeat microscopy on day 0, 2, 4, 6, 8 & 10 by Technicians. **Stage 3:** Training of staff laboratory supervisors at all SCCs & MCs in the two intervention districts. Addition of 1% CF to sputum samples under the program before transportation. Perceptions of staff and technicians recorded pre and post intervention.
Results: Macroscopic examination revealed no putrefaction in any of 188 samples at RL and additional yield of 22% observed with no false error in 140 samples at DTCs. In stage 3, comparison of intervention area showed higher smear positivity (8.4%) compared with randomly chosen non-intervention districts of Patan and Rajkot (5.2%) with odds ratio of 1.67

Table   Sputum smear results with and without intervention of adding 1% carbol fuchsin to sputum samples (equal amount) before transportation to microscopy center, Gujarat, India

Sputum Smear Results / Intervention	Positive	Negative	Total
Yes	250 (8.4%)	2732 (91.6%)	2982
No	104 (5.2%)	1896 (94.8%)	2000
Total	354 (7.1%)	4628 (92.9%)	4982

Odds ratio = 1.67 (1.31–2.13)

(1.31–2.13) in total sample of 1982 and 2000 respectively. Overall impact of intervention on sputum microscopy showed increase positivity of sputum positivity from 10.6% to 11.6% as compared to same period of previous year with incremental yield of 10% over baseline. Out of 270 health officers and staff interviewed before intervention 85% reported problems of dried samples and foul smelling in samples which reduced to 17% post intervention.

Conclusion: It feasible to add 1% CF in sputum samples before transportation with incremental yield in positive smear results, without increasing false positives, prevents sputum putrefaction and foul smelling and participation of health workers and technicians in sputum collection and transportation system increases with high acceptability.

OP-116-01   Evaluation of the effectiveness of magnetic bead fluorescence microscopy in tuberculosis diagnosis

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Setting: National Reference Laboratory of mycobacteria of National Tuberculosis Programme in Ouagadougou, Burkina Faso.

Objective: To compare the efficacy of routine staining with fluorescence microscopy (FM) before and after use of TB-Beads assays.

Methods: Sputum samples were treated with auramine then subjected to the 'TB-Bead': the sputum samples were decontaminated with NaOH, 0.4% for 15 min. Mixture was added to an equal volume of solution of TB-Bead. After 2 min, the mixture tube was placed on the magnetic rack 1 min. The supernatant was poured and the pellet resuspended in an equal volume NaOH 0.04% and then left at room temperature 5 min. The beads were captured by the magnet and the supernatant was discarded. The tube was removed from the rack and the pellet resus-

pended in 100 µl buffer eluate. Smears were made on slides precoated with 1.25% alginate for 5 min before being washed, dried and stained with auramine. The McNemar χ^2 test was used to compare pairs of results; significance level, $P = 0.05$.

Results: Without concentration, 24 (30%) samples were AFB-positive: 8 (10%) scanty, 16 (20%) score 1–3+. After TB-Beads, 26 (32.5%) were AFB-positive: 6 (10%) scanty, 20 (20%) score 1–3+, an increase of 2.5%; there was no significant difference between magnetic bead FM and direct FM, $P = 0.513, 0.05$.

Conclusion: We have a slight increase in sensitivity with magnetic bead FM compared to direct FM; TB-bead FM requires longer time and does not seem to be useful tool in TB detection for referral laboratories. Our results have to be confirmed in larger studies with unselected patients.

CIVIL SOCIETY PERSPECTIVE ON TUBERCULOSIS CONTROL

OP-117-01   Patient-centred approach intervention in tuberculosis care: impact using a realist inquiry perspective in five countries

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Background: The aim of the study was to provide information from the patient's perspective on the extent to which TB services in the selected areas were patient centered through impact analysis of its results based using a realist perspective. The specific objectives were to: (1) assess the extent to which TB services ensured patients' rights and reflected patients' responsibilities, (2) assess the meaning of quality from the patient's perspective, (3) describe the direct and indirect costs to patients for TB care, (4) describe patients' experience of stigma and discrimination and stigma in daily life and in seeking TB related health care, and (5) determine patients' general knowledge about TB and HIV.

Design/methods: We used a prospective, mixed methods, quasi-experimental study design with a non-equivalent control group to answer the study objectives across 5 countries: Indonesia, Cambodia, Zambia, Mozambique, and Nigeria. A package of 5 Patient Centered Approach tools was applied in intervention areas. Data were collected before and after the 6 month intervention period in both intervention and non-intervention areas. Per country: quantitative research included a survey of 180 TB patients; qualitative methods employed 4 focus group discussions with TB patients and 4 with community members, 10–12 in-depth-interviews with TB patients,

and 10–12 key informant interviews with health facility staff and 4–6 with community leaders. A framework of analysis (see figure) guided data analyses using SPSS (for survey data) and Excel (for thematic extraction for qualitative data).

Results: Synthesis of findings across countries highlighted that 1) TB patients are mostly unaware of their rights and responsibilities, albeit efforts and introduction of the Patient's Charter on TB, 2) stigma and discrimination at individual, community and health worker level prevail and masqueraded in various forms, 3) inefficiencies of TB services and service providers contributes to already unaffordable indirect costs related to travel and time.
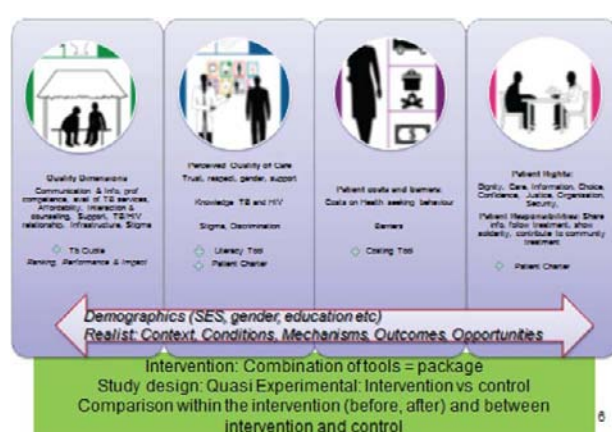
Figure   Framework of analysis.

Conclusion: Implementation of the package improved patient centeredness in all countries, several challenges warrant attention and further research. For example, patients' thorough understanding of their rights and embracing of their responsibilities, lack of sufficient attention for provider, community and self-stigma, persisting indirect patient costs, the context(s) in which they occur and the influencing mechanisms.

OP-118-01   'Please sir, I want some more.' Advocating nutritional supplements for tuberculosis patients in India's Food Security Bill

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Background: Nutritional deficiencies can delay the recovery time of TB patients receiving treatment especially if they are from a low socioeconomic status. 26% to 44% of all Indian TB patients live in households with a monthly income of less than Rs 2000. Poverty exacerbates treatment timelines especially if the primary breadwinner begins treatment and is tempted to return to work and not complete his treatment at the first signs of improvement in order to provide for his family. The need for state support for nutritional supplements thus required a new form of public health advocacy.

Intervention/response: In March 2012, under the District TB Patients' Forum of Project Axshya, TB patients in Kerala submitted a petition to the state Government's District TB officer (DTO) for additional nutritional supplements. This was supported and sent onward to the District Collector. Taking cognizance of this, similar memoranda were also submitted to various district Collectors, State TB officers and DTOs in other states. As the momentum built, this Memorandum was presented to Mr. K T Thomas, India's Union Minister for Food and Civil Supplies. Last October, a team from The Union and its NGO partners under Project Axshya, presented a Policy Brief advocating the inclusion of TB patients in the Food Security Bill. Mr. Thomas forwarded this to the Ministry and, onward to the Parliamentary Standing Committee for the Food Security Bill.

Results and lessons learnt: A truncated and somewhat diluted version of the Food Security Bill was passed by the Indian Parliament in March 2013, which has been disappointing. But this process has taught us that even TB patients, who are a vulnerable and marginalized community, can have their voice
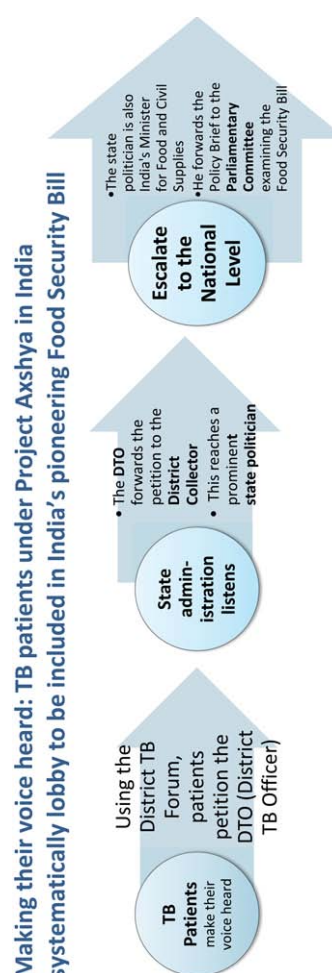
heard with the assistance of strategically positioned support. Through the efforts of The Union's NGO partners, well-timed policy briefs and meetings with political leaders, the voice of this group was heard.

Conclusions: India's democratic system is open even if it is unresponsive to the specific needs of India's TB patients in this single instance. Strategic engagement with Indian policy- and decision-makers is recommended on a sustained basis to educate them. Working to systematically build up a critical mass of both sensitized politicians and rights-aware TB patients can open a path to augment resources needed to continue the fight against TB.

OP-119-01   KAP in tuberculosis treatment and care among government and private health providers: baseline KAP survey in 30 districts in 15 states, India, 2011

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Background: Knowledge, Attitudes and Practices towards Tuberculosis (TB) by the health service providers (HSPs) are key in treatment and control of TB. In a country with high burden of TB, it is essential that the HSPs have the correct knowledge on TB diagnosis, treatment and control. In the context of RNTCP's new strategy of involving all the HSPs including private practitioners in TB care and control, the current analysis aims to establish a baseline level of knowledge of HSPs on TB and assess the differences among the HSPs from government and private sector.

Design/methods: A cross-sectional community based survey was conducted in 30 districts from 15 states in India from January–March 2011. The HSPs practising in the 300 primary sampling units were enlisted and those who consented to participate were interviewed using a semi-structured questionnaire with questions related to knowledge on TB symptoms, diagnosis, preferred test of diagnosis, treatment and cure, DOTS, MDR-TB, diagnosis centres, and others including contact examinations, source of TB medicines and separate record maintenance.

Results: Of 614 HSPs interviewed, complete information was available for 582 providers. Of them, 66% were private HSPs, 10.65% were female, mean age is 43 years and 54.5% were qualified in allopathic system of medicine. The level of knowledge among government practitioners on disease, diagnosis, referral and contact examination of tuberculosis patients was higher as compared to private HSPs (see Table). Only 54% of the private practitioners were aware of MDR-TB and said sputum microscopy for the most preferred test for TB. Also, the level of knowledge was greater among practitioners of allopathy as compared to other systems (allied) of

Table   Knowledge, attitude and practice with regards to tuberculosis (TB) in government and private practitioners, baseline KAP study, India, 2011

Variable	Private practitioner ($n = 385$) n (%)	Government practitioner ($n = 197$) n (%)	P value
Aware of DOTS			
Yes	367 (95.3)	194 (98.5)	0.06
No	18 (4.7)	3 (1.5)	
Aware of average duration of treatment			
Correct (6–8 weeks)	296 (76.9)	166 (84.3)	0.04*
Incorrect	89 (23.1)	31 (15.7)	
Main symptom for diagnosing TB			
Cough of 2 weeks	363 (94.3)	185 (93.9)	0.85
Others	22 (5.7)	12 (6.1)	
Aware of MDR-TB			
Yes	207 (53.8)	160 (81.2)	<0.01*
No	178 (46.2)	37 (18.8)	
Aware of correct investigation to diagnose MDR-TB**			
Yes	181 (87.5)	138 (86.3)	0.74
No	16 (12.5)	22 (13.7)	
Most preferred investigation for TB			
Sputum microscopy	208 (54)	157 (79.7)	<0.01*
Others	177 (46)	40 (20.3)	
Site of referral for sputum examination			
DMC (government)	268 (69.6)	190 (96.4)	
DMC (private)	89 (23.1)	5 (2.5)	<0.01*
Non-DMC	28 (7.3)	2 (1)	
Knowledge of pulmonary TB patient being cured			
Improvement in symptom	240 (62.3)	81 (41.1)	
Sputum turned negative	83 (21.6)	88 (44.7)	<0.01*
Improvement in X-ray	31 (8.1)	6 (3)	
Others	31 (8.1)	22 (11.2)	
Source of TB medicines			
Government	264 (68.6)	181 (91.9)	0.01*
Private	121 (31.4)	16 (8.1)	
Maintaining separate records for TB patient			
Yes	99 (25.7)	135 (68.5)	<0.01*
No	286 (74.3)	62 (31.5)	
Contact examination			
Yes	153 (39.7)	102 (51.8)	<0.01*
No	232 (60.3)	95 (48.2)	
Attitude of effectiveness of DOTS			
Good outcome	336 (91.5)	182 (93.8)	
Average outcome	28 (7.6)	11 (5.7)	0.73
Bad outcome	1 (0.3)	0 (0.0)	
Don't know	2 (0.5)	1 (0.5)	

* Statistically significant by χ² test.
** This is only for those who are aware of MDR-TB (pvt. practitioner = 207, public. practitioners = 160).
KAP = knowledge, attitude and practice; MDR-TB = multidrug-resistant tuberculosis; DMC= designated microscopy centre.

medicine. Private allopathy practitioners (67%, $n = 118$) were aware of MDR-TB when compared to private allied practitioners ($P < 0.01$). Government allopathy practitioners (83%, $n = 123$) preferred sputum test for diagnosis when compared with government allied practitioners ($P < 0.01$).

Conclusion: This analysis demonstrates the lack of correct knowledge about TB diagnosis, treatment and care among majority of private practitioners and government allied practitioners. As RNTCP prepares to include all health service providers in TB care and control program according to the new strategies it developed, it is crucial that we consider the knowledge level of each group of health service providers based on initial assessment and their qualification and equip them through tailor-made trainings for effective TB care and control.

OP-120-01   Cookstoves for carbon credits: innovatively leveraging networks for a sustainable solution to indoor air pollution

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Background: In a recent survey done for the Union-South East Asia (USEA), it was found that 90% of the TB patients surveyed used solid and fossil fuels for their cooking. A majority of this population was female, and lived in rural areas; these women were exposed to high degrees of indoor air pollution and increased their likelihood of contracting TB. Thus indoor air pollution, which kills 2 million people annually globally, was a key contributor to TB for which the USEA sought an innovative solution that could be sustainable, viable and practicable.

Response: To devise an innovative intervention for the problem of indoor air pollution, we came up with a market-based business plan leveraging the wide USEA network of 1000+NGOs and the idea of Carbon Emission Reduction (CERs) credits. CERs are a global market-based instrument traded on global stock exchanges under the Clean Development Mechanism of the Kyoto Protocol. Emission credits can only be generated in the Global South in projects that mitigate carbon emissions, and CERs can only be purchased by firms and entities in the developed countries of the North. Taking advantage of this positioning, the USEA team prepared a business plan leveraging the wide network of partners in India to procure and distribute energy-efficient CER-certified cookstoves to rural women. This business plan was submitted to the 'Power of Ideas' national business plan competition organized by the elite Indian Institute of Management, Ahmedabad.

Results: After three rounds of competition, the USEA business plan ranked in the top 75 out of 14000 submitted business plans. Two members of the USEA team were provided free training and mentoring for 10 days at IIM-Ahmedabad, gaining exposure to all aspects of running a startup enterprise (from advertising, staffing and financing to accessing venture capital) in addition to gaining access to an exclusive network of key business entrepreneurs in India.

Cookstoves for Carbon Credits. The Union proposes a simple intervention with multipronged effects

2. DISTRIBUTE

The Union is present in 300 districts and 20 states of India

1. PROCURE

3 MONETISE & REDISTRIBUTE

The Union will procure CER-certified efficient cookstoves, distribute it through our wide network, generate revenue by monetise usage and return the Union's share of CERs generated back to the community. (1 CER = 5 Euros at present)

Conclusions: The largest challenge to the Cookstoves for CERs project has been the global carbon market, which has witnessed depressed prices in recent months. But the concept itself is based on an innovative approach to public health which leverages existing resources in unforeseen ways to tap the power of our public health network with the market mechanism and deliver a solution for TB patients. Marrying market-based mechanisms with public health goals as our project did is one way to think outside the box for innovative TB control.

OP-121-01   Building representative capacity of civil society in tuberculosis control: England's local tuberculosis partnerships

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Background: England has the largest burden of tuberculosis (TB) in Western Europe. Unlike other Western European countries, where TB incidence has halved on average since 2000, TB incidence in England continues on an upward trajectory. England has high incidence 'hot spots', comparable to many developing countries. Public health interventions must be based on a co-beneficial relationship between health care providers and communities at risk of TB. Building opportunities for such reciprocity into public health activities increases impact and sustainability of TB services, one of the goals of The Truth About TB programme, the UK's flagship TB awareness programme. Health outcomes sought by The Truth About TB are to: reduce the time between onset of symptoms and diagnosis; reduce transmission; improve service design and delivery from the prism of a social model of health.

Intervention: One of several initiatives is the formation of Local TB Partnerships (LTBPs), which provide a mechanism to develop the role of civil society in TB care and control, including developing relationships between Community Based Organisations (CBOs), People Affected by TB (PATB) and state agencies. LTBPs give communities a structure for planning and implementing their ideas based on the following principles: being representative of, and owned by, affected communities; being recognised by state agencies as legitimate and necessary for TB control; working with state agencies to improve the design and delivery of local TB services.

Results and lessons learnt: 5 LTBPs have been developed in areas of high TB incidence. There has been varying models of implementation in each area. A gradual but certain paradigm shift in the way TB control is administered is evident: PATB and community engagement are now seen as vital components; change from 'doing to' to 'working with' affected communities; it is valuable to combine the knowledge of professionals with the experiences of patients.

Conclusion: The impetus for building the representative capacity of civil society in TB control can come from community members or CBOs seeking to understand, influence and contribute to TB services. The creation of successful partnerships needed to build this representative capacity depends on the local context, including governance structure and the ability of the lead state agency to create trust and a shared vision among partners addressing TB.

OP-122-01 Establishing the parliamentary front to fight tuberculosis in Brazil

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Background and challenges to implementation: In accordance to the STOP TB Partnership international guidelines related to community involvement to fight tuberculosis, in 2009 the National TB Programme (NTP) conducted a national seminary gathering all federal units' representatives from different sectors: parliamentarians, researchers, public managers and social activists. This meeting resulted into 32 refereed recommendations, in which one of them was the establishment of a national parliamentary front to fight TB. In March 2011, the National Health Council recommended the HIV and AIDS Public Policy Council and Parliamentary Fronts that the TB theme should be included as a priority in their agenda at local, state and national levels.

Intervention and response: In response to the National Health Council's recommendation, NTP technical advisors and social activists conducted a series of meetings aiming to raise awareness among parliamentarians on the importance of discussing the theme in the national congress. During these meetings a parliamentarian who was sensitive to the cause was identified, and he accepted the challenge of implementing the Front. The deputy therefore, convened a public hearing throughout the week of 24 March (World TB Day) in order to widen the debate and bring visibility to the theme in the parliament. The establishment of Parliamentary Mixed Fronts (having both Senate and Chamber of Deputies' representatives) is possible if 198 signatures are gathered, which represents one third of the total number of congressmen from both Houses (171 deputies and 27 senators). The Parliamentary Front to Fight TB assembled 217 parliamentary signatures, among deputies and senators.

Results: The Parliamentary Front to Fight TB was duly established on May 8, 2012.

Conclusion and recommendations: During the first operational year, the Parliamentary Front to Fight TB presented an amendment to the Budget Guidelines Law which allowed more flexibility in the access to public resources. The beneficiaries are community-based organizations aiming to develop actions and promoting health in areas such as TB, HIV/AIDS, viral hepatitis, leprosy, malaria and dengue. In 2013, the Front has pursued the development of a sub-commission aiming to analyze and diagnose the government efforts managing poverty related diseases, in which TB is correlated to.

OP-123-01 Partnerships between civil society and state structures in response to fighting HIV-TB epidemics in Ukraine

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Background and challenges to implementation: Ukraine is burdened with dual epidemics HIV and TB. The level of co-infection TB-HIV increases every year (from 3.2 per 100 000 in 2005 to 10.4 in 2012). 62.5% newly registered AIDS-patients in 2011 suffered with TB which makes the TB leading cause of death among people living with HIV/AIDS. 10.2% HIV-infected patients have active TB in 2011 (2010– 8.8%). Collaboration between the specialized healthcare system relies on personal relationships rather than institutional procedures.

Intervention and response: Based on its experience AU extended its activities in the field of HIV prevention among TB patients and TB prevention among HIV patients. AU supports NGOs to provide typical harm reduction services in integrated medical and psychosocial care (syringes exchange, condoms distribution, and advocating services, PITC) settings to prevent HIV in TB-patients. TB-screening, IEC

materials distribution among HIV-patients is provided in the integrated care sites. NGO's signs a MoU with each health care institution as a commitment of partnership to implement these prevention activities. 81 Health care institutions provide integrated services including early TB detection, PITC for IDUs on SMT-sites.

Results and lessons learnt: 163 NGOs were supported during the implementation in 2012 and providing consultation and other services to 278 representatives of vulnerable groups with HIV by TB-doctors within the project. 8066 TB-patients received HIV prevention services.

Conclusions and key recommendations: CSO's intervention in programs for prevention of TB and HIV/AIDS epidemic provides the possibilities for vulnerable groups to access prophylaxis of TB and HIV in an integrated setting, which leads to further reduction of HIV and TB burden in the community.

OP-124-01   A framework for sustainable partnerships with NGOs and the private sector for tuberculosis control in Bangladesh

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Background: The Society for Empowerment, Education and Development (SEED) is a registered non-governmental organisation in Bangladesh. Since 2004, SEED has been pioneering a public-private partnership (PPP) model to engage NGOs, private sector organisations and civil society within the National TB Control Programme in order to improve access and quality of TB care. Developing and piloting of the PPP model took place in four selected research sites in Dhaka city. Based on the successful outcomes, this model has been scaled up in two other big cities— Chittagong and Sylhet in 2008.

Design/methods: We used NTP service statistics to compare the TB control outcomes between the intervention and control areas. To capture detailed insights of NGOs, private medical practitioners (PMPs), TB managers and garments workers about the process and outcomes of the study, we conducted a series of in-depth interviews, focus group discussions (FGDs), and workshops. Quantitative data were analysed using Microsoft Excel and qualitative data were systematically analysed using a thematic approach.

Results: The systematic involvement of NGOs, PMPs and garment factories, coordinated by SEED, 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 smear-positive TB cases—contributing about 36% of all TB cases registered in the project areas. Moreover, during 2008–2010, a total of 3372 garment workers from a workforce of 69 000 were examined for sputum microscopy and 598 were diagnosed with smear positive TB, 145 of which received care at their workplace—the overall treatment success rate was 100%. We identified eight steps and four principles which were critical for engaging NGOs and private sector providers in the NTP's activities. Our participatory approach to planning and designing the partnership played a crucial part in securing commitment and ownership for sustainable scale up. The framework also guided the public, NGO and private sector providers to work together for achieving the common goal for TB control, although PMPs and garment factory owners were initially sceptical about the partnership.

Conclusion: The model is simple, effective, and sufficiently robust to provide guidance in developing partnerships with NGOs and private sector for sustainable health service delivery.

HAND IN HAND: SCREENING FOR TUBERCULOSIS AND HIV

OP-125-01   Intensified tuberculosis case finding in a cohort of HIV-infected children in Johannesburg, South Africa

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Background: The WHO's Intensified TB Case-Finding (ICF) guidelines recommend that HIV-infected children presenting with current cough (C), fever (F), weight loss (W) or contact with a TB case (Co) should be evaluated for TB. We aimed to assess these recommendations in a cohort of South African children initiating HAART.

Methods: Children (0–8 years), receiving care at an outpatient HIV care and treatment clinic in Johannesburg were included in the analysis. First, children were screened for TB by routine clinic staff using standard of care procedures. Subsequently, research staff screened all children not diagnosed with TB and not receiving TB treatment for TB symptoms or contact with active TB using a standard questionnaire. Screenings were done on the day of starting HAART, 2, 4, 6, 8 and 12 weeks and every 3 months thereafter for 2 years. Symptomatic children were assessed by chest X-ray (CXR), tuberculin skin test, smear microscopy and culture on a single sputum specimen. Adjusted odds ratios and 95% confidence intervals

(CI) were estimated for associations between child or visit characteristics and presence of TB symptoms.

Results: Among 277 participating children, 220 (79%) underwent 1151 screenings while not on TB treatment. Half (52%) were male, median age at enrolment was 2.1 years (IQR: 0.74–4.79). The median baseline CD4% was 18.4% (IQR: 12.6–24.8). Of the 1151 screenings, 67 (5.9%) were positive: 0.1% for CFW, 0.9% for CW, 0.2% for CF, 0.2% for FW, 0.1% for CCo and 4.4% for only one of CFWCo. Of those with W, 75% had <5% decrease in weight. In addition to CFWCo, symptoms of ear discharge and enlarged lymph nodes were present at another 3 screening visits. These 70 positive screenings occurred in 54 individual children. A decision to start TB treatment was made in 5 (9.3%) children based on CXR ($n = 2$), empirically ($n = 2$) or on TB culture results ($n = 1$). Screening visits were more likely to be positive on the day of starting HAART (OR = 3.2; CI: 1.2–3.2) and in children with a baseline CD4% < 15% (OR = 1.9; CI: 1.8–5.8).

Conclusions: In this cohort of children initiating ART, we found a low prevalence of TB symptoms despite the use of a highly sensitive TB symptom screen. The proportion of children with positive ICF screening started on TB treatment was high (9.3%), suggesting that routine use of a simple but sensitive symptom screen improves case finding in this vulnerable population.

OP-126-01 Overcoming barriers to tuberculin skin testing and isoniazid preventive therapy in HIV clinics in Rio de Janeiro, Brazil

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Aim: To determine if a TB-HIV Integration Specialist (THIS) nurse increases provision of TST and IPT in four HIV clinics in Rio de Janeiro, Brazil.

Design/methods: Between 2005 and 2009, 29 HIV clinics received intensive training for provision of TST and IPT as part of the TB-HIV in Rio (THRio) study. After receiving the THRio training intervention, HIV clinics implemented TST and IPT markedly faster, however, significant delays for both TST and IPT remained. In 2012, 4 of these clinics employed a THIS whose responsibility was to expedite all aspects related to TB-HIV. The THIS were trained to approach all patients in the HIV clinics, review medical records, place and read TST, implement IPT, screen for symptoms, order CXR for ruling out TB, and record CD4 and viral load values. We compared the following outcomes between 2008 (THRio) and 2012 (THIS) across the clinics among eligible patients: 1) proportion receiving a TST; 2) proportion initiating IPT and 3) prevalence of latent tuberculosis infection.

Results: In 2008 during the THRio study, there were 2456 HIV-infected patients eligible for a TST and 812 (33%) had a test placed and read, compared to 2033 of 2507 (81%) eligible patients during the THIS study. TST proportion ranged from 30%–41% in clinics in the THRio period and from 76%–87% in the THIS period. TST positivity declined from 13% (clinic range: 10–17%) in the THRio period to 10% (clinic range: 7–12%) in the THIS period, with declines observed in each of the clinics. The proportion of TST positives initiating IPT increased from 82% in the THRio period (clinic range: 75%–91%) to 89% during the THIS period (clinic range: 75%–97%). When first approached during the THIS period, 49% of HIV-infected patients reported no history of receiving a TST; 34% reported receiving a TST more than one year ago; and, 17% received a TST less than one year ago.

Table TST and IPT provision during the THRio study period (2008) and the THIS study period (2012)

	2008				2012			
	N	TST tested	TST+	Start IPT	N	TST tested	TST+	Start IPT
Clinic 1	741	219 (30%)	28 (13%)	24 (86%)	568	431 (76%)	44 (10%)	37 (84%)
Clinic 2	635	205 (32%)	23 (11%)	21 (91%)	600	520 (87%)	47 (9%)	36 (77%)
Clinic 3	481	196 (41%)	20 (10%)	15 (75%)	571	467 (82%)	34 (7%)	32 (94%)
Clinic 4	599	192 (32%)	32 (17%)	24 (83%)	768	615 (80%)	76 (12%)	74 (97%)
Total	2456	812 (33%)	103 (13%)	84 (82%)	2507	2033 (81%)	201 (10%)	179 (89%)

Conclusion: Hiring a TB-HIV integration specialist nurse in four HIV-clinics in Rio de Janeiro markedly increased the number of HIV-infected patients who received a TST and IPT. IPT has been shown to reduce TB risk in HIV-infected patients in Brazil and elsewhere, but recent evidence suggests that patients with a positive TST benefit most. TST can be challenging to operationally implement and often causes delays. However, we have shown that a dedicated nurse can have a strong impact on reducing these delays. A cost analysis will be conducted to assess the sustainability of this intervention.

OP-127-01 An integrated community HIV and tuberculosis testing model: using routine data to compare stand-alone and mobile HCT services

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Background: The South African government has acknowledged that knowing one's HIV status is vital and views HIV counseling and testing (HCT) as a key component of HIV care and prevention. HCT

services offered at health facilities cannot test everyone. Community based HCT services provide the opportunity to increase universal access. An integrated community model was developed to increase access to HIV and TB testing and included both stand-alone centers and mobile services. This study reviewed the routine data collected from both these services to better understand the populations who accessed these services and the benefits of each.

Methods: A model was developed where nine community HCT stand-alone centers were established and maintained in partnership with non-governmental organizations from 2008 to 2012, in high TB-HIV burden communities around Cape Town. Services were provided from either the stand-alone centre or on a mobile 'outreach' basis. Mobile services were provided from tents and caravans that were set up at busy community thoroughfares and transport hubs. All clients were tested for HIV and screened for TB according to national guidelines. Routine data was collected in HCT registers and entered into a database. The chi-square test was used to determine if either the stand-alone or mobile service was associated with any of the HIV or TB indicators collected in the routine data.

Results: 96 137 clients accessed these services. The mobile services accessed a greater proportion of clients (80%) than the stand-alone service (20%) and had a greater proportion of male clients (50%) compared to the stand-alone centers (45%). The stand-alone centers diagnosed a significantly higher proportion of clients with HIV (13%, $P < 0.001$) and a significantly higher proportion of co-infected clients (16%, $P < 0.001$) than the mobile services. The stand-alone centers were also better able to link HIV-infected clients to care ($P < 0.001$) than the mobile services.

Table   HIV and TB indicators from routine data collected for clients who accessed either a stand-alone or mobile service in the community

Indicator	Stand alone n (%)	Mobile n (%)	Total n (%)
Total clients	19 398	76 739	96 137
Males	8 744 (45)	38 188 (50)	46 932 (49)
Tested	18 087 (93)	72 164 (94)	90 251 (94)
HIV diagnosed	2 331 (13)	4 148 (6)	6 918 (7)
HIV+ve referred	2 140 (92)	4 148 (90)	6 288 (91)
HIV+ve linked to care	1 574 (74)	2 825 (68)	4 399 (70)
Total TB symptoms (100% screened)	2 169 (11)	4 405 (6)	6 574 (7)
HIV+ve with TB symptoms	470 (22)	535 (12)	1 005 (15)
HIV+ve TB tests	388 (82)	387 (72)	775 (77)
HIV+ve TB diagnosed	63 (16)	29 (7)	92 (12)
HIV+ve commenced TB Rx	59 (94)	28 (97)	87 (95)

Conclusion: This model was able to successfully integrate HIV and TB testing for stand-alone and mobile services. The mobile service was able to access a more 'well' population and provide early case detection, referral and linkage to care for a higher number of clients. Policy makers who wish to expand access to HCT should consider an integrated community model that includes both a stand-alone and a mobile arm for improved coverage. Future research should consider a cost analysis of these two services.

OP-128-01   Engaging informal health care providers in case detection for tuberculosis and HIV in rural Malawi

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Introduction: The poor and vulnerable face structural barriers in accessing TB and HIV/AIDS services. We implemented a randomised, controlled health system intervention trial involving informal health care providers (IHP): 'Triage Plus' in rural Malawi. We aimed to determine the overall effect on: a) diagnostic uptake for TB and HIV and b) TB and Anti Retroviral Therapy (ART) treatment initiation.

Methods: The intervention consisted of training non-paid IHP (such as store-keepers) in TB and HIV disease recognition, sputum specimen collection, referral to the public health system, and raising community awareness. Front line public health personnel and community leaders were sensitised to support the intervention. A phased, matched, parallel cluster design was used with a 1:1 randomisation of six clusters (average total population size per cluster = 205 139) to an early intervention arm (received the intervention early in the first 12 months) and a delayed intervention arm (received the intervention after one year). Repeated measurement Poisson models were used for evaluation of incidence rate ratios between the two arms over 23 months. Development, set up, and recurrent cost data were collected and adjusted for inflation.

Preliminary results: The number of presumptive TB cases accessing diagnostic sites was 15.2% higher in the early arm ($P = 0.003$) after the first 12 months, but there was no difference between the two arms after the next 11 months (i.e., after the intervention was rolled out to the delayed arm). The number of TB cases starting treatment was non-significantly higher (18%) in the early arm ($P = 0.112$) after 12 months, but 45% lower ($P < 0.001$) after the next 11 months. HIV testing uptake was 61% higher in the early arm ($P < 0.001$) after the first 12 months but there was no difference between the two arms after the next 11 months. ART initiation was 34.7% higher ($P = 0.048$) in the early arm after the first 12 months and again there was no difference between

the arms after the next 11 months. The incremental cost-effectiveness of the intervention was $16 per additional HIV test and $600 per additional new case starting ART. As duration and coverage increase, the fixed cost proportion will reduce, improving cost-effectiveness.

Conclusions: Engagement of IHP in integrated TB and HIV services at community level was associated with a substantial increase in services access and HIV treatment initiation. There may be several explanations for the decrease in TB treatment initiation over time.

OP-129-01   Intensified tuberculosis case finding in PMTCT settings in Nigeria

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Background and challenges to implementation: Nigeria ranks 10th among the 22 high burden TB countries, with estimated TB prevalence rate of 118/100 000, an HIV sero-prevalence rate of 4.1%, and TB-HIV co-infection rate of 30%. TB-HIV collaboration has been shown to increase TB and HIV case finding among the two groups. Intensified TB case finding has been established in FHI360 supported HIV counseling and treatment sites but not in PMTCT settings. HIV-infected pregnant women are ten times more likely to have active TB than HIV-uninfected pregnant women and TB has serious implications during pregnancy. Antenatal care (ANC) is an important point of contact between pregnant women and the health system. This paper describes a pilot intervention to intensify TB case finding among antenatal attendees in four facilities providing PMTCT services in Nigeria.

Intervention or response: Health providers at antenatal and DOTS clinics and the AFB laboratory received orientation on TB-HIV collaboration and referrals. The HCT client intake form was modified to include WHO TB symptoms screening among pregnant women attending ANC. The clients with a score of >1 were referred for AFB microscopy or GeneXpert machine. Results were entered into a modified ANC register from which a monthly summary was derived.

Results and lessons learnt: Out of the 2793 pregnant women clinically screened for TB, 189 had a score of >1. Only 103 out of the 189 women had productive cough and 64 were tested using AFB microscopy while 39 were tested with GeneXpert. Only one pregnant woman was diagnosed with active TB (sputum smear positive) and was referred to the DOTS clinic for anti-TB treatment.

Conclusions and key recommendations: Intensified TB case finding in PMTCT setting appears to be a low yield intervention and may not be cost effective. It however provides an opportunity for TB awareness and education.

OP-130-01   Experience with the Xpert® MTB/RIF assay in routine programme conditions with different HIV prevalence and risk of MDR-tuberculosis

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Background: The Xpert® MTB/RIF (Xpert) assay was introduced in over 30 tuberculosis (TB) programs operated by Médecins Sans Frontières using different diagnostic algorithms according to HIV prevalence and risk of multidrug-resistant (MDR) TB. We monitored the yield of patients detected with TB, rifampicin resistance, and started on treatment in routine conditions in four sites after Xpert introduction.

Methods: The monitoring took place from March 1 until November 30, 2012, in Nhlangano, Swaziland (high HIV, high MDR); Mathare, Kenya (high HIV, low MDR); Sukhumi, Abkhazia (low HIV, high MDR); and Kampong Cham, Cambodia (low HIV, low MDR). Smear microscopy was done systematically to all TB suspects in all sites, as well as Xpert in high HIV settings. In low HIV settings, Xpert was used for *Mycobacterium tuberculosis* detection in smear-negative pulmonary or extra-pulmonary TB (EP-TB) suspects upon clinical request, and for rapid rifampicin detection in MDR-TB suspects and, in Abkhazia, in all smear-positive patients. Data were collected using the routine Xpert MTB/RIF laboratory register and program TB registers.

Results: In high HIV settings, Xpert MTB/RIF positivity rate was 11% in Swaziland (123/1006), 22% (268/2420) in Kenya, and 15% and 24% in HIV patients, respectively. Initial inconclusive results were 6% in Swaziland and 11% in Kenya, where they were reduced to 4% after repeated testing. Among pulmonary TB patients started on treatment, the proportion of smear-negative cases detected by Xpert was 21% in Swaziland and 5% in Kenya, with a median delay from first specimen collection to treatment start of 5 and 3 days, respectively. In low HIV settings, Xpert was requested in 46% (220/475) of smear-negative TB suspects in Abkhazia with an 8% positivity rate. In Cambodia, Xpert was performed in 51% (778/1531) of smear-negative pulmonary TB suspects and 93% (155/167) EP-TB suspects providing a specimen, with 5% and 13% positivity rate.

Rifampicin resistance was detected in 4% of Xpert MTB/RIF positive patients in Cambodia, 5% in Kenya, 11% in Swaziland and 20% in Abkhazia, where the median delay from first specimen collection to start of MDR empiric treatment was 12.5 days.

Conclusions: These results illustrate the variety of use and added value of Xpert compared to traditional methods according to the contexts and algorithms used. Xpert was particularly useful for the confirmation of pulmonary TB in Swaziland, EP-TB in Cambodia and in early MDR treatment start in Abkhazia.

OP-131-01   HIV testing among presumptive tuberculosis cases in routine implementation, Karnataka, India

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Background: Based on evidence generated in operational research studies, the National Tuberculosis (TB) Control Programme and National AIDS Control Programme in India made a joint policy decision in January 2012 of implementing Provider Initiated HIV Testing and Counselling (PITC) among presumptive TB cases in high HIV prevalence states. We present here the first year's implementation findings of the state of Karnataka (population: 60 million), India.

Intervention: All the presumptive TB cases coming to the microscopy centre were offered voluntary counselling and testing for HIV. The programme records (laboratory form for sputum examination and laboratory register) and reports (monthly programme management report) were modified to capture HIV status of presumptive TB cases. We collected data on —number of presumptive TB cases assessed for HIV and found HIV positive—from the monthly reports of all 31 districts and aggregated at state level for the period January–December 2012.

Results: Of 498 292 presumptive TB cases examined for sputum microscopy, 232 156 (47%) had their HIV status ascertained and 21 899 (9%) were found to be HIV positive. The key reason for non-testing was because sputum samples were transported from periphery to microscopy centre instead of patients.

Conclusion: The policy of PITC among presumptive TB cases has been implemented successfully in Karnataka. Challenges of ascertaining the HIV status of presumptive TB cases whose sputum samples come to microscopy centre need to be addressed—this may include decentralizing HIV testing services at the peripheral health institutions.

THE EVOLVING EPIDEMIOLOGY OF TUBERCULOSIS IN CHILDREN

OP-132-01   Bacille Calmette-Guérin lymphadenitis among Saudi Arabian children is a growing menace. Is this the right time to reconsider vaccination policies?

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Background: Bacillus Calmette Guerin (BCG) is the only available vaccine for the most infectious tuberculosis (TB) disease since 1921. However its efficacy and admissibility to different population is still controversial though it gives confirmed protection against military TB and tubercular meningitis among children. Saudi Arabia recently faced several outbreaks of BCG related lymphadenitis around the country and that lead us to trace the outbreak using molecular techniques.

Design/methods: A nationwide collection of 42 mycobacterium isolates (during 2009–2010) from children aged less than 18 months and three BCG vaccine strains (SSI, Danish 1331, Connaught and Japan) were subjected to fingerprinting and drug susceptibility testing. All the isolates were underwent spoligotyping, 24 loci MIRU-VNTR typing followed by susceptibility testing to first line anti-TB drugs; streptomycin, isoniazid, rifampicin and ethambutol. Phylogenetic data analysis was conducted by using online database (www.miru-vntrplus. org).

Results: The study population was dominated by male children (63%) and all the cases were Saudi nationals. Majority (78.6%) of the children were aged between 1–5 months. Of the total, 41 (97.6%) isolates were genotypically matched completely with the SSI Danish 1331 strain and one with Japan strain. All the SSI 1331 strain isolates were resistant to isoniazid. The phylogenetic analysis and clinical data clearly showed an outbreak of lymphadenitis caused by the SSI 1331 strains and this must be related to the change of vaccine to SSI 1331 since 2005.

Conclusion: The uniqueness of Saudi population with the high rate (56%) of consanguinity is a major predisposing factor for high incidence of primary immunodeficiency disorders and makes the population vulnerable to BCG complications. In addition previous studies reported Saudi Arabia with the highest number of severe combined immunodeficiency (SCID) incidence in the world. Furthermore a rare genetic condition, Mendelian susceptibility to mycobacterial disease (MSMD), which associated with mutations in 6 genes result in 13 inherited conditions, is frequently reported among Saudi nationals than expected. It is evident that, this is the right time to conduct a nationwide community based study to find the real

magnitude of problems and efficacy of BCG vaccine followed by implementing the vaccination policies according to the findings.

OP-133-01 Drug resistance surveillance in children with culture-confirmed tuberculosis in the Western Cape: a downward trend?

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Aim: To determine the prevalence of drug resistance and HIV-co-infection among children with culture-confirmed tuberculosis (TB) and to compare results with 4 previous surveys.
Method: Prospective surveillance was done from March 2011 through February 2013 at Tygerberg Children's Hospital, Cape Town, South Africa. Drug-susceptibility testing (DST) was done by line probe assay (GenoType MTBDR*plus*®; LPA) for INH and rifampicin (RMP) on one isolate from each child <13 years with culture-confirmed TB. Further DST was done if resistance was found. HIV status was documented.
Results: 324 children, 167 (52%) male, median age 32 months (range 1 day–156 months) were diagnosed with culture-confirmed TB. HIV testing increased from 60% (period 2) to >90% (period 5) of TB cases, but HIV infection decreased significantly from 29% (period 3) to 15.7% (period 5), OR 0.46 (95%CI 0.30–0.70). The results of three surveillance periods (periods 1, 3 and 5) are presented in the table due to abstract restrictions. Significant differences in resistance: RMP-monoresistance 1st and 5th period—$P = 0.03$; MDR-TB decreased period 3 to 5—OR 0.50 (95%CI 0.26–0.96), $P = 0.04$. Previous treatment in children decreased from 17% (period 3) to a low 9.9% (period 5)—OR 0.53 (0.33–0.86), $P < 0.01$.

DST	2003–2005 Period 1n %	2007–2009 Period 3n %	2011–2013 Period 5n %
Culture-confirmed TB	323	294	324
DST completed	320 (99.1)	292 (99.3)	324 (100)
Any resistance to			
INH or RMP	41 (12.8)	45 (15.4)	41 (12.7)
INH monoresistance	22 (6.9)	15 (5.1)	20 (6.2)
RMP monoresistance	0	4 (1.4)	6 (1.9)
Multidrug resistance	19 (5.9)	26 (8.9)	15 (4.6)

Conclusions: Overall proportion of drug resistance shows a declining trend, associated with a significant decrease in MDR-TB cases. Increase in RMP-monoresistance is not only due to genotypic LPA DST, which may miss some INH resistance. The significant decrease in HIV infection in TB cases is likely due to a well-functioning prevention of mother-to-child-HIV-transmission programme.

OP-134-01 Childhood tuberculosis in Israel: epidemiological trends and treatment outcomes, 1999–2010

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Introduction: Pediatric tuberculosis (PT) poses high risk of severe diseases and death for children. This study describes the characteristics of PT in Israel, and examines treatment outcomes during the last decade.
Methods: Data source was the National Tuberculosis Registry. The denominator used to calculate tuberculosis rates was the national census. All children younger than 18 years of age who were diagnosed with tuberculosis (pulmonary and extra pulmonary) between 1999 and 2010 were included.
Results: During the study period, 416 children were diagnosed with PT in Israel, in an average of 1.5 per 100 000 children (range 0.6–3.2), in a declining trend. Tuberculosis rates and trends were similar for boys and girls. The average PT proportion of all cases reported annually was 8.4% (range 5.4–11.8). Most ($n = 320$, 78.8%) of the PT had pulmonary tuberculosis. Of the 88 (21.2%) of children with extra pulmonary tuberculosis, the most common site was lymph node ($n = 55$, 62.5%), followed by the pleura ($n = 9$, 16.4%) and menings ($n = 5$. 5.7%). The majority of PT was at the age group of 0–4, followed by 5–9, 15–17 and 10–14. TB rates were highest for the age group 0–4 and lowest for 10–14. Of all PT, 259 (62.2%) were not Israeli-born: 214 (51.5%) were born in Ethiopia and 22 (5.3%) were children of migrant-workers, who were not Israeli citizens. The number of PT in the latter group is increasing. The PT incidence in 2010 was 1.05/100 000 children, among Israeli-born children was 0.55/100 000 children, among children of Ethiopian origin was 15.8/100 000, and 50–100/100 000 for children of migrant-workers. Most migrant children with PT were diagnosed within the first two years following their arrival in Israel. Cultures were performed only in of 60% of all PT, and 54.5% of those were positive. Average treatment success was 97.8%, and three cases (0.7%) died due to tubercular tuberculosis meningitis.
Conclusions: Overall PT rates in Israel are decreasing, which may suggest a low rate of mycobacterial transmission in the community. However, children or siblings of parents born in high-prevalence are at high-risk for PT. Treatment success among PT is high, but 3 died. Analysis of bacteriological confirmation of PT should be encouraged to improve childhood tuberculosis control.

OP-135-01   Prevalence of non-tuberculous mycobacteria in children investigated for pulmonary tuberculosis in Southern Mozambique

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Background: Non-tuberculous mycobacteria (NTM) are ubiquitous environmental bacilli frequently encountered in gastric aspirates and induced sputum samples.These microorganisms can cause disease, especially in severely immunosuppressed children, which can be undistinguishable from tuberculosis (TB). Moreover, NTM can complicate the diagnosis of TB and interfere with clinical endpoints for TB vaccines.
Objective: To determine the prevalence of NTM isolates from children under investigation for tuberculosis within the Manhiça District, South of Mozambique.
Design/methods: TB suspect children under the age of three years were recruited through active and passive case finding during a period of one year in a study to determine the minimum incidence of tuberculosis within the Manhiça HDSS. Patients fulfilling any of the TB screening criteria were defined as suspects and further studied through chest X-ray, HIV and tuberculin skin testing as well as gastric aspirate and induced sputum sampling. All samples were processed for smear testing using LED Microscopy, liquid and solid culture, and mycobacterial molecular identification by GenoType® Mycobacterium CM.
Results: Mycobacterial culture demostrated NTM isolates in 183 of the 806 TB suspect cases and *M. tuberculosis* isolates in 13 patients. The crude diagnostic yield of NTM was 9.7% (207/2133), 9.8% (106/1077) for gastric aspirate and 9.6% (101/1056) for induced sputum. Most prevalent NTB was *M. intracellulare* (*n* = 106), followed by *M. scrofulaceum* (*n* = 25) and *M. fortuitum* (*n* = 8). There was no significant difference between the prevalence of the NTM in HIV positive and negative cases (25 vs. 30%). Twenty-eight percent (52/183) of the patients with NTM isolates initiated TB treatment, compared to 10% (61/615) in those with negative cultures.
Conclusion: NTM were isolated in 22% of all children investigated for pulmonary tuberculosis. NTM may complicate the diagnosis of PTB in regions that lack capacity for mycobacterial species identification. The clinical significance of NTM isolates requires further investigation.

OP-136-01   Trends in childhood tuberculosis case notifications over the past years in 23 countries

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Background: Many children with TB remain undetected. We present data from 23 countries regarding the number of registered children with TB, focussing on time trends in TB childhood registration.
Methods: Descriptive analysis of GDF (Global Drug Facility) country mission reports on notified paediatric TB cases in 23 countries; calculated was (i) the proportion of paediatric TB cases compared to all TB cases (all ages); (ii) the percentage change in the annual number of paediatric TB cases registered, using the two most recent years for which paediatric TB data were available; and (iii) the proportion of children aged 0 to 4 years over all registered children (0 to 14 years) with TB.
Results: Most countries do not report to WHO complete paediatric TB registration data and not all GDF mission reports contain comprehensive paediatric TB data. In 2010 or 2011, the proportion of paediatric cases over all TB cases (all age groups included) ranged from 2.9% in Kazakhstan to 23.6% in Myanmar; in only nine countries was this proportion 10% or above. Looking at the two most recent years for which data were available, we found that in twelve of the 23 countries, there was an increase in the number of paediatric TB cases (range: 0.5% to 64.3%). In
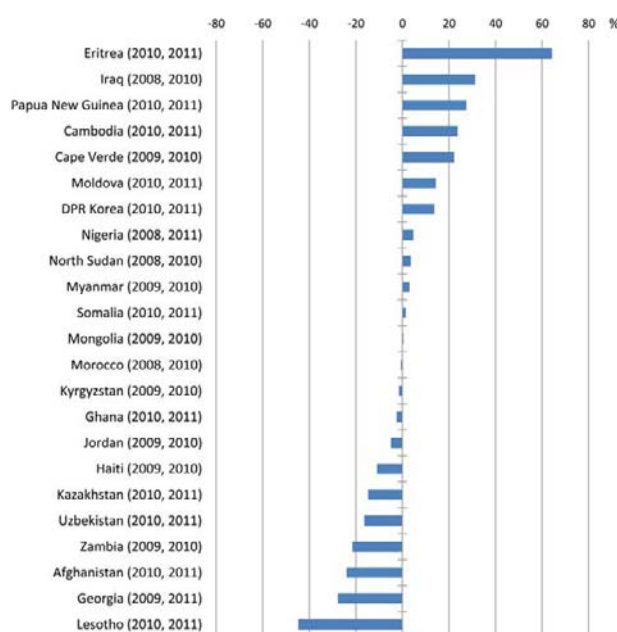
Figure   Percentage change in the number of paediatric TB cases registered. Comparison of the annual numbers from the two most recent years for which paediatric TB data are available.

eleven countries, there was a decrease (range: 0.6% to 44.7%) (see figure). In 19 countries, paediatric TB cases by the two age groups 0 to 4 and 5 to 14 years were available. In only three countries (Lebanon, Lesotho and Somalia) was the proportion of children aged 0 to 4 years over cases aged 0 to 14 years above 50%. In eight countries, this proportion was between 25% to 50% and in another eight, it was below 25%.
Conclusions: 1) Accurate recording and reporting regarding paediatric TB cases is essential to track progress in paediatric TB care. A challenge is that countries are slow in adapting their data collection tools for WHO.

2) In at least 14 of the 23 examined countries, further efforts are needed to detect more paediatric TB cases.

3) Regarding a recent increase of the number of paediatric TB cases, our analysis suggests that such progress occurs in some countries only. A limitation of the study is that data from just two years may not describe true trends in notification.

4) Assuming that the widely held assumption that among children with TB around 66% are aged 0 to 4 years is correct, significant under-detection of TB among children aged 0 to 4 years is common.

OP-137-01   High tuberculosis burden among HIV-infected children enrolled in HIV care in Kenya: results of a national retrospective study

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Background: Tuberculosis (TB) remains a major cause of morbidity and mortality among HIV-infected children. We assessed the burden of TB and the effect of anti-retroviral therapy (ART) on incident TB in HIV-infected children enrolled in care.
Design/methods: We conducted a retrospective cohort study of HIV-infected patients aged <15 years enrolled in care in 50 randomly selected Kenyan health facilities from November 1, 2004 to March 31, 2010; follow up was through July 2012. At each selected health facility, we abstracted data from medical records for all children aged <2 years and 89 randomly selected children aged ≥2 years. We computed median values with interquartile ranges (IQR) to describe patients' characteristics and logistic regression model to assess risk factors for TB. We computed incident rates and their 95% confidence interval (CI) to assess the effect of ART on TB incidence.
Results: A total of 7710 children (51.2% male) were identified. At enrolment, median age was 2.5 (IQR 1.1–6.3) years, CD4 was 16.0% (IQR 10.0–24.0) and 37.7% were classified as WHO stage III or IV; 4984 (64.6%) initiated ART. Median follow-up time

from enrolment was 2.5 (IQR 0.6–4.2) years. Overall, 2151 (27.9%) children had an episode of TB; of these 966 (44.9%) had TB diagnosis before or at the time of enrolment into HIV care. The incidence of TB during follow-up was 2.1 per 100 person-years [py; 95%CI 2.0–2.2]. In adjusted analysis, history of positive TB contact ($P < 0.0001$), severe immunosuppression ($P = 0.002$), and advanced clinical disease ($P < 0.0001$), were independently associated with increased risk of TB while age and gender were not. TB incidence decreased with time on ART, from 4.4 per 100 py (95%CI 3.8–5.1) in the first 6 months to 0.3 per 100 py (95%CI 0.2–0.3) after 6 months on ART. Overall, ART was associated with 78.2% reduction in incident TB [relative risk 0.2 (95%CI 0.2–0.3)].
Conclusion: The burden of TB in HIV-infected children in Kenya is high. Advanced immunosuppression and TB contact are associated with increased risk of TB disease while ART use is strongly protective. Efforts should be made to ensure early identification of HIV-infected children and timely initiation of ART. There is also need to emphasize TB screening among these children as well as contact tracing.

OP-138-01   High rates of multidrug-resistant tuberculosis amongst children in Pakistan

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Background: Childhood tuberculosis (TB) despite having a high global burden with an estimated 0.5 million cases and 64 000 deaths, remains a neglected entity. Pakistan's National Tuberculosis Control Program (NTP) data in 2001–2004 reveals that 4% of all TB registered cases are seen in children. No prior data on drug-resistant TB in children from Pakistan is available. Being a high multidrug resistant TB (MDR-TB) burden country there is a need to evaluate extent of drug resistance TB in children. Therefore this study aimed to determine resistance to first line anti-tuberculosis drugs amongst *Mycobacterium tuberculosis* isolates from <15 year-old children from Pakistan.
Design/methods: Data of *M. tuberculosis* strains isolated amongst < 15 year-old children in Aga Khan University Hospital (AKUH) laboratory, Karachi, Pakistan (2008–2012) was retrospectively analyzed. Patients were divided in three groups (aged 0–4, 5–10 and 11–15 years). Antimicrobial susceptibility profile of isolates was evaluated for resistance to isoniazid, rifampicin, pyrazinamide, ethambutol and streptomycin. MDR-TB was defined as *M. tuberculosis* resistant to at least both rifampicin and isoniazid.
Results: During the study period 468/14634 (3.2%) *M. tuberculosis* strains were isolated from patients less than 15 years old. Of these, 28 strains were from ages 0–4 y, 46 from 5–10 y and 394 from 10–14 y. Overall resistance to at least one of the first line drugs

was seen in 257 (55%) and MDR was seen in 181 (39%) strains. Proportion of MDR-TB was lower in ages 0–4 y (4/28, 14%) compared to 5–10 y (16/46, 35%) and 11–15 y (161/394, 41%).

Conclusion: High rate of MDR-TB in children in this setting reflects a high rate of transmission of drug-resistant TB in our population. These results highlight an urgent need to develop methods for rapid detection of drug-resistant TB in pediatric population to optimize management.

OP-139-01   The burden of childhood tuberculosis in Botswana, 2008–2012

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Background: Botswana has the 10th highest annual incidence rate of TB globally, 503 cases per 100 000 population. TB among children significantly impacts child health and survival but the magnitude of the problem is unknown as data on childhood TB incidence are scarce. We aimed to describe the epidemiology of childhood TB in Botswana.

Design/methods: We conducted a retrospective descriptive study of children <15 years old who were diagnosed and treated for TB during January 2008 through August 2012 in 9 of 27 health districts in Botswana. Districts selected were those with the highest reported TB burden. TB registers at each clinic and district were reviewed for all children and adult cases. Data recorded for each pediatric case included: age, sex, type of TB, new or retreatment case, HIV status, and treatment outcome. We defined good outcome as treatment completion or cure and bad outcome as death, treatment default, or failure.

Results: Of the 12 061 cases of TB identified, 1141 (9.5%) were children, which varied from 6.4% to 15.7% across districts. Of the 1141, 1056 (93%) of these were new cases, and 830 (73%) were pulmonary cases. Among 1041 childhood cases with complete data, 47% were female and the median age was 4 (interquartile range 2–9 years); 369 (35%) were ⩽ 2 years old at time of diagnosis. HIV test results were documented for 701 (61%) children, 230 (33%) of whom tested positive; HIV prevalence varied from 3.7% to 40% across the nine districts. Of the 1108 expected to have a treatment outcome, 769 (69%) were cured or completed treatment, 147 (13%) were transferred out, 50 (5%) defaulted from treatment, 5 (1%) had treatment failure, 25 (2%) died, and 112 (10%) did not have an outcome recorded.

Among the 555 with documented HIV status and TB treatment outcome, children without HIV were more likely to have a good outcome than those with HIV (odds ratio: 3.1; confidence interval: 1.7–5.8).

Conclusion: Childhood TB represents a substantial burden of TB in Botswana. HIV co-infection is high among children with TB tested for HIV, but HIV status was unrecorded for a large proportion of children. HIV was associated with poor outcomes, and because treatment of HIV may improve outcomes for children with HIV and TB, efforts should be undertaken to expand HIV testing in this population. Improved reporting and recording will provide data needed to target interventions to improve outcomes and allow for better allocation of resources.

INNOVATIONS IN STUDYING THE TRANSMISSION OF TUBERCULOSIS

OP-140-01   Genomics meets public health: insights from a tuberculosis outbreak in Switzerland over 21 years

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Background: One of the first molecular epidemiological tuberculosis (TB) studies in Switzerland identified a TB outbreak of 22 Swiss-born patients in the Canton of Bern between 1991 and 1992. The aim of the present study was to revisit this historical outbreak and analyse its propagation until today using genomic methods.

Methods: All culture-confirmed TB cases in the Canton of Bern diagnosed between 1991 and 2011 with an available *Mycobacterium tuberculosis* isolate were included (1642 from 1940 cases, 84.6%). Isolates were screened by an outbreak-specific single nucleotide polymorphism (SNP) assay based on whole genome sequences of three known outbreak and five control strains. We generated whole genome sequences for all putative outbreak strains, and performed 24-loci MIRU-VNTR. In addition, we collected sociodemographic and clinical data.

Results: We identified a total of 80 *M. tuberculosis* isolates from 72 TB patients which belonged to the TB outbreak based on the molecular screening. Median age was 42 years (interquartile range 34–54), 56 (78%) were male, 58 (81%) were born in Switzerland, and 14 (19%) were HIV-infected. Overall, 51 (71%) of all cases were diagnosed within the first
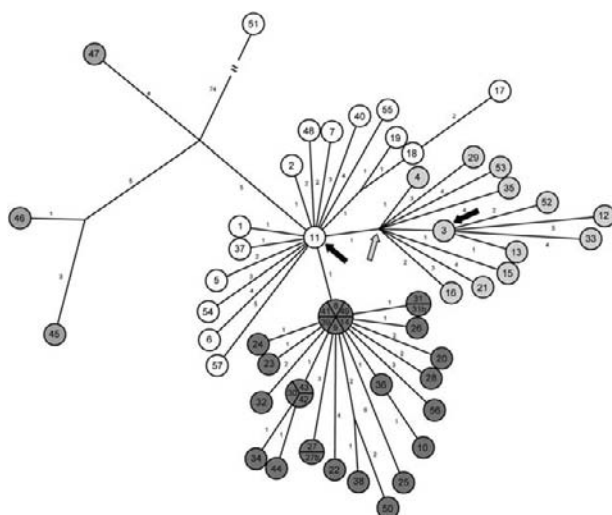
Figure Maximum parsimony tree of the first 59 *Mycobacterium tuberculosis* outbreak genome sequences, Canton of Bern, Switzerland, 1991–2011. Subclusters are in different shades of gray. Black arrows indicate potential superspreaders, and the gray arrow a potentially unidentified tuberculosis case in the transmission chain. Numbers in circles correspond to strain numbers, and branch lengths represent the number of single nucleotide polymorphisms (SNPs) which separate the isolates. Analyses are based on preliminary SNP calling. Sites with more than two variants, as well as gaps in at least one isolate were excluded from SNP analyses. Isolate 51 showed 74 SNPs difference to the rest of the outbreak strains, and was therefore excluded from genomic analyses.

five years of the outbreak. This particular *M. tuberculosis* genotype mainly spread within a defined social group of homeless people, alcohol and injecting drug abusers, but rarely to the general population. All outbreak isolates belonged to the Euro-American lineage (spoligotyping family S). Preliminary analyses of the first 59 genome sequences revealed four main subclusters within the outbreak, which included 4, 12, 15 and 28 TB cases (Figure). Despite identical MIRU-VNTR patterns, these isolates differed by up to 20 SNPs. In addition, we identified two potential superspreaders (black arrows). Finally, we found a vacant central node in the genetic tree which may indicate a potentially unidentified TB case, or alternatively represents an isolate not yet sequenced (gray arrow).

Conclusion: We present a TB outbreak in a low incidence country over 21 years in a defined social group at high risk. In contrast to traditional molecular genotyping, whole genome sequences provided insight into a high-resolution transmission network with different subclusters and superspreaders. Real-time whole genome sequencing has the potential to guide and improve public health interventions in the future.

OP-141-01 'Eggcrate UV': a novel, more efficient, whole ceiling upper room ultraviolet germicidal irradiation system for air disinfection in occupied rooms

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Aim: Upper-room ultraviolet germicidal irradiation (UVGI) can significantly reduce TB transmission in congregate settings such as hospitals, clinics, and prisons. However, louvers on conventional wall fixtures (Fig. A), required for safety in the lower room, greatly reduce UV output. To more efficiently produce the required UV dose in the upper room while preventing UV over exposure in the lower room we created a novel, whole ceiling, UVGI system using bare UV lamps above a commercially available 'eggcrate' suspended ceiling (Fig. B).

Methods: Suspended 2 ft $\times$ 2 ft ceiling panels were replaced with commercially available black plastic eggcrate panels in a room-size test chamber. The prototype system used bare UV lamps from conventional UVGI fixtures, mounted on a square aluminum plate, set atop the eggcrate ceiling. The plate (Fig. B) prevent direct irradiation of the lower room. A common ceiling fan in the middle of the room ensured air mixing. Air disinfection experiments with aerosolized *Mycobacterium parafortuitum* were (a surrogate for MTB) were performed for both the new eggcrate UV system and conventional UVGI wall-mounted fixtures. Eye level UV irradiance was measured to assess occupant safety.
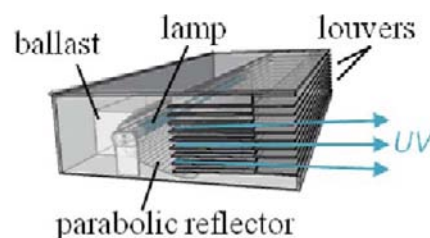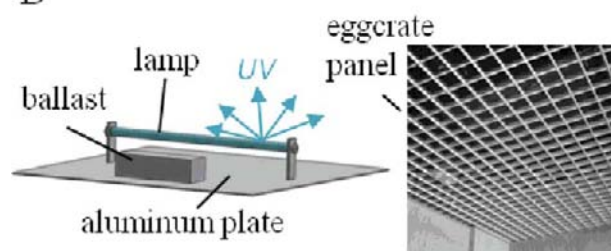
Figure **A**) Conventional wall-mounted UVGI fixture and **B**) UV panel and eggcrate tiles used in the whole ceiling UVGI system.

Results: The eggcrate configuration with 1 UV lamp resulted in inactivation of 84% of airborne *M. parafortuitum*, while 1 conventional louvered UVGI wall fixture achieved 55% inactivation. The eggcrate system with 2 bare lamps inactivated 91% compared to 63% with 2 conventional wall fixtures. Conventional UVGI fixtures produced 8 and 10 equivalent air changes per hour (EqACHUV) for *M. parafortuitum*, whereas the eggcrate UV configuration produced 33 and 62 EqACHUV for 1 and 2 lamps, respectively. Maximum eye level irradiance in the lower room was equal to or less than 0.4 μW/cm², a safe limit for realistic exposure times. Experiments using eggcrate panels with 45 degree angled vanes further reduced the maximum eye-level irradiance to 0.1 μW/cm². Reduced air mixing and pathogen removal with the angled panels were restored by additional UV lamps and fan adjustments.

Conclusion: Whole ceiling eggcrate UV is the first new approach to upper room UV germicidal air disinfection in many decades. It has the advantage of greater efficiency, that is, greater efficacy per UVGI lamp, compared to conventional fixtures while still preventing UV over exposure of occupants. Its components are readily available and this approach should be adaptable to high burden settings.

OP-142-01 Towards a practical method for estimating natural ventilation performance for existing buildings

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Background: Ventilation is a key component of air quality and risk mitigation for airborne infection transmission. Natural ventilation has the potential to deliver the air changes recommended, but performance is dependent on a variety of factors such as room volumes, apertures and ambient conditions. Methods for measuring ventilation may be cumbersome, and require specialised skills and equipment. Isolated measurements may not be meaningful in determining peaks, troughs and averages of effective ventilation rate over time and under different building use conditions. Recently international guidance for healthcare building has moved from expressing ventilation requirements from air-changes per hour (ACH) to volumetric flow rates per capita (l/s/person). Applying limits to occupancy levels through administrative control potentially empowers facility managers to systematically address overcrowding for airborne infection control. To do this a practical, robust, rapid method for estimating natural ventilation performance and deriving 'safe' occupancy levels for existing indoor spaces is needed

Design/methods: A set of 39 naturally-ventilated clinic buildings were identified in one priority district

within SA. The floor plans were analysed with respect to room volumes, plan configuration, room use and risk allocation, aperture size, position and obstructions. A modest baseline wind speed of 1 m/s was assumed. A generic reference room of constant dimensions and variable aperture size and relative positions was modelled and studied using computational fluid dynamics. These findings were used to quantify the effect the ratio of aperture to room floor area has on ventilation rates. An algorithm was devised empirically to relate these variables to an estimated volumetric flow-rate (ACH). These algorithms were written into bespoke software which was used to analyse and compare the identified clinics. Occupancy maxima per room were derived from the data.

Results: A total of 1163 spaces were analysed. The derived occupancy maxima per room varied between 266 persons (164 ACH) and 0 persons (for internalised spaces). An average maximum occupancy of 6.6 persons was calculated.

Conclusion: Further research is required to validate the constants and re-evaluate empirical algorithms and expand variables (wind vectors). This will be undertaken in a series of dynamic, modular wind-tunnel experiments using scaled tracer gas decay analysis and additional computational fluid dynamic studies.

OP-143-01 The importance of integrated system design for the effectiveness of portable air cleaners in airborne infection control

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Background: The results of the recent study into the effectiveness of portable air cleaners (PACs), as an infection control measure against TB, delivered unexpectedly low results. That finding initiated a further study to understand the contribution of system design to the effectiveness of PACs in airborne infection control.

Objective: To quantitatively evaluate the contributions of combined ventilation and PAC systems and identify factors with the potential to reduce the functional effectiveness of such systems.

Design/methods: In this study, the performance of both the mechanical ventilation system and PAC unit was validated (7 and 12 air changes per hour (ACH) respectively). The validation of the ventilation system included volumetric airflow measurements and quantitative air change efficiency assessments. The compliance with design criteria of the PAC was assessed by volumetric airflow measurements, filtration efficiency

tests and the derivation of effective clean air delivery rates (CADR). A computational fluid dynamics (CFD) simulation of the wards was developed to model the system contamination removal effectiveness (CRE) at designed and measured capacities with the PAC running and idle. Streamlines were simulated to visualise airflow interactions between the PAC and HVAC systems.

Results: Even with high total filter leakage (15% vs. 0.05% specified), an acceptable effective CADR of 11.9 ACH was measured from the PAC. The ventilation system's air change rate measured higher than specified at 10.8 ACH with near fully-mixed flow. The simulation using the system's design capacities showed a significant contribution by the PAC to the CRE. The simulation using the higher airflow rates, measured during validation, showed little contribution by the PAC. The simulated airstreams indicated that the PAC operation could reduce the performance of the HVAC system by stimulating airflow short-circuiting.

Conclusion: The study indicates that the contribution of PACs in airborne infection control may be limited to spaces with inadequate pre-existing ventilation systems or low ventilation rates. Where spaces are fitted with effective mechanical ventilation, the addition of PACs may offer no real improvement to infection control. The CFD results demonstrated the potential of PACs to disrupt and reduce the contamination control effectiveness of well-designed and functioning ventilation systems if their location within the room is not well considered.

OP-144-01   Quantification of shared air: an innovative technology platform to measure potential tuberculosis transmission

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Aim: It is widely acknowledged that tuberculosis (TB) transmission occurs through small droplet nuclei transfer in the air and it is reasonable to conceptualise the spread of these droplets following the same patterns as seen in gas diffusion.

Methods: We designed a small monitor ($10.3 \times 6.0 \times 2.7$ cm) that can be worn by study participants to measure environmental carbon dioxide (CO_2), relative humidity, temperature and a Global Positioning System (GPS) location at 1-minute intervals for 22 hours between charges. The monitor has a data capacity in excess of 20 days of continuous measurement. The machine was tested by monitoring the daily activity, as kept by a diary, of 30 youths (age 12 to 20 years) living in a peri-urban community in Cape Town, South Africa who were assumed to be at high risk of TB and comparing these data to a perceived low risk group of 15 adults working in an office environment.

Results: An estimate of the instantaneous rebreathed amount from others was calculated using the formula derived from [1]:

$$(C - Co)/Ca \times (n - 1)/n \times P$$

C is the concentration of CO_2 in indoor air (parts per million, ppm); Co is the concentration of CO_2 in outdoor air (ppm), identified as the minimum value in each monitoring period; Ca is the concentration of CO_2 added to exhaled breath during breathing (set to 38 000 ppm); n is the total number of people at the location (we thus calculate the number of 'other' people); P is the breathing rate per person (set to 8 litres per minute).

The sum of the instantaneous measures gives total rebreathed litres from other people for either the location or the time period under investigation.

In this pilot study we showed a range of 11 to 228 litres of air rebreathed from other people in a day ($l.day^{-1}$, Figure). The youth group, who within this community have been shown to have a very high annual risk of TB infection of 4.2% [2], had a significantly higher median value of 82 $l.day^{-1}$ when compared to the adult group (43 $l.day^{-1}$, Kruskal-Wallis $P < 0.001$). The distribution of this rebreathed air by location was also investigated.
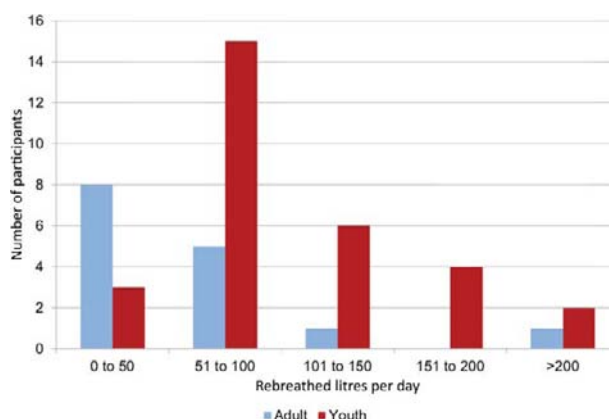
Figure The distribution of daily shared air from other people among adults working in an office environment and youths living in a township community in Cape Town, South Africa ($n = 45$).

Conclusion: This innovative tool can be used in epidemiological investigations of social mixing to identify hotspots of potential disease exposure through an integrated measure of the number of people present in the environment, the ventilation of the site and time of exposure.

References
1 Rudnick & Milton. Indoor Air 2003; 13: 237–245.
2 Middelkoop, et al. BMC Infectious Diseases 2011; 11: 156.

OP-145-01　The possibility of respirator multiuse: issues from 'what for' to 'which' and 'how long'

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Setting: Limited material resources spent on engineering means IC TB and architectural solutions make respiratory protection more significant but at the same time dictate their reusability and lead to procurement of the cheapest models.

Objective: To study the possibility (efficacy) of the respirator multiuse in the conditions of its exposure to infectious aerosol; to determine the effect of the model and way of getting the filtration material on the respirator efficacy in its multiuse; to determine the safety and economic expediency of the respirator.

Methods: Seven models of respirators, of them, four models of two protection classes FFP2 and FFP3, were studied. The respirators were of different construction: formed half mask (2), panel type (3), non-formed type (2). The technologies of the non-woven material of the respirators were taken into consideration: solid (5) and liquid (2) ways of extrusion. Eleven kinds of respirators, total of 72 items, were tested. The cost of the respirators varied from US$0.65–US$11.18. The compactness of the respirator conformity was assessed by fit-test with Bitrex, the penetrability of the filter material was estimated by a particle counter and a particle generator. The contamination of the internal surface of the respirator was biologically studied.

Results: Two models did not pass fit-test before their use, one more model did not pass the test after one work shift of 12 hours, i.e., four tests of six. The rest of the respirators preserved their perfect conformity for 4, 5, 8 and 11 work shifts. Two respirators (before their use) did not correspond to the claimed protection classes according to the filtration efficacy by 5.5 and 14.2%. Only two models preserved their filtration to the extent of the stated class in the maximum period of their use. No mycobacteria were detected on the internal surface of all the items.

Conclusion: The multiuse of respirators (filtering half masks) is possible only after preliminary testing of the respirator models, as a number of factors influence the period of their effective use. To avoid procurement of the respirators not meeting the requirements, it is advisable to test the respirators during the tendering. In the right operation of the respirator the contamination of the internal surface with its own microflora is not hazardous. In the multiuse of the respirators, the purchase of brand models is economically expedient.

OP-146-01　Requirement of isolation room and risk assessment in tuberculosis control in clinical settings

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Aim: To estimate the requirements of isolation rooms for open pulmonary tuberculosis (pTB) by model simulation.

Design/methods: Datasets were collected from two hospitals (Hospital A [2581 beds] and B [1076 beds]) to obtained the utilization of isolation rooms. The configurations of facilities in hospitals were collected from annual national health statistics in Taiwan (TB incidence 67/100 000 in 2006). The mathematical equation was simulated by Monte-Carlo method under different scenarios and was tested by using the results from datasets. Risk assessment was performed to determine which factors related to the failure of isolation for hospitalized patients with pTB.

Results: Of the 542 and 342 newly diagnosed patients with tuberculosis, 362 and 142 of patients were pTB in hospital A and B, respectively. The hospitalization rates for patients with pTB were 59%(216/362) and 93%(132/142), and with mean stay in isolation rooms for 21 and 20 days, respectively. Fifteen percent and 6.3% of culture-positive pTB patients were not isolated during hospitalization in hospital A and B, respectively, and 20% of non-TB patients were over-isolated in both hospitals. The incidences of pTB among employees in 2006–2009 ranged from 0~112/100 000 and 0~248/100 000 in hospital A and B, respectively. Failure of isolation was estimated by calculating the difference between the need of isolation and isolation capacity in different circumstances. The minimal requirement of isolation room was then obtained when the lowest value for failure of isolation was reached, with predicted/actual isolation bed ratios 0.84 (16/19) and 0.52 (13/25) in hospital A and B, respectively. On the basis of fixed number of isolation room, risk assessment by Tornado plots method indicated the isolation days for pTB was the major determinant in decreasing failure of isolation (regression coefficient [r] = −0.9); other factors including incidence case number for tuberculosis in hospitals (r = −0.2), proportion of pTB (%) among TB patients (r = −0.2), percentage of pTB patients who need to be hospitalized (r = −0.18), and isolation days for pTB patients receiving adjustment of anti-TB chemotherapy (r = −0.18) were also related to failure of isolation. It indicated that isolation policy in TB management and diagnosis capabilities were determinant in control of pulmonary TB in clinical settings with limited isolation room.

Conclusion: The model was helped to estimate and evaluate the utilization of isolation room in health agency.

FACTORS IMPACTING DIAGNOSIS, TREATMENT AND SPUTUM DISTRIBUTION OF TUBERCULOSIS

OP-147-01   Investigating the impact of health care visits on incident tuberculosis in Taiwan: population-based study

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Background: TB patients can be infectious for up to several months before being diagnosed and treated. During this period, the TB patients may seek medical attention and transmit the disease to other patients. We hypothesize that the health care setting may be an important site for TB transmission and frequent health care visit may increase the risk of TB.

Material and methods: We conducted a population based case-control study to investigate the association between frequency of health care visit and risk of tuberculosis. The source population consisted of one million individuals in the health insurance database from Taiwan. Incident cases of TB were identified through ICD-9 code and prescription of anti-TB drugs. For each case, four controls were selected and matched by age, gender, date of diagnosis (index date), and presence and severity of medical co-morbidities (diabetes, chronic obstructive pulmonary disease, cancer by site, chronic kidney disease, receiving immunosuppressants, silicosis, gastrectomy, and jejunoileal bypass). Based on previous studies on diagnostic delay of TB in Taiwan, we assumed a 3-month delay between TB onset and diagnosis. We enumerated each health care visit in the previous year before TB onset. Conditional logistic regression was used to estimate the association between frequency of health care visit and risk of TB.

Results: We included 4088 TB cases and 15 321 controls. The median (IQR) frequency of health care visit was 18 (7–34) and 16 (5–31) per year for cases and controls. Compared to those with less than 5 health care visits per year, the risk of TB increased with increasing visit: the odds ratio was 1.28 (1.16–1.43) for 6~15 visits, 1.37 (1.23–1.53) for 15~30 visits, and 1.57 (1.40–1.75) for >30 visits per year. Further analysis revealed that emergency room and internal medicine visit were particularly associated with high risk of TB. Using another independent dataset from a nationally representative sample, we found that smoking, alcohol use, and education attainment could not explain the observed association between health care visit and TB.

Conclusion: Frequent health care visit was associated with increased risk of TB in Taiwan. Although further molecular typing studies are needed to confirm this finding, we suggest education should be given to general population to discourage hospital shopping, and active case finding for TB and enhanced infection control should be considered to prevent TB transmission.

OP-148-01   A novel DNA chip based on modified DigiTag2 assay for high throughput species identification and genotyping of *Mycobacterium tuberculosis* complex

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Background: High throughput genotyping technologies for epidemiological study of *M. tuberculosis* are urgently required. We proposed to differentiate *M. tuberculosis* complex species and classify *M. tuberculosis* genotype by modified condition of DNA chip based on DigiTag2 assay.

Design/methods: For development of multipurpose DNA chip, fifty-one well characterized SNPs spanning *M. tuberculosis* complex genome were selected. The first four SNPs were selected for MTBC speciation. The next forty-seven SNPs were chosen for genotyping *M. tuberculosis*, two SNP positions for determination of principle genetic groups (PGG) and forty-five SNPs for characterization of *M. tuberculosis* into SNP cluster groups (SCGs). The DNA chip was tested with thirteen *M. tuberculosis* complex reference strains and 331 well characterized *M. tuberculosis* clinical isolates from Thailand.

Results: The developed DNA chip revealed 99.85% call rate, 98.94% accuracy, 100% conversion rate, and 99.75% reproducibility. The total running times for the assay was around 6 hours for identifying and genotyping 96 DNA samples.

Conclusion: For molecular epidemiological purpose, DNA chip based on modified DigiTag2 assay is a promising simple, rapid and cost-effective tool for tracking the spreading of tuberculosis.

OP-149-01   Evaluation of diagnostic practices for tuberculosis in South Africa: implications for new technologies

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Background and challenges to implementation: The rollout of the Xpert® MTB/RIF test in South Africa has the potential to provide local and widespread

access to simple, accurate, and rapid laboratory diagnostic testing for tuberculosis (TB) based on a single sputum specimen. Currently the South Africa National TB Guidelines define a person as having TB disease based on evidence of a positive sputum smear; however, current clinical practices utilized for TB diagnosis are not well known.

Intervention or response: We conducted a study nested within an evaluation of South Africa's TB surveillance system to examine programmatic practices for diagnosing TB disease among new patients in Quarter 1 2009. Using data from multiple sources (TB patient file, TB patient register, and Electronic Tuberculosis Registry), if a diagnostic method was indicated on any data source, we considered it affirmative as being utilized in TB screening and diagnosis. We used chi-square tests to compare differences in proportions of diagnostic methods between patient subgroups. We used multivariate modeling to calculate risk ratios to assess differences in sputum collection practices based on programmatic and patient level factors.

Results and lessons learnt: Our analysis included 1071 patients that were newly diagnosed with TB. Among these patients, 745 (70%) had record of a sputum specimen obtained for bacteriologic determination of TB, 268 (25%) were diagnosed without record of a sputum specimen being collected, and 58 (5%) had no diagnostic method recorded. Chest radiography was the sole diagnostic method for 189 (18%) patients. In analysis using multivariate modeling of factors associated with sputum collection, we found that persons with documented HIV infection were significantly less likely to have a sputum sample collected than persons without documented HIV infection (Risk Ratio = 0.87; 95%CI 0.81–0.94; $P < 0.001$).

Conclusions and key recommendations: We documented that sputum was not collected for nearly one third of all patients that were newly identified by health facilities as having active TB disease. Our findings suggest inconsistencies in sputum collection practices by clinical and programmatic factors. Many current diagnostics, such as smear, culture, and Xpert, are dependent on providers obtaining a biological specimen. The incorrect use of TB diagnostic methods can result in an increase of undetected cases thereby increasing morbidity, mortality, and disease transmission. Improving TB diagnosis in a high HIV prevalence setting will need to address ongoing challenges of sputum collection if diagnostic tests are to be successfully implemented. If this practice is not routinely implemented then the utility of rolling out of Xpert and other promising new technologies cannot be realized.

OP-150-01   Rates and determinants of household catastrophic payments for tuberculosis care in rural Nigeria

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Background: A major limitation of cost of illness studies on tuberculosis patients is that these costs are reported as averages and the economic impact estimated using average income. Averages do not represent the poorest because they spend less on treatment compared to other economic groups, and this makes up a higher proportion of their income. Second, the extent to which tuberculosis expenditures risk sending their household into, or further into, poverty and its determinants, is unknown. To assess the rate and determinants of catastrophic payments that households incur on services which are supposedly free-of-charge, using the example of tuberculosis care in rural Nigeria.

Design/methods: We assessed patient/household direct costs and income from a survey of 452 pulmonary tuberculosis patients sampled from three rural health facilities in Ebonyi State, Nigeria. We analysed the incidence of household catastrophic payments using as thresholds the traditional >10% of household income and ≥40% of non-food income, as recommended by World Health Organisation. We used logistic regression analysis to identify the determinants of catastrophic payments.

Results: Average direct household costs for tuberculosis were US$157 or 14% of average annual income. The incidence catastrophic payment was 44%; with 69% and 15% of the poorest and richest household income-quartile experiencing catastrophe respectively. Independent determinants of catastrophic payments were: age >40 years (aOR 3.9 [2.0–7.8]), male gender (aOR 3.0, [1.8–5.2]), urban residence (aOR 3.8 [1.9–7.7]), formal education (aOR 4.7 [2.5–8.9]), care at a private facility (aOR 2.9 [1.5–5.9]), poor household (aOR 6.7 [3.7–12]), household where patient is primary earner (aOR 3.8 [2.2–6.6]), and HIV co-infection (aOR 3.1 [1.7–5.6]).

Conclusion: Current cost-lowering strategies are not enough to prevent households from incurring catastrophic out-of-pocket payments for tuberculosis care. Financial and social protection interventions are needed for identified at-risk groups, and community-level interventions may reduce inefficiencies in the care-seeking pathway. These observations should inform the post-2015 tuberculosis strategies and influence policymaking on health services that are meant to be free-of-charge.

OP-151-01   Superior yield of morning specimens during an active case-finding intervention in Karachi, Pakistan

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Background: In 2011, just 66% of tuberculosis (TB) cases were detected and notified worldwide, below Millennium Development Goal targets. Improvements in case detection must come from more active approaches to case-finding, the implementation of new diagnostic tests and by optimizing the sputum submission and testing process.

Methods: All individuals visiting six private laboratories located across Karachi, Pakistan were verbally screened for symptoms of TB and resultant TB suspects were asked to produce a spot sputum specimen for testing. Those who could not, were asked to return with an early morning specimen. All TB suspects who provided a specimen received a smear-microcopy test, chest X-ray, and when indicated, a GeneXpert MTB/RIF test. Active case-finding (ACF) activities lasted for 9 months and were followed by 3 months of passive case-finding. Data were abstracted from electronic medical records and a multivariate model was constructed to assess which factors contributed to the yield of bacteriologically-positive (B+) TB cases.

Results: 4900 TB suspects submitted a specimen during ACF activities. Early morning specimens yielded significantly more B+ TB cases compared with spot specimens [morning = 135 (17.1%) vs. spot = 518 (12.5%), aOR 1.27 (1.01, 1.59)]. Other factors, including young age and presence of TB-related symptoms, were also significantly associated with increased yield of B+ TB. During the passive case-finding phase, 864 TB suspects submitted a specimen for testing.

	9 Months active case-finding	3 Months passive case-finding
Sputum collection time		
Early morning	1.27 (1.01, 1.59)	1.04 (0.55, 1.94)
Spot	Ref	Ref
Gender		
Female	1.18 (1.00, 1.41)	1.37 (0.94, 1.99)
Male	Ref	Ref
Age		
15–24	3.12 (2.35, 4.16)	2.38 (1.34, 4.23)
25–59	1.28 (0.97, 1.69)	1.02 (0.59, 1.76)
⩾60	Ref	Ref
Weight loss (WL), fever (FV) and/or night sweats (NS)		
WL, FV, NS	5.12 (2.72, 9.63)	12.27 (1.63, 92.61)
WL, FV, no NS	3.62 (1.93, 6.79)	11.63 (1.55, 87.49)
no WL, FV, no NS	2.53 (1.35, 4.73)	8.39 (1.12, 62.70)
no WL, no FV, NS	2.48 (1.05, 5.85)	5.37 (0.56, 51.35)
WL, no FV, no NS	1.68 (0.79, 3.55)	2.42 (0.21, 28.08)
WL, no FV, NS	1.18 (0.31, 4.42)	4.34 (0.25, 76.50)
no WL, FV, NS	0.93 (0.95, 1.34)	1.55 (0.09, 26.15)
no WL, no FV, no NS	Ref	Ref

Young age and presence of TB-related symptoms were again significantly associated with increased B+ TB yields. However, there was no difference in yield between morning and spot specimens [morning = 15 (17.8%) vs. spot = 133 (17.1%), aOR 1.04 (0.55, 1.94)].

Discussion: During an ACF intervention, the testing of morning sputum specimens can result in significant increases in the number of B+ cases which are detected. TB cases with a short history of symptomatic disease likely produce paucibacillary sputum specimens and would benefit from the testing of sputum which has accumulated *Mycobacterium* bacilli overnight. More research is needed to understand the incremental yield of morning specimens over paired spot specimens during ACF interventions using enhanced diagnostic algorithms that include chest X-ray and GeneXpert testing.

OP-152-01   Spatial clustering characteristics of tuberculosis in China, 2005–2011

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Background: China is one of the 22 tuberculosis (TB) high-burden countries in the world. As TB is a major public health problem in China, spatial analysis could be applied to detect geographic distribution of TB clusters for targeted intervention on TB epidemics.

Methods: Spatial analysis was applied for detecting TB clusters on county-based TB notification data in the national notifiable infectious disease case reporting surveillance system from 2005 to 2011. Two indicators of TB epidemic were used including new sputum smear-positive (SS+) notification rate and total TB notification rate. As one of indicators of Global spatial autocorrelation by ArcGIS, Global Moran's I was used to assess whether TB clustering and its trend were significant. SaTScan software which used the Kulldorf method of retrospective space-time analysis and Possion probability model was utilized to identify geographic areas and time period of potential clusters with notification rates on county-level from 2005 to 2011.

Results: Two indicators of TB notification had presented significant spatial autocorrelation globally each year ($P < 0.01$). Global Moran's I of total TB notification rate had positive trend as time went by (t = 6.87, $P < 0.01$). The most likely clusters of two indicators had similar spatial distribution in the south-central regions of China from 2006 to 2008, and the secondary clusters in two regions: northeastern China including Heilongjiang province and the

parts of Inner Mongolia and Jilin provinces, and western China including Tibet and Xinjiang Autonomous Region. Besides, the secondary clusters of total TB notification rate had two more large clustering centers in Inner Mongolia, Gansu and Qinghai provinces and several smaller clusters in Shanxi, Henan, Hebei and Jiangsu provinces.

Conclusion: The total TB notification cases clustered significantly in some special areas each year and the clusters trended to aggregate with time. The most-likely and secondary clusters which overlapped among two TB indicators had higher TB burden and higher risks of TB transmission. These were the focused geographic areas where TB control efforts should be prioritized.

OP-153-01   Are patients who recovered from tuberculosis still at risk of premature death? Results of a 10-year follow-up of all Israeli patients

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Background: Long-term mortality and causes of death among patients who recovered from tuberculosis (TB) are poorly documented. The aim of this study was to estimate excess in mortality among patients that completed treatment and to identify their causes of death.

Design/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 the Cox analysis was performed.

Results: Of all 3394 TB patients who were followed for 21 503 person-years, 412 (12.1%) died in an average of 2.1 (standard deviation = 2.5) years after treatment completion, with 41% dying within the first year. Overall, patients recovered from TB 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 had higher risk 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 than 65 years of age had additional risk of dying (HR = 1.4, 95%CI 1.3–1.4). The leading cause 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: Israeli 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. Physicians who treat individuals who recovered from TB should increase their index of suspicion their higher risk to develop malignancies and other morbidities.

OP-154-01   Recurrent tuberculosis after successful treatment in an urban area in China

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Background: Information on recurrent tuberculosis (TB) can identify potentially modifiable gaps in TB treatment and control activities. Recurrent TB in China has not been well studied. The objective of this study was to determine the incidence of, risk factors for, and the frequency of endogenous re-activation or exogenous re-infection in, recurrent TB after successful treatment in Shanghai, China.

Design/methods: A retrospective study of all pulmonary TB patients reported in Shanghai during 2000–2008 was conducted. Recurrent TB was defined as a new diagnosis of pulmonary TB in any patient who had correctly completed treatment for their first episode. Kaplan-Meier and Cox-regression were used to determine the survival and the hazard ratio (HR). Variable number of tandem repeats (VNTR) genotypings from initial and subsequent episodes of TB were compared to determine whether recurrence was due to endogenous re-activation or exogenous re-infection.

Results: Of 31 323 pulmonary TB patients who were successfully treated, 1266 (4.0%) developed a recurrent TB. The incidence of recurrent TB was 0.756 per person-years of follow-up, which was 18.9 times higher in the cohort than the incidence of a first TB episode in the general population (40 cases per 100 000 population). Patients who were male (aHR = 1.5, $P < 0.001$), age ⩾30 years (aHR = 1.3, P = 0.003), had cavitory (aHR = 1.4, $P < 0.001$), had diabetes (aHR = 1.4, P = 0.001), were smear positive (aHR = 1.4, $P < 0.001$), had any drug resistance (aHR = 1.6, $P < 0.001$) and had multi-drug resistance (aHR = 3.0, $P < 0.001$) were more likely to have recurrence. Paired VNTR genotypings were available in 94 recurrences: 52 (55.3%) pairs were

identical (endogenous re-activation) and 42 (44.7%) were different (exogenous re-infection).

Conclusion: The rate of recurrent TB after successful treatment was higher than the rate of new TB in general population, suggesting that patients with a history of TB must be considered as a group at risk of having TB despite having successfully completed treatment. Subpopulations at increased risk of recurrent TB may benefit from additional medical or public health interventions. Exogenous reinfection is an important cause of TB recurrence in Shanghai, China.

TUBERCULOSIS RESEARCH FROM THE BENCH TO PROGRAMME OUTCOMES

OP-155-01 Linkage of presumptive multidrug-resistant tuberculosis patients to diagnostic and treatment services in Cambodia

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Setting: National Tuberculosis Programme, Cambodia.
Objective: In a cohort of TB patients, to ascertain the proportion of patients who fulfil the criteria for presumptive MDR-TB, assess whether they underwent investigation for MDR-TB, and the results of the culture and drug susceptibility testing (DST).
Methods: A cross-sectional record review of TB patients registered for treatment between July–December 2011.
Results: Of 19 236 TB patients registered, 409 (2%) fulfilled the criteria of presumptive MDR-TB; of these, 187 (46%) were examined for culture. This proportion was higher among relapse, failure, return after default (RAD) and non-converters at 3 months of new smear positive TB patients (>60%) as compared to non-converters at 2 months of new TB cases (<20%). Nearly two thirds ($n = 113$) of the samples were culture positive; of these, three-fourth ($n = 85$) grew *Mycobacterium tuberculosis* complex (MTBc) and one-fourth ($n = 28$) grew non-tuberculous *Mycobacteria*. DST results were available for 96% of the MTBc isolates. Overall, 21 patients were diagnosed as MDR-TB (all diagnosed among retreatment TB cases and none from non-converters) and all of them were initiated on MDR-TB treatment.
Conclusion: There is a need to strengthen mechanisms for linking patients with presumptive MDR-TB to culture centers. The policy of testing non-converters for culture and DST needs to be reviewed.

OP-156-01 Low treatment initiation among newly diagnosed multidrug-resistant tuberculosis patients in Gauteng, South Africa, 2011

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Background: South Africa has the largest burden of multi-drug resistant tuberculosis (MDR-TB) in Africa. The aim of this study is to determine treatment uptake among newly diagnosed multi-drug resistant tuberculosis (MDR-TB) patients and risk markers for non-initiation of treatment.
Design/methods: A cross-sectional study was conducted including all newly diagnosed MDR-TB patients in Gauteng province of South Africa in 2011. Socio-demographic and clinical characteristics of those that attended Sizwe hospital, the designated MDR-TB hospital, were extracted from their medical records. District health offices provided data on patients not seen at Sizwe hospital. Univariate and multivariate analysis were used to determine risk markers for non-initiation of treatment.
Results: Of the 942 newly diagnosed MDR-TB patients in Gauteng, only 593 (63%) initiated treatment. Of these, 70 (11.8%) did not maintain treatment up to the fourth month. Among the 349 (37%) who did not initiate treatment, 31.2% died and 46.4% could not be accounted for. Referral for laboratory diagnosis from hospitals, health district of laboratory diagnosis, HIV infection and place of residence were independently associated with non-initiation of MDR-TB treatment.
Conclusion: Untreated patients continue the transmission of MDR-TB in communities. The study findings highlight the need to identify and target the causes of non-initiation of treatment in specific settings. In Gauteng, we recommend the intensification of follow-up of MDR-TB cases, particularly those identified in hospitals.

OP-157-01   Are household contacts with high IFN-γ levels in response to *M. tuberculosis*-specific antigens in the QuantiFERON-TB Gold in-Tube assay at high risk of developing tuberculosis?

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Background: Although the use of Quantiferon-TB Gold In-Tube (QFT-GIT) is rapidly expanding, some questions remain unanswered. It has been postulated that individuals with strong and/or rising interferon-gamma (IFN-γ) responses to *M. tuberculosis* specific antigens may be at greater risk for progressing to disease.

Objective: To determine whether individuals with high levels of IFN-γ in response to *M. tuberculosis* specific antigens in the QFT-GIT assay compared with lower levels are at higher risk of developing TB.

Methods: A cohort of TB free adult household contacts (HHCs) of newly diagnosed TB patients notified at government clinics in Zambia and South Africa. HHCs were visited twice over a 4 year period. QFT-GIT, TST and HIV testing were performed at baseline. A standardized questionnaire was used to collect information on risk factors for TB. High and low levels of IFN-γ were defined as ≥ 10 and between 0.35 and 10 U/ml, respectively. Cox regression models were used to assess the relationship between high IFN-γ responses levels and incidence of TB.

Results: A total of 1789 HHCs were enrolled, 1113 (62.2%) attended at least one follow-up visit, and of these 707 had a positive IFN-γ at baseline (>0.35) and were included in the analysis. Overall 73% (516) were male and median age was 31 years (IQR 21, 46). Among 694 HHCs with HIV status recorded 159 (22.9%) were HIV positive. 171 (24.2%) HHCs had IFN-γ levels ≥ 10 IU/ml.

38 TB episodes occurred in follow-up, giving an overall rate of 24.4 per 1000 person-years (pyrs). TB incidence was 24.5 (9 cases/367.2 pyrs) and 24.4 (29 cases/1191 pyrs) among those with high and low levels of IFN-γ respectively, giving an unadjusted hazard ratio (HR) of 1.0 (95% confidence interval (CI) 0.5–2.2).

TB incidence in those with high levels was 19.6 (6 cases/306.7 pyrs) among HIV negatives and 51.9 (3 cases/57.8 pyrs) among HIV positives (Table).

Among HIV negatives, the HR for high IFN-γ levels was 1.70 (95%CI 0.6–4.7) while in HIV positives it was 0.8 (95%CI 0.2–2.8), though evidence for interaction was weak ($P = 0.4$). In multivariable analysis adjusting for age and sex, results were similar; among the HIV negatives, HRs for high IFN-γ levels was 1.70 (95%CI 0.6–4.8) while in HIV positives it was 0.9 (95%CI 0.3–3.0).

Conclusion: There was no evidence to suggest that household contactst with high levels of IFN-γ in response to *M. tuberculosis* specific antigens in the QFT-GIT assay were at a higher risk of developing TB than those with low levels.

Table   TB incidence rates and incidence rate ratios, stratified by HIV status; all TB cases ($n = 38$)

Variable	n (col %)	TB cases/ pyrs	Incidence rate/ 1000 pyrs (95% CI)	Incidence rate ratio (95%CI)	P value
HIV negatives ($n = 535$)					
Low IFN-γ levels	394	10/871.7	11.47 (6.17–21.32)	1	
High IFN-γ levels	141	6/306.7	19.56 (8.79–43.54)	1.70 (0.51–5.18)	0.16
HIV positives ($n = 159$)					
Low IFN-γ levels	130	19/291.0	65.29 (41.65–102.36)	1	
High IFN-γ levels	29	3/57.8	51.94 (16.75–161.04)	0.79 (0.15–2.70)	0.38

Missing HIV status: 13.

OP-158-01   Preclinical trials of anti-tuberculosis drugs based on nanotechnology

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Background: The relevance of research is determined by the necessity to develop and to introduce into TB treatment practice the new anti-tuberculosis drugs with enhanced bioavailability, the ability to directly penetrate into the lesion focus, to provide a prolonged effect, thereby reducing the number of intakes and reduce the risk of adverse effects and thus increase the effectiveness of TB treatment, adherence to treatment and improve the quality of life of patients with TB.

Design/methods: Preclinical comparative trials of anti-tuberculosis activity and acute toxicity of nanorifampicin, nanolevofloxacin and nanocycloserine with substances of these drugs in their original form were carried out. Anti-tuberculosis activity was estimated in vivo on male mice of C57BL/6 inbred line. The mice were infected by intravenous injection of lethal dose (5×10^6 CFU/ml) of *M. tuberculosis* strain H37RV. Anti-tuberculosis activity was estimated according to *M. tuberculosis* inoculation (the number of colony forming units (CFU) from the lung and spleen on the 7th and 21st day of treatment. The study of acute toxicity of drugs was carried out on mice of Balb/c line and assessed by LD50 of substance and nano-forms of drugs under consideration (mg/kg).

Results: It is ascertained that the anti-tuberculosis activity of rifampicin, levofloxacin and cycloserine nanoforms exceeds the specific activity of substances of these drugs in the usual form 2–2.5 times on average. The acute toxicity of levofloxacin nanoform was higher than of its substance, while the acute toxicity of rifampicin and cycloserine nanoforms decreased compared with the substances of these drugs in the usual form.

Conclusion: The performed preclinical trials of nanoforms of anti-tuberculosis drugs showed that their anti-tuberculosis activity exceeded the anti-tuberculosis activity of the drugs in the usual form, they did not cause adverse effects and that testified for great potential of further medical trials of the developed nanoforms of anti-tuberculosis drugs.

OP-159-01   A qualitative study to understand reasons for loss to follow-up during treatment for drug-resistant tuberculosis under programme conditions, Andhra Pradesh

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Background: In Andhra Pradesh, India, rates of loss to follow-up (LTFU) during treatment for drug-resistant tuberculosis (DRTB) were 11% in 2011. We sought to understand reasons for these high rates of LTFU from DRTB treatment using qualitative methods.

Design/methods: We attempted to locate and interview all patients who were lost to follow up during DRTB treatment registered at four DRTB centres in Andhra Pradesh, from January, 2010 through June, 2012. Our sample included patients LTFU for DRTB who were still living in their respective districts as of April, 2012. We interviewed patients with open-ended questions to understand their reasons for being LTFU. We also conducted focus group discussions (FGD) with medical officers, treatment supervisors and DOT providers to understand provider's perspectives regarding reasons for LTFU. FGD and patient interviews were continued until no new themes emerged. All FGD were voice recorded and transcribed into text and then analysed for emerging themes.

Results: Out of 141 patients with DRTB reported as having been LTFU, 22% (*n* = 31) died and 19% (*n* = 27) had moved out of district. Among the remaining 83 patients, we successfully found and interviewed 57% (*n* = 47). Sex and age did not differ between those interviewed and those not interviewed. Themes which emerged as reasons for LTFU by patients were adverse side effects from anti-TB medications and the inability to address these side effects by the providers. Other themes included pill burden, lack of family support, lack of food, attitude of medical staff, no clinical improvement, lack of faith in ability of treatment to help them, and misconception of cure when TB symptoms subsided. Themes emerged from the six FGDs involving 10 medical officers, 30 treatment supervisors and 10 DOT providers were similar with exceptions like: misguidance from private practitioners, availability of investigations and speciality consultation under one roof were important themes that emerged in the FGDs.

Conclusion: Both patients and providers reported that side effects were the most important reason for LTFU. Patients expressed frustration with the inability to address these side effects, which ultimately led to LTFU. Programmes need to address both clinical challenges and social support challenges to reduce LTFU. More attention needs to be given to involving private providers in standards of TB care.

OP-160-01   Experience of a quality management system in a tuberculosis laboratory in Kisumu, Kenya

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Background: Laboratories are a fundamental component of tuberculosis (TB) control, providing diagnostic testing, surveillance, and treatment monitoring. New initiatives and resources to strengthen laboratory capacity and implement new rapid diagnostic tests for TB require keen detail to quality standards.

Design/methods: To prepare the laboratory for new diagnostics and expanded capacity, the KEMRI/CDC TB laboratory in Kisumu focused on strengthening quality management systems (QMS) through external quality assessment (EQA) programs for microscopy, culture, drug susceptibility testing and molecular diagnostics in addition to monitoring key quality indicators since January 2011. The laboratory participated in the Stepwise Laboratory Improvement Process Towards Accreditation (SLIPTA) in preparation for accreditation, a CDC funded program through A Global Healthcare Public Foundation (AGPHF). Annual surveys were carried out by administering questionnaires to clients.

Results: A preparatory baseline assessment conducted on 16–17 February 2012 gave the laboratory a 3-star rating. The laboratory thereafter developed key strategies to improve quality and address identified nonconformances. Performance changes included monitoring turnaround time for all tests, verification of

results integrity, reducing culture contamination rates, improved efficiency of workflow, improved staff motivation, and attainment of 98% client satisfaction from the 2012 annual survey. During a subsequent assessment between 29th–30th August 2012, the laboratory attained a 5 star rating. The laboratory applied for ISO 15189 accreditation in January 2013 and is currently waiting for an assessment with the accreditation body.

Conclusion: Implementation of quality management system ensures adherence to standards and improves quality of laboratory processes and reaffirms credibility of laboratory systems.

OP-161-01   Improving tuberculosis control by removing health system barriers in Georgia

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Background and challenges to implementation: Despite significant health system reforms aimed at facilitating universal access to TB diagnosis and treatment services, Georgia lags behind many countries in the European region on key TB indicators. In 2011, the Government of Georgia began a major health sector reform, privatization of the health service delivery, which included the integration of previously vertical TB program into the general health care system. While an integrated TB care model has the potential to improve access to and quality of TB services, concerns remain about the handling of TB by the privately managed health care system. Sound evidence is needed to support the integration process and overcome barriers which may have negative impact on effectiveness and efficiency of TB service delivery. USAID Georgia TB Prevention Project undertook study to explore barriers to effective TB care and to identify approaches for structural and functional improvements to services.

Intervention: The assessment methodology comprised a mix of site visits and observations, face-to-face semi structured interviews with national and regional stakeholders, as well as desk-based research.

Results and lessons learnt: The assessment revealed that governance and management of TB service provision is fragmented; most TB suspect patients refer to TB specialists directly and therefore, rural primary health care sector remains largely underutilized; the functions of village family practitioners and nurses are poorly defined; provider payment system creates perverse incentives for effective TB service provision; district hospitals do not meet international infection control standards; state program does not provide adequate funding to motivate private hospitals for effective TB service delivery; no single entity is responsible for monitoring and quality assurance.

Conclusion and key recommendations: Complex health system barriers existing in the country undermined integration efforts and lead to fragmentation of TB services thus posing a significant risk to developing well functional integrated TB service delivery model.

OP-162-01   Tuberculosis treatment outcomes in Singapore, 2002–2011

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Background: A national treatment surveillance module (TSM) was launched in 2001 as one of the key initiatives of the Singapore TB Elimination Programme. Its main functions are to monitor national treatment outcomes (an indicator of programmatic performance), and to perform real-time tracking of the treatment progress of patients so that timely measures may be taken should patients default treatment. We report the treatment outcomes of TB cases among Singapore residents and permanent residents (PRs) for the decade 2002–2011.

Methods: Every TB patient treated in Singapore was required to have a submission by the treating physician regarding his or her treatment progress at each clinic visit. Information pertaining to treatment adherence, TB drugs prescribed, treatment delivery mode and final outcome was captured. Treatment outcomes were specified as 'completed treatment' (with or without 'cure'), 'lost to follow-up', 'death' (with cause of death specified), 'left country', 'diagnosis revised' and 'still on treatment/no final outcome' and were determined for quarterly cohorts at the end of the corresponding quarter of the following year. The outcomes of the four quarterly cohorts of each year were combined to generate the treatment outcomes for that year.

Results: Over the decade 2002 to 2011, the treatment completion rates of the yearly cohorts increased from 73.4% to 82.8%. The proportion of patients who were 'lost to follow-up' decreased from 3.4% to 1.7% while that of patients categorized as 'still on treatment/no final outcome' decreased from 10.5% to 4.4%. Death rates remained stable at between 10.1% to 11.7%, of whom the majority died from non-TB causes. The improvement in our treatment completion rate could be attributed to multiple factors: the use of the legal act to compel TB treatment in recalcitrant defaulters since 2004, the implementation of a non-governmental organization-funded incentive scheme of providing grocery vouchers to needy patients undergoing Directly Observed Therapy since 2009, and to the effect of the TSM itself. The relatively high death rate in our treatment cohorts is due to TB being a disease of the elderly in Singapore.

Conclusion: The TB treatment completion rate among Singapore citizens and PRs has improved since 2002 as the likely result of several initiatives over the past decade.

ASSESSING KNOWLEDGE, ATTITUDES AND PRACTICE IN THE TREATMENT OF TUBERCULOSIS

OP-163-01   Community perspective of causes, transmission and prevention and its effect on health seeking behaviour for tuberculosis in Nigeria

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Background and challenges to implementation: Despite the availability of proven interventions and free availability of treatment and TB services, there is still a high level of apathy towards patronizing such services in Nigeria. This necessitated a national survey in 2012 in assessing the knowledge, attitude and perception of Nigerians on TB with a view to understand best ways in improving patronage of TB services.
Method: The study employed a prospective cross-sectional method through a multi-stage random design to select 3021 households (513 in Ondo, 518 in Benue, 525 in Akwa Ibom, 518 in Katsina, 424 in Ebonyi and 523 in Gombe), 12 FGD and 24 IDIs in six states across Nigeria.
Result: Only about 27% of the study population had correct knowledge of the cause of TB. About 71% of respondents believed that TB is curable, about half of the respondents believed that TB patients should be isolated. About 23% of the respondents were not in agreement that TB patients should be cared for. Three key preventive measures with the highest reporting across the respondents are: controlled spitting and coughing (55%), proper disposal of sputum (49%), and avoidance of direct spitting (48%). About 85% of respondents will attend a clinic when having persistence cough of more than 2–3 weeks, while ease of access to TB DOTS facility (72%) and availability of anti-TB drugs (98%), 3% reported high cost of TB services as barrier. Of the 3012 respondents, 5%, 20% and 63% will first consult traditional healers, self-medication and DOT facility for treatment respectively. Qualitative evidences further buttress some of these findings in greater details though further logistic regression analysis is on-going to identify significant individual and community level variables.
Conclusions and key recommendations: The preliminary analysis showed that there is a wide gap in the communities on knowledge, attitude and perception towards TB. Increasing awareness in the community contributes to increasing access to TB services. There is the need to developing and stepping up behavioural change communication on TB in Nigeria.

OP-164-01   University students' knowledge on tuberculosis

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Background and challenges to implementation: Students' knowledge and opinion about tuberculosis (TB) are very important in recognizing early symptoms and signs of the disease, prevention of delay in diagnosis of TB and influence on outcome of the disease. The research was conducted among the students of University of Novi Sad in Serbia.
Intervention or response: Goal: To define the non-medical students' knowledge about TB (risk factors, symptoms, different procedures in diagnostic and treatment, possible side effects and complications, comorbidity).
Material and methods: Prospective study comprised six faculties of the University of Novi Sad. The data were obtained through the questionnaire filled in during October and November 2010 and 2011.
Results and lessons learnt: The total of 1930 students were included in the study. The majority of the students had a good knowledge about TB (80.98%). Most of the queastioned students know that TB is infectious disease (96.9%), that the main cause of the disease is bacteria (80.5%), as well as that it is curable disease (95.9%). Over 94% of them knew that cauhg is the main cause of TB transmission. 67% of questioned students considered risk factors as a contributive factor to the appearance of TB (47.3%, alcoholism, 69.8%, poor nutrition, 74%, comorbidity such as diabetes, HIV infection, tumors and 77.4%, smoking habit). A lot of the students (43.9%) thought TB incidence in the country is increasing.
Conclusions and key recommendations: Students of all faculties at the Unversity of Novi Sad showed a good knowledge about TB. The best knowledge was noticed among the students of Faculty of Agriculture and Medical Faculty. They are not well informed about the situation with TB in the country and the effects of national and international guidelines implemmentation. In order to inform them better, National Comitee for TB should use media, workshops, flyers, etc.

OP-165-01   Overcoming resistance to the use of smear microscopy for tuberculosis diagnosis: the need for new strategies

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Background: Namibia has a high TB incidence (566/100 000 in 2011), and is sparsely populated with long distances to health facilities. The extent of implementation of smear microscopy as the cornerstone of diagnosis of TB done in the respective regions in Namibia has been variable across regions. A large number of patients (up to 65% in some regions) with pulmonary tuberculosis (PTB) were being diagnosed without smear examination in 2004.

Intervention: Intensive trainings of doctors and nurses on the national TB guidelines were conducted starting in 2006, focussing on diagnostic algorithms. Sputum specimen collection was decentralised to all health facilities, with smear microscopy being performed at 31 of the 34 district laboratories. Emphasis was placed on follow-up smear examination for all smear positive cases on treatment.

Results and lessons learnt: There has been a gradual decline in the proportion of PTB patients diagnosed without sputum smear examination (SND) from 37% in 2004 to 24% in 2011. Use of smear microscopy for PTB diagnosis thus remains sub-optimal. There are however significant variations across regions, suggesting lack of inter-regional uniformity in diagnostic approaches (see Figure). Age-specific data on the proportion of children for whom smear examination was performed are not routinely aggregated and reported, and were therefore not available for analysis. The routine data collection does not capture the reasons for not performing smear examination. Anecdotal reports identify doctors as the staff category most likely to commence patients on treatment without smear-microscopy.
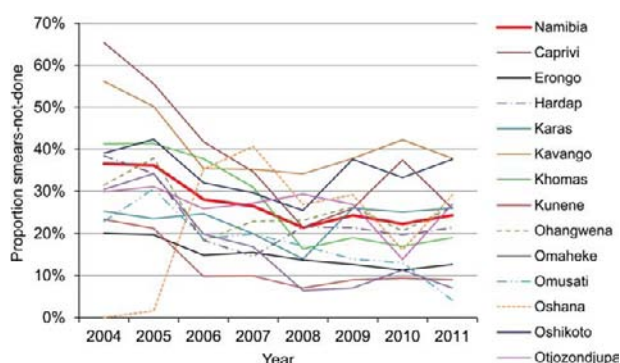
Figure Trends and regional variations in the proportion of patients with pulmonary TB in whom sputum smear examination was not performed, Namibia, 2004–2011.

Conclusions and key recommendations: There is continued need to improve the utilisation of smear examination for the diagnosis of PTB. Further studies should be conducted to determine some of the reasons why patients are not having sputum smear examination. There is need to collect age-disaggregated data to ensure that children-specific diagnostic challenges are elucidated. Smear microscopy is also cru-

cial for infection control and early detection of treatment failure, given the relatively high rates of DR-TB in Namibia. Region-specific interventions should be implemented to address local issues. Including smear microscopy as a requirement for patient registration can be explored, regardless of diagnostic category.

OP-166-01   Assessing knowledge, attitudes and beliefs about tuberculosis among the community in Yunnan Province, China

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Background and challenges to implementation: Multi-drug resistant tuberculosis (MDR-TB) is a threat to tuberculosis elimination. Studies have shown that lack of TB knowledge prevents appropriate healthcare seeking behavior by TB-infected individuals, resulting in diagnostic delays and non-compliance with TB treatment. In 2011, China ranked second highest in the world in both TB and MDR-TB incidence, with the percentage of previously treated patients well above the global average. The aim of this study was to identify barriers to TB diagnosis and treatment due to a lack of knowledge and personal beliefs about TB in Yunnan Province, China.

Intervention or response: We conducted a cross-sectional survey of 442 participants convenience-sampled from the community in Kunming City, Yunnan Province, China during March and April of 2013. All participants were interviewed by outreach workers using a pre-validated structured questionnaire consisting of socio-demographic and socio-economic characteristics; knowledge about TB symptoms, transmission and treatment; health seeking behaviors; and access to healthcare providers. Descriptive analysis was used to elaborate demographic information. Inferential statistics (χ^2) were used whenever appropriate using SPSS software.

Results and lessons learnt: Respondents tended to have a secondary school educational level (44%) and were employed (64%) and married (86%). Among the 442 participants interviewed, 149 (33.7%) had never heard of TB, with more men (41%) than women (26%) lacking this basic knowledge on TB ($P = 0.0012$). In addition, only half (52%) of those who had heard of TB were aware that cough with blood was a symptom of TB, and only 19% aware that weight loss was also a symptom. Lack of knowledge was also found in how TB is cured: 48% of the participants reported that Chinese medicine could cure TB.

Conclusions and key recommendations: Educational strategies for community outreach in Kunming City, Yunnan Province, China should address gaps in TB knowledge. These strategies could include targeting male-dominated sectors of the community (businesses and factories) and engaging those who practice Chinese herbal medicine to advocate and educate on TB. Improving knowledge on TB transmission and treatment could potentially improve access to diagnosis and treatment compliance, if attitudes are also addressed. This could ultimately improve TB and MDR-TB case detection and treatment success.

OP-167-01 Assessment of various pedagogical techniques in tuberculosis programme performance in Delhi, India

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Background: Developing capable and competent health workforce is essential to achieve national and global health goals, especially with respect to tuberculosis (TB). To achieve excellence in program service delivery by effective learning practices, it is essential to embrace various pedagogical techniques in the training curriculums implemented by TB control programs.
Design/methods: Various pedagogical techniques were synchronized with different training sessions undertaken by Revised National TB Control Program Delhi in 2012. The adult pedagogical techniques used were: 1) problem based learning; 2) supportive learning; 3) differential learning; 4) applied learning; 5) interactive learning; 6) assessment of learning; 7) cognitive learning; 8) audio-visual learning; 9) simulation learning and 10) kinesthetic learning. Delhi Program Management Records were reviewed to ascertain the training needs of key program staff and to assess the impact of pedagogical techniques on specific program outcomes achieved in 2012. The outcomes chosen were three months sputum smear conversion rates, percentage entries of electronic medical records under the national web-based patient tracking system, percentage drug resistant TB patients initiated on treatment and uptake of TB-HIV services among registered TB patients.
Results: In 2012, 60% (590/988) of key program staff was trained and retrained by modular technique which was supplemented by specific pedagogical techniques. For practical training of all key program staff (50) and sensitization workshops for other stakeholder's (733) different pedagogical techniques were used. The effectiveness of these techniques was assessed in two domains—skill and cognition development. Skill development was quantified on the basis of deliverables like sputum conversion rates (which

increased to 90% from an average of 88% in previous years), electronic patient record entries (>90% in 2012), drug resistant TB patients initiated on treatment (93% in 2012 from 73% in 2011) and uptake of TB-HIV services (73% in 2012 from 58% in 2011) in Delhi. Cognitive development was quantified based on pre and post-test assessment. McNemar's chi-square test was used to find out the significant difference between pre and post-test results.
Conclusion: Inclusion of specific pedagogical techniques in the training methodology of National Tuberculosis Program leads to development of a competent workforce in short span of time, thereby improving program performance.

OP-168-01 Participatory governance as a determinant of urban tuberculosis control in Delhi, India

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Background and challenges to implementation: Significance of participatory governance as a positive catalyst in any urban public health program needs an empirical study for its adoption in policy design. The participatory governance model effected through active interaction among stakeholders focuses on community empowerment by creating valuable social capital, which, in turn, impacts the outcome of public health programs. The study situates itself in context of an urban TB program witnessing positive growth in program outcomes against the backdrop of a unique participatory governance initiative started by Delhi Government called-Bhagidari program.
Intervention or response: Bhagidari (meaning collaborative partnership) is a model of participatory urban governance initiated in the year 2000. This citizen government partnership has re-engineered the process of service delivery through a unique public-private-community participation approach, which makes the system more responsive to the citizens need. Through the Bhagigari model, all national health programs and social security schemes have received enhanced advocacy and outreach among the beneficiaries who include TB patients and their families. The interrelationship between Bhagidari and TB program service delivery in Delhi was examined in 2012. A wide range of published government records pertaining to selected social determinants of TB which reflect social development in an urban setup and TB program surveillance records pertaining to the year 2001–2011 were studied.

Results and lessons learnt: The decade saw a significant growth in most of the social development parameters in the state. TB program performance showed stable trends in TB case detection and treatment success rates by annual cohorts, 56% increment in lives saved and 29% reduction in TB deaths. The 8% reduction in incident TB case notification rates translate to logarithmic decline of 5.4 new TB cases per 100 000 population for each year since 2001. Decline in new TB cases was higher in males than females ($t = 1.8$; $P < 0.05$). Except literacy rates and net migration rates, other social determinants showed significant correlation with decline in TB incidence.

Conclusions and key recommendations: Participatory governance leverages the efforts of government and citizens for the improved program outcomes. Strong policy inducement promoting participatory governance as a determinant of urban TB care needs to be reckoned in the public health policy framework for TB control in an urban set up.

OP-169-01   Creating instructional material targeting the decentralisation of primary care services

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Introduction: The state of Rio de Janeiro has the highest incidence rate of tuberculosis in Brazil. In 2011, 14 756 cases were reported, with an incidence of 72.3/100 000 population. The State of Rio de Janeiro has the largest number of new cases and cases where the living conditions of the population are poor, with large clumps. On 29 and 30 September 2011 the Management of Sanitary Pneumology (GPS) participated jointly with the Office of Primary Care and Superintendency of Surveillance and Environmental/SES-RJ and the Secretariat for Primary and Surveillance and Health Promotion/SMS-RJ in organizing the Workshop line care of tuberculosis in the Municipality of Rio de Janeiro, where he attended the coordinators of CAPs, to discuss strategies to combat tuberculosis. This meeting, a report was prepared with information that led to the instructional manual of tuberculosis for professional training of primary care aims to decentralize the actions for primary health.

Objective: Describe planning workshop and action plan of the PCT for the city of Rio de Janeiro.

Methods: The workshop included presentations and group activity. For the group activity was designed practical guide, based on the pedagogy of problematization, with nine situations problems.

Results: Participated approximately 200 professionals. One hundred and one answered the questionnaire, predominantly female (90.1%), aged between 20 and 39 years (50.5%), nurses (66.3%), bond Employment Laws (50.5%) and inclusion in FHS (44.6%).

The main causes of the problems were attributed to the PCT people (professionals and patients) and the work process. The planned activities relate to job training, combat stigma and the preparation and dissemination of flows.

Conclusion: It was considered likely that the action plans will be implemented with favorable change in the indicators of the PCT. It was recommended development of instructional material to facilitate capacity building and monitoring and evaluation of action plans.

OP-170-01   Assessment of knowledge, attitudes and practices on tuberculosis in ten zones of Amhara and Oromia Regional States, Ethiopia

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Background: TB is the leading cause of morbidity and second cause of death in Ethiopia. Understanding knowledge, attitudes and health-seeking practices (KAP) is critical to inform effective health interventions that improve TB case detection and treatment outcomes. PATH and partners of the USAID-funded and MSH-led HEAL TB Project conducted a mixed-methods study in ten project zones in Amhara and Oromia Regions to identify TB KAP among general population, TB patients and health workers.

Methods: A community-based cross-sectional survey of 1920 members of the public; qualitative interviews with 15 TB patients and 20 health workers; 4 focus groups. Data were collected using a structured questionnaire and semi-structured interview guides in national languages.

Results: Basic knowledge of TB symptoms, transmission and cure was widespread, however perceived and real knowledge were consistently higher in Oromia Region and in urban areas. Awareness of free TB treatment was low (45.2% urban; 26.8% rural). Respondents in Oromia were more likely to feel at risk for TB infection, to state that TB is a 'very serious' problem, and to say their reaction to a TB diagnosis would be 'fear' or 'sadness'. Half (53.7%) of respondents felt others would think less of them if they had TB; 29.7% said they would be embarrassed or ashamed. A majority (71.9%) felt that they would not have a problem finding a marriage partner, however 56.9% reported that if they had TB it would be a social problem for their children. Preferred sources of TB information included health workers (65.3% Amhara; 42.8% Oromia), HEWs (23.3% Amhara; 49.4% Oromia) and radio (15%)/TV (12.2%). Lack of risk perception and financial barriers contributed to delay in seeking diagnosis for TB patients. The

majority of patients said they discussed their disease with family members and friends and reported that their social, family and sexual relations were affected by their diagnosis. Potential barriers to treatment adherence include substance addiction and social or financial instability.

Conclusions: Study findings emphasize the need for implementing targeted communication strategies to correct misinformation, increase awareness of risks for TB, reduce social stigma. Communication channels and messages should be tailored to the zones and to rural/urban residence. Results suggest that TB treatment services should be patient centered and decentralized to the community level through HEWs.

OP-171-01   Impact of a TB-HIV integrated approach (the 5 I's) in a deep rural resource-limited border-setting in North West Province, South Africa, 2006–2012

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Background: South Africa has one of the highest tuberculosis (TB) burdens in the world with more than 60% of all TB patients co-infected with HIV. The integration of services at clinic level has been identified as a priority yet in many instances there are barriers to implementation. The that'sit programme provides evidence of the success of the WHO and IUATLD approach to integrated care, by decreasing the burden of HIV in TB and TB in PLWHA patients. A comprehensive community-based systems strengthening approach to support the TB programme in rural settings in South Africa called that'sit, was introduced during 2006 in Bray, a small community (local population 12 000) at the Botswana border in the Kalahari desert. The area is characterized by limited resources, poor infrastructure, variable internet connectivity, a high rate of poverty (many farm labourers), cross-border migration and poor access to clinic services.

Methods: Following a needs assessment the that'sit programme introduced the following activities to support integration of services:

- Introduction of a one-patient-one-file approach that decreased waiting times and improved clinical management of patients
- Training of all staff in TB-HIV management, recording, reporting and infection control
- Integration of all professional services, rotation of staff through all service points
- TB screening and counselling and testing for all early initiation of ARTs
- Prophylactic care (CPT/IPT), nutritional assessments during the pre-ART phase
- TB technical support was provided by the appointment of key trained staff to oversee all activities

and to ensure that National TB programme protocols were adhered to. Collaboration with the mobile clinic services of the Department of Health ensured that defaulter rate was minimized especially in those clients living on the farms.

Results and lessons learnt: During this period of time more than 5000 patient were counseled and tested and 609 patients were diagnosed and treated for TB. Data recorded in the electronic TB register was compared from the initiation of the project in 2006 until Quarter 4 in 2011. All the National TB indicators illustrated a positive trend over the time period; e.g., cure rate increased from 56% to 85% and the number of patients initiated on ART increased to above 80% in 2011 from zero in 2006.

Conclusion: A integrated approach to TB-HIV can change the course of an epidemic effectively.

OP-172-01   Treatment-seeking behaviour of tuberculosis patients in India: findings from a cross-sectional study from six high burden states of India

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Background: India is one of the high burden countries for tuberculosis and Project Axshya a civil society initiative is implemented by Population Services International across 30 districts with the objective to improve the access to TB services to marginalised and vulnerable populations. A study was conducted to understand the risk perception and treatment seeking behaviour of the TB patients in order to address the needs of the target group. The objectives of the study was to identify TB patients and symptoms experienced, actions taken by the TB patients with symptoms and identify delays if any.

Design/methods: A cross-sectional study was conducted across 30 districts covering 21 748 households. Multi-staged sampling design was adopted; probability proportionate to size (PPS) was done as per the district population to give a representative sample of the target population. Respondents were selected from the sampling frame prepared through household listing. The survey was conducted across rural and urban locations and targeted at men and women 18–54 years of age. An almost equal proportion of men and women were contacted and 172 were TB patients. A semi-structured questionnaire was used to determine the self-risk perception about TB symptoms and the treatment seeking behaviour of the TB patients.

Results: The survey reported that of the 172 TB patients contacted, 80 were on DOTS and 92 on other regimens. The following symptoms were common: cough for two weeks or more (84.6%), temperature

rise (52%), hemoptysis (44.7%), chest pain (42.3%) and weight loss (33.3%).The actions initiated were: visit private providers for diagnosis (46.8%); public sector hospitals (36.3%), self-medication (6.5%), pharmacists (5.6%) and nothing (5%). The delays that were reported were: 16.7 days for initiation of action from day of symptoms; average 31.5 days for initiation of any investigation (31.5 days). On an average the TB patients went to 2.09 providers to seek treatment.

Conclusion: The study has shown that there are substantial delays in diagnosis and initiation of treatment. TB patients go provider shopping and different regimens are used. Large number of patients also access the private sector providers for treatment. The findings of the study have given insights for program designing and implementation to improve access to TB diagnosis and treatment in the six states.

OP-173-01   Individual and service delivery barriers affect anti-tuberculosis treatment adherence in Punjab, India

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Background: 39 569 TB cases have been registered in the Punjab during 2012. Among new smear-positives (NSP), treatment success rate has remained steady during 2006–2012 in the range of 85% to 88%. Treatment success rate has declined to 62% in 2012 from 75% in 2011. The default rate among NSP cases varies from 4% to 7% in last 5 years, the same in smear-positive retreatment cases varied from 10% to 13%. Defaulting is the major concern in some parts of the districts. Irregular/default cases back into treatment with follow up from RNTCP, Axshya Project and other civil society organisations. The objective of this paper is to find out the barriers in treatment adherence at 4 levels—individual, family, community and service delivery.

Design method: 65 cases (46 M and 19 F) were surveyed in 8 districts of Punjab, especially where The Union supported Axshya Project is being implemented by using a semi-structured questionnaire. The data collected in terms of category, patient type, comorbidities, smoking/tobacco, alcohol use and reasons for irregularity/default in treatment and analysed from the gender perspective.

Results: Out of 65 cases irregular and default cases surveyed, 3 in every 5 persons, i.e., 40 patients (30 M and 12 F) are in the age group of 15–45. Fourteen (12 M and 2 F) cases are between 46–60 years of age and 8 cases were beyond 60 along with a child

case of 12 year old. Among all, 35 (24M; 11F) are in CAT-I and 30 (22 M, 8 F) in CAT-II treatment regimen. 29 CAT-II cases are from RNTCP including 8 relapses. 15% (10) cases are both current smoker and alcohol consumer.

Out of 65 cases, 39 (60%) said they are not interested in continuing medicine which include 26 male. 10 male patients migrated to other places, 3 cases discontinued medicine as they feel well. Only 2 cases discontinued due to self and societal stigma. 6 cases (10%) became irregular due to other disease and drug reactions. 41 cases retrieved back to treatment, 3 cases died 2 cases shifted to private service provider and result of others are still not known.

Conclusion: In 4 stage barrier analysis, the major barriers identified at the level of 'individual' and 'service delivery'. That of at the level of family or community doesn't carry much significance. Patients lack adequate knowledge on TB and its implication on him/her, family and the society. Proper counselling, regular follow up and re-vitalising faith on the quality services are the key to eliminate those barriers at the level of individual and service provisions.

OP-174-01   Knowledge about tuberculosis diagnosis and management using DOTS among final year medical students in south western Nigeria

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Background information: Equipping medical graduates with the competence to manage tuberculosis (TB) is not just imperative but also urgent as the diseases have been consistently listed as one of the major causes of morbidity and mortality in Nigeria. However, there were no baseline studies done on knowledge of final year medical students on various aspects of TB diagnosis and management under DOTS which forms the basis of this study.

Methodology: A total of 241 final year medical students from three medical colleges in Nigeria were interviewed. The questions assessed their knowledge about various modes of transmission, symptoms and management of tuberculosis under the DOTS strategy.

Results: More than half of the respondents (i.e., 69%) had poor knowledge about TB disease. Only 33.6% mentioned sputum smear as the best tool of diagnosing TB according to guideline. Poor knowledge was also exhibited when asked of various categories under DOTS treatment regimen, as 46.1% correctly mentioned cat 1 and 2. Minority 18.7% and 6.7% had complete knowledge of 6 months duration for new TB cases and 8 months for re-treatment cases

respectively. Less than one tenth, i.e., 4.6% and 2.9% could correctly define what is called a new TB case and re-treatment cases according to standard guideline.

Conclusion: The study reveals gross inadequacies in TB knowledge and management practices among Nigerian final year medical students. There is urgent need for incorporation of national TB guideline into existing undergraduate medical education curriculum as well as students rotation through activities in DOTS clinic.

POSTER DISCUSSION SESSIONS

HOLDING HANDS TOGETHER: LINKING TB-HIV COLLABORATION

PC-301-01   Quality of care for integrated tuberculosis and HIV services in Ekurhuleni North sub-district, South Africa: taking patient perceptions into account

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Background: Limited knowledge exists about the experiences and perceptions of patients seeking both TB and HIV care in primary health care settings where efforts are being made to improve integration of TB and HIV services. We compare patients' experiences of integrated TB and HIV care with the status quo in the context of the 'MERGE' study, a cluster-randomised trial evaluating a health systems intervention to improve delivery of integrated TB and HIV services.

Methods: Semi-structured interviews were conducted with 58 adult HIV-co-infected TB patients accessing TB and HIV services between September 2012 and February 2013 at six primary healthcare clinics (3 intervention, 3 control) in Ekurhuleni North sub-district, Gauteng, South Africa. The interviews collected basic demographic data and information about patients' treatment-seeking experiences and perceived quality of care received.

Results: Of the 58 adults interviewed (28 intervention, 30 control), 27 (47%) were female, median age 35 (IQR 28, 39) and 36 (62%) were employed. The most common reasons for attending the clinic were collection of TB drugs ($n = 49$, 84%), collection of antiretrovirals (ART) ($n = 13$, 22%), and ART initiation ($n = 9$, 16%). Patients in clinics in the intervention arm had a lower median clinic waiting time (15 vs. 30 minutes, $P < 0.05$) and a lower proportion

reported being seen by a third health care worker at the clinic visit (3.6% vs. 20.7%, $P < 0.05$). In both arms, patients valued staff that were caring and supportive, and provided a quick service. Patients were dissatisfied with long waiting times, harsh and rude staff attitudes, receiving inadequate information, having to go to different rooms to see different providers and having to come on separate days for TB and HIV care. Sentiments did not vary by study arm. Areas highlighted for improvement were an appointment system to avoid coming for TB and HIV care on separate days, provision of better information regarding treatment and more caring attitudes from the staff.

Conclusions: Despite reduced waiting times and a reduction in the number of health care providers seen by patients, rationalisation of care through integration does not always equate to better perceived quality of care but may be influenced more directly by the interaction with health care providers. Efforts to deliver joint TB and HIV services more efficiently must be mindful of the need to retain quality in patient-provider interactions.

PC-302-01   Improving cross-referrals of tuberculosis and HIV through community follow-up

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Background and challenges to implementation: PLHIVs are more susceptible to TB. PLHIVs co-infected with TB have an annual risk of 60% of developing active TB as compared with 10% lifetime risk in HIV negative. TB if diagnosed timely amongst PLHIVs reduces the morbidity.

Project Axshya aims to reach the most vulnerable and marginalised including PLHIV. MAMTA is implementing project Axshya in 14 districts of Rajasthan.

Intervention or response: To increase the cross referrals from HIV to TB and TB to HIV, two activities were implemented, that included Training of District level network of positive people and Facilitation of Quarterly meeting of ICTC and DMC.

1 Two trainings annually were organised at state level for District PLHIV network on TB care and control in Rajasthan in year 2011 and 2012, wherein representatives from network participated and trained on TB care and control with an aim to increase the referrals of HIV positive for TB testing.

The trained representatives of district PLHIV network discussed this in their monthly meeting and encouraged referral to DMC for TB testing.

2 To review the district wise cross referrals, quarterly DMC-ICTC meetings were facilitated and cross referrals were discussed in all 14 districts of Rajasthan where project Axshya is implemented by MAMTA.

Results and lessons learnt: The total number of registered TB cases with known HIV status from 34 districts rose from 27 369 (Year 2011) to 34 943 (Year 2012). In case of 14 districts where MAMTA-HIMC is implementing Axshya Project the figure increased from 15 881 to 19 157. Similarly, in 2011, from ICTC to DMC 12 515 cases were referred and tested for TB. In Year 2012, 16 544 cases were referred from ICTC to DMC for testing out of which 1436 were diagnosed as TB (717 NSP, 629 NSN and 90 extra-pulmonary) and 693 were put on DOTS.

Conclusions and key recommendations: Sensitizing the network of PLHIV is useful for increasing the TB testing of PLHIVs. Similarly, reviewing the cross referrals periodically could be an important means for achieving the maximum cross referrals from both the departments. This is evident from the study that it can help future interventions and also in planning to increase cross referrals in near future.

PC-303-01   Seven years (2006–2012) of implementing TB-HIV collaborative activities in Nigeria: what worked and lessons learnt

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Background: TB and HIV constitute major public health problems in Nigeria, the country is among the high ranking countries globally in terms of TB and HIV burden. The National programme in order to address the impacts of the TB-HIV developed and implement the National TB-HIV strategic framework in collaboration with the partners.

Aim: To assess what worked, the challenges and lessons learnt since implementation of TB-HIV collaborative activities commenced in 2006.

Design/methods: A retrospective review of quarterly TB-HIV reports from the states programme was conducted from 2006 to 2012. A structured questionnaire was also administered to TB and HIV programme managers from six states.

Results: The weak structure for HIV health sector response at lower levels unlike the well established structure of the TB programme is a major hindrance to effective collaboration between the TB and HIV programme at lower level (the state and LGAs); the TB-HIV information from the DOTS sites are readily available while that of HIV sites are rarely available due to heavy dependent on partners for such informations. The TB-HIV collaboration has worked in the following areas when the progress is compared with the set target: the provision of HCT at DOTS sites with the proportion of TB patients tested for HIV increasing from 10% in 2006 to 85% in 2012; the provision of CPT for co-infected patients has also

increased from 17% in 2006 to 81% in 2012. Limited progress were made in the area of access of TB-HIV co-infected patients to ART from 23% in 2006 to 56% in 2012; part of the reasons for this is the number of DOTS sites (4642) which outnumbered that of the ART sites (516). HIV patients are routinely screened for TB with 78% (582 098) PLHIV screened for TB in 2012, 2%(10 584) of whom had TB. The following areas has not worked in the TB-HIV collaboration: access of eligible PLHIV to IPT with less than 5% having access to IPT; infection control implementation is also very minimal.

Conclusion: A strengthened structure for HIV health sector response at all levels like the TB programme is essential for effective TB-HIV collaboration at lower levels; ART services must be decentralized to DOTS clinic to increase access of TB-HIV co-infected patients to ART; HIV programme must consciously scale up implementation of IPT and IC.

PC-304-01   An enhanced role for lay screening officers in integrated TB-HIV services? Insights from the MERGE trial in primary care clinics, Gauteng, South Africa

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Background: In May 2010, the South African Department of Health introduced WHO four-symptom TB screening for HIV-positive people coming into contact with the health system. Little is known about how primary care clinics are implementing screening, and how screening activities contribute to the broader goal of integrating TB and HIV services at primary care level. In the context of a health systems intervention trial to improve delivery of integrated services for TB and HIV in South African primary care clinics, nine screening officers (SO) were placed in the nine intervention clinics to promote intensified case finding (ICF).

Design/methods: In-depth interviews were carried out with the nine SOs approximately 6 months after placement to explore their perceptions of roles, responsibilities, and strategies deployed to carry out prescribed tasks.

Results: Three of the eight SOs were enrolled nurses; the remaining six were lay persons educated to Grade 12 with prior experience in health settings. Beyond administering the symptom screening checklist, SO reported a range of activities related to patient communication, education, and retention in care. Moving between clinic spaces, they filled in 'gaps' in the care continuum by completing registers, following up on

patients, and communicating across staff divides. SOs adapted the screening tool in order to probe patient histories, and took on other clinic activities in order to 'fit in' as part of the clinic staff. Professional boundaries between staff nurses and SOs undermined screening activity in some clinics where this was perceived to be a lowly task. SOs felt most able to contribute to integrated care where they had the active support of clinic managers and staff.

Conclusion: Beyond implementing four-symptom screening, SOs can play a vital role in supporting co-infected patients' pathways to care, and in mediating across divisions in TB and HIV services. In order to fulfil this enhanced role, however, SO must gain adequate professional recognition and managerial support.

PC-305-01 Reduced mortality in a high TB-HIV prevalence setting through improved TB-HIV integration: Ventersdorp District, Dr Kenneth Kaunda, North West Province

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Background and challenges to implementation: South Africa continues to face the dual epidemic, with 993/100 000 TB cases reported in 2011, 65% of which were co-infected with HIV. The United States Agency for International Development (USAID) TB project run by University Research Corporation (URC) provides technical support Ventersdorp sub-district in Dr Kenneth Kaunda District, North West Province to improve the quality of TB services, increase TB treatment availability, increase the demand for TB services, and improve TB management support. In 2010 the Project investigated the factors influencing the high TB mortality reported, after which intervention plans to address the recommendations were jointly developed.

Intervention or response: A retrospective cohort analysis of routine data to identify factors influencing the high mortality in Ventersdorp sub-district. Analysis of data to describe baseline characteristics was performed. Kaplan Meier survival analysis was used to describe time to death. The findings from the study indicated that there was poor recording of data—40% of HIV results, 54% of ART results and 50% of CD4 count results were not recorded. Sixty-three percent of TB patients had the HIV results, 8.9% had CD4 count done, 55.2% on cotrimoxazole and 15.4% on ART. The death rate in 2009 was 18% in the facilities assessed. Quality improvement plans were jointly developed to address the challenges identified. Interventions included training on TB-HIV management, DRAT, support supervision with in service training and coaching.

Results and lessons learnt: The death rate improved from 15.8% in Q1/2009 to 5.4% in Q3/2011, while 98% of TB patients have HIV status recorded compared to 63.3%; CD4 count improved 82.1%; ART improved to 83.6% over the same period. The treatment success rate improved from 63.2% in Q1/2009 to 78.4% in Q3/2011.

Conclusions and key recommendations: Timely implementation of research recommendation can be used to improve the quality of care provided to patients and also influence TB treatment outcomes. The results of the mortality study highlighted challenges which were used to improve the TB-HIV programme and treatment outcomes.

PC-306-01 Community information needs and involvement in tuberculosis and HIV/AIDS: needs assessment study in rural Lilongwe, Malawi

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Background: The main purpose of the study was to assess communities' information needs and informal health providers' capacity to implement the health communication package for a randomized controlled trial, 'Triage Plus' which aims at involving informal community based health care providers in the promotion of early access to TB and HIV/AIDS diagnosis and treatment.

Methods: Qualitative research methodology was utilized in this study. The study was conducted in 7 traditional authorities in Lilongwe. Study participants included community members, traditional leaders, health care workers and informal community based health care providers. It consisted of 12 focus group discussions, 30 in-depth interviews and 8 workshops. All interviews were recorded to maintain quality and transcribed verbatim in MS word. Analysis was done using MaxQDA software.

Results: The results revealed that respondents had relatively poorer knowledge on TB issues than HIV/AIDS and were more comfortable discussing HIV/AIDS issues. They were not sure how the two diseases relate to one another. Respondents raised questions about MDR-TB, how it is caused and thereby questioned the effectiveness of TB treatment. Diagnosis for both TB and HIV/AIDS was said to be at a formal health facility. The source of information frequently mentioned was radio, the preferred channel of information was through community systems (informal community based health care providers) which just needed capacity as said can provide information anytime unlike radio. With low TB knowledge and fear

of stigma, respondents highlighted that people access the services only when very sick.

Conclusion and recommendations: The communities have limited information on TB which demonstrated that TB information is not as readily available at community level compared with information on HIV. This is due to the different communication channels used. There are NGOs in the communities that train communities and disseminate HIV/AIDS information. TB information is usually communicated by the NTP only. Communities expressed their willingness to learn more about TB and HIV and participate in further dissemination of information in their communities. To facilitate this process, the authors recommend more integration of TB and HIV/AIDS services at community level in terms of provision of services and spreading of information. Coordination between the NTP and HIV/AIDS unit would focus on proposed community channels and strengthen them.

PC-307-01   Tuberculosis and HIV coinfection in Bangladesh

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Background and challenges to implementation: Bangladesh is a low HIV prevalent country with high-risk situation. The number of PLHIV is constantly increasing and becoming a vital issue. Estimated figure of PLHIV in Bangladesh is around 7500. Cumulative number of reported PLHIV in Bangladesh as of 1 December 2012 is 2871. TB is a major public health problem in Bangladesh and ranks sixth among the 22 high burden countries of TB globally. HIV/AIDS pose a potential threat to TB control efforts.

Intervention or response: Ashar Alo Society (AAS) is a community based registered organization working for care and treatment of PLHIV in Bangladesh. It started with 10 PLHIV in 1998. Now the total beneficiaries (members) are 1427 till 31 March 2013. Male 898, female 445, children 72, transgender 12. Between 1st January 2010 and 31st December 2012, total 164 HIV positive patients received TB treatment. Of them male: 128, female: 34, children: 2. Out of total 164 patients, smear positive: 46, smear negative: 25, extrapulmonary: 26 and re-treatment cases 16. Ashar Alo Society with its 3 centers and other 2 PLHIV organization covers TB and HIV co-infection treatment in whole Bangladesh. Baseline sputum test was done for all symptomatic patients. X-ray chest done for smear negative symptomatic cases and FNAC/Biopsy for extra pulmonary cases. TB treatment outcomes were described as per national TB treatment indicators. Weight and CD4 cell count were analyzed and adherence to cotrimoxazole and ART were measured. Maximum patients CD4 cell count was <100 cells. As of 31 March 2013, total 619 PLHIV are receiving ART.

Results and lessons learnt: A total of 164 TB and HIV co-infected patients were co-managed in the clinic. The majority were males 78%. The average age was 34.2 years. Treatment success rate of total 2 years such as 2010 and 2011 are 73% for smear positive pulmonary TB, 46% for smear negative pulmonary TB, 73% for extra pulmonary TB and total 26% died. There were an average weight gain and CD4 cell count rise. Almost 90% of TB and HIV co infection patient were started cotrimoxazole and antiretroviral therapy.

Conclusions and key recommendations: Tuberculosis is one of the commonest opportunistic infections seen among HIV positive patients. With the success of ART in reducing morbidity and mortality, HIV infection has become a chronic, manageable disease. Prompt ART initiation decreases the risk for OIs including TB.

PC-308-01   Designing and implementing a point-of-care TB-ART electronic medical record system in Malawi

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Background and challenges to implementation: TB infection among HIV positive patients is as high as 60% in Malawi. An integrated TB-ART management was adopted by the Malawi MoH to ensure continuum and access to care. Although integration of services has been achieved, the information systems are parallel creating a challenge for continuum of care for patients. In order to improve adherence and management of data for TB and ART patients, the Lighthouse Trust worked with Baobab to develop an integrated point of care Electronic Medical Record (EMR) system.

Intervention or response: A user centered design was used in the development of the EMR. At the heart of this design was task analysis to understand the workflows required in the co-management of patients enrolled in the TB and ART programme. The users and policy makers were engaged in development of system specification and series of testing. This design approach took into consideration fundamental theorems of medical informatics such as recognizing that a doctor working in partnership with an information resource is better than a doctor working alone.

Results and lessons learnt: The development and implementation of the system has shown that work

flows required in the management of TB-HIV con-infected patients can be embedded in a point of care EMR. Up to 7 workflows have been embedded in the EMR.

Conclusions and key recommendations: The EMR has been deployed at Martin Preuss Centre in March 2013. The outputs of the system in terms of optimizing workflow are being observed and will be shared.

PC-309-01 Predictors of mortality among TB-HIV co-infected patients being treated for tuberculosis in Northwest Ethiopia: a retrospective cohort study

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Background: Tuberculosis (TB) is the leading cause of mortality in high HIV-prevalent populations. HIV is driving the TB epidemic in many countries, especially those in sub-Saharan Africa. The aim of this study was to assess predictors of mortality among TB-HIV co-infected patients being treated for TB in Northwest Ethiopia.

Design/methods: An institution-based retrospective cohort study was conducted between April 2009 and January 2012. Based on TB, antiretroviral therapy (ART), and pre-ART registration records, TB-HIV co-infected patients were categorized into 'On ART' and 'Non-ART' cohorts. A chi-square test and a *t*-test were used to compare categorical and continuous variables between the two groups, respectively. A Kaplan-Meier test was used to estimate the probability of death after TB diagnosis. A log-rank test was used to compare overall mortality between the two groups. A Cox proportional hazard model was used to determine factors associated with death after TB diagnosis.

Results: A total of 422 TB-HIV co-infected patients (i.e., 272 On ART and 150 Non-ART patients) were followed retrospectively for a median of 197 days. The inter-quartile range (IQR) for On ART patients was 140 to 221 days and the IQR for Non-ART patients was 65.5 to 209.5 days. In the Non-ART cohort, more TB-HIV co-infected patients died during TB treatment: 44 (29.3%) Non-ART patients died, as compared to 49 (18%) On ART patients. Independent predictors of mortality during TB treatment included: receiving ART (Adjusted Hazard Ratio (AHR) = 0.35 [0.19–0.64]); not having initiated co-trimoxazole prophylactic therapy (CPT) (AHR = 3.03 [1.58–5.79]); being ambulatory (AHR = 2.10 [1.22–3.62]); CD4 count category being 0–75 cells/μl, 75–150 cells/μl, or 150–250 cells/μl (AHR = 4.83 [1.98–11.77], 3.57 [1.48–8.61], and 3.07 [1.33–

7.07], respectively); and treatment in a hospital (AHR = 2.64 [1.51–4.62]).

Conclusion: Despite the availability of free ART from health institutions in Northwest Ethiopia, mortality was high among TB-HIV co-infected patients, and strongly associated with the absence of ART during TB treatment. Higher hospital setting mortality also needs attention in the service provision and should be investigated in other studies.

PC-310-01 Tuberculosis, a neglected disease: outcomes of monitoring the availability and accessibility of tuberculosis and TB-HIV services in Uganda

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Background: Tuberculosis (TB) remains a major global health problem The WHO indicates that TB caused almost 9 million new TB cases in 2011 and 1.4 million TB deaths. In Uganda according to the National TB and Leprosy Program; there were approximately 49 000 new TB cases in 2011. TB has not being given the priority it deserves in relation to resource allocation to prevention, diagnosis, treatment, community education, research and advocacy. The International Community of Women Living with HIV Eastern Africa (ICWEA), a regional advocacy network carried out an assessment on the availability and accessibility of TB, TB-HIV services in Mityana and Mubende Districts in Uganda in 2012 to identify barriers to access to TB, TB-HIV services and gaps in service delivery.

Intervention: ICWEA developed a monitoring tool based on the national TB-HIV guidelines. Carried out in-depth interviews with the District TB and HIV focal persons and district medical officers, staff of 24 health facilities and focus group discussions with community members who were or had been on treatment for TB, HIV or both from the community. 98 community members were interviewed. Organized policy dialogue meetings at the district and national levels, carried out follow up visits to health facilities to check in on what had been addressed.

Results and lessons learnt: Low information about TB in the community coupled with high TB related stigma and discriminations leading to low uptake of services. Adherence to TB treatment is challenging and poor completion rates and yet not mechanism to trace patients. No routine TB screening for PLHIV and yet ICF tool availed in the health facilities. None functional laboratories duration for drug-susceptible TB is still 8 months despite WHO recommendation of the 6 months regimen a cause and consequence to poor treatment completion. MDR-TB is in the 2 districts with 5 patients diagnosed in Mubende Hospital but sent back to the community with no treatment,

despite the treatment in Mulago Main referral Hospital, there is no mechanism to trace them.

Conclusion: Commitment from the Uganda government for fight TB is needed to provide comprehensive TB, TB-HIV care for patients. We need tuberculosis regimens of shorter duration which would facilitate treatment completion and improve individual and public health. TB advocates must scale up efforts to government to scale up of investment in TB and to ensure that quality access to TB, TB-HIV services.

PC-311-01   Outcomes of integrated tuberculosis and HIV services in Uthukela District, South Africa

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Background and challenges to implementation: WVSA and Medical Research Council (MRC) implemented that'sit (Tuberculosis, HIV & AIDS Treatment Support and Integrated Therapy) project in Uthukela District in responding to the high rates of co-infection with Human Immunodeficiency Virus (HIV) and tuberculosis (TB) in TB patients. Provision of healthcare services to HIV infected TB patients was limited or non-existent in remote mountainous areas. Mobile clinics provided health services at over 100 points, but patients in these areas did not receive services. Evaluation of that'sit project was conducted in 2009 using a mix of observational, descriptive and cross-sectional designs. Data sources included key informant interviews, existing baseline, project follow-up surveys, and routinely collected TB and HIV statistics.

Intervention or response: Among key activities were integrating TB and HIV services through establishment and strengthening of referral networks and nutritional and economic support to patients.

Results and lessons learnt: In Okhahlamba municipality HIV testing rate in TB patients increased from 72% in 2007 to 82% in 2009. CD4 testing in TB patients increased; 38% of HIV infected TB patients started on ART per quarter. Average proportion of patients with CD4 count 200 cells/µl and less was 86%. All clinics used integrated patient files. The referral networks substantially contributed to increased level of HIV testing in TB patients through active case-finding and nutritional and economical support.

Conclusions and key recommendations: Facility-level and community based activities to integrate TB and HIV services through strengthening referral networks combined with nutritional and economical support can improve quality of services. These integrated TB-HIV services should routinely be provided at healthcare facilities throughout South Africa.

A POTPOURRI OF TUBERCULOSIS AND HIV ISSUES

PC-312-01   Tuberculosis treatment outcomes in integrated TB-HIV care clinics in Lusaka, Zambia

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Background: In Zambia, 65% of new tuberculosis (TB) patients are co-infected with HIV. Typically TB and HIV services are offered in vertical programs causing diagnostic and treatment delays. In 2011 the Centre for Infectious Disease Research in Zambia and the Zambian Ministry of Health piloted integrating HIV care into two TB clinics. While integrated care is intended to improve HIV care we sought to confirm that TB treatment outcomes were not being adversely affected by this integration.

Intervention: Antiretroviral therapy was initiated by clinical officers within 4 weeks of TB diagnosis in co-infected, eligible patients. We retrospectively collected TB outcome data from national TB registers for co-infected patients. We collected 6 months of data pre- and post-implementation. The pre-implementation cohort began 14 months prior to the intervention to allow sufficient time for completion of TB treatment (6–8 months). We classified TB treatment outcomes as successful (cured or completed) and unsuccessful (died, defaulted or failed). Patients who transferred out or had missing outcomes (200) were excluded. We compared the proportion of successful outcomes in each clinic pre- and post-implementation using chi-squared tests. Ethical approval was received by the University of Zambia and the University of North Carolina.

Results: We implemented Clinic A in August 2011. They had 151 evaluable co-infected patients pre-implementation and 102 patients post-implementation. The proportion with successful outcomes was 84.1% pre- and 85.2% post-implementation ($P = 0.80$). Clinic B was implemented in October 2011. They had 98 evaluable patients pre-implementation and 144 post-implementation. The proportion of successful outcomes pre- vs. post-implementation was 74.5% vs. 75.7% ($P = 0.83$).

Conclusions and key recommendations: In these early experiences, TB treatment outcomes were not adversely affected by integration of HIV care into TB clinics in Lusaka. This finding is reassuring, suggesting that consequences of new integration strategies such as early ART initiation, multiple drugs and increased pill burden are not obstacles to TB treatment

success. Limitations to this analysis include threats to validity due to the small sample size and losses to follow up. Challenges in integrated clinics included staff shortages, staff 'buy-in', and shortage of space. Further evaluation of the impact of integrated care on HIV outcomes in this setting is still required.

PC-313-01   Declining rates of HIV-TB co-infection in British Columbia and the efficacy of current Canadian tuberculosis screening practices in the HAART era

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Rationale: HIV-TB co-infection represents an important challenge to the clinical and public health management of both diseases. Current guidelines recommend one-time screening for all HIV positive individuals, annual screening for patients at high risk of developing tuberculosis, as well as treatment for LTBI when applicable. The impact of our current screening practices and LTBI treatment in HIV-TB co-infected individuals remains unclear in the HAART era.
Objective: To describe the incidence rate of active TB in the HIV population in British Columbia in the HAART era. Secondary objectives included describing the manifestations of HIV-TB co-infection and estimating the rate of missed opportunities for preventing active TB.
Methods: We performed a retrospective study on all HIV-TB co-infected individuals in BC between Jan 1, 2003 and Dec 31, 2012. We queried the BC Center for Disease Control TB registry for active TB cases, and from this population, clinical and demographic variables were extracted for all known HIV co-infected patients.
Results: 126 cases positive for both active TB and HIV were determined (estimated TB incidence of 124 per 100 000 HIV positive population), with a median age of 43.34 years, and 92 (73.02%) males. 63 individuals (50.00%) had at least one previously documented screening TST. Of the 39 individuals with a prior positive TST, 38 (97.43%) did not complete preventative therapy for LTBI. Of the 24 TST negative individuals, 20 (83.33%) did not have repeated testing within 12 months of developing active TB. However, TB-HIV co-infection rates have decreased significantly over the past 10 years ($P < 0.01$).
Conclusions: This study of a provincial TB screening program reveals that HIV-TB co-infection rates have decreased significantly over the past 10 years. Current screening practices in the HIV positive population and LTBI treatment rates are low. Consideration should be given to intensifying screening efforts and LTBI chemoprophylaxis uptake in order to further reduce HIV-TB co-infection rates.

PC-314-01   Tuberculosis among people living with HIV/AIDS: long-term incidence and risk factors in the German ClinSurv HIV Cohort

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Background: In Germany, surveillance yields no information on the burden of tuberculosis (TB)/HIV co-infection due to different reporting rules. To bridge this gap, we aimed to 1) describe the characteristics of TB-HIV patients in Germany, 2) estimate TB incidence density rate in people living with HIV/AIDS (PLWHA), and 3) identify risk factors for TB in PLWHA in terms of receiving/not receiving combination antiretroviral therapy (cART).
Design/methods: We performed a retrospective cohort study of PLWHA enrolled from January 2001 through December 2011 in the German ClinSurv HIV cohort. TB incidence density rates (IDR; cases/ 100 person-years [PY]) were calculated overall and for subgroups. Two multivariable Cox regression models for PLWHA with and without cART were constructed specifying hazard ratio (HR) to identify demographic factors (age groups, gender and geographical origin) and clinical factors (CD4+ cell count and viral load (VL)) associated with TB.
Results: Of 11 693 HIV-positive patients, a total of 233 (2%) patients were diagnosed with TB either at enrollment ($n = 62$) or during follow-up ($n = 171$). These TB-HIV patients were predominantly male (72%), and of foreign origin, mostly from sub-Saharan Africa (37%). The IDR of TB during follow-up was 0.4 cases per 100 PY overall and was higher in patients originating from sub-Saharan Africa compared to those from Germany (1.2 vs. 0.2 cases per 100 PY, respectively; $P < 0.001$). The highest IDR was found among cART-naïve patients compared to those receiving cART (1.3 vs. 0.3 cases per 100 PY, respectively; $P < 0.001$). In the two multivariable analyses, both patients (a) without cART and (b) those receiving cART shared the same risk factors for TB, namely: originating from sub-Saharan Africa ((a) HR, 4.0 [1.9–8.6]; $P < 0.001$ and (b) HR, 4.9 [2.6–9.5]; $P < 0.001$), CD4 cell count < 200 cells/μl ((a) HR, 9.4 [4.8–18.5]; $P < 0.001$ and (b) HR, 2.8 [1.2–6.6]; $P = 0.02$) and viral load >5 log10 copies/ml ((a) HR, 2.6 [1.4–4.9]; $P = 0.002$ and (b) HR, 1.8 [1.1–2.8]; $P = 0.02$).
Conclusion: The lower TB-IDR among patients receiving cART suggests that early cART initiation can avert incident TB. In particular patients originating from sub-Saharan Africa, and those with low CD4+ cell count and high viral load might benefit from it. However, patients on cART are still at risk for TB. Thus raising awareness and early diagnosis

of TB as well as isoniazid preventive therapy should be considered in addition to cART in the TB control strategy.

PC-315-01   Prevalence of latent tuberculous infection in HIV-infected persons in the Sylvanus Olympio teaching hospital of Lome

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Objective: To determine the prevalence of latent tuberculous infection (LTBI) in HIV-infected people.
Method: Using a cross-sectional study on HIV-infected persons monitored in the Department of Lung and Infectious Diseases of CHU Sylvanus Olympio of Lomé from August 10, 2010 to November 10, 2010. All patients are receiving antiretroviral therapy and have no clinical or radiological symptoms of TB, and had never received tuberculin skin test (TST) in the last 3 months. The CD4 rate of all patients was more than 200 cells/μl. The diagnosis of LTBI is based on the measurement of at least 5 mm of skin induration, 72 h after a subcutaneous injection of 5 IU of purified tuberculin.
Results: Of 154 persons included in the study, 107 were female and 47 were male. The median age was 40 years. Eleven patients were exposed to a risk of TB and only 70.7% of patients had a BCG scar. Approximately 45% of patients were very immunocompromised with a CD4 rate between 200 and 350. The prevalence of LTBI was 76%.
Conclusion: The prevalence of LTBI obtained with the TST is high in this study. A similar study using the interferon-gamma release assay, which is more specific, would be more helpful to obtain more reliable epidemiological data on patient outcomes and to determine the appropriateness of the use of chemoprophylaxis with isoniazid.

PC-316-01   Tuberculosis control at a reference hospital for infectious diseases: operational research, Sao Paulo, Brazil

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Background: The public reference services are an essential and strategic part of TB-HIV care for co-infected patients. Given the importance and complexity of TB-HIV cases, these services deserve constant supervision, self-evaluation, and monitoring of epidemiological and assistance indicators. The purpose is to analyze the outcomes of TB-HIV cases in the context of public reference hospital for infectious diseases.
Method: The first phase of study consisted a retrospective data analysis of inpatients discharged from IIER from July 2008–June 2009 with diagnosis of TB-HIV co-infection utilizing TB Information System of Sao Paulo State (TBWEB). After the conclusion of first phase began the second phase with a short interview based in a questionnaire. The study was approved by Ethic Committee.
Results: It was found 240 discharged cases corresponding to 219 patients. Thus, 178 TB-HIV patients were properly notified at TBWEB and treated. From those 178, 75 (55.6%) presented exclusively pulmonary TB, and other 60 (44.4%) were extrapulmonary, while 43 (24.2%) presented an associated co-infection, primarily represented by TB meningitis and TB lymphadenitis cases. According TBWEB culture of sputum/other specimen was performed in 109/178 (61.2%), which 72 samples were positive. The sensitivity test was performed in 56/72 samples (77.8%); 17/56 (30.4%) presented any type of TB-drug resistance. Regarding case type, 109 cases (61.2%) were new, 33 (18.5%) re-treatments after default, 3 (1.7%) re-treatments after failure, and 33 (18.5%) relapses. Concerning treatment outcome, the respective rates were: 41.6% cure, 28.1% default; 3.4% remaining in treatment; failure (2.8%); change of diagnosis (2.8%) due to non-tuberculosis mycobacteria, and death (21.3%). Variables such as 'pulmonary clinical presentation' and 'outpatient facility' remained as default predictors of TB outcome.
Conclusions: The high rates of under-reporting, failure to solicit relevant cultures and sensitivity tests, along with a low cure percentage rate achieved revealed critical deficiencies of key reference centers despite the importance of their status for TB care and demonstrate an urgent need to adopt practical and effective measures to improve the situation in order to assist those in treatment. According opinions of interviewed physicians, the agents and sectors more capable to transform this situation are in hospital itself. Furthermore it should be necessary the implementation of TCP at IIER.

PC-317-01   The relative infectiousness of TB-HIV co-infected patients

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Background: Previous studies indicate that co-infection with HIV may modify the transmissibility of tuberculosis. Some data suggests that co-infected HIV-TB patients are less likely to transmit infection while others do not support this conclusion. Here, we estimated the relative transmissibility of HIV-infected TB patients by measuring tuberculin skin test positivity in their household contacts.

Design/methods: Between September 2009 to August 2012, we identified and enrolled 5128 household contacts of 1609 patients with drug sensitive tuberculosis in Lima, Peru. Data was collected on the HIV status of index patients and their CD4 counts as well as other risk factors for infection specific to the index case, the household and the exposed individuals. Contacts underwent tuberculin skin testing to determine TB infection status. We estimated the association between exposure to an HIV-infected index TB case stratified on CD4 count and TB infection through multivariate modeling using the Poisson generalized estimating equation (GEE).

Results: After adjusting for covariates, we found that household contacts of HIV-infected TB patients with CD4 ⩽ 250 were less likely to be infected with TB (RR = 0.50, 95%CI = 0.29–0.88) compared to HIV-negative TB patients. When we restricted the analysis to children under 15 years old, we found that no children exposed to HIV-positive patients with CD4 ⩽ 250 were infected with TB, compared to 22% exposed to non-HIV infected patients. There was no significant difference between HIV-infected index cases with CD4 counts of > 250 and those not HIV-infected.

Conclusion: HIV infected index patients with CD4 counts 250 are less infectious than those with higher CD4 counts and without HIV infection.

PC-318-01   Demography and not HIV predicts active tuberculosis in a community sample in rural South Africa

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Background: Intensive case finding (ICF) for TB has been endorsed by the WHO as a TB control strategy in HIV-positive patients. Community-based integrated TB and HIV ICF (CBICF) is a promising approach particularly in hard to reach rural populations but available evidence about factors associated with successful case finding is limited. We report on factors associated with TB cases detected in a CBICF program in a high HIV and TB prevalence area in rural South Africa.

Methods: A team of nurses, health educators, and HIV counselors provided health education and voluntary integrated TB-HIV screening at community congregate settings, including taxi ranks, prisons, social grant pay points, municipality and home-based care events. Participants were questioned regarding TB symptoms; if present, a sputum specimen was requested for microscopy and culture and drug susceptibility testing. In conjunction with the DOTS office,

patients were notified of any positive sputum results and referred for treatment.

Results: Three hundred twenty-two community visits were conducted 2010–2012; 5457 local residents were screened and 35 cases of microbiologically confirmed TB were detected, leading to an overall 641/100 000 case notification rate. Predictors of TB included female gender ($P = 0.03$), lack of household electricity ($P = 0.04$), and community screening site ($P = 0.001$). Municipality events were the community site with the highest rate of notified TB cases (711/100 000; NNS 141). HIV status was not associated with a positive sputum result ($P = 0.22$). Symptoms associated with TB cases included cough ($P = 0.0002$), night sweats ($P = 0.03$), weight loss ($P = 0.05$), and chest pain ($P = 0.002$). Multivariate analysis of TB symptoms demonstrated that cough >2 weeks was the only significant symptom in this CBICF sample (sensitivity 38.2%, specificity 85%, negative predictive value 99.6%).

Conclusion: Predictors of microbiologically confirmed TB in a community-based case finding strategy included gender, poor socioeconomic status, and type of screening site. Despite high HIV prevalence, HIV status did not predict active TB in this community sample. In contrast to known HIV patient populations which utilize 4 symptom screen, cough >2 weeks may be sufficient for screening at the community level. These data point to the need to adapt approaches in different regions and populations and may be used to refine TB case finding strategies in resource-limited settings.

PC-319-01   Epidemiological and clinic profile of TB-HIV coinfection in Brazil by age group from 2007 to 2011

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Purpose and challenges: In Brazil TB is a public health issue of great magnitude, transcendence and vulnerability. National researches show that people living with HIV/AIDS present 35 times more chances of having TB, representing the main cause of death for infectious diseases. The study analyzes the clinic and epidemiologic profile of TB-HIV coinfection in Brazil, according to age, aiming to develop strategies to support this population.

Methods: A retrospective cohort study was conducted on TB-HIV coinfection. Data was obtained from the National Information System for Notification of Diseases and TB cases profile was established according to the variables: age, clinical TB form and classification of outcome therapy, from 2007 to 2011. The data analysis was based on the Qui-quadrado test and the 18th SPSS statistic software.

Results: From 2007 to 2011 Brazil presented about 363 625 new TB cases, in which 202 015 were HIV tested (55.0%) and 34 125 presented positive HIV serology, representing 9.4% of the TB-HIV coinfection. From the total of TB-HIV coinfection cases, the majority was part of the age group from 15 to 64 years old. Pulmonary TB was more common (62.6%) regardless of age, in relation to extrapulmonary TB. The pulmonary + extrapulmonary TB represented 37.4%. Comparing the coinfected population in the ⩽14 year old, 15–64 year old and ⩾65 year old age groups and the therapy outcome of pulmonary TB, extrapulmonary cases and pulmonary + extrapulmonary TB, there was a statistical difference for the 15–64 year old group. No statistical difference was found among coinfected people, clinical TB forms and outcome therapy, in the ⩾65 year old group when compared to the others.

Conclusion: There is a need to widen access to specialized care services for TB-HIV coinfection, especially for the 15 to 64 year old group, through strengthening adherence strategies, providing comprehensive health care services to the coinfected population, and developing a specific network for complex cases.

PC-320-01   Effectiveness of a partner notification pilot programme of newly HIV diagnosed persons in Barcelona, Spain

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Background: The contribution of HIV partner notification (PN) has been neglected in HIV prevention and little research on the effectiveness of HIV PN for getting people with undiagnosed HIV is available in Spain.

Methods: In 2012, every newly HIV diagnosed case was invited to participate as an 'index case' in a PN survey by providing contact information of sexual contacts in the last 12 months at two healthcare centres (hospital and non hospital) in Barcelona (Spain). The PN includes a test to rapid detection of HIV status. A descriptive study was performed. The effectiveness was determined by the proportion of newly HIV diagnosed among of studied contacts.

Results: A total of 119 index cases were identified, of whom 97 (81.5%) provided partner locating information. A total of 1955 partners were elicited, 147 (7.51%) were evaluate and the rest were not contactable. Thirty-four partners (23.12%) were known HIV-infected. Of the 113, who were tested by the PN Program, 23 cases (20.35%) were newly diagnosed with HIV. The total prevalence among the studied contacts was 38.8%.

Conclusions: Partner notification is useful for identifying HIV infections, and is an important HIV prevention intervention, with benefits to public as well as personal health. PN Program should be commissioned as a prioritised and essential part of sexual health services with appropriate funding for Health Advisers.

NEW INSIGHTS INTO THE EPIDEMIOLOGY OF TUBERCULOSIS IN CHILDREN

PC-321-01   Tuberculosis control in the paediatric population of a central hospital in Malawi

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Background and challenges to implementation: Malawi is one of the countries in sub-Saharan Africa with high TB notification rates, related to the high HIV prevalence (11% in the general population). By 2012, the HIV prevalence among all forms of TB was 60%. The NTP has put in place a recording and reporting system for TB cases, including TB-HIV services data for several years; however, paediatric TB has not been systematically reported to the NTP.

Aim: To determine the number of paediatric TB cases (0–14 years) who accessed TB-HIV management at Kamuzu Central Hospital (KCH) in Malawi over a ten-year period.

Methods: TB patients' records (registers) from 1st January 2003 to 31st December 2012 were reviewed. The existing national data for all patients (children and adults) reported at the national level was used as a control.

Results: TB case notifications (all forms) among paediatric patients at KCH decreased at an average rate of 8% per year from 2003 to 2012. This has also been observed among all other patients, though slightly lower, at 5% decrease per year. Paediatric TB cases with known HIV test results ranged from 42% to 69% from 2007 to 2012; no HIV test results were recorded before 2007. In contrast, 86% to 93% of all other TB patients had a known HIV status during the same period. ART uptake among paediatric TB-HIV patients was very low (5% in 2007 and 8% in 2012), with the highest rate in 2009 (27%); in contrast, ART uptake in all other patients increased from 17% in 2007 to 79% in 2012. Treatment success rates have been similar to all other patients, ranging between 78% and 88%, with low mortality rates between 3%

Table Tuberculosis in a paediatric population in a central hospital in Malawi (2003–2012)

Year	No. of paediatric TB patients evaluated (all forms)	% of paediatric TB patients with known HIV status	% of paediatric TB patients tested HIV+	% of paediatric TB-HIV patients on CPT	% of paediatric TB-HIV patients on ART	Treatment success rate	Mortality rate	% of paediatric TB patients T/O	% of paediatric TB patients lost to follow-up
2003	1031	0	0	0	0	87	4	3	7
2004	804	0	0	0	0	88	5	3	6
2005	846	0	0	0	0	84	3	4	8
2006	800	0	0	0	0	86	3	5	7
2007	764	12	71	49	5	88	3	3	6
2008	598	43	50	19	5	87	4	2	7
2009	709	83	67	36	27	81	6	6	8
2010	641	91	51	100	11	86	4	4	6
2011	457	97	55	82	3	78	4	9	9
2012*	724	97	42	78	8	86	3	5	7

* Evaluation was done for only 346 cases registered between January to June 2012.
TB = tuberculosis; T/O = transfer out.

and 6%; however, rates for lost to follow-up have been higher, varying from 6% to 8%, compared to 2% and 3% for adult patients over the past 10 years. **Conclusions and recommendations:** Low uptake of HIV services among pediatric TB patients at KCH may be attributed to poor coordination between TB and HIV clinics within the hospital and documentation problems at the TB clinic. High rate of lost to follow-up may be due to lack of interest by TB clinic staff to follow-up children who are not coming for TB treatment. The NTP needs to put in place interventions to improve pediatric TB management in the country especially in central hospitals.

PC-322-01   Epidemiology of paediatric tuberculosis in Kenya

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Background: Children are estimated to account for 6% of reported global tuberculosis (TB) cases; however, the burden is likely underestimated due to challenges with diagnosis, and reporting and recording, especially in resource-limited settings. In high TB and HIV-burden settings, such as Kenya, children are at an increased risk of TB because of frequent and close contact with adults with infectious TB. The Kenya Ministry of Health routinely collects surveillance data on adults and children registered for TB treatment, but has not previously described the epidemiology and trends of TB among children.
Design/methods: We analyzed data collected from five of eight provinces in Kenya where district level staff utilize personal digital assistants for routine reporting of TB data. We reviewed data for all children aged 0–14 years who were registered for TB treatment between January 2009 and December 2011.

Results: In 2011, 2121 children were registered for TB treatment comprising 4.8% (2121/44 087) of the total cases reported. The median age was 6 years (IQR 3, 11). The highest proportion of cases occurred in the youngest age group, with the age 0–2 years reporting 457 or 21.5% of all cases. Rift Valley North reported the highest number of cases (700 cases; 33%) followed by Nyanza North at (465; 21.9%). These trends were consistent throughout the previous 3 years. Most (89.4%; 1898) children received DOT from a household member during the intensive phase. Pulmonary TB was the most common form of TB, with 1504 (71%) of 2121. However, sputum was only collected in 28.9% (613/2121) of the children, with the majority (60%) collected from the adolescent group of 11–15 year olds. Among the 0–2 years, sputum was done for 19/457 (4.2%). The majority of pulmonary TB cases were diagnosed clinically as positive sputum results were only available in 40.8% (226)/1504 patients. Only 27 children had a sputum culture, and of these only 1 had a positive result and the rest the results were unknown either due to no documentation or delays in getting the results back. These findings were similar in the previous years with rates of PTB being similar.
Conclusion: The highest burden of paediatric TB is among the youngest children. Majority of cases are not laboratory confirmed, especially in the youngest children who are at highest risk of developing TB disease after infection. The national TB program needs to improve the strategies to prevent and diagnose disease in the young children.

PC-323-01   Surveillance of multidrug-resistant tuberculosis among children in South Africa

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Background: South Africa has the highest prevalence of multidrug-resistant tuberculosis (MDR-TB) in Africa. Released in 2012, the first global estimates of TB and MDR-TB among children were based on limited data. WHO estimates the risk of MDR-TB to be higher among children than adults in S. Africa. The extent to which existing recording and reporting systems capture pediatric drug-resistant (DR) TB in S. Africa is unknown.
Design/methods: We collected surveillance data for children <13 years diagnosed with MDR-TB in three S. African provinces from 2008–2010. We abstracted data from: 1) patient records at MDR-TB hospitals,

2) national Electronic DR TB Registers (EDR), and 3) the National Health Laboratory Services (NHLS) system. We created a comprehensive listing of patients within and across data sources using deterministic algorithms based on first name, surname and date of birth (DOB) or age. Then, we applied fuzzy logic probabilistic matching on the remaining entries using first name and surname within 3 letters, and matching 2 of 3 additional variables (registration year, DOB/age, or gender). Any unmatched entries were then manually compared, declaring a match if >3 of 5 criteria matched.

Results: Of 206 children with diagnosed MDR-TB, 173 (84%) were documented by NHLS, 90 (44%) were documented in hospital records, 85 (41%) were documented by EDR, and 59 (29%) were documented by all systems. Of 173 children with lab-confirmed MDR-TB, 84 (52%) were female with a median age of 5 years (IQR 0–10); 166 (96%) had MDR-TB and 7 (4%) had extensively drug-resistant (XDR) TB. Among 90 children registered at MDR-TB hospitals, 50 (56%) were female with a median age of 9 years (IQR 4–10). Among 173 patients with lab-confirmed MDR-TB, 111 (64%) were not registered at a designated MDR-TB hospital. Children <2 years were 5.9 times more likely to be unregistered for treatment at a designated facility than older children (95%CI 2.7–12.8).

Patients (<13) with MDR TB Documented in Selected Recording and Reporting Systems
South Africa*, 2008-2010
Unique Patients (Any Source) : N=206

National Lab System
N=173 (84%)

EDR Register
N=85 (41%)

MDR TB Treatment Unit
N=90 (44%)

N=101
N=10
N=3
N=59
N=5
N=11
N=17

* Eastern Cape, Gauteng, and Limpopo Provinces
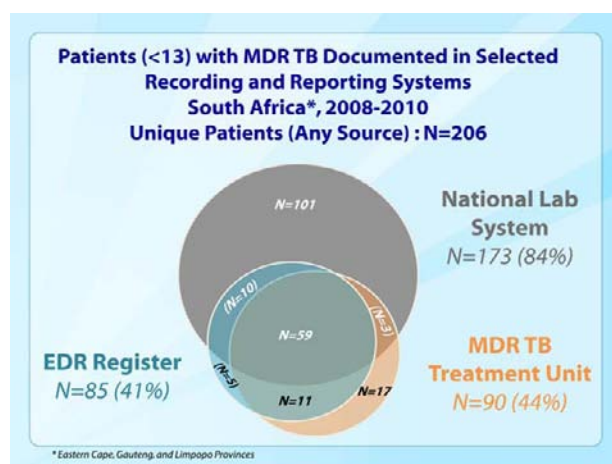
Conclusion: All systems underestimate the burden of diagnosed MDR-TB among children in S. Africa. The laboratory system captures the majority of children diagnosed with MDR-TB, but no single system includes all of them. Among children with laboratory-confirmed MDR-TB, nearly two-thirds were not on record at designated MDR-TB hospitals. Many children with MDR-TB, especially young children, are being lost between diagnosis and treatment.

PC-324-01   Clinical spectrum and hospital burden of childhood tuberculosis and MDR-TB at two hospitals in Kenya

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Background: Childhood TB is common and potentially serious. However good quality data on the burden and clinical spectrum of childhood TB are limited due to the difficulties making a diagnosis, particularly in low resource, high burden settings. Better quality data are needed to inform both clinical practice and allocation of public health resources.

Methods: We prospectively investigated all children who presented to a rural and an urban Kenyan hospital with one or more defined clinical features suggestive of TB. Following clinical assessment, chest X-ray, tuberculin skin test, mycobacterial culture and PCR of spontaneous/induced sputum, careful follow up, and other investigations as indicated, we assigned children to pre-defined diagnostic categories based on published definitions.

Results: Between 2009 and 2011 we investigated 2041 children for TB. 70 (3%) had bacteriologically confirmed TB, 63 (3%) had clinically highly probable TB, and 581 (29%) had possible TB (of whom 144 received TB treatment); TB was excluded in 1327 (65%) children. The figure shows the age distribution of confirmed and highly probable TB (CHPTB) cases. 107/133 (80%) CHPTB cases had pulmonary TB encompassing the full spectrum of radiological presentations; 8/107 (7%) were smear positive. 52/133 (39%) had extra-pulmonary TB, including 26/107 (24%) PTB cases. 31 (23%) were HIV co-infected and 61
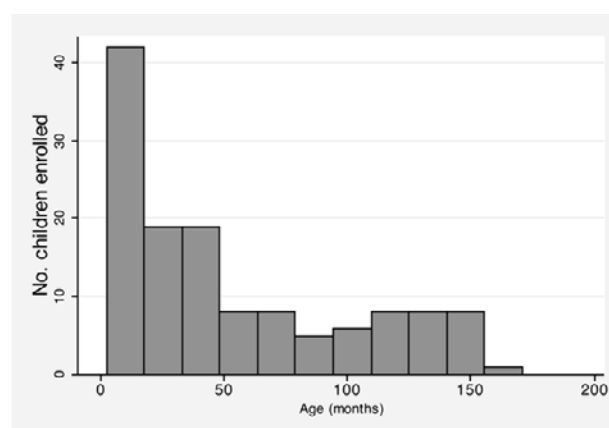
Figure Age distribution of confirmed and highly probably TB cases.

(46%) severely malnourished. 1 child had multi-drug resistant (MDR) TB (prevalence 1.4% [95%CI 0.0–7.7%] among confirmed cases). Children investigated and treated for TB accounted for 8% and 1% of the paediatric inpatient burden, respectively.

Conclusion: Based on broad, clearly defined inclusion criteria, this is the first comprehensive, prospective description from East Africa of the hospital burden and clinical spectrum of childhood TB, and one of very few from high burden settings. The proportion of childhood TB cases with MDR-TB provides valuable insight into the proportion of currently circulating strains that are multi-drug resistant. The true burden of TB on inpatient services derives from the large number of children in whom TB suspected, the resources for proper investigation of whom are unavailable in most African hospitals. Better and more affordable diagnostics for childhood TB are urgently needed to improve diagnosis in low resource, high burden settings like Kenya.

PC-325-01 Prise en charge de la tuberculose chez les enfants aux cliniques universitaires de Kinshasa

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Background: la tuberculose pédiatrique est un challenge diagnostic et thérapeutique en milieu défavorisé. L'objectif est de rapporter les déterminants cliniques et paracliniques et l'issue thérapeutique des enfants suivis pour tuberculose au département de Pédiatrie des Cliniques Universitaires de Kinshasa.

Design/methods: Etude rétrospective et descriptive, série des cas avec analyse des données sociodémographiques, cliniques et d'explorations réalisées de janvier 2006 à décembre 2011. Elle a concerné les enfants âgés de 0 à 15 ans, admis pour tuberculose sous toutes ses formes. Les fréquences et les moyennes ont été rapportées pour les variables d'intérêt.

Results: Sur 16 621 enfants reçus durant la période d'étude toutes causes confondues, 283 (1,7%) ont été traités pour tuberculose, avec un sex ratio de 1,17 en faveur des garçons. Parmi eux, 15 (5,3%) étaient âgés de 0 à 6 mois, 31 (10,9%) de 7 mois à 2 ans, 48 (16,9%) de 3 à 6 ans, 88 (31%) de 7 à 10 ans, et 101 (35,6%) de 11 à 15 ans. Seulement 249 (87,9%) patients ont pu réaliser l'examen du Ziehl, tandis que 102 (36%) seulement ont réalisé la culture sur milieu Lowensteïn. Au total 86 (30,4%) patients avaient une TP−, 40 (14,1%) avaient une TP+, 150 (53%) présentaient une TEP et 2 (0,7%) avaient une tuberculose chronique dont 1 avait une TB-MR documentée. Le patient avec tuberculose chronique est décédé avant de débuter son traitement. Au cours du traitement, 17 patients ont présenté une anémie, dont 3 ont

nécessité une transfusion, 4 patients ont présenté une légère élévation du taux d'acide urique. Chez 32 enfants, les transaminases étaient légèrement élevées entre le deuxième et le cinquième mois de traitement. Sept enfants (2,5%) avaient une co infection avec le VIH. Pour l'évolution, 200 (70,6%) patients ont terminé le traitement, 7 (2,5%) ont présenté un échec thérapeutique, 5 (1,8%) sont décédés, 48 (17%) ont été référés vers des centres de santé plus proche du domicile et 23 (8,1%) ont été perdus de vue.

Conclusion: Bien que le traitement des enfants atteints de tuberculose soit facilité par l'implantation du programme DOTS, cette enquête révèle que la prise en charge est encore insuffisante dans notre contexte. Ceci justifie le développement des techniques alternatives de diagnostic et la mise à disposition des formes galéniques pédiatriques.

PC-326-01 Pulmonary tuberculosis in childhood and adolescence in Portugal

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Background: In 2011, it was estimated half a million cases and 64 000 deaths in children (age < 15) due to TB. Some authors state that the incidence of PTB in children is still poorly documented and discuss diagnosis challenges at such young ages. In order to better understand the transmission of PTB and to contribute for the PTB control among children and adolescents, we studied the delay in diagnosis (time between the first symptoms and the diagnosis) and the number of PTB notified cases of children and adolescents between 2000 and 2010 in Portugal mainland.

Design/methods: The data sources were the National Tuberculosis Surveillance System (SVIG-TB) and National Statistical Institute. We performed a descriptive and analytic study for PTB notified cases, using the variables: sex, age, level of PTB burden in residence area, HIV co-infection, number of previous treatments, type of diagnosis and delay in diagnosis. Classical statistic techniques and survival analysis methods were used to characterize the age groups.

Results: From the total of 28 612 all notified cases of PTB, from Portugal mainland for the reviewed period, 985 were children and adolescents (from these about 49% were under 15). The average age is 11.9 years (sd = 6.1), 52.5% are male. The municipality with the highest number of cases of PTB was Oporto (31.6%) followed by Lisbon (26%). Only 1.8% of the cases were identified as HIV positive and 74.6% were diagnosed only when symptoms were present. 3.7% had at least one previous treatment (2.1% over 14 years). Concerning the delay in diagnosis, we observed a median of 41 days for ages under

15 and 45 days for age group 15–18. The log-rank test only revealed differences in survival curves for the number of previous treatments and the type of diagnosis ($P \leqslant 0.043$).

Conclusion: Among the studied group, it was found a higher incidence for the age group 15–18 years, consistent with other studies. The median delay for PTB diagnosis observed is lower than the one for the all population, found in a previous study. The possible reasons for this delay must be better understood so Public Health decision makers are able to adapt their actions towards an effective PTB control. As expected, known risk factors related to PTB for adults (alcohol, tobacco, drugs, reclusion and homeless) revealed to be not significant for children and adolescents.

PC-327-01   Epidemiological study of the distribution of paediatric tuberculosis patterns in Kenya

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Background and challenges to implementation: In Kenya about 11% of the total TB cases notified are in children below 15 years. Children continue to bear the brunt of TB especially because of challenges in diagnosis and complications of other lung diseases. Understanding the epidemiology and spatial distribution of TB in this population will help target interventions.

Intervention or response: All paediatric TB cases notified in the years 2009, 2010 and 2011 were included in the study. Aggregation was used to summarize district data points. Summary statistic was assigned to counties and expressed as a function of the population size to provide estimates of incidence rate per unit area. The arcGIS 10 software was used to develop choropleth maps showing information by 'filling' (colouring) each component area with colour, providing an indication of magnitude of the variable of interest. Global Moran's I statistic allowed us to find the characteristics of the global pattern (clustered, dispersed, random). LISA, the localised version of Moran's index was used to identify clustering, outliers, and map the polygon with statistically significant relationship with its neighbours and the type of relationship. A local statistic for measuring the concentration of spatially distributed attribute variable helped us identify hotspots in our spatial data.

Results and lessons learnt: A total of 24 962 pediatric TB cases were reported during the three years of study. The LISA statistic showed that majority of the counties had an insignificant relationship with its neighbours but Kitui, Embu, Isiolo and Meru counties were found to be having a high-high relationship with its neighbours implying clustering. Tharaka-

nithi and Machakos counties (with z-score > 2.58) were identified as the hot spots for year 2010 while counties surrounding it showed tendency towards becoming hotspots. Baringo, Uasin-Gishu, Nandi, Kisumu and Kericho were identified as cold spots in the year 2010. Isiolo and Meru showed some tendency towards being hot spots while Baringo showed tendency towards being a cold spot in 2011.

Conclusions and key recommendations: The spatial-temporal distribution of the disease provided an understanding of the dynamics of disease spread and clustering. The detection of space-time clustering was useful in identifying higher risk areas, where surveillance and control needed to be targeted. Studies to identify risk factors of pediatric TB in these areas are recommended.

PC-328-01   The changing pattern of paediatric tuberculosis infection during two time periods in Tygerberg Hospital, Cape Town

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Background: Tygerberg hospital is a central hospital with a general paediatric and subspecialist division. It serves the Eastern Metro of Cape Town which is known to have a high incidence of tuberculosis (TB). The areas referring to the hospital includes poverty-stricken parts of Cape Town with higher childhood morbidity and mortality rate expected. The aim of this study was to the assess change in the paediatric tuberculosis burden of disease in children <13 years during two defined time periods a year apart.

Design/methods: This study took place in the short stay ward at Tygerberg Hospital (TBH), Cape Town and is a retrospective interrupted time series study of routine health information undertaken during similar respiratory seasonal periods 1 April 2011 to 31 August 2011 and 1 April 2012 to 31 August 2012. Study participants and data were systematically identified from the routine short stay inpatient ward admission registers for the two periods. Data was analysed for age, sex, malnutrition status, TB diagnosis and discharge/or admission data from the ambulatory care clinics, using standard parametric and non parametric methods with SPSS software. The study was approved by the Stellenbosch University Ethics Committee.

Results: There were 2446 children admitted in 2011 and 2470 admitted in 2012 to the short stay ward in TBH. 6% (228/3809) of children had a TB diagnosis. 59% (130/219) were male. Median age (IQR) was 22.15 months (10.63–44.33). Tygerberg subdistrict accounted for the majority of referrals (45%; 96/212). The Eastern and Khayelitsha subdistrict accounted for 29% and 12%, respectively. There was a slight decrease in TB diagnosis, 7% in 2011 to 5% in 2012. CNS TB had a tremendous increase from 15% to

32%, but pulmonary TB (PTB) decreased from 64% to 43% and miliary TB was similar (2%). The majority (80% vs. 82%) were below the age of 5 years with respectively 34% and 28% younger than 1 year of age. Nearly a third were moderately to severely malnourished (26% in 2011 and 29% in 2012). Median length of stay remained 1 day in both periods, but more patients required admission to a ward for on-going care, with an increase from 45% in 2011 to 58%. Children with CNS TB were older than children with PTB (median 30.31 vs. 19.6 months, $P = 0.03$) and more likely to be admitted (88% vs. 43.9%, $P = <0.001$). Malnutrition was similar in the 2 groups ($P = 0.5$).

Conclusion: TB diagnosis was similar in the 2 study periods with a decrease in pulmonary TB. Of concern is the increasing number of patients with CNS tuberculosis at diagnosis (from 15 to 32%). The majority were younger than 5 years of age and malnourished in both time periods.

PC-329-01   Factors associated with extensively drug-resistant tuberculosis among children in four provinces of South Africa, 2005–2010

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Background: Pediatric drug-resistant TB accounts approximately 10–15% of the global drug-resistant TB burden. Factors, associated with extensively drug-resistant (XDR) TB are not well described in children.
Objectives: To identify predictors of XDR-TB among children being treated for drug-resistant TB in Eastern Cape, Gauteng, KwaZulu-Natal, and Limpopo provinces of South Africa (SA).
Design/methods: We analyzed demographic, clinical and laboratory data abstracted from TB registers, medical and laboratory records of TB patients < 13 years old, starting treatment for drug-resistant TB from January 1, 2005 to June 30, 2010 in health facilities of four provinces of SA. We used multivariable logistic regression to identify factors independently associated with XDR-TB disease compared to other forms of drug-resistant TB.
Results: Of 657 children starting treatment for drug-resistant TB, 383/657 (71%) were HIV positive, 431/657 (66%) had bacteriologically-confirmed MDR-TB, 42/431 (10%) had XDR-TB. 19/42 (45%) XDR cases had a prior history of TB disease, 3/19 (16%) previously had MDR-TB. 16/42 (38%) XDR cases had contact with drug-resistant TB within the family. Factors associated with XDR-TB included contact with a person with drug-resistant TB (aOR =

2.5; 95%CI 1.2, 5.3) and history of previous MDR-TB (aOR = 6.8; CI 1.6, 28.2, compared to no TB history). Of 657 children treated for drug-resistant TB, 300 (46%) were new TB cases; of these, 176 (59%) had primary MDR-TB, 7/176 (4%) had primary XDR-TB. Primary XDR-TB was significantly associated with contact with a known drug-resistant TB case (OR = 9.7; CI 1.8, 51.2).
Conclusion: XDR-TB occurred in 10% of all children diagnosed and treated for MDR-TB. Overall, XDR-TB among children was associated with the presence of a drug-resistant TB contact and previous history of MDR-TB. Primary XDR-TB disease was only associated with a drug-resistant TB contact in the family. Early detection of drug-resistant TB among family contacts is needed to appropriately diagnose and treat children with TB.

PC-330-01   The association between HIV infection and child tuberculosis deaths

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Background: The World Health Organization (WHO) has called for more accurate numbers of tuberculosis (TB) deaths among children by 2015. The annual incidence of TB for children in the Free State, South Africa, has been above 80/100 000 since 2009, with an estimated mortality of 2–4%. This study documented the child TB mortality in the Free State and evaluated associations with death, focusing on human immunodeficiency virus (HIV) infection.
Design/methods: The provincial electronic TB register, which records all TB cases on treatment in the province, was used to extract line data on all cases aged between 0 and 18 years recorded for the years 2009–2011. Duplicate entries were deleted, and entries with no age or outcome, were excluded from the analysis. Outcome was compared among three groups of children: unknown HIV status, HIV-infected and HIV-uninfected. Other associations (age, sex, microbiologically proven TB, type of TB and treatment, antiretroviral treatment, district) with outcome were also analyzed.
Results: There were 8863 child TB cases and the analysis done on the final database of 6453 cases for which the outcome was known (cure, completion of treatment, death, treatment failure). Of these cases, the overall mortality was 4.0% ($n = 259$), 46.0% had unknown HIV status (mortality 2.8%), 19.3% were HIV-infected (mortality 11.0%) and 34.6% were HIV-non-infected (mortality 1.7%). Mortality among 0–4 year old children was 3.2% (2.3% if HIV

status unknown, 12.3% if HIV-infected, 1.5% if HIV-non-infected), 5.1% among 5–14 year old children (3.7% if HIV status unknown, 10.1% if HIV-infected, 1.3% if HIV-non-infected), 4.6% among 15–18 year old children (3.2% if HIV status unknown, 11.4% if HIV-infected, 2.6% if HIV-non-infected). From 2009 to 2011 the percentage of HIV unknown cases dropped from 60.9% to 42.3% to 31.4%, as did the percentage of HIV-infected children for whom it was unknown whether they were receiving antiretroviral treatment (ART), from 64.8% to 47.4% to 26.2%.

Conclusion: HIV infection was associated with a 2.8× higher mortality rate compared to overall mortality. Comparing the three different age groupings used in the WHO reports, mortality rates were much higher in the HIV-infected children than the HIV-non-infected children (8.2× for 0–4 years, 7.8× for 5–14 years, 4.4× for 15–18 years). Our study suggests that if more children with TB are tested for HIV and started on ART, the mortality rate in children with TB will decrease.

PC-331-01   Burden of tuberculosis among infants in a rural cohort in Eastern Uganda

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Background: A well defined background rate of tuberculosis (TB) is needed to determine the sample size required for assessing the efficacy of new TB vaccine. Infants are the likely targets for new vaccines being developed. Estimates of incidence of TB in infants available to the National TB program are likely underestimates and aggregated for all children 0–14 years. Moreover, definitive diagnosis of TB in children is a challenge and requires diagnostic algorithms based on a combination of history, radiological and mycobacteriology.

Methods: We used active case finding methods to measure the incidence of TB in a cohort of 2500 BCG vaccinated infants aged 0–2 years in Iganga and Mayuge districts over 2 years of follow up as part of TB vaccine preparedness studies. The study was done between 2008 and 2011. TB suspects defined by presence of TB symptoms, history of contact and a positive TST were evaluated for active disease. We performed fluorescent microscopy, culture on both solid and liquid media, tuberculin skin testing and chest X-rays

on all TB suspects. Cases were classified into definite, probable and possible TB using an algorithm developed in South Africa. Person time was calculated from date of enrolment.

Results: We found one culture confirmed definite TB case, 27 probable TB cases and 34 possible TB. The combined incidence rate of definite and probable TB was 62 per 10000 (or 0.62%) person years (95%CI 41, 90). The median person time was 1.9 years. None of the confirmed TB cases were HIV infected. Using the Cox proportional hazards, gender, age, history of TB contact and presence of cough for more than 14 days were statistically significant predictors for TB. Cohort retention at 1 year was 89.5% ($n = 2097$) and 85.8% ($n = 1896$) at the 2 year follow up.

Discussion: The incidence of TB in this study was found to be much lower than what would be needed for a trial expected or reported in other parts of Uganda. This is not surprising given that active case finding was done in this mostly rural setting with a relatively low incidence of HIV both of which factors may have contributed to the low TB incidence observed. A more sensitive diagnostic test may have yielded a higher incidence. The site demonstrated ability to adequately form and track a cohort with a good cohort retention.

Conclusion: This setting and population therefore may not be suitable as a TB vaccine trial site but could be used for study of other diseases.

DEVELOPMENTS IN THE DIAGNOSIS OF TUBERCULOSIS IN CHILDREN

PC-332-01   Accuracy of Xpert® MTB/RIF in diagnosing smear negative childhood tuberculosis in Kampala, Uganda

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Background: Diagnosis of childhood tuberculosis (TB) is still a challenge because of its paucibacillary nature, the nonspecific signs of the children and difficult sample collection. Its detection and control is often a low priority in TB endemic regions as children often develop smear negative sputum and rarely transmit TB. The aim is to assess the accuracy of Xpert MTB/RIF in smear negative sputum samples compared to Ziehl Neelsen (ZN) staining procedure, and liquid culture (MGIT 960).

Methods: A prospective study was carried out from June 2011 to February 2013 at Nsambya Hospital, Uganda, one of the multicentre trial sites of the EDCTP TB CHILD Project. 191 and 245 children and adult smear negative sputum samples respectively were tested with Xpert MTB/RIF, ZN and MGIT 960. Additional information including chest X-ray, HIV status, tuberculin skin test and new TB diagnostic tests are also available. For children under 2 years, sputum induction was performed. Statistical analysis to evaluate Xpert MTB/RIF performances was included.

Results: Considering the 436 smear negative samples among children and adults, the analysis of Xpert MTB/RIF compared to MGIT 960 as reference test showed an overall sensitivity of 61.1% (95% Confidence Intervals, 44.9–75.2), specificity of 100.0% (99.1–100.0), positive predictive value of 100% (85.1–100.0) and negative predictive value of 96.6% (94.4–98.0). In particular, the sensitivity of the assay for children was 40.0% (16.8–68.7), and for adults 69.2% (50.0–83.5). Interestingly, among the samples collected from children with probable clinical diagnosis of TB, 4 Xpert MTB/RIF tests showed positive results on blood although negative on sputum and liquid culture. Moreover, 8 Xpert MTB/RIF positive/MGIT 960 negative samples were detected on adult patients, who showed a positive TB clinical outcome.

Conclusions: Since TB diagnosis is still a challenge in children, the use of Xpert MTB/RIF in the high TB burden country Uganda revealed its effectiveness in increasing TB case detection on smear negative patients, therefore allowing an early initiation of treatment. The statistics of Xpert MTB/RIF obtained from the analysis of smear negative adult TB cases in Nsambya Hospital within this EDCTP Funded Project are in the average output of other studies.

PC-333-01   Feasibility of using non-respiratory specimens for diagnosis of child tuberculosis

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Background: Child tuberculosis (TB), although cover 6% of the total incidence, has long been neglected and still under reported due to lack of gold standard diagnostic tool. Respiratory sample is very difficult to collect from children and the diagnostic yield is also very poor. There is an urgent need to develop effective TB diagnostic tool for children. We aimed to find out the diagnostic feasibility of non-respiratory samples for child TB and to compare their effectiveness with the existing ones.

Design/methods: We enrolled 103 children with symptoms suggestive of TB and 27 children as hospital control from the Dhaka Hospital of icddr,b and from the Chest Disease Clinic, Shyamoli. Diagnosis was mostly done clinically. Sputum, induced sputum and gastric lavage were collected for smear microscopy & culture (L-J & MGIT). T-SPOT.TB (Oxford Immunotec) and QuantiFERON-TB Gold in Tube (QFT-GIT, Qiagen) tests were performed on the blood samples and LAM Ag detection (Alere Determine™ TB LAM Ag kit, Alere Medical) and TB-LAMP (Eiken) tests on the urine samples.

Results: Among 58 out of 67 confirmed TB cases, positivity of smear microscopy, L-J & MGIT were found 18.9%, 25.9% and 25.9%, respectively. Urine LAM strip results were almost same in between MGIT positive and negative (25% vs. 23.9%). Urine LAMP positives were not significantly different between MGIT positive and negative (21.4% vs. 4.3%). We found QFT positive between MGIT positive and negative; 81.8% vs. 43.5%, $P = 0.022$ and T-SPOT positive; 75% vs. 22%, $P = 0.006$ respectively.

Conclusion: Urine tests were found less effective compared to MGIT in this small setting for child TB diagnosis. QFT and T-SPOT.TB tests were found more positive among TB patients. However, large scale studies might be beneficial to establish their effectiveness.

PC-334-01   Yield of one, two and three gastric aspirates to diagnose microbiological PTB in Botswana's children, 2008–2010

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Background: Botswana has the 10th highest annual incidence rate of TB globally, 503 cases per 100 000 population. Since September 2008, we have trained nurses in Botswana to do gastric aspiration (GA's) to enhance the diagnosis of pediatric pulmonary tuberculosis (PTB). Botswana's 2011 pediatric TB diagnostic algorithm recommends sending two samples when investigating a child for PTB. We aimed to determine the yield of one, two and three gastric aspirates to diagnose microbiologic PTB.

Design/methods: This project occurred while national TB management guidelines recommended collection of 3 samples, prior to their revision in 2011. We conducted a retrospective descriptive operational research

project in three health districts of southern Botswana that included all children (<13 years) referred from September 2008 to December 2011 for a GA due to suspicion of PTB. Subjects were excluded if on anti-TB treatment, culture results were unavailable, or a *Mycobacterium* other than TB was isolated. Microbiologic TB was defined as the presence of acid fast bacilli on sputum microscopy or culture of *Mycobacterium tuberculosis*. For yield of microbiologic PTB and equivalence testing between 1, 2 and 3 GA's, the point estimate and 90% confidence intervals (CI) were calculated. We used 90% confidence intervals to assess yield equivalence between 1, 2 and 3 GAs, and considered the impact of sample contamination on our results.

Results: Of 502 subjects referred for GA's, 415 were eligible for analysis. Of these, 217 (52%) were male, median age was 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 yield of microbiologic TB by number of GA's is shown (Table). Depending on whether or not our analysis included patients whose samples were partially contaminated, our estimates varied slightly. When including all contaminated samples (Table), results suggest no statistically significant difference in the diagnostic value of having a third GA sample.

Table   Yield of 1, 2, and 3 gastric aspirates collected to diagnose microbiologic TB in children

No. of GA's	Sample size *n*	Mean TB positive yield of those who had a GA %	90%CI
Excluding subjects with any contaminated samples			
1	374	14.7	11.8–18.1
2	316	23.4	19.5–27.7
3	264	25.8	21.4–30.6
Including subjects with >1 contaminated samples			
2	374	22.2	18.7–26.0
3	342	27.5	23.5–31.7

Conclusion: Although doing 2 GA's gave a higher yield than doing 1, the yield of doing a third GA was not consistently greater than doing just 2 GA's. Future studies should consider the complementary role of clinical diagnoses and cost per TB case detected in this setting. Improved data including documented HIV status is needed.

PC-335-01   Evaluation of Xpert™ MTB/RIF and Ustar TB IAD in fine needle aspirates for the diagnosis of paediatric tuberculosis lymphadenitis

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Background: At least 9 million new cases of tuberculosis (TB) disease occur annually, 31% in the African region. Approximately ten per cent of the global burden is in children, who often suffer severe disseminated forms of TB, most commonly lymphadenopathy. The value of fine needle aspiration biopsy (FNAB) in diagnosing mycobacterial lymphadenitis has been established. Two new nucleic acid amplification techniques applied on FNAB were evaluated in this prospective study.

Design/methods: Consecutive recruitment of children aged 8 weeks to 16 years, was done at Temeke District Hospital, Dar es Salaam, Tanzania. Recruitment criteria were clinical suspicion of TB lymphadenitis, palpable lymph nodes (≥1 cm) persisting for ≥4 weeks despite oral antibiotics and no TB treatment 12 months prior to recruitment. Palpation guided FNAB was performed and assessed by Xpert MTB/RIF, Ustar TB IAD, AFB microscopy, cytology and culture. Treatment was based on clinical assessment, chest X-ray and subsequent laboratory outcomes. Follow-up was done 5 months after recruitment.

Results: 53 children were recruited, of which 4 dropped out and 3 were lost to follow-up. Tests were

Xpert	Ustar	Cytology	Culture *M. tuberculosis*/ NTM	Anti-TB Rx
+	−	Suspected TB	*M. tuberculosis*	Yes
+	−	Suspected TB	*M. tuberculosis*	Yes
+	+	Suspected TB	*M. tuberculosis*	Yes
+	+	Suspected TB	—	Yes
+	−	Suspected TB	—	Yes
+	−	Acute lymphadenitis	—	Yes
+	−	Suspected TB	—	Yes
+	−	Suspected TB	Contaminated	Yes
+	+	TB & ZN positive	Contaminated	Yes
+	−	Necrotising suppurative lymphadenitis	Contaminated	Yes
+	−	Chronic reactive lymphadenitis	Contaminated	Yes
−	−	TB & ZN positive	*M. tuberculosis* BCG bovis	Yes
−	−	Chronic reactive lymphadenitis	*M. tuberculosis*	Yes
−	−	Reactive lymphadenitis	NTM	Yes
−	−	Reactive lymphadenitis	NTM	Yes
−	−	Suspected TB	Contaminated	Yes
−	−	Suspected TB	—	Lost
−	+	Unknown	—	No

+ Positive; − negative.

done on 51 patient samples available. Results from patients with at least one test positive are listed in Table. Xpert was positive in 21%, Ustar in 8%, Cytology in 21% and Culture MTB/NTM in 14%. After 5 months lymphadenopathy resolved in 27 cases of which 5 were not treated for TB.

Conclusion: Xpert™ MTB/RIF in FNAB appears superior in diagnosing TB compared to the established gold standard liquid culture and correlates fairly well with cytological examination. The combination of the three approaches should improve the diagnostic accuracy for paediatric TB lymphadenitis. Application of the Ustar TB IAD system seems to be not beneficial for the diagnostic algorithm.

PC-336-01   Rapid diagnosis of pulmonary tuberculosis in African children in a primary care setting using Xpert® MTB/RIF on respiratory specimens

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Background: Rapid, accurate diagnosis of pulmonary TB (PTB) in hospitalised children using Xpert® MTB/RIF is possible, but there are no paediatric studies in primary care, where most children are managed, and where microbiologic diagnosis is rarely attempted. The aim of this study was to investigate the diagnostic accuracy of Xpert in children in primary care.

Methods: Repeated induced sputum (IS) and nasopharyngeal (NPA) specimens were obtained from children with suspected PTB at a clinic in South Africa and diagnostic accuracy of Xpert compared to a reference standard of IS culture and to smear.

Results: 384 children (median age 38.3 months; 31 [8.1%] HIV-infected) had one paired IS and NPA; 309 had 2 paired specimens. A positive smear, Xpert or culture occurred in 5 (1.3%), 26 (6.8%) and 30 (7.8%) children respectively. Xpert on IS detected 17/30 culture-confirmed cases (56.7%, 95%CI 39.2–76.2) compared to Xpert on NPA [12/30 (40.0%, 95%CI 24.6–57.7), $P = 0.2$]. Similar accuracy was obtained in children with 2 paired samples. Incremental yield from a second IS was 16.7% for culture and 33.3% for Xpert. Specificity of Xpert on IS and NPA was 98.9% and 99.3% respectively. Xpert results were available sooner than culture (median 1 vs. 13 days, $P < 0.005$).

Conclusion: Xpert on respiratory specimens enabled rapid detection of PTB in children in primary care. Xpert detected almost 5 times the number of cases as smear microscopy; the yield increased substantially with a second test.

PC-337-01   Molecular genetic methods in the diagnosis of tuberculosis in children

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Background and challenges to implementation: In children with TB bacteriologic confirmation of diagnosis is rarely observed only in 3–10% of cases by cultural methods.

Intervention or response: To estimate of real-time PCR (RT- PCR) efficiency in diagnosis of tuberculosis in children.

Results and lessons learnt: In department of children's in institute of phthisiopulmonology during the period of time 2006–2012 were examined 296 patients age from 4–14 years with TB. Diagnostic complex included: Diaskintest® (DST)—immunological skin test with the use of recombinant allergen of *M. tuberculosis* specific proteins: ESAT-6 and CFP-10, QuantiFERON®-TB Gold (QFT-G), and multislice computer tomography (MCT). Bronchoalveolar lavage was simultaneously examined by RT-PCR (IS*1110* DNA fragment based) and culturing on Löwenstein-Jensen medium and BACTEC MGIT960.

Results: After examination on 217 children (91.9%) was diagnosed tuberculosis with intrathoracic lymph nodes, 10 children (4.2%)—with generalized tuberculosis and 9 children (3.8%)—with pulmonary TB. RT-PCR results were positive in significantly often compared to culture methods (13.1% [31] vs. and 4.1% [9], $\chi^2 = 13.32$, $P < 0.001$). In 71 children with tuberculosis of intrathoracic lymph nodes RT-PCR results were positive in 25.4% (18) in significantly often compared to culture methods (25.4% [18] vs. and 7.0% [5], $\chi^2 = 8.76$, $P < 0.01$). Specificity PCR in diagnosis generalized tuberculosis—90.0%, in diagnosis of pulmonary TB—55.6% in children.

Conclusions and key recommendations: RT-PCR was more sensitive in diagnosis of generalized tuberculosis and pulmonary TB in children in lungs compared to microbiological tests.

PC-338-01   Urinary lipoarabinomannan for the diagnosis of paediatric pulmonary tuberculosis: a pilot study

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Background: Urinary lipoarabinomannan (uLAM), a mycobacterial cell wall lipopolysaccharide, is useful for the diagnosis of tuberculosis (TB) in severely immunosuppressed HIV-infected adults, who are frequently sputum smear negative. Paediatric TB is also typically paucibacillary, although young children

progress rapidly to severe and disseminated forms of TB following infection. A rapid, point-of-care lateral flow test is currently available for the detection of uLAM. There are no published data on the performance of uLAM in children with suspected TB.

Methods: Prospective diagnostic cohort; children <5 years of age with suspected intrathoracic TB were consecutively enrolled from Tygerberg Children's Hospital, Cape Town, 30 April 2012–28 February 2013. Entry criteria were symptoms suggestive of TB, or atypical symptoms with ≥1 of: 1) recent close contact with a TB source case; 2) reactive Mantoux skin test; 3) chest radiograph suggestive of TB. From every participant, 2 gastric aspirates and 2 induced sputum samples were obtained for mycobacterial smear and culture. A urine sample obtained at enrolment was tested at room temperature using Determine TBLAM Ag ([Determine TB-LAM] Alere, Waltham, MA, USA), and was read by 2 independent blinded readers within 96 hours of collection.

Results: Urine was tested in 41 (11 female, 8 HIV positive, median age 13.4 months) of 59 children: in 18 urine collection failed. Of 22 children diagnosed with TB, 10 (45%) had culture-confirmed TB by any sample. uLAM was positive in 6 children: 3/10 (30%) of culture confirmed cases, 2 additional children with a clinical diagnosis of TB and 1 child with chronic respiratory symptoms. Among children with TB, all those with positive uLAM results were severely malnourished (weight-for-age Z-score <−2) compared to 6/17 with negative uLAM. Only one HIV positive, severely immunosuppressed child (CD4 count 21, 1.3%) had culture confirmed TB: he was uLAM positive. One case of confirmed TB had discordant uLAM result between readers.

Conclusion: More studies are needed to investigate the value of uLAM for the diagnosis of childhood TB.

PC-339-01   Detection of *Mycobacterium tuberculosis* antigens or DNA impacts the rapid diagnosis of tuberculous meningitis in children

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Background: Tuberculous meningitis (TBM) is the most common form of neurotuberculosis and the fifth most common form of extrapulmonary TB. Early diagnosis and prompt treatment are the cornerstones of effective disease management. The accurate diagnosis of TBM poses a challenge due to an extensive differential diagnosis, low bacterial load and paucity of cerebrospinal fluid (CSF) especially in children.

Design/methods: This study was designed to assess the utility of molecular approaches for the diagnosis of TBM by 1) quantifying *M. tuberculosis* GlcB, HspX, MPT51, Ag85B and PstS1 proteins as well as *M. tuberculosis* DNA in CSF filtrates and 2) comparing the performance of antigen and DNA detection tests, and 3) assessing the impact of these tests on the standard diagnosis of TBM. CSF specimens were categorized according to the uniform case definition rule based on clinical criteria, CSF parameters, CT findings and presence of extraneural TB.

Results: We compared the utility of ELISA and qPCR for the detection of *Mycobacterium tuberculosis* proteins (GlcB, HspX, MPT51, Ag85B and PstS1) and DNA for the rapid diagnosis of TBM. CSF filtrates ($n = 532$) derived from children were classified as 'Definite' TBM (*M. tuberculosis* culture positive, $n = 29$), 'Probable and Possible' TBM ($n = 165$) and 'Not-TBM' including other cases of meningitis or neurological disorders ($n = 338$). ROC curves were generated from ELISA and qPCR data of 'Definite' TBM and non-tuberculous infectious meningitis (NTIM) samples and cut-off values were derived to provide ≥95% specificity. devR qPCR, GlcB, HspX and PstS1 ELISAs showed 100% (88;100) sensitivity and 96–97% specificity in 'Definite' TBM samples. The application of these cut-offs to 'Probable and Possible' TBM groups yielded excellent sensitivity (98%, 94;99) and specificity (98%, 96;99) for qPCR and for GlcB, HspX and MPT51 antigen ELISAs (sensitivity 92–95% and specificity 93–96%). A test combination of qPCR with GlcB and HspX ELISAs accurately detected all TBM samples at a specificity of ~90%. Logistic regression analysis indicated that these tests significantly added value to the currently used algorithms for TBM diagnosis.

Conclusion: The detection of *M. tuberculosis* GlcB/HspX antigens/devR gene DNA in CSF is likely to improve the utility of existing algorithms for TBM diagnosis and also hasten the speed of diagnosis. These tests may also have the potential to be used for the rapid and accurate diagnosis of other paucibacillary forms of TB.

PC-340-01   Comparison of the diagnostic use of *Mycobacterium tuberculosis* LAM-ELISA and LAM strip tests in childhood tuberculosis

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Background/objectives: Diagnosis of tuberculosis is usually established by the detection of mycobacteria

through smear microscopy or culture. Both methods rely on the presence of mycobacteria in the sample. Due to the paucibacillary nature of the disease in children, detection of acid-fast bacilli often fails and diagnosis can be difficult. Lipoarabinomannan, a cell wall component of mycobacteria, is released into the urine of TB patients. Advantages of LAM detection in urine include the ease of sample collection and test performance, especially when using the new lateral strip test. In this study we compare the diagnostic performance of the *Mycobacterium tuberculosis* LAM-ELISA and the new LAM lateral strip test in children with suspected tuberculosis.

Methods: In a prospective study with a follow-up of at least 12 months, 133 TB suspected children were enrolled and subsequently assigned to predefined diagnostic subgroups, based on microbiological and clinical findings. Sensitivity and specificity of *M. tuberculosis* LAM-ELISA and the LAM strip test at time of diagnosis were assessed in comparison to mycobacterial culture and/or clinical TB diagnosis as reference standard.

Results: Sputum culture confirmed the diagnosis of tuberculosis in 18 (13.5%) of 133 children. The LAM-ELISA detected 8 (44%, 95% confidence interval [CI] 21.5–69.2), the LAM-strip 5 (28%, 95%CI 9.7–53.5) of these cases on the first day of the study. The sensitivity of both tests was higher in HIV positive compared to HIV negative children, with 70% (95%CI 34.8–93.3) vs. 13% (95%CI 0.3–48.2) for the LAM-ELISA and 50% (95%CI 18.7–81.3) vs. 0% (95%CI 0.0–33.6) for the LAM strip test, respectively. In terms of specificity, no child where TB could be reliably excluded had a positive LAM test.

Conclusion: In this paediatric cohort both tests demonstrated an acceptable sensitivity in HIV positive TB infected children. For HIV negative children, the sensitivity was extremely poor. The *M. tuberculosis* LAM-ELISA detected considerably more TB cases than the easier to use LAM strip test.

FLOODS, MIGRANTS, CAMPS: INNOVATIONS IN TUBERCULOSIS PATIENT CARE

PC-341-01 Social capital and tuberculosis treatment adherence in a study of alcohol treatment among tuberculosis patients in Russian Federation

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Background: Alcohol use disorders (AUD) are associated with decreased tuberculosis (TB) treatment success and increased risk of developing drug resistance among TB patients. Patients with AUDs are often less able to adhere to treatment. This analysis assessed the effect of social capital on TB treatment adherence in a randomized controlled trial of alcohol treatment among TB patients with AUDs in Russian Federation.

Methods: This is a secondary analysis of the IMPACT study: a randomized controlled trial of 196 TB patients with AUDs who received alcohol use interventions through TB providers. Interviews at baseline, 3 and 6 months captured demographic, clinical, substance use behavior and social-emotional factors. Instruments included the Timeline Follow-Back Calendar (alcohol use); depression (CESD); consequences of alcohol use (Addiction Severity Index) and questions assessing social capital. Cognitive social capital was defined as higher access to resources, greater trust in people, belief in honesty of other people, and ability to turn to family or friends in time of need, based on a verbally administered questionnaire. Missing data for 6-month visit was multiply imputed (MI). MI-adjusted association of social capital, demographic, clinical and treatment factors on treatment adherence (defined as documented taking >80% of prescribed doses) were assessed using logistic regression. Models were determined using stepwise regression including a priori determined variables.

Results: Overall, TB treatment adherence was high (89%). In univariable analysis, increased cognitive social capital at baseline and age over 40 were statistically significantly associated with better adherence ($P < 0.05$). Diagnosis with multi-drug resistant tuberculosis, incarceration history, higher baseline alcohol use, higher ASI alcohol composite score, and higher CESD score were negatively associated with adherence ($P < 0.05$ for all). The final model included cognitive social capital (OR 1.65, 95%CI 1.09–2.51),

number of heavy drinking days per month at baseline (OR 0.91, 95%CI 0.83–0.99) and baseline MDR status (OR 0.45, 95%CI 0.19–0.84).

Conclusion: Higher social capital was significantly associated with greater adherence to TB treatment in this study population, when controlling for baseline drinking behavior and MDR status. Interventions aimed at increasing social capital and support among TB patients with AUDs could increase TB treatment adherence and improve treatment outcomes.

PC-342-01   MTB by front-line workers in a tribal district in India: a pilot study

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Background and challenges to implementation: Front Line Workers/Rural Health Care Providers (RHCPs) are most often 'first point of contact' for curative services in many villages especially in tribal and remote geographic areas. A paper based referral mechanism is used to capture the data on referrals made, results of their sputum examination and the management of those diagnosed with TB. However, Front Line Workers (FLWs) including RHCP's and Lab Technicians (LTs), often lack information about referred chest symptomatic cases. Validating the referrals at designated microscopic centers is resource intensive, time consuming and difficult. It is also difficult to attribute the contributions made by FLWs towards strengthening National TB Control Programme.

Intervention: 'ComCare' is an easily customizable mobile platform that tracks the referred cases, supports FLWs and creates a central database on real-time basis. The ComCare application is being piloted in three blocks of Khunti, a tribal district in Jharkhand, India covering a population of 255 372 (80% district population). Two ComCare applications have been developed. One application is being used by RHCP and NGO supervisor and one by LTs. FLWs are provided with 10 Lava Android phones. ComCare aids FLWs with guidance on key counselling points also. Each counselling point is reinforced by image and audio clip that FLW uses to engage their clients. Messages displayed regardless of the result of sputum examination are focused on 'Shared Air, Safe Air' (Flow chart of intervention attached).

Results and lessons learnt: ComCare based management system assists in follow up of referred chest symptomatics by FLWs for diagnosis and treatment of tuberculosis efficiently. It reduces the delay in communication of the test results and saves resources by reducing the number of visits by FLWs to the diagnostic centres. It helps to assess the contribution of FLWs in total symptomatic cases examined and TB

Flow Chart of Mobile Application
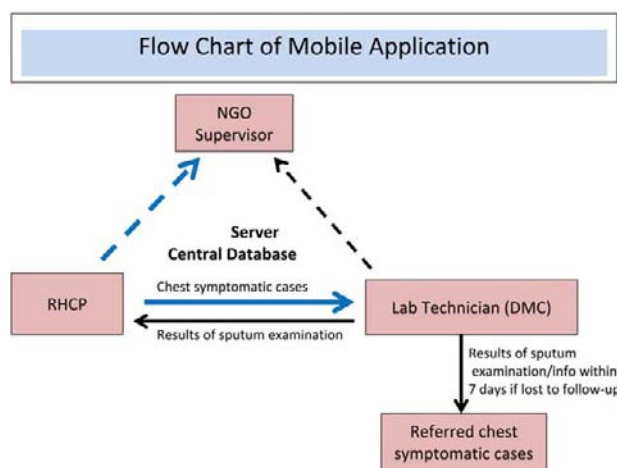
cases diagnosed. This application gives the data of lost to follow up cases and creates a real-time central database which in turn helps in retrieval of cases.

Conclusion: Targeted intervention in tribal district is getting benefitted by deploying ComCare. Monitoring and evaluation of the project intervention has strengthened through usage of this mobile platform. Retrieval of lost to follow up cases could be simplified by using this mobile platform. This also facilitates compilation and analysis of data.

PC-343-01   Identification of tuberculosis cases among flood affectees in Sindh: an innovative approach

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Background: In 2010 flood brought an enormous destruction and misery for Pakistani people, in all 17 flood affected Districts of Sindh about 7.27 million people were displaced, 100 000 houses, 350 health facilities were destroyed and this resulted in about 2800 TB cases discontinuing their TB treatment.

Objectives: 1) To identify TB patients living in the camp, who had discontinued their anti-TB treatment due to displacement. 2) To detect and register new TB cases among residents of camp.

Design/methods: The intervention was conducted at a relief camp established by the government authorities at Razzak Abad flood relief camp ten kilometers away from city Karachi. Total population of the camp was 8509[3] including children, women and men from different parts of province Sindh affected by flooding. Established TB clinic was managed by a TB trained team like doctors, field officers and one lab technician. Announcement on mega phone was made by team on a daily basis and visited families to inform them about availability of TB clinic and delivered educational messages about TB. All other four clinics were also requested to refer the confirmed and

suspected new cases to the TB clinic. All clients attending TB clinic were asked complete history and clinical examination was performed by trained physician. Recording and reporting tools were filled for those who were already on anti TB treatment and their treatment was discontinued due to displacement. They were provided anti-TB treatment and were advised for follow-up during their stay in camp.

Results: A total of 411 clients attended TB clinic during 42 days, out of which 18 TB patients were identified who had discontinued their treatment due to displacement. Total 40 new TB suspects were identified among them 03 were diagnosed for TB, all 21 cases were registered for treatment during their stay in the camp and referred back to nearest TB DOTs centre on their return to their homes for continuation of treatment.

Conclusion: Through above innovative approach we were able to find 18 TB patients who had discontinued treatment due to displacement and re-started their treatment, 3 new TB cases were diagnosed. This public private partnership in TB provides evidence that similar type of work can be repeated at any place in disaster situation to identify TB cases to prevent transmission of TB infection in displaced populations and prevent drug resistance and other consequences.

PC-344-01   Expérience d'une caravane de lutte contre la tuberculose chez les populations nomades dans le Sahel du Burkina

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Background and challenges : Burkina Faso est un pays à forte incidence de tuberculose avec 55 TPM+ pour 100 000 Hbts (2010). Cette prévalence est encore plus dans la Région du Sahel. L'union des religieux et coutumiers du Burkina est une organisation qui regroupent les structures religieuses et traditionnelles du Burkina. Elle a pour objectif de créer une synergie dans les interventions. A cet effet elle met en œuvre depuis 2009 un projet de prévention et de dépistage de la TB. Dans le cadre de ses activités elle a organisé en juin 2012 une caravane de lutte contre la TB dans la Région du Sahel au Nord du Burkina. Le Sahel est comprend des populations transhumante.

Intervention or response : L'objectif de cette intervention a été de contribuer à la prévention et au dépistage de la TB dans la Région sanitaire du Sahel. La stratégie a consisté à organiser dans un village des visites portes par une équipe composée d'un agent de santé, deux animateurs communautaires. Au cours de la visite un entretien avec les personnes composantes du ménage que l'on trouve à l'heure de la visite est organisé. Les animateurs font une sensibilisation de proximité sur la TB avec les membres de la famille sous la supervision de l'Agent de Santé. L'agent de

santé procède à des prélèvements de crachat chez les personnes suspectes de la famille qui sont envoyés au laboratoire. Au cas où il y a nécessité d'une confirmation, le 2ème animateur communautaire (qui connaît individuellement les suspects) se charge du 2ème prélèvement de crachat.

Results and lessons learnt : En 10 jours 942 ménages ont été visités, 5637 personnes ont été sensibilisées à la prévention de la tuberculose, 379 crachats soumis au dépistage, 14 TPM+ ont été dépistés et mis sous traitement.

Les leçons apprises de cette intervention sont :

- La caravane se révèle être une activité à gain rapide en ce sens qu'elle a permis de dépister et mettre sous traitement 14 malades en 3 jours de travail par district sanitaire
- La collaboration entre les acteurs communautaires et les agents de santé a été renforcée par un renforcement de capacité des acteurs communautaires pour le prélèvement de crachats
- L'implication des leaders religieux et coutumiers a une forte influence sur l'adhésion des populations aux programmes de santé

Conclusions and key recommendations : La caravane permet de toucher les populations et de dépister en peu de temps beaucoup de cas de TPM+. Elle est de ce fait une activité à gain rapide.

PC-345-01   Drivers of treatment interruptions among private-sector tuberculosis patients in Myanmar

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Background: Myanmar is one of 22 high TB burden countries. Poor adherence during the treatment of drug sensitive TB can lead to the development of drug resistance, and approximately 10% of retreated TB cases in Myanmar are multidrug-resistant. Since 2004, PSI/Myanmar has been providing TB treatment through the 'Sun Quality Health' (SQH) franchised network of private doctors. These providers are trained in TB case management and provided ongoing support to ensure quality care.

Aim: To study examine provider behaviors linked to treatment interruption among patients attending SQH clinics.

Design/methods: Analysis was conducted using client exit interview data from 716 TB patients attending SQH clinics between 2010 and 2013. Patients were asked whether the doctor provided information about TB drugs, if the doctor took any action to ensure they took TB drugs regularly and whether they had stopped taking their TB drugs for one or more

days. Chi-square test and simple logistic regression were run using SPSS V15.0.

Results: Among all TB patients studied, 8.2% reported interrupting treatment by at least one day. Data indicate that drug interruption was significantly associated with provider behavior. For examples, individuals who answered 'No' to the question 'Did the doctor do anything or ask to make sure you take TB drugs regularly?' were 2.5 (95%CI 1.4, 4.7) times more likely to interrupt treatment compared to those who did receive reminders from their doctors. Individuals who answered 'No' to the question 'Did your doctor explain to you about TB drugs?' were 3.5 (95%CI 1.5, 7.8) times more likely to interrupt treatment compared to those who were provided information about TB drugs. From 2010 ($n = 124$) to 2013 ($n = 181$), key provider behaviors associated with the prevention of treatment interruption have decreased. The proportion of patients saying that their doctor did remind them to take drugs regularly has fallen from 92.7% to 78.5% ($P < 0.05$), whilst the proportion of patients who remember having TB drugs explained to them has fallen from 98.4% to 95.0% ($P > 0.05$).

Conclusion: These findings indicate that treatment adherence is enhanced by providers giving patients critical information on TB drugs and reminding patients about the importance of adherence. Given the decreasing frequency of these behaviors among SQH providers, provider refresher trainings and routine support and supervision should concentrate on the importance of these behaviors.

PC-346-01   Gender and tuberculosis: burden of tuberculosis among women living in IDP camps in Afghanistan

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Background and implementation challenges: Afghanistan is among the 22 TB high burden countries in the world with low case detection rate of 48% in 2011. During 2012, ATA-AP/ACREOD implemented active TB case detection within 15 internally displace populations (IDPs) camps of 6 provinces of Afghanistan to contribute increases case detection in the country. The project was financially supported by TB REACH grant which started in November 2011 and ended in August 2012. Beyond TB REACH project, IDPs were neglected from the TB care services of the system.

Intervention or responses: Active case finding among IDPs was done by Mobile TB teams which consisted of a doctor, a nurse and a lab technician. The Mobile TB team performed TB symptoms screening among IDPs in each of the target six provinces through door to door visits. Mobile Teams informed IDPs about TB symptoms, identified TB suspects among them

and collected sputum samples from identified suspects and delivered the samples to the designated fixed laboratory for microscopic examination. This study reviewed and analyzed the data to find difference between SS+ diagnosed among men and women.

Results and lessons learnt: Totally, 66135 adults (50% male and 50% female) were screened for TB in IDPs camps. Among them, 286 SS+ cases (109 males and 177 females) were diagnosed. The data shows though equal number of men and women were screened, but 62% of cases were diagnosed among women.

Conclusions and key recommendations: Study results reveal that women are more vulnerable, getting TB infection and developing TB in IDPs camp's settings. Thus, further studies are needed to explore associated factors. Now, awareness generation targeting women on TB symptoms, early treatment benefits, route of TB transmission and prevention should be sustained.

PC-347-01   Health education intervention delivered by mobile telephone SMS to improve the knowledge and adherence of tuberculosis patients in hospitals

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Background: Central Java Province has shown an improvement of treatment service since establishment of DOTS strategy in early 2000. Unlike health center which showed a very good case holding for years, hospital's treatment outcome remains below the expected result. Low adherence of TB patients treated in hospital was often found as a result of long communication channels between health provider in hospital and non-adherence patients. This study aims to improve tuberculosis-related knowledge of treatment observer by providing health education intervention delivered by mobile telephone short message service (SMS). It is expected, the improvement of treatment observers' knowledge will in turn improve tuberculosis patients' knowledge and adherence.

Design/methods: A clustered randomized controlled trial was designed to compare knowledge improvement and adherence of 95 pairs of patient and treatment observers as treatment group to 61 pairs of control. A six week intervention consisted of tuberculosis-related information for treatment group and health-related information for control group was delivered via SMS every two days. A multivariable-logistic regression analysis was employed to measure the estimated effect of intervention by comparing the indicators before and after intervention.

Results: Beside improving adherence, SMS improved comprehensive knowledge of TB patients better than its improvements on basic knowledge. The likelihood of improvement among patients in treatment group was 11 times higher for comprehensive knowledge and 2 times higher for basic knowledge. Male treatment observers were 2 times more likely to improve comprehensive knowledge than female observers. After being adjusted by group, gender, age and education level, it was found that patients with comprehensive knowledge improvement are 2 times more likely to comply the TB medication compare to those who have no comprehensive knowledge improvement.

Conclusion: SMS significantly improve patients' adherence by improving comprehensive knowledge of TB. Males can be given higher priority as treatment observer for any health education intervention using information and communication technology.

PC-348-01   Nursing interventions to decrease treatment failure among smear-positive tuberculosis patients along the Thai Myanmar border

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Background and challenges to implementation: High treatment failure rates had been observed among smear-positive TB patients in a Thai setting with diverse populations including non-Thai migrants and marginalized populations. Between 2008 and 2009, the failure rates were reported as 6.6% (5/76) and 7.7% (5/65), respectively. These rates were much higher than WHO recommendation (3%).

Intervention or response: This action research was to evaluate the rate of treatment failure among smear-positive TB patients who participated in the nursing intervention and to assess patient satisfaction with the nursing intervention. The study was carried out in a tertiary 350-bed hospital near Thai-Myanmar border which is situated with shops and business. The nursing intervention was provided to 35 consecutive smear-positive TB patients registered from January to May 2011. The nursing intervention included: (a) an appointed full-time TB nurse manager, (b) patient-centered care planning with interdisciplinary approach, (c) referral system linking hospital with community and (d) patient's home visit. The multidisciplinary team consisted of 89 members from each hospital department and local TB program. Patient satisfaction was assessed at baseline and at the end of treatment. Patient characteristics were collected from TB register. Data were entered into SPSS. Frequency, percentage, mean, standard deviation and pair-sample t-test were used for data analysis.

Results and lessons learnt: Over half of patients were male (63%) and an average age was 45 years. Patients were registered as 29 new smear positive, 3 re-

lapse and 3 treatment after failure. All patients had known their HIV status and 9% had HIV infection. The treatment failure rate was 2.9% and treatment success rate was 82.9%. Patient satisfaction at the end of treatment was significantly higher than at the baseline ($P < 0.05$, a mean score of 56.9 for the baseline and 61.2 for the end of treatment).

Conclusions and key recommendations: The nursing intervention could help reduce the treatment failure rate among smear-positive patients. This intervention can be applied in other settings and non-Thai patients whom patient-centered approach is tailored to meet their needs.

TUBERCULOSIS CONTACT INVESTIGATIONS

PC-349-01   Assessment of chest X-ray screening among tuberculosis household contacts in Metro Manila

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Background: In 2010, CATCH TB project used household CI to find more TB cases in Metro Manila. Symptom screening was used by 87 health centers. By June 2012, there were 8676 index cases with 30 226 contacts identified. Only 86% of these contacts were evaluated or seen by health workers, and 589 secondary TB cases were found. Quarterly yield ranges from 1–4%. To improve case finding, we included chest X-ray (CXR) as additional screening in 4th quarter of 2012. All household contacts in selected health centers were sent for CXR. The cost for the procedure was borne by the project. We want to determine if adding CXR is more effective than symptom screening only, and compare the yield of secondary TB before and after it was introduced.

Design/methods: A retrospective cohort study was done. All household contacts from October to December 2012 were included. A case-control study was also done. Contacts evaluated and secondary TB cases found in selected health centers in 4th quarter of 2011 (controls) were compared to same period in 2012 (cases). Data were encoded and analyzed using EpiInfo.

Results: Cohort study: there were 5396 contacts identified from 1651 index cases. Age ranged from 0–86 years (median 22), 33% were 0–14 years, and 52% were females. Eighty-eight percent were evaluated and 55 (1%) had TB. Of the 1469 contacts for CXR, only 157 (3%) availed. This was due to administrative

constraints, and financial barriers among contacts. Compared to those screened by symptoms only, those with CXR were 23 times more likely to be diagnosed with TB (CI = 13.7–37.8). There was no difference between secondary TB cases found from contacts of smear positive or negative index cases (RR = 0.65, CI = 0.38–1.09). Case-control: there were 962 and 1262 contacts identified, and 76% and 88% of them were evaluated in 2011 and 2012 respectively. Fifteen (2%) secondary TB were seen in 2011, and 23 (2%) in 2012. Contacts in 2012 where two times more likely to be evaluated (OR = 2.34, CI = 1.86–2.95). There was no difference in the yield of secondary TB cases (OR = 0.99, CI = 0.49–2.01) in 2011 and 2012.

Conclusions: CXR when added to TB symptom screening was more effective in detecting secondary TB cases than symptom screening only. Free CXR may have encouraged contacts to consult, as shown by the increased proportion of contacts evaluated in 2012. However, it failed to show any difference in improving the yield of secondary TB. Ensuring accessible CXR services is important to take advantage of its effectiveness.

PC-350-01 Risk of developing tuberculosis according to interferon gamma release assay results among tuberculin converters in a contact investigation

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Background: Follow-up tuberculin skin test (TST) 8–10 weeks later after initial contact investigation is recommended to the tuberculin negative responders in Korea. A booster effect by the previous BCG vaccination at newborn or NTM infection can cause TST conversion by the initial tuberculin stimulation. The tuberculin converters who aged less than 35 years old are recommended to receive preventive treatment without interferon gamma releasing assay (IGRA) after exclusion of active tuberculosis. This study is aimed to compare the risk of developing tuberculosis according to the results of IGRA among tuberculin positive converters (defined as follow-up TST; ⩾10 mm and increasing 6 mm or more than initial TST) at the end of the window period.

Design: Prospective cohort study. Adolescent contacts of infectious tuberculosis patients were reexamined with TST and IGRA performed with the Quanti-FERON-TB Gold In-Tube 3–6 months later after initial contact investigation. Development of tuberculosis was traced by periodic chest X-ray screening and matching with tuberculosis surveillance system

up to 28 months. Chest CT was taken for confirmation if active TB lesion was suspected on chest X-ray. **Results:** A total of 2704 participants were evaluated with the initial and follow up investigation. Among the 245 tuberculin converters at the follow-up TST, 59 (24%) participants showed positive IGRA results. Others showed negative response. Preventive therapy was administered to 35 IGRA positive and 4 IGRA negative participants. Pulmonary tuberculosis was developed in 10 participants including 3 bacteriologically confirmed cases. All the tuberculosis cases were positive to IGRA and not received preventive therapy. Periodic follow up screening detected 8 cases including 1 bacteriologically confirmed case. Five cases were diagnosed at the first follow-up.

Conclusion: IGRA might be considered to the recent tuberculin converters who were initial tuberculin negative responders in contact investigation when preventive treatment is provided.

PC-351-01 Successful investigation of household tuberculosis contacts In Buriram Province in Thailand during 2011–2012

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Background: Tuberculosis remains a major public health problem in Thailand. The goal of the National TB Program is to find TB cases and ensure high treatment success rates. Household contacts of TB patients have a high risk of developing tuberculosis. Therefore the search for TB in household contacts is a critical component of an active case finding strategy.

Objective: To evaluate approaches for screening and diagnosing household contacts of index TB patients in 2011–2012 at Buriram Provincial Hospital.

Design and methods: After identification of an index case in the TB clinic, the TB nurse interviewed the patients on potential household contacts. A one stop service to screen household contacts of index cases was set up where all contacts were invited for screening. They were interviewed of any symptoms and examination by chest X-ray in children under 15 year chest X-ray (AP Lateral) and TB skin test was conducted.

Results: Of 283 index cases in 2011, 138 families (48.76%), were screened involving 528 individuals. Of these 464 cases (87.88%) were actively screened and TB was identified in 9 children below age 5 (1.70%) and in 60 cases (11.36%) who were adults. In 2012, among 359 index TB cases, 84 families were screened (23.39%) with 274 individuals, all of whom were actively screened. TB was found in 4 children (1.46%) ⩽5 and in 23 adult cases (8.39%).

Conclusion: Active screening of household contacts is feasible at the local level and yields a high proportion of cases. This is an important strategy to improve

treatment outcomes by early identification and preventing ongoing transmission in the community. The approach does not require massive investment but only taking an active approach to case finding by health care staff in the TB clinic.

PC-352-01 Significance of contacts in the manifestation of tuberculosis as an infectious disease

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Aim: To evaluate the importance of contact in the manifestation of tuberculosis, i.e., to answer the question: what age, which forms manifest tuberculosis in this category of patients and what is the connection with the source of infection, i.e., which is the period of contact to the manifestation of tuberculosis as an infectious disease.

Method: The histories of 88 cases of tuberculosis in persons who have been in contact with a person sick from tuberculosis, for the period 2010–2012, retrospectively were analyzed.

Results: The number of patients with tuberculosis who were in contact accounted for 7.5% of the total number of registered patients (1177). 42 (47.7%) were male and 46 (52.28%) female. 28.4% belonged to the age group of 0–14 years, 54.5% of the age group 16–44 years and 17% of the age group older than 44 years. 58 of the 63 analyzed (92%) were pulmonary, and 5 of 63 (8%) out of pulmonary tuberculosis. In 44.9% (26/58) *Mycobacterium tuberculosis* was isolated from sputum. Retrograde analyzing the source of infection, it is usually a close family member in 32/42 (76%). In 5/42 (11.9%) source is another member of the family (grandmother, grandfather, aunt). In 2/42 (4.76%) source is a roommate from the prisoner's room, and 1/42 (2.4%) source is classmate or neighbor. In 75.6% of the source of infection in the family is one of the parents, in 13.5% brother or sister, and at 8.1% is one of the spouses. Analyzing the time period for manifestation of tuberculosis after the contact, most often (in 17/30 or 56.7%) tuberculosis is diagnosed within the first 3 months after the contact, with 23.3% of tuberculosis manifests itself in a period of 3 to 6 months, and after 6 months of contact tuberculosis manifested in 6/30 (20%) of the respondents. Length of time of contact to manifest tuberculosis is correlated with the age of the diseased.

Conclusion: In 7.52% of registered TB patients, contact with person suffering from tuberculosis is confirmed. In 76% of the cases source is in the family, and the most common source in the family is one of the parents (75.6%). After the contact with the source of infection, tuberculosis usually manifests in the first three months (56.7%). Taking into account the fact that tuberculosis can manifest after 6 months of contact, there is a need for contact tracing in an extended period of time.

PC-353-01 Experiencia exitosa en el manejo operativo de tuberculosis en la Nahualtl población en Zacatlán, Puebla, Mexico, en 2011

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Background and challenges to implementation: Se ha demostrado que la TB afecta preferentemente grupos específicos (personas privadas de su libertad, indígenas, etc.). Aproximadamente un 35% de la población total en Puebla es indígena; los usos, la calidad de los servicios de salud es deficiente si no se considera los usos y las costumbres de la población indígena; sobre todo en TB afecta la adherencia obteniendose como resultado deteccion y curación baja por lo que es necesario establecer estrategias operativas a nivel local con personal de salud capacitado y sensibilizado.

Intervention or response: Se desarrolló en Jilotzingo, Zacatlán en Puebla de Enero a Junio de 2011; la población de esta jurisdiccón es Nahuatl y es habitual que no acudan a las unidades de salud para solicitar atención. Se brinda información en Nahualt con oferta de baciloscopía; al desarrollar la búsqueda de casos y la visita al domicilio a una de las personas con diagnóstico de TBP se encuentran 4 casos de TB entre los convivientes. Se brindó información en su lengua sobre la enfermedad durante toda la duración del tratamiento. Se trabajó de manera conjunta con el Curandero de la Comunidad, se brindó información sobre los mitos y realidades de la TB; sin embargo los afectados pidieron que se guardara discreción por temor al estigma y la discriminación en la comunidad. el tratamiento fue otorgado en el domiclio.

Results and lessons learnt: Se revisaron 13 personas de este núcleo familiar, se encontraron 5 casos de TB el 100% curaron, se identificaron 3 menores de cinco años, 3 personas de entre 5 y 14 años y 2 personas mayores de 15 años a quienes se les tomó baciloscopía resultando negativas, se brindo Terapia preventiva con Isoniazida a los contactos que lo requieren; se hace vigilancia posterior al término del tratamiento cada 6 meses por 2 años.

Conclusions and key recommendations: Es necesario manejar la Tuberculosis con el enfoque de interculturalidad que garantice la adherencia y la curación de las personas con TB que son indígenas, la participación de la comunidad y del personal de los servicios de salud es fundamental; la información y la capacitación reducen el estigma y la discriminación.

PC-354-01   Evaluation of the tuberculosis contact tracing system in Khartoum State, 2008

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Background: The contact tracing procedures in Khartoum state had been established many years ago, no proper assessment was carried yet. So, this research represents a crucial need that is aiming to evaluate the system and discover its strengths, weakness and gaps.
Materials and methods: This is a cross-sectional, descriptive study of pulmonary TB contact tracing procedures in Khartoum state. The study population included: sputum-positive TB patients and 159 health care providers at 53 TBMUs distributed in 7 localities. All smear-negative and extra pulmonary TB patients had been excluded from the study. The representative sample of contacts ($n = 361$) was used to assess the procedures and effectiveness of contact tracing through a standardized administered questionnaire while the indicators relevant to the number and incidence of cases among contacts have been applied on all contacts ($n = 1780$). Number of sputum positive cases of pulmonary TB patients in each locality (seven localities) were obtained using TBMUs records (NTP information office), and found to be 1780. Estimated number of contacts was calculated using household number of three and found to be 5340.
Results: About 52% of contacts of TB patients in this study were not registered (the percentage of the difference between the estimated and the registered number of TB contacts) in the contacts records in the TBMUs and were not detected. This is expected as the current contact detection procedure in Khartoum State is passive rather than active, this means that the procedure is lagging behind the actual number of contacts which should be detected. 78.8% of the registered contacts were not sputum tested for AFB, while 21.2% were tested. The detection rate among contacts who were sputum tested was found to be 8.8%, which was based on single sputum test. Mostly the practice is carried without a standardized checklist; this may result in loss of many contacts before requesting them for sputum test. The incidence of smear positive among contacts of sputum smear positive pulmonary TB patients was found to be (8.8%), 83 times the estimated incidence in the general population. 76.5% of the interviewed health care providers were exposed to on-job training, mostly carried by the NTP staff during the routine supervisory visits. However the knowledge of the health care providers as assessed by the scoring system showed to be poor for 52.4% of them.
Conclusions:
• The practice of primary screening which was carried without a standardized check-list was not satisfactory. About 52% of the contacts of smear positive pulmonary TB patients were not registered.
• The contact tracing procedures were inadequate, the case detection rate incidence of smear positive among contacts of sputum smear positive pulmonary TB patients was found to be (8.8%), 83 times the estimated incidence in the general population.

PC-355-01   Contact investigation for tuberculosis and factors associated to risk of active disease

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Background: Tuberculosis (TB) remains a threat to the health of people worldwide. About one-third of the human population would have harbor the *Mycobacterium tuberculosis* and be contained as latent infection representing an important reservoir of potential reactivation of TB. Contacts of TB patients are a high-risk group for developing active TB.
Objective: To assess risk factors to active TB among household contacts of TB patients from Instituto Clemente Ferreira a reference center for tuberculosis for the City of Sao Paulo, Brazil.
Design/methods: A prospective analysis of TB contact was undertaken from January 2008 to December 2010. It was analyzed 404 patients and excluded 65 whom tuberculin skin test did not perform. It were obtained medical information regarding age, sex, size of tuberculin skin test (TST), associated diseases, time and type of intimacy to TB patients, BCG vaccination and latent TB treatment outcome.
Results: A total of 339 TB contacts was evaluated, 105 (31%) were children and 234 (69%) adults. The incidence of positive TST among all contacts was 55%. Among the contacts analyzed 18 (10%) develop TB during the study period. From those patients, 15 did not take ILTB treatment, and 3 stopped it before completing two months. In 13 (72%) the active TB occurred in first two years of TB exposition. There was no correlation between TB developed and tobacco, presence of comorbidities was not higher in contact with active TB.
Conclusion: The main risk factor for TB development was no treatment of latent TB infection and having a positive tuberculin skin test.

PC-356-01   Household contact tracing of MDR- and XDR-TB patients in Tugela Ferry, KwaZulu-Natal, South Africa, 2006–2012

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Background: In 2006, the world's largest cluster of XDR-TB and MDR-TB was reported from Tugela Ferry in Msinga sub district. Extremely high rates of

HIV co-infection, morbidity, mortality, and health care and community transmission was documented. Since then the number of MDR XDR-TB cases are decreasing and fewer cases are identified through contact tracing.

Interventions: Since 2006, Department of Health contact tracing mobile teams are visiting MDR XDR-TB households. This is one component of the response to the epidemic implemented with the support of a multinational collaboration.

A comprehensive integrated TB and HIV strategy was implemented, including:

- Strengthening TB DOTS program facilities, staffing and policies and practices
- Evaluating, improving and monitoring inpatient and outpatient infection control
- Reducing reliance on inpatient hospital care
- Integrating TB and HIV diagnosis, care and treatment
- Initiating antiretroviral therapy: ~12 000 people through 2012
- Implementing TB & HIV healthcare facility and community intensive case finding
- Implementing decentralized integrated community treatment of MDR-TB.

Results and lessons learnt: From 2006 through 2012, a total of 523 MDR and 456 XDR-TB index cases were reported. In temporal association with above strategies, a significant and sustained decrease in both XDR and MDR cases has occurred, dropping to 6 XDR and 30 MDR cases in 2012. A significant drop on household transmission has also been reported with 3 positive MDR-TB contacts in 2010, 2 in 2011 and 3 in 2012.
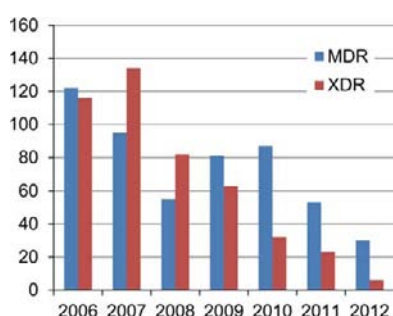
Conclusions and key recommendations: XDR/MDR-TB epidemics remain extremely serious in Tugela Ferry, but, in association with strengthened, resourced, comprehensive and integrated TB and HIV public health and clinical strategies, this experience stands in contrast to increasing global cases of XDR/MDR-TB and demonstrates that explosive drug resistant TB epidemics, even in impoverished, high HIV prevalence rural communities in sub-Saharan Africa can be successfully combatted.

PC-357-01 Concurrent tuberculosis infection and disease among close contacts of active pulmonary tuberculosis in Bandung

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Background: Tuberculosis remains a major health problem in Indonesia with a mortality rate estimated at 27/100 000 in 2011. People in contact with TB patients are a high-risk group for developing the disease and active screening of these people may improve case detection rates and improve disease control. Unfortunately, active screening has not yet been implemented as a national policy in Indonesia.

Methods: A cross-sectional study was conducted from January to December 2012 at a Latent TB Clinic in Bandung, West Java. Close contacts of newly diagnosed smear-positive TB patients were invited for TB screening. Initial screening included a Tuberculin Skin Test (TST). For those who were TST positive (induration ≥ 10 mm) a chest radiograph was obtained to determine TB disease. Those with radiographs suggestive of TB disease were referred to DOTS Clinic in Hasan Sadikin Hospital or primary health care clinics for further investigation. The CDC TB Classification System was used to define TB disease in close contacts.

Results: From 211 TB pateints, 828 close contacts were identified. Of these, 729 were eligible for TB infection screening and 478 (66%) were willing to be screened. Of these 268 were adults and 210 were children (<18 years old). There were 20/268 (7.5%) adults and 43/210 (20%) children classified as Class 3 (TB, clinically active); 140/268 (52%) adults were in Class 2 (TB infection, no TB disease). Of all children screened 59/210 (28%) received preventive treatment.

Conclusions: Among close contacts of active pulmonary TB, the concurrent TB infection and active disease found in people who came for screening is high especially among children. Actively screening contacts of people with confirmed tuberculosis makes an important contribution to TB disease control.

PC-358-01 Feasibility and yield of tuberculosis contact investigation under program conditions in Dar es Salaam, Tanzania

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Background: Tuberculosis contact investigation is an efficient, targeted approach to case finding routinely implemented in high resource settings. However, in most low and middle-income countries where the TB burden is concentrated, contact investigation is not undertaken and data on impact of contact investigation are scarce. In 2012, WHO released guidelines to aid programs in establishing strategies for contact investigation. We initiated a randomized controlled trial of contact investigation in Tanzania utilizing the WHO guidelines. We report the yield and feasibility of contact investigation among household contacts of sputum smear positive pulmonary TB cases under program conditions.
Design: Index cases were enrolled from 5 clinics in Kinondoni District, Dar es Salaam. Cases were consented, asked to name their contacts, and randomized to an intervention group (contact investigation) or control group (standard of care). 9 TB Contact Investigators (TBCIs) were trained and stationed at study clinics. TBCIs visited households of intervention cases within 1 week of diagnosis, conducted a TB symptom review, and referred those with symptoms for clinical evaluation. The clinic registers were reviewed monthly to determine whether contacts from either group were diagnosed with TB.
Results: From March 2012 to March 2013, 632 index cases were enrolled (331 intervention, 301 control). In the intervention, mean age of the index case was 33.8 years, 70.7% were male, 19.3% were HIV+, 7.3% reported prior TB, and each named a mean of 4.5 contacts. The control cases were not significantly different for any of these variables. 1160 contacts were named by the intervention cases; 690 (59.5%) contacts were screened; 12.5% had at least one symptom consistent with TB. Mean time spent conducting a household visit was 127 minutes; mean number of visits/household was 1.1; mean number of contacts screened/visit was 2.7. Thirteen secondary cases were found, indicating a yield of 1.9% of evaluated contacts or 15.1% of symptomatic contacts.
Conclusions: Despite an extended pilot phase where contact investigation procedures were optimized, the yield was lower than expected. Possible reasons include an incomplete % of contacts screened, or cases resulting from reactivation rather than rapid progression to disease. In response, we implemented a second household screening 3–6 months after the index case was diagnosed to evaluate whether this window is more efficient in finding secondary cases.

MOLECULAR DIAGNOSTIC TESTS FOR TUBERCULOSIS

PC-359-01 Laboratory costing for new molecular diagnostics in Cape Town, South Africa

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Background: A costing study was undertaken as part of the Technology, Research, Education and Technical Assistance for Tuberculosis (TREAT TB) research study, 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).
Aim: To determine the total laboratory cost of Line Probe Assay (LPA) in the National Health Services Laboratory in Cape Town in 2012, under routine operational conditions.
Methods: Costing was performed using the Foundation for Innovative New Diagnostics (FIND) excel-based laboratory costing analysis tool developed as part of FIND demonstration project (2008). It used an ingredients approach and time-observation studies of laboratory procedures. Cost inputs were reviewed and updated to 2012 costs, and several assumptions were revised based on current laboratory practice. Laboratory costs were sub-divided into: (1) overhead, (2) building space (3) equipment (4) staff, (5) supplies (reagents, chemicals and consumables), (6) training, (7) transport.
Results: Cost per sample tested for smear, culture and LPA was US$35.72 (ZAR 259.2) and with second line drug sensitivity testing (SL DST) US$45.23 (ZAR 328.25). Cost per valid test result for smear, culture and LPA was US$36.84 and with SL DST US$46.35. Currency conversion is based on average rates in 2011.
Conclusions: Limited resources require the National TB Control Programme to utilize tests in a cost conscious manner. Costing is a key component in the decision to implement new diagnostic tests. Costs in this study were found to be higher than had been presented in the FIND demonstration study. This suggests that costing analysis should also be done under routine operational conditions to inform the scale-up of new diagnostics. A comparative costing study is being undertaken for Gene Xpert in the same setting.

PC-360-01 EXPAND-TB: experience of establishing tuberculosis laboratories in resource-limited settings—laboratory strengthening and sustainability

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Background: Phasing out development support projects in resource-limited settings remains challenging. EXPAND-TB is a UNITAID-supported six-year project implemented as a collaboration with WHO (GLI, GDF–Stop TB Partnership) and FIND. The project focuses on accelerating access to new, rapid and WHO-endorsed diagnostic technologies for patients at risk of MDR-TB in 27 low and middle-income countries in Africa, Central Asia, Eastern Europe, Latin America, and South-East Asia. We describe a transitioning model that will allow the project to be effectively phased-out while maintaining laboratories operations beyond 2014.
Methods: The EXPAND-TB project has entered its fifth year of operations, which is critical time to ensure meeting project goals and successfully transitioning the laboratory support to partners. Throughout the project we have assured political commitment and policy review; upgraded laboratory facilities; delivered commodities for liquid culture and drug susceptibility testing (DST), line probe assay (LPA), and rapid speciation; and initiated a capacity building and mentoring program for laboratory staff in collaboration with partners. At present we are developing a transitioning strategy to ensure that this level of operations is maintained beyond the project, including a set of tools that will allow governments and local/international partners to provide the necessary support. These include budgeting; procurement and forecasting; and laboratory strategic plan tools.
Results: By the end of 2012, 36 965 cases of MDR-TB were detected in 65 laboratories in 24 countries (32% of the global target), excluding three countries which are still at the early stages of implementation. In the operational laboratories the supported technologies have been integrated into the national diagnostic algorithms but continued support is required to ensure their rational use. Costly infrastructure and biosafety upgrades, inadequate and high turnover of human resources, complex importation regulations and poor sample transportation systems are amongst the major limitations to improved laboratory diagnosis of MDR-TB, which we aim to address through our transitioning strategy model.
Conclusion: The EXPAND-TB project has successfully supported TB laboratory work in 27 countries, contributing to narrowing a dignostic gap for MDR-TB cases. We currently focus on continuous improvement while developing a transitional strategy to ensure long-term sustainability.

PC-361-01 Are there any cost savings from using the line-probe assay for MDR-TB diagnosis in the Archangelsk region of Russia?

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Background: LPA and MGIT tests are currently used for diagnosis of multidrug-resistant (MDR) TB in Archangelsk region.
Objectives: To determine the additional cost (or savings) associated with LPA speedier diagnosis.
Design/methods: As a part of the cost-effectiveness analysis conducted alongside clinical trial (PROVE-IT), the cost data on 112 patients were collected at the baseline and two subsequent interviews. MDR-TB diagnosis was established with LPA test, and a control test with MGIT was done on the same patients. In addition the 'historic' cohort ($n = 161$) of 'matched' patients provided a control sample of MDR-TB diagnosis. Cost-effectiveness analysis was conducted from the societal perspective and included the costs to the health system and patient costs. Health system costs were identified using accounting data specific to the universal health care coverage in Russia and included cost of tests (equipment, consumables and reagents), clinical personnel time and medications. Patient costs were collected with the STOP-TB questionnaire adapted to Russian socio-economic conditions and included travel cost incurred by patients and guardians, lost productivity, additional expenses associated with hospitalization, supplementary medicine and food. The preliminary results correspond to the first follow up.
Results: In comparison to MGIT, LPA-based diagnosis corresponded to the speedier assignment of the correct treatment (by mean value of 27 days in sm+, and by 16 days in sm− patients) and immediate increase in cost of MDR-TB medications (by $717 per sm+ patient and $468 per sm− patient). However, assuming that the speedier diagnosis and treatment correspond to the earlier seroconversion and subsequent discharge, the increased cost of medications was offset by reduction in hospital costs for a sm+ patient (by $436). There was no equivalent cost reduction in sm− patients who received ambulatory treatment before and after MDR-TB diagnosis. After a speedier discharge sm+ patients faced higher expenditures (by $17) due to travelling to a DOT place

and supplementary food. In sm− patients the increase in expenditures was almost entirely due to supplementary food ($17).

Conclusion: LPA is associated with additional cost of $7 per extra day with correct diagnosis in sm+ patients and $28 per extra day with correct diagnosis in sm− patients.

PC-362-01   LPA technology for rapid detection of *Mycobacterium tuberculosis* complex directly from AFB-positive slides

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Background: All the pulmonary tuberculosis patient cases need to be investigated following diagnosis of the suspected case and then at regular follow-up intervals of treatment especially in case of failure as tuberculosis or another else with a basic method, sputum smear microscopy (SSM), in both modern and remote areas in every country. But, AFB positive by SSM cannot be differentiated between *Mycobacterium tuberculosis* and non-tuberculous mycobacteria (NTM) including susceptible or resistant strains.

Design/methods: A total of 222 AFB positive slides both Ziehl-Neelsen stain and fluorescence stain were performed the DNA extraction and used LPA technology, HAIN Genotype MTBDR*plus*®, for detection of *M. tuberculosis* and MDR-TB.

Results: The LPA results demonstrated that *M. tuberculosis* could be detected 187 in 222 slides (84.23%). Out of 187, 157 *M. tuberculosis* AFB positive-stained-smear slides could provide the drug resistance information as MDR-TB 14.01% (22/157), rifampicin resistant 2.55% (4/157), isoniazid resistant 20.38% (32/157) and susceptible for rifampicin and isoniazid 63.06% (99/157).

Conclusion: This study provides the new information in TB laboratory from positive-stained-smear slides for the possible advantage of the increased bacteriological confirmed for TB cases and MDR-TB suspected cases. The method of extraction DNA from AFB positive-stained-smear slide together with LPA technology should be an appropriated method to improve bacteriological yield for mycobacterial confirmation in the limited culture laboratories.

PC-363-01   Evaluation of real-time polymerase chain reaction for direct identification of mycobacteria in clinical samples and liquid culture bottles

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Background: The direct identification of mycobacteria with polymerase chain reaction (PCR) is becoming a very interesting issue, especially regarding its efficacy and feasibility. Reduced identification rate when PCR is applied on acid-fast bacilli (AFB) smear-positive sputum samples of low positivity (AFB1+) was recently noticed. The aim of our study was to determine would it be reasonable to perform PCR only on smear-positive clinical samples of higher positivity (AFB 2+ and AFB 3+). Furthermore, we wanted to determine is it more convenient to use PCR on smear-positive liquid culture bottles because of larger amount of present mycobacteria than in a clinical samples.

Methods: The study was conducted at the University Hospital Centre Zagreb, Zagreb, Croatia. We performed PCR for mycobacteria on smear-positive clinical samples and diagnostic yield was evaluated according to the AFB score (AFB 1+, AFB 2+, AFB 3+). PCR was also done on smear-positive Mycobacterium Growth Indicator Tube (MGIT) culture bottles. LightCycler real-time PCR assay (LightMix®, TIBMOLBIOL, Berlin, Germany) to discriminate between *Mycobacterium tuberculosis* complex and other *Mycobacterium* spp. was used. Conventional auramin stain and culture on solid Löwenstein-Jensen medium was also done.

Results: Fifty-two smear-positive clinical samples included 33 sputum samples, 12 bronchoalveolar lavage (BAL) samples, 6 bronchial aspirates and 1 pleural fluid. Among them 51 *M. tuberculosis* complex and 1 non-tuberculous mycobacteria (NTM) was isolated by conventional culture. The PCR had

Table   Results of direct detection of mycobacteria from 52 smear-positive specimens by PCR

Smear result (no.)	Culture result (no.)	No. of isolates identified by the PCR		
		M. tuberculosis complex	*Mycobacterium sp.*	Negative
AFB 1+ (28)	*M. tuberculosis* complex (27)	14 (52%)	0	13 (48%)
	M. xenopi (1)	0	0	1 (100%)
AFB 2+ (11)	*M. tuberculosis* complex (11)	11 (100%)	0	0
AFB 3+ (13)	*M. tuberculosis* complex (13)	13 (100%)	0	0

100% identification rate for AFB 2+ and AFB 3+ samples, but only 14 out of 27 (52%) AFB 1+ samples were identified by PCR (Table). Among the 28 smear-positive MGIT bottles, 21 *M. tuberculosis* complex and 7 NTM isolates, including *M. gordonae* (*n* = 6) and *M. intracellulare* (*n* = 1) were identified by conventional culture. PCR had 100% identification rate for smear-positive MGIT bottles.

Conclusion: PCR efficacy is related to the mycobacterial burden in tested clinical sample. It is excellent and rapid method for identification of mycobacteria grown in MGIT culture bottles. PCR used on clinical samples is not reliable enough to rule out the diagnosis of tuberculosis in paucibacillary pulmonary tuberculosis, but should be used on clinical samples with higher AFB positivity (AFB 2+ and AFB 3+). With this approach financial and practical demands regarding the influence of PCR on diagnostic process and choice of treatment would be justified.

PC-364-01 Development of a molecular platform for the rapid diagnosis of multidrug-resistant tuberculosis

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Background: The emergence of multidrug-resistant (MDR) tuberculosis (TB), defined as resistance to at least rifampin and isoniazid, represents a threat for TB control, especially in high burden countries and Eastern Europe. Conventional drug-susceptibility testing is slow and rarely available due to the lack of adequate laboratory facilities to perform it. A faster diagnosis through the use of cost-effective and user-friendly tools is needed for the detection of MDR-TB cases. A first generation of a rapid molecular diagnostic assay for MDR-TB detection by a lab-on-chip (LoC, VereMTB™), suitable for testing other poverty related diseases, was developed within the FP7 TM REST Project, and an improved version is under evaluation.

Methods: The VereMTB™ provides an all-in-one device for fast-PCR amplification and detection of targets on a low-density microarray. Most clinically relevant mycobacterial species are identified by targeting the 16S rRNA gene and IS*6110* insertion sequence. A multiplex PCR and specific probes were designed for the analysis of rpo*B*, kat*G*, and inh*A* as the most frequently mutated genes involved in the MDR phenotype of *M. tuberculosis* complex (MTBC).

Results: The assay allows identifying MTBC, and 10 clinically relevant non-tubercular mycobacterial (NTM) species, including *M. abscessus*, and *M. avium* complex. The most common mutations involved in DR TB are detected by targeting D516V, S531L, H526D/Y (rpo*B*), S315T (kat*G*), and c-15t, t-8c, t-8a (inh*A*); other mutations can be identified by a negative signal from wild type probes. The performances of the LoC were improved in the current version of the assay by optimizing the multiplex PCR and the array layout, targeting the L511P mutation (rpo*B*), including 3 replicates for each probe instead of 2, and amplification controls for each gene. The VereMTB™ shows overall sensitivity and specificity similar to those of the molecular tests endorsed by the WHO for MDR-TB detection on clinical isolates. More than the 94% of preliminary tests performed on smear positive specimens showed valid results.

Conclusions: This fast and affordable integrated chip tool represents an innovation for MDR-TB identification and it's easily adaptable for other diagnostics purposes, making this assay indicated for the laboratory routine. A field test in high TB burden country Uganda within the EDCTP TB CHILD Project was conducted and large comparative study in China is ongoing.

PC-365-01 Feasibility of TB-LAMP, a simple and rapid nucleic acid amplification test, in Haiti

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Background: The situation of tuberculosis (TB) in Haiti is worst among countries of WHO Region of the Americas. The case detection rate of Haiti is 62% (2010). Sputum smear test is the standard diagnostic technique, but nucleic acid amplification test (NAAT) and culture are very limited. TB-LAMP (EIKEN Chemical Co., Ltd) is a packaged commercial kit of the LAMP (loop-mediated isothermal amplification) which is rapid and much simpler NAAT than conventional PCR. In order to improve the case detection rate, we tried to introduce TB-LAMP in Haiti. First, we confirmed whether the technique could be operated by Haitian laboratory technologists in the field settings of Haiti, and then we applied TB-LAMP to the TB-suspected patients.

Design/methods: From November 2011 to January 2012 TB-LAMP tests were performed and the results were compared with those of smear sputum tests (First phase). Then, from March to June 2012 TB-LAMP tests were performed for the TB-suspected patients who were difficult to diagnose with sputum

smear tests, such as children, HIV-positive patients, and smear-negative but highly suspicious patients for TB due to X-ray findings (Second phase). Before starting the field operations, we held two to three day training courses for the Haitian technologists.

Results: In the first phase, 1066 sputum samples from 699 patients were tested with TB-LAMP. In a total of 80 runs of TB-LAMP tests, all positive and negative controls showed right results. Among 440 patients for diagnosis, there were 86 patients with positive smear and 100 patients with positive TB-LAMP. 5.6% of smear negative samples for diagnosis were TB-LAMP positive. In the second phase, 1026 patients were tested with TB-LAMP test. Among 257 patients who were smear-negative but highly suspicious for TB based on X-ray findings, 11 (4.3%) were TB-LAMP positive. The sample size of children and HIV-positive patients are 58 and 41, respectively, and no additional advantage of TB-LAMP was shown compared with smear microscopy. All of ten technologists reported that they felt TB-LAMP technique easier than sputum smear microscopy.

Conclusion: About one in twenty smear-negative samples were positive on TB-LAMP test in Haiti, and this technique may be useful, as a simple, rapid and sensitive point of care test in Haiti where the use of culture test is very limited. For evaluating the TB-LAMP for children or HIV-positive patients, a study with a larger sample size is needed.

PC-367-01   Applicability of DNA and RNA amplification assays in diagnosis of *Mycobacterium tuberculosis* complex in extra-pulmonary samples

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Background: This study aimed at evaluating the role of molecular tests: real-time polymerase chain reaction (PCR) and the Amplified Mycobacterium Tuberculosis Direct Test (AMTDT) in rapid detection of *Mycobacterium tuberculosis* complex from extra-pulmonary samples.

Methods/design: It was a laboratory based prospective study over a period of one year and ten months (May 2011–Feb 2013) including a total of 238 suspected extra-pulmonary tuberculosis cases. Clinical presentations were obtained and samples were processed for culture by Bact/ALERT 3D automation method, Real Time PCR by Genosen's MTBC kit using primer targeting 16s rRNA segment of *M. tuberculosis* complex genome using Rotor gene 6000, Corbett Research System, Australia and AMTDT (Genprobe, San Diego, CA) as per manufacturer's guidelines. Molecular tests were analysed statistically using both clinical suspicion and culture as gold standard.

Results: 165/238 (69.32%) cases were PCR-positive

followed by AMTDT 117/238 (49.15%) and culture 77/238 (32.35%). On comparing with culture, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for PCR was 84.2%, 45.8%, 55.2%, and 78.5% and for AMTDT was 81.1%, 53.6%, 45.7% and 85.5% respectively. On comparing with clinical suspicion, for PCR they were 75.8%, 66.7%, 89.3% and 42.9% and for AMTDT were 70.2%, 89.2%, 94.8% and 51.6% respectively. PCR had a higher sensitivity than AMTDT but the specificity of AMTDT remained high with both the gold standards.

Conclusion: The present study concludes that both the molecular tests have performed reasonably in statistical terms. AMTDT was very specific with higher PPV as it detects RNA and live bacilli which correlated well with clinical symptomatology. The cost for AMTDT is approximately Rs 1000/test and real time PCR ~Rs 550/test in our hospital. Real time PCR has equivalent performance with marginally lower specificity but is cost effective and has a sturdier laboratory protocol as compared to AMTDT.

IMPROVE TUBERCULOSIS CASE DETECTION INNOVATION

PC-368-01   Tuberculosis-free subdistrict strategy to improve the performance of the TB Control Programme

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Background and challenges to implementation: Low case detection (58% in 2010) is one of TB control problem in East Java Province. Primary Health Center is often implementing TB program by them self without support from any other sectors. It was needed to intensify other sectors involvement to improve TB case detection, such as sub district administrator, empowerment and local Family Welfare Organization, education sector and people affected TB. TB services network in sub district also should be strengthened.

Intervention or response: This study is action research. The objective of the research is solving the programmatic challenge, especially low case detection. The study in 2011 at 9 districts in East Java Province, Sumenep, Pamekasan, Sampang, Bangkalan, Pasuruan, Probolinggo, Jember, Bondowoso dan Situbondo. The serial interventions consisted of 1) coordination meeting with 9 districts health office officers; followed by 2) coordination meeting with public health center and the stake holder (sub districts leader, informal leaders, teachers, village's woman organizations and cadres) from selected sub district in each districts (total 87 sub districts); 3) strengthening public health

center networking and supported by stake holder in sub district level; 4) promotion and case detection activities that involving the communities (cadre) and 5) the case holding by tracing activities for non adherence patients. The performance of program compared by previous year as the evaluation. We access the impact of the strategy on case detection and treatment outcome.

Results and lessons learnt: The case detection was increasing 14% in average and the highest is 25% compared previous year. Treatment success was increasing in 4 districts but there was 1 district decreased the treatment success. Non goverment stake holder is the important part of the program.

Table   Case detection improving comparison between districts that implemented TB-free sub-districts strategy and not implemented

	Districts	
Case detection	Implemented TB-free sub-districts strategy	Not implemented TB-free sub-districts strategy
Increase	9	20
Decrease	0	8
No increase or decrease	0	1
Total	9	29

Conclusions and key recommendations: TB-Free Sub District Strategy can improve the performance of TB program at district level. It can be an alternative activities to increase case detection without lowering the quality of treatment outcome.

PC-369-01   Intensified community-based DOTS services for increasing access to all tuberculosis patients in Bangladesh

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Background and challenges: Tuberculosis is a major public health problem in Bangladesh. BRAC, a development organization initiated community-based tuberculosis control program in 1984 in one subdistrict covering 220 000 population. This model was gradually expanded since 1994 in collaboration with National Tuberculosis Control Program (NTP) and currently covering 93 million population in two-thirds of the country. TB case notification and treatment outcomes were low in many slums, urban, peri-urban and hard to reach areas. Thus TB control interventions were further intensified in BRAC supported areas throughout the country to increase case notification of all forms of TB and improve treatment outcomes during last 2 years.

Intervention: BRAC frontline health worker known as Shasthya Sebika (SS) plays an important role in implementing community-based DOTS interventions.

They disseminate TB messages in the community during household visits. TB symptomatic identified during household visits are referred for sputum examination at NTP designated laboratories. Outreach sputum collection centers are expanded in different remote areas to improve access to diagnosis. People with persistent TB symptoms and negative smear results are referred to higher lever health facilities for X-ray, FNAC and biopsy. Treatment for all TB patients is initiated by medical officers and ensured daily intake of treatment through frontline health workers. TB services were further expanded to many hospitals/clinics and referral mechanism established with large number of private medical providers during last two year.

Results and lesson learnt: In 2011 and 2012, additional 700 and 1484 outreach sputum collection centers were held in remote areas. Referral linkage was established with 1066 additional private medical practitioners as a special intervention in 101 sub-districts. Case notification of all cases in 2011 and 2012 were 99 and 111 per 100 000 respectively. Service intensification resulted improved case notifications from 93 646 in 2011 to 104 984 in 2012 by maintaining treatment success rate over 92%.

Conclusions: Intensifying community based TB services in underserved areas and linkage with hospitals and individual private medical practitioners increased access for improving case notification and treatment outcomes.

PC-370-01   Innovative community-based approach to increase detection of sputum smear positive tuberculosis cases in the low case notification districts in Odisha, India

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Background and challenges to implementation: Odisha, India, has 31 districts, each of which is divided into microscopy centre areas (MCA) with a population of 100 000. Each of the MCA, in turn, is divided into health sectors with a population of 30 000 each. Odisha suffers from low tuberculosis (TB) case detection rates. To improve the situation, the Government of Odisha's Department of Health provided TB awareness campaigns followed by increased access to sputum microscopy. The intervention was implemented between April and June 2012, in 10 districts with the lowest case detection rates in Odisha.

Intervention or response: The unit for intervention

within these districts was a sector. The selected districts, with a total population of 12 million, carried out this intervention in 25 sectors each. The intervention consisted of two days of using speakers mounted on vehicles to increase awareness of TB followed by a health camp on the third day. Community volunteers from each village in the sector brought persons with suspected pulmonary TB and their morning sputum sample to the camps. These persons submitted their second spot sputum sample at the camp for microscopy. For the purpose of comparison, the percentage change in sputum positive cases detected between 2Q11 and 2Q12 in the MCAs with intervention sectors were compared with MCAs without intervention sectors.

Results and lessons learnt: In the 8 districts from which data were available, a total of 203 such activities were held in which 8582 persons suspected of having TB were screened. Of these, two sputum samples were collected and tested from 8507 (99%) persons suspected of having TB. 240 (3%) of those tested were found to be smear positive on sputum microscopy. A comparison of change in number and percentage of patients with smear positive TB in intervention and non-intervention MCAs showed a 10.75% increase in the intervention areas vs. a 0.82% increase in number of smear positive cases in the non-intervention areas.

Conclusions and key recommendations: This was the first large intensified case finding activity conducted in Odisha under programmatic conditions. We are unaware of any other activities which could explain this substantial increase in diagnosed sputum smear-positive cases. Hence, the results of the study indicates the potential of regular awareness programs along with sputum camps, to increase case finding effectively.

PC-371-01 Tuberculosis suspect registry improves tuberculosis case finding: results from a community-based cohort study in south Ethiopia

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Aim: We examined if a registry of patients with symptoms suggestive of tuberculosis can improve case finding.

Methods: We did a census of 36575 people in rural Sidama in south Ethiopia. Based on interviews, we identified 724 (2%) chronic coughers. We then did a prospective cohort study of these 724 chronic coughers and 1448 neighbourhood controls. Every three months, we interviewed them, and did sputum microscopy.

Results: Between September 2011 and June 2012, 23 chronic coughers and 3 controls developed smear positive tuberculosis. We observed higher risk of smear positive tuberculosis among chronic coughers (adjusted HR 15.5, 95%CI 4.2–56.7) and the poor (adjusted HR 2.5, 95%CI 1.1–5.8). Also, chronic coughers had a higher risk of death (adjusted HR 9.3, 95%CI 1.8–49.1).

Conclusion: This study provides evidence on the benefit of a tuberculosis suspect registry for improving smear positive tuberculosis case finding in high tuberculosis burden communities.

PC-372-01 Is DOTS expansion synonymous to increased case notification? What Nigeria needs to do differently

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Background: Early diagnosis and administering appropriate treatment are major interventions for the control of tuberculosis. Therefore, access to quality laboratory services and treatment are key strategies employed. To assess this, TB programmes uses DOTS coverage by population of 1/25000 population and 1/80000 for microscopy centers. Population coverage was used based on the assumption of being synonymous with access whilst undermining population distribution within a given area and availability, distribution and utilization of existing health facilities.

Objective: Assess both DOTS and microscopy coverage by population in comparison with case notification rates and health facility coverage in the same geographical area.

Methods: This is a retrospective descriptive study reviewing 5 years of National TB programme data (2005–2009) and 7 selected states within the northwest zone of Nigeria. The case notification rates of 2009 were compared among these states with different population coverage indicators and health facility coverage.

Results: The DOTS and microscopy coverage increased from 36% and 38% in 2005 to 54% and 57% in 2009, respectively. While, the case notification rate increased from 51/100000 in 2005 to 61.8/100000 in 2009, however it leveled at an average of 60/100000 pop for 3 years (2007–2009). Analysis of TB data for 2009 from the selected states comparing population DOTS coverage, health facility DOTS coverage and case notification rates showed that DOTS coverage by health facility ranges from 6.6% to 11% only. The data shows that DOTS coverage by population is not directly proportionate to CNR. A state with the least DOTS coverage by population of 28.3% has the highest CNR in the zone of 67.4/100000 compared to state with the highest
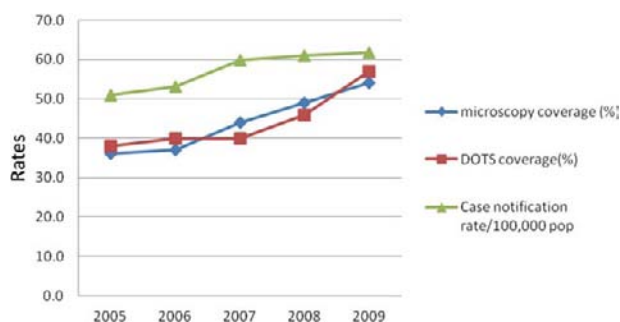
Figure Trend of CNR, Mic and DOTS coverage for 2005–2009 in Nigeria.

DOTS coverage by population of 49%, notifying only 37.9/100 000. The data equally shows that facility coverage is not proportionate to CNR, as seen in state with the least DOTS coverage by facility of 6.6% and a CNR of 63/ 100 000, while state with 11% DOTS coverage by facility had a CNR of 26.1/100 000.

Conclusion: DOTS and microscopy expansion alone without critical analysis of 'where most of the population access health care services will not directly lead to increased CNR. Programmes should identify facilities highly utilized by the population for expansion of its services while enhancing community participation and strengthening the ACSM for TB control.

PC-373-01   Innovative strategies to enhance additional case finding of smear positive cases in Pakistan

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Background: Despite of progress towards MDG Targets and increasing case detection up to 64% still NTP Pakistan face challenge of missing TB cases from high risk areas such as slums. The enhanced efforts are needed to improve case notifications such as adopting active case findings in high risk areas such as slums, prisons, etc.

Design/methods: We evaluated a retrospective community-based strategy for TB case detection in 5 randomly selected districts with urban slums of Sindh Province Pakistan. The integrated strategies like chest camps with frontloading strategy and LED based fluorescence microscopy were applied to enhance prompt case detection of smear positive cases. This project was funded by TB REACH and implemented by engaging the private providers practicing in slums who were trained and managed the suspects and cases detected through chest camps. Main objective was to increase the additional case detection of smear positive TB cases.

Results: From March 2011 to September 2012, project assessed 165 280 individuals of whom 7747 sus-

pects were identified by GPs and 13 481 were by camps. A total of 3117 tuberculosis positive cases were detected and notified to NTP: 1707 through chest camps, out of which highest contribution observed in Dadu (566) and 1410 from GPs clinics in which highest 1260 were in Karachi. During the project, the total number of smear positive TB notification rate increased from 5158 to 8275 progressively from chest camp intervention over the intervention period.

Conclusion: Community-based strategies involving chest camps by engaging private providers can significantly increase the number of TB suspects in urban slums areas which are otherwise missed from notifications.

PC-374-01   Field assessment tool for advocacy, communication and social mobilization under the Revised National Tuberculosis Control Programme, Delhi

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Background and challenges to implementation: Empowering TB patients and the affected community helps to achieve timely diagnosis and treatment completion. Advocacy, Communication and Social Mobilization (ACSM) is a multi-level strategy for promoting and sustaining safe behavior among individuals and communities by disseminating health messages through a variety of communication channels. Despite a substantial budgetary allocation (8%–10%) for the ACSM activity under the Revised National Tuberculosis Control Program, there are no process indicators under the National program monitoring strategy which could act as a tool for monitoring and implementing these activities in the field.

Intervention or response: State TB Department of Delhi devised a simple field assessment tool for monitoring of various ACSM activities at each treatment center. Basic questions regarding awareness about disease and advocacy events in the community along with willingness to become a treatment provider need to be entered during continuation phase of treatment by field supervisory staff in the TB treatment card. These questions help to understand about TB disease, DOTS strategy, importance of counseling for adhering to the TB treatment and also provide a database of probable community DOT providers.

Results and lessons learnt: As a consequence, total case notification rates increased by 8% in the year 2012 as compared to 2011. There was a significant increase in various ACSM activities across the state which resulted in improved case finding and case holding efforts in 2012.

Conclusions and key recommendations: Incorporation of a field monitoring tool in the TB treatment card acts as a ready reference tool for assessing ACSM activities in the field. National TB Control Programme should incorporate basic ACSM activity questionnaire in the TB treatment card.

PC-375-01   Using quality improvement model to improve tuberculosis case finding in Cambodia

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Background and challenges to implementation: The national TB programme in Cambodia is engaging community DOT watchers (DW) and private care providers (PPs) to identify and refer TB suspects to public health facilities. While this has contributed to increased case detection, the proportion of TB suspects referred by PPs and DWs arriving at the health centres remained below 50% in 2011. QI model was used to guide a team of service providers to test system changes through the use of the PDSA tool. The main steps are to identify explicit improvement aim; develop the improvement measurement system; generate ideas for changes using known change concepts; and test system changes. If a specific change yields improvement, it is sustained and replicated. If not, the change is abandoned and another change tested.

Intervention or response: Five health centres (HC) in Kampong Cham province applied the QI model to improve successful referrals of TB suspects referred by PPs and DW. Service providers used QI tools to identify root cause of problems and generate change ideas. The change package implemented were: 1) engaging commune council members in HC activities; 2) joint review of HC performance by all stakeholders (DWs, PPs, and commune councils); 3) monthly meetings to compare patient referrals and arrivals with systematic follow up of those patients who did not report to the HC; 4) prepare run charts on HC performance and display in public area. In addition, some commune councils supported transportation costs for poor patients.

Results and lessons learnt: The proportion of referred TB suspects reporting to the HCs increased from 63% (184/292) in Nov–Dec 2011, when the project was initiated, to 87% (470/539) in Oct–Dec 2012. 429 TB cases (all forms) were diagnosed during the first year of intervention (Nov 2011–Oct 2012), compared to 314 TB cases detected in the prior 12 months–36% increase in case detection. In addition, these five QI HCs detected an average of 86 TB cases/per HC/per year, compared to 39 TB cases/
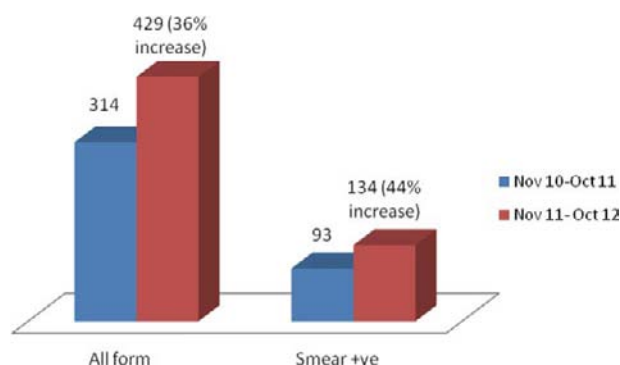
Figure   TB cases diagnosed in five HCs implementing QI.

per HC/per year in the remaining HCs of the intervention districts.

Conclusions and key recommendations: QI model can be successfully applied to improve referrals and case finding for TB. Involvement of commune councils in activities of health centres can help address problems faced by the community. QI tools empower service providers to identify issues, find solutions and implement improvement plans based on their context and priority.

PC-376-01   Establishing tuberculosis control services to cover underserved population in South West Delhi: experience of Damien Foundation–India.

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Background and challenges to implementation: Tuberculosis control program in urban areas faces many challenges due to lack of health infrastructure, high population density, floating population, settlements and influence of private sector. There is a need to document the experience gained while establishing sustainable urban TB control models in partnership with private sector.

Intervention or response: Damien Foundation, a NGO has initiated TB control activities in underserved population in South West district of Delhi in 2002. Initially covered one TB unit with a population of 500 000 and it was extended to one more TB unit in 2004 in same district. The services are provided through ten designated microscopy/DOT centres are managed by one Microscopist/Field Worker (MFW). There is one senior laboratory supervisor and one senior TB supervisor managing each TB Unit. The chief medical officer is overall responsible to manage complications with supervision and monitoring of both TB units. The MFWs are trained in both sputum microscopy and DOT supervision including arranging DOT in the community. The program follows the

guidelines laid by Revised National Tuberculosis Control Program.

Results and lessons learnt: Case notification for total TB cases registered has increased from 17 in 2002 to 258 in 2012 per 100 000 population. The new sputum positive case registered has increased from 6.8 in 2002 to 82.5 in 2012/100 000. All the patients are treated under DOT either at the centre or with RMPs and community volunteer. In 2012, during routine supervisory work it was found that 77% of community DOT providers are functioning correctly. An analysis of 779 tuberculosis patients data to identify the referral sources found that 20% were self-reported; 22% were referred by government hospitals; 38% by private doctors including rural medical practitioners; 20% by community including patients and DOT providers. Analysis of treatment outcomes showed an increase in the cure rate among new sputum positive cases from 85% in 2002 to 89% in 2011. The defaulter rate has remained below 4% in the last 10 years.

Conclusions and key recommendations: This model with one person for diagnosis and treatment can be easily replicated in other urban areas in partnership with private sector with minimum human resource without compromising the quality.

PC-377-01   Community screening and GeneXpert® for active tuberculosis case detection in a rural district in KwaZulu-Natal

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Background and challenges to implementation: TB-HIV Care Association received a TB REACH grant to increase diagnosis and treatment of drug susceptible and drug resistant TB (DRTB) in Sisonke district, KwaZulu-Natal.

Intervention or response: TB symptom screening and sputum collection was done by mobile HIV counseling and testing (HCT) teams and community health workers (CHWs) with sputum examination by Xpert MTB/RIF (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 and lessons learnt: From October 2011 to September 2012, 21 712 GeneXpert tests were done in Sisonke and 1474 (6.8%) detected MTB. Of these, 1314 had sputum smear microscopy at baseline for program monitoring and 479 (32.5%) were smear-

Table   Decreased time to treatment—Pholela CHC

Time from sputum collection to starting TB treatment	April-June 2011	April-June 2012
<24 hours	0	11/18 (61%)
24-48 hours	0	3/18 (17%)
2-5 days	1/10 (10%)	2/18 (11%)
> 5 days	9/10 (90%)	2/18 (11%)

negative. Of the 1474 TB cases, 1372 (93%) had an HIV test and 72% were HIV-positive. Out of 1474 TB cases, 127 (8.6%) were rifampicin-resistant and were referred for treatment of multidrug-resistant TB. The average time from sputum collection to treatment for drug resistant TB decreased from 136 days in April–June 2011 to 15 days in April to June 2012.

Conclusions and key recommendations: 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 to increase case finding and decrease time to treatment of drug susceptible and resistant TB in a rural setting.

INFORMATION TECHNOLOGY TO IMPROVE TUBERCULOSIS CONTROL

PC-378-01   Effect of surveillance system strengthening initiatives on quality of tuberculosis data in Afghanistan: a cross-sectional study

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Background: Tuberculosis (TB) data are vital to adequately monitor performance, plan programs and projects, make strategic decisions, direct resources, and evaluate programs for improved TB control. Since 2009, USAID-funded projects (TB CAP and the follow on, TB CARE I) have been helping the Afghanistan's National TB Program (NTP) strengthen the nation's TB surveillance system and data quality. In 2012, the NTP and TB CARE I staff conducted an assessment to determine the effect of the project's surveillance system strengthening initiatives on Afghanistan's national TB data quality.

Methodology: From November 2012 to January 2013 Staff from the NTP and TB CARE I conducted a cross-sectional study among 61 health facilities in 14 provinces. (DF = 1; total health facilities 442; frequency of outcome 24% and 95%CI). Data collection

tools include NTP reporting forms and a standard questionnaire. The team reviewed documents to assess five dimensions of TB data, trace reported TB cases for verification, and cross-check reported cases with past records. During this assessment, we collected information on validity/accuracy; ability of system to yield accurate data, reliability; protocol/procedure for data collection, precision; sufficient details of TB data, system integrity; security of data from bias and manipulation, confidentiality; data security, and timeliness. We compared the result of data accuracy assessment of 2008 and 2012.

Results: Among the 61 health facilities, the average score for all five data quality dimensions was 80.1% with 71% validity, 80% reliability, 89.8% system integrity, 90.2% precision and 73.7% timeliness. There was variation in data quality among provinces: Samangan province's health facilities scored 64.9% and facilities in Kandahar and Ghazni both had an average score of 98%. In summary, data quality improved by 5% (from 76% in 2008 to 81% in 2012). Health facilities in two provinces scored less than 70%, facilities in five provinces scored between 71–80%, facilities in five provinces scored between 81–90%, and facilities in only two provinces scored above 90%.
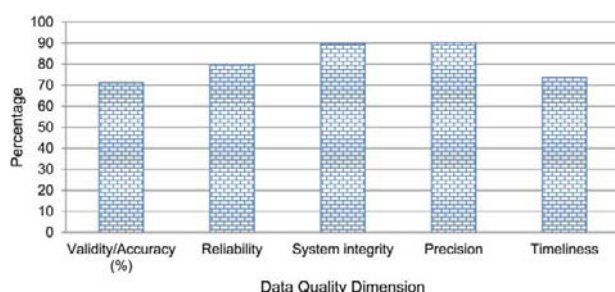
Figure Comparison of data quality dimension in 14 provinces of Afghanistan, Nov 2012–Jan 2013.

Conclusion: Study results showed that TB data quality has been improving in Afghanistan, but more needs to be done. Afghanistan's NTP and its partners should focus on all data quality dimensions particularly validity/accuracy, reliability, and timeliness. We strongly recommend implementation of electronic data reporting and training of frontline health staff on recording and reporting.

PC-379-01   Deploying web-based SMS alert system for delivering sputum smear test results

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Background: In Cambodia, health center (HC) staff collect, prepare, and deliver sputum smears to the nearest tuberculosis (TB) sputum microscopy laboratory once a week. During the weekly trip to the lab, HC staff collects results for samples submitted in the previous week. Sputum smear results are usually available within two weeks, but could be longer during public holidays or when staffs are on leave.

Intervention: In January 2012, a web based SMS system was introduced to provide sputum smear results to HC staff and community volunteers in order to promote earlier diagnosis and treatment. Four TB laboratories and 15 HCs in Kampong Cham province participated. Community volunteers identify and refer presumptive TB patients to the nearest HC who collect sputum samples from patients and prepare sputum smears. At the time of transporting the sputum smears to the laboratory, HC staff sends a coded SMS message containing specimen details to the SMS system which automatically relays this information via SMS to the concerned laboratory technician. Once the sputum smears are received and examined, the laboratory technician sends the results as a coded SMS to the system that in turn automatically relays the results to the concerned HC staff and community volunteer assigned to the patient. Only positive sputum smear results are transmitted to the community volunteer.

Results: The number of smear samples registered in the system increased from 471 in January–March 2012, the first quarter of implementation, to 736 in January–March 2013. The proportion of sputum samples registered for which results were sent using the system increased from 74% (347/471) in January–March 2012 to 99% (726/736) in January–March 2013. The turnaround time from the date of registering specimen details in the system to delivery of results decreased from 8 days in January–March 2012 to 3 days in January–March 2013, while remaining below 5 days since July 2012.
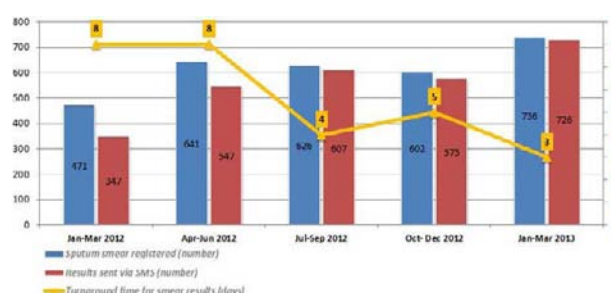
Figure Performance of TB SMS system for delivering sputum smear results.

Conclusions and key recommendations: The web based SMS system is a feasible and acceptable intervention, enabling over four-fold decrease in the turnaround time for delivering sputum smear results to HC staff and community volunteers. Providing mobile phones with capability for Khmer text SMS would

address the difficulties faced by users in using English text SMS. Geographical coverage as well as use of the system for other applications should be expanded.

PC-380-01 Bulk text messaging via mobile phones: an innovative way of increasing tuberculosis case finding

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Background: Tuberculosis (TB) case finding in Abia state, Nigeria has been low when compared to the national target and estimates. This may not be unconnected to the low level of awareness at community levels about TB. If persons know when to suspect TB and access free services they would seek for health services on time. Use of SMS has come to stay as a simple, fast, efficient and cost effective means for communication and was employed as the primary tool in this study.
Objective: To describe the role of bulk text messaging approach in increasing case finding.
Methodology: A comparative prospective study between two populations. In collaboration with a Global System Mobile (GSM) company, simple messages were sent at random primarily to 200 000 GSM lines of persons residing in Abia State with an estimated population of 3.3 million persons and about 1 million registered GSM lines. All messages were delivered to a mixed population of which 56% were males cutting across various age groups of which 70% ranged from 18–50 years. The text message provided information on the when to suspect TB, whom to call, where to go for free TB diagnosis and treatment. The text messages were sent as bulk messages in batches of 20 000 to 40 000 of 12 batches over a period of 3 months (October–December 2012). Data was reviewed looking at case finding in the period of intervention in the same state and comparing with the same period in the control state.
Results: A total of 364 patients were notified in Q4, 2012 which is a 17% increase compared to Q4, 2011 and a 20% increase compared to Q3, 2012 in the same state, while the control state experienced a decline in case finding by 13% in the same quarter. Of all cases, 74% were smear +ve, 58% males; 52% within age groups of 25–44 years and a TB-HIV co infection rate of 22% was observed amongst the cases.
Conclusion: Text messaging is a simple, cost effective and efficient means of communication. It should be used to create awareness on tuberculosis with the aim of increasing case finding.

PC-381-01 Innovations that improved the external referral acceptance rate at East Avenue Medical Center DOTS Clinic, Quezon City, Philippines

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Background: In 2010, the East Avenue Medical Center (EAMC) DOTS Clinic was one of the 11 public hospitals engaged in the CATCH TB Cases Project managed by the National TB Program (NTP) and supported by the WHO-CIDA. Based on the project, the majority (80%) of the TB cases were eventually referred to peripheral DOTS facilities. The external referral system is the agreed processes and arrangements among the DOTS Clinic and peripheral DOTS facility staff to ensure continuity of care to TB patients. Its effectiveness is measured by the number of TB patients successfully referred to peripheral DOTS facilities that were actually accepted, treated and reported to the NTP. This study will discuss innovations that significantly improved the external referral system thus contributing greatly to the number of reported TB cases.
Methods: A descriptive study was done in January 2013 to compare the number of accepted external referrals in 2011 to that of 2012 when the EAMC DOTS Clinic intensified the use of the Short Message Service (SMS) or text messaging in following up referrals of TB cases made to peripheral DOTS facilities. A cellular phone was provided to be used by the Clinic Nurse to communicate with the patients or the receiving health facilities by sending a text message, inquiring if the referrals were accepted. A patient is considered successfully referred once he is assigned a TB case number by the receiving facility. Communication allowance was also provided which enabled the DOTS Clinic staff to immediately text the patients within a day after the referrals were made to determine the outcome.
Results: In 2011, the external referral acceptance rate ranged from 52% to 75%. With the innovation
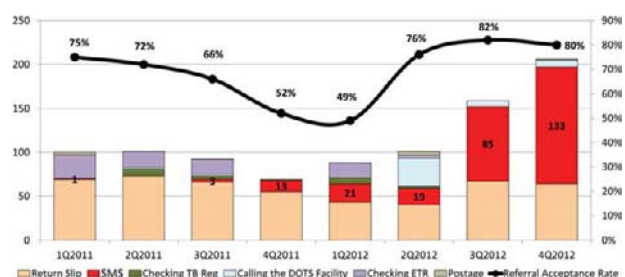
Figure External referral acceptance rate and modes of knowing the outcome of referrals, EAMC DOTS Clinic, Quezon City, Phillippines, January 2011–December 2012.

implemented in 2012, the external referral acceptance rate increased from 49% in the 1st quarter to 80% in the 4th quarter. Comparing the mode of knowing the outcome of referrals from 2011 to 2012, a dramatic increase was noted particularly in the SMS component with the introduction of the innovation. In 2011, only 17 (5%) of the total 363 accepted referrals were communicated via SMS, as compared to 258 (48%) of the 553 patients successfully referred in 2012 (Figure).

Conclusion: The use of SMS, coupled with the logistic support of providing communication allowance, and the pro-active attitude of the referring facility in following up the referrals to the peripheral DOTS facility, contributed greatly to the improvement of the external referral acceptance rate.

PC-382-01   Tuberculosis programmes incorporating mobile phones as tools may overlook the most vulnerable tuberculosis patients in low-resource countries

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Background: Socioeconomic factors are closely related to tuberculosis (TB) with poverty being one of the strongest risk factors for contracting TB infection and subsequent TB disease. The use of mobile phone technology has been suggested as a useful tool in TB control programmes. Ownership of mobile phones may vary depending on socioeconomic status. We aimed to assess the ownership of mobile phones amongst TB patients from an impoverished community in the tropics and examine whether ownership was associated with socioeconomic status and TB disease outcome.

Intervention: We recruited 2342 laboratory-proven TB patients from 16 contiguous shantytowns in Ventanilla, on the outskirts of Lima, Peru. Patients provided socio-demographic data via a nurse-led questionnaire. These data included: poverty (equal or below median income), poor nutrition (equal or below median monthly spending on food per person) and ownership of a landline and mobile phone. Further data regarding TB resistance, smear positivity, poor outcomes on treatment (death, delay or abandonment of treatment), or TB recurrence, was collected from visits to local health-posts or patients' homes. We then analysed the association of these factors with ownership of a mobile phone and landline.

Results: Median patient age was 28 years old and 62% of patients were male. 80% of patients had a mobile phone and 57% had a landline. Patients who had mobile phones were more likely to be younger
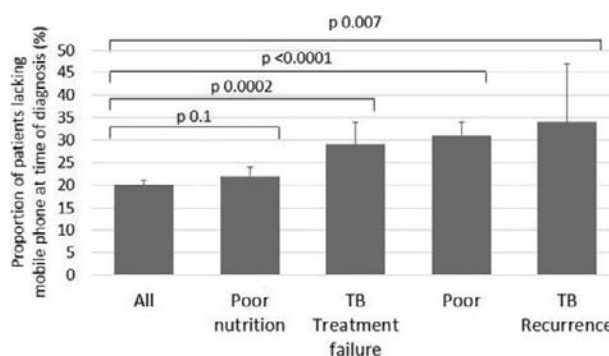
Figure Socio-economic and health variables associated with patients not having a mobile phone.

(33 years vs. 36, $P = 0.0004$). Those who did not own a mobile phone were more likely to be poor (78% vs. 64%, $P < 0.0001$), have poor nutrition (54% vs. 47%, $P = 0.01$), have a poor treatment outcome (27% vs. 18%, $P = 0.0001$) and to have developed recurrent TB disease (4.1% vs. 2.0%, $P = 0.01$) than those with mobile phones all patients (Figure). These associations remained true for ownership of a landline only for being poor and developing recurrent TB disease. No associations were found between mobile phone ownership and sex, sputum smear microscopy positivity or TB drug-resistance profile. In multiple logistic regression analysis, not owning a mobile phone was independently associated with an approximately two-fold increased risk of being poor and having a poor TB treatment outcome (both $P < 0.001$).

Conclusions: Mobile phone ownership was frequent in this impoverished Peruvian shantytown. Whilst this may initially suggest scope for use of mobile phones in supporting national TB programs in low-resource settings, further analysis showed that those patients who did not own a mobile phone were poorest, least nourished and had the worst outcomes on TB treatment. Expansion of mobile phone use in national TB programs may neglect the most vulnerable patients.

PC-383-01   Mobile health technology (smart phones) use for supportive supervision improves performance and tuberculosis outcomes in Nigeria

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Background and challenges to intervention: The WHO ranks Nigeria 10th among high TB burden counties. Based on in-country consultations, capacity to provide high-quality TB/TBHIV services is suboptimal and not unrelated to weak supervision. Within the NTP in Nigeria, supervision is entirely paper based;

time consuming and structured in a way that rapid review of results is not available. Focusing initially in 16 facilities in 4 states and full scale up to all TB facilities in 2 states. Due to its success in improving supervision system, the NTP decided to scale up to additional 4 states.

Intervention: The National TB and Leprosy Control Program and Abt Associates-led, USAID-funded project automated a national supervisory checklists into smart phones for the purpose of supervision. The phones automatically calculate TB indicators at the facility-level and then analyze them against national standards. This rapid analysis becomes the platform for clinical supervisors to devise immediate, data-driven quality improvement plans during routine monitoring/supervision. LGTBLS were trained and 3 supervisory visits using the smart phones were conducted within 3 consecutive quarters in each TB facility. After a successful pilot, the project scaled to over 200 facilities in 2011–2012.

Results and lesson learnt: In Lagos Mainland, the proportion of TB-HIV co-infected patients on preventive treatment (CPT) jumped to 100% in March 2012 from 33% in March 2011. The new TB smear positive cure rate increased from 62% in March 2011 to 79% in May 2012. The treatment success rate in the Abia state TB facilities increased from 78% in 2011 to 85% in 2012. The time spent on supervision was reduced to 2 hour per facility using smart phones compared to 6 hrs when using paper based checklist. Supervision now concentrates on the performance of clinical tasks and resolution of problems.

Proportion of TB/HIV co-infected patients on preventive treatment (CPT)

Before Intervention 33%	After Intervention 100%

New TB smear positive cure rate.

Before Intervention 62%	After Intervention 79%

The treatment success rate in the Abia state.

Before Intervention 78%	After Intervention 85%

Conclusions: The use of smart phones for supervision has a model for sustainability. Training is done locally in-country. The technology is kept simple and collects useful information in a timely manner. It has also eliminated the need for printed forms, minimized human error in data entry, reduced the lag time, and helped pinpoint ways to improve delivery of care. Based on the experience from the first 3 rounds of data collection, a rollout of the approach is recommended.

PC-384-01   Development of an online system for requesting special anti-tuberculosis drugs, 2012, São Paulo State, Brazil

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Background: Information technology is a tool that tends to generate data quality with the purpose to lower the uncertainty in the decision making process. Health information must be worked reinforcing human rights, contributing to eliminate misery and social inequalities and at the same time to subsidize the decision process in the field of health.

Method: The development of an online flux for requesting special medicines for the treatment of tuberculosis (TB) was a challenge to the Sao Paulo Tuberculosis Control Program (TCP). The system was developed on the Google Docs® platform and uses the Microsoft Excel® database. The system implementation took place in June 2011 showing satisfaction among applicants of medications and staff of TB Division—the Sao Paulo State TCP.

Results and conclusions: Since the system was constructed it has become easier to manage each case individually, analyzing and monitoring the treatment. It was suggested by the applicants, there was a space in the form to describe special situations presented by patients, reinforcing their request. We have observed a time reduction in the dispensation of these drugs, making agile the correct treatment of these patients by preventing the worsening of their health condition of this population, and the appearance of extremely drug-resistant cases (XDR), including preventing deaths due to TB.

PC-385-01   Challenges in rolling out NIKSHAY, an online patient repository in Kerala, India, as part of the Revised National Tuberculosis Programme

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Background: In May 2012, the Government of India introduced an online web portal called NIKSHAY (www.nikshay.gov.in). It was envisioned as a web repository of all TB patients for monitoring and research purposes. NIKSHAY has been presently operated at national, state, district and tuberculosis unit (TU) levels. The first stage from June 2012–December 2012 consisted of entering the data from TB treatment cards into the web portal, so that quarter 4's patient's database may be entered into the portal.

Challenges: Kerala the most literate state in India

faced teething troubles in rolling out this innovative project. District data entry operators (DEO), who were identified as the nodal person for data entry retrospectively, started digitalising data from TB treatment cards from January 2012. Although trained and sensitised by the programme, card entry at district level was slow and tardy.

Intervention: A root cause analysis was done and a semi-structured interview was administered to 14 DEOs over telephone. Practical, field problems faced by the DEO and their feedback was recorded and analysed. Problems like issues in the web software, power failure, poor web connectivity and gaps in human resource were identified as challenges. It was observed that the data entry operators were overloaded with routine programme management tasks and were on the brink of a burnout due to the 'enforced' NIKSHAY card entry. They were discussed with state programme managers. The technical issues faced by the Data Entry operator were conveyed to the Central TB Division of Government of India for fine tuning the portal. Operational issues were discussed with the District TB Officers (DTOs) and taken care at the district level. Computer literate TB workers were identified in each district and were encouraged to contribute to data entry. DEOs were supported and encouraged repeatedly to keep up their morale.

Results: All districts were able to complete data entry as scheduled with technical and administrative support as problems were identified at ground level and from user feedback interviews. From a backlog of 11 184 patient cards in September, all 17 218 cards of 2012 were entered by January 2013.

Lessons learnt: Understanding of field reality is crucial in solving out problems in public health programmes, especially those involving information technology. The invisible digital divide must be scientifically understood and solved with a quintessential human touch.

PC-386-01   Implementation of the eCompliance system in Uganda for management of TB-DOTS

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Background: In 2011, the Millennium Villages Project site in Ruhiira, Uganda diagnosed over 50 tuberculosis (TB) patients, with a 19% lost to follow-up rate and 8 TB deaths. Typically nurses and community health workers (CHWs) manually track patient visits—meaning missed doses can easily go unnoticed. When TB patients are lost to follow-up they are at high risk of discontinuing their drug regimen and developing drug resistant TB.

Intervention: The eCompliance biometric system addresses the challenges inherent in the manual system by requiring both the patient and the responsible health worker to scan his/her fingerprints using a biometric terminal at each visit—limiting the possibility of human error or fabrication. The system then creates an easily accessible list of patient visitation schedules, upcoming observations and missed doses. The health workers are then able to easily view patient visit records and quickly identify patients at risk of being lost to follow-up. The eCompliance pilot project took place at 3 clinics in the Ruhiira cluster selected for TB patient loads and terrain that provides unique barriers to access of TB DOTS. A senior CHW from each clinic was selected based on past performance and demonstrated commitment to the community. Study subjects were selected from previously identified TB patients. eCompliance was introduced to the cluster through a series of classroom training sessions and supported patient enrollments in the field.

Results: The study was an interrupted time series where data for a cohort of 31 patients enrolled on eCompliance in July 2012 and completing or discontinuing TB treatment was compared to data from two time periods before the eCompliance intervention was introduced: July 2011–January 2012 and January 2012–June 2012. After all 31 patients left the system the death and lost to follow rates were both zero (0); 100% of patients have successfully graduated out of the treatment through drug completion. Community members and patients also expressed their gratitude for the time and thoroughness with which the health workers now attend to TB patients.

Conclusions: eCompliance allows for ease of access by health workers and thereby supports TB DOTS follow-up and completion leading to significantly reduced rates of patients lost to follow up in Uganda. By implementing eCompliance in resource limited settings the incidence of lost to follow up may be halted and the occurrence of drug resistance reduced.

PC-387-01   Innovative programme management of tuberculosis, leprosy and lung disease using an electronic information system (TIBU): experience from Kenya

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Background and challenges to implementation: Demands from governments, partners, communities and patients have increased leading to challenges in accountability for resources used in program management. Disbursement and accounting for activity funds,

data collection and reporting, supervision, and management of drugs and lab supplies amongst other programmatic responsibilities remain a big challenge in resource limited settings. Quality of data collected from the field including completeness, accuracy and timely submission remains a big task.

Intervention or response: NTP introduced the use of PDAs in 2008 but PDAs did not adequately respond to programmatic needs. NTP in partnership developed a concept on an electronic program management system. An organizational structure that included policy and operations levels were agreed upon by all partners. Type of equipment to be used and the level of implementation were settled upon during regular consultative meetings. Three reputable organizations were engaged to develop the solution. Development was divided into 3 phases based on available resources, time and focus of the project. Phase 1 captured TB/MDR-TB data collection and reporting and payment of patient support. Phase 2 covered IPT, EQA, leprosy, supervision, funds disbursement and reporting. The final phase covers commodity management and other program areas. Developers collected requirements from program officers and clarifications were sought as ongoing engagements until the final product. The product was piloted to improve the system. District TB coordinators were trained on the use of the solution.

Results and lessons learnt: TIBU was rolled out in September 2012 and covers 220 of 250 districts across 47 counties. Over USD 153 000 mobile payments have been processed for supervision and MDR patient support from January to April 2013 and 87 379 patients registered in the system. Electronic program management system confers multiple advantages and improves governance, accountability and performance in low resource settings. It motivates staff because of the equipment used and simplification of work. Integration with other existing systems such as the national Health Information System (DHIS2), lab information system, GeneXpert and national commodity management system is possible.

Conclusions and key recommendations: It is possible to use electronic systems in program management. Programs should adopt innovative electronic data collection methods.

PC-388-01 Use of helpline and mhealth for tuberculosis care and control: results from a pilot innovation in India

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Background: Project 'Axshya' supported by The Global Fund Round 9, aligned with the national TB control strategy and the WHO Stop TB Strategy is being implemented by Population Services International in thirty districts across six states inIndia. The objective of the program is to create demand generation and improve access TB diagnosis and treatment services through advocacy, communication and social mobilisation strategies.

Intervention: Population Services International along with the Union and BBC WST launched a 360 degree mass media campaign with an integrated toll free helpline to raise self risk perception in individuals with cough for two weeks or more and take a specific call to action to visit nearest microscopy center for diagnosis of TB. The pilot helpline was introduced to guide individual callers about the nearest microscopy center for free TB diagnosis. The helpline is the first of its kind introduced in India for TB with free inbound call facility. It was implemented across thirty districts of six states in India for a month and operated for twelve hours in a day. The helpline was promoted through mass media campaign and other local channels of communication. Mhealth component was also integrated and the callers who registered were informed through sms of the nearest designated microscopy center (DMC) for free diagnosis of TB.

Results: There were 1856 calls during the month 95% callers were males and 5% were females. SMSes were sent to 316 persons providing information about the location of the nearest microscopy center for diagnosis of TB. The pilot helpline was also appreciated by the government stakeholders and was suggested to scale and run the same for a longer duration.

Conclusions and key recommendations: Through the toll free helpline it has been possible to reach out to substantial number within a short span of time and inform people and make them aware of the diagnostic center in their vicinity where free services were being provided. It is recommended to replicate the successful pilot model is recommended for scale-up to other project locations.

PC-389-01 Geolocation of patients as a tool for improved tuberculosis care and information systems

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Geographic information system (GIS) data have been used in different countries to map the distribution of tuberculosis (TB) patients and identify hotspots of disease. Scaling up such efforts could help TB programmes to identify individuals at increased risk of TB infection, disease or unfavourable outcome of treatment, and to follow up more closely patients receiving treatment, thus ensuring better adherence. The impact could be substantial given that global TB

case detection was estimated to be only 66% in 2011, and 7% of new TB patients were lost to follow-up or not evaluated (20% of previously treated) and only 19% of patients with multidrug-resistant TB (strains resistant to, at least, isoniazid and rifampicin) were detected. The global expansion in the availability of handheld devices, including affordable cellular phones, which facilitate the rapid capture and transmission of GIS data opens up new frontiers for TB programmes to map the exact location of their patients and to better plan for efficient provision of services.

We provide examples from four settings—urban Lima (Peru) and Karachi (Pakistan), Republic of Moldova, and Swaziland—to illustrate how the spatial analysis of GIS data has been used to improve the understanding of epidemiology of tuberculosis, such as clustering of drug-resistant TB, and programme performance, as for instance to locate the site of observed treatment encounters. We use these experiences to draw up a provisional framework to evaluate the effectiveness of these interventions, to generate more evidence and to inform future guidance to countries for a wider and generalised use. The World Health Organization (WHO) will be assessing the information available and work towards innovating care and monitoring systems.

PC-390-01   Using GIS to effectively monitor resources for managing tuberculosis in West Arsi Zone, Ethiopia

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Background and challenges to implementation: Effective management of TB requires that managers have access to timely and accurate information on the distribution of TB cases, the location of skilled human resources, and diagnostic facilities. Geographic Information System (GIS) is a valuable management tool, allowing health care managers to collect, and compare relevant demographic, epidemiologic, resource, and service data to inform program planning and human resource allocation.

Intervention or response: USAID's projects, TB CARE I and MEASURE Evaluation, are collaborating with the West Arsi Zonal Health Bureau to pilot test the use of GIS as a health management tool. In five woredas, the project team used GIS to collect, display, and link information on TB case distribution, population density, human resource capacity, drug stockouts, and the accessibility and availability of TB service and laboratory facilities. The team collected data using a structured questionnaire and then displayed this data on maps. Zonal and woreda TB focal staff will be trained on using this GIS tool for planning and human resource allocation.

Results and lessons learnt: In the five woredas, TB case distribution corresponded to the population density and the number of facilities offering TB diagnostic and treatment services. The data revealed that many laboratories had poorly functioning microscopes and an uneven distribution of trained staff in the facilities. Sixty percent of the facilities (6 of 10) in Arsi Negela and Kore, the two woredas with the highest case rates, had three or more health care staff trained in TB management compared to 93.5% (1 of 15) of facilities in the other three woredas with lower case rates. While 80% of the facilities provided services to persons with HIV and TB, these services were integrated in approximately one-third (6/20) of the facilities.
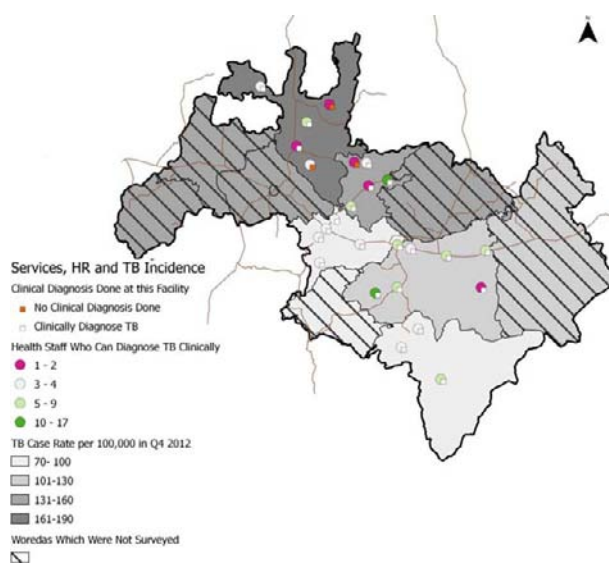
Figure   TB health staff distribution in West Arsi Zone, Ethiopia.

Conclusions and key recommendations: The TB data collected and entered into the GIS allowed program managers to effectively show the relationships between TB case distribution, service availability, laboratory facilities, drug stockouts, and available human resources in West Arsi. These GIS displays can also assist health workers to quickly identify areas and facilities where deficiencies exist and develop targeted action plans to quickly correct these and improve service quality. While piloted for TB, GIS can also be used to inform programming and decision making in relation to other diseases.

PC-391-01   Is it possible to replace paper-based tuberculosis reporting with electronic systems in Namibia, a resource-limited country?

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Background: Namibia is a high TB incidence country with a case notification rate (all forms of TB) of 529/100 000 in 2012. The National Tuberculosis Programme (NTP) at district level is run by non-substantive District TB and Leprosy Coordinators (DTLCs). The NTP has been using a paper-based data system since 1991, making retrospective TB data analysis beyond routine indicators difficult. TB-HIV and drug-resistant TB have increased the need for patient level data tracking and inter-system triangulation, which is difficult with a paper-based system.

Intervention: In 2006, Namibia introduced the ETR.net, an electronic TB register. DTLCs were trained and computers were procured and the ETR.net was rolled out to all 34 districts (excluded the regional level) in 2007. The DTLCs entered data which were electronically forwarded to national level on a quarterly basis. Trouble-shooting visits from national level were conducted to 'problematic' districts, with no technical backstopping at regional level. Annual national level ETR.net data were compared to the paper-based data as a measure of coverage of the ETR.net, and health workers (HWs) were periodically asked on their experience with the ETR.net.

Results and lessons learnt: There was variable implementation of the ETR.net in the districts, with the country reaching 95% concordance in 2012 (Figure). Constraints included: limited computer skills, poorly maintained computers with frequent breakdown, limited internet access for data transmission, rapid staff turnover, and poor supervisory capacity at

Figure   Comparison of the total number of patients reported through paper-based system and the 2012 ETR.net in Namibia, 2006.

regional level. Data entry into the ETR.net significantly lagged behind the paper-based register. HWs perceive the ETR.net as not adding value to patient management.

Conclusions and key recommendations: Implementation of an electronic TB data system in a resource limited settings requires attention to baseline infrastructure and system-wide capacity building on computer skills, as well as an adequate pool of hardware and technical backstopping. Dedicated DTLCs are key and on-site refresher trainings and supervision can address the rapid staff turnover. A dual system with paper and electronic registers should be maintained until computer skills among HWs have significantly improved. Addition of a web module to the ETR.net can ameliorate data transfer challenges. Electronic systems that address direct patient management in addition to reporting requirements are likely to get easier buy-in with HWs.

DRUG CONSIDERATIONS IN THE TREATMENT OF TUBERCULOSIS

PC-392-01   Clofazimine for the treatment of multidrug-resistant tuberculosis: a multicenter, randomised controlled study

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Background: Multidrug-resistant tuberculosis (MDR-TB) has recently emerged as a global public health problem. The treatment outcome of MDR-TB was poor due to lack of effective drugs. Clofazimine has shown activity against *Mycobacterium tuberculosis*, including multidrug-resistant strains in vitro and in animal studies. However, clinical experience with clofazimine in MDR-TB is scarce. To evaluate the clinical efficacy and safety of using clofazimine to treat MDR-TB.

Methods: We enrolled 92 patients who had sputum-culture-positive MDR-TB in 8 major tuberculosis specialized hospital in China. Patients were randomly assigned to clofazimine therapy group ($n = 46$) and control group ($n = 46$). All patients had positive sputum-smear microscopy results at the time of MDR-TB diagnosis. Patients in two groups were adopted individual-based chemotherapy regimens based on the patient medication history and drug susceptibility test results. Meanwhile, clofazimine therapy group was added to 100 mg of clofazimine once daily for 21 months.

Results: 3 patients in each group discontinued therapy because of side effects or other reasons. The sputum culture conversion rates of clofazimine therapy
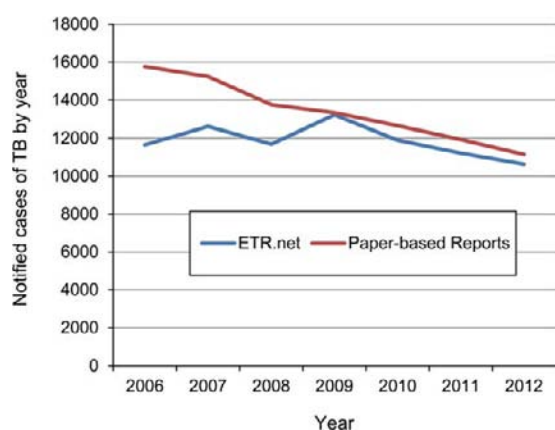
group were 74.41% (32/43) in the 21th month after treatment, higher than those of control group (58.13%, 25/43) ($P < 0.05$). The lesions absorption rates of clofazimine therapy group were 81.39% (35/43) in the 21st month after treatment, higher than those of control group (60.46%, 26/43) ($P < 0.05$). Of clofazimine therapy group, 39 had cavitary changes noted on initial chest computed tomography, and of control group, 38 had cavitary changes. The cavity closure or reduced rates of clofazimine therapy group were 71.79% (28/39) in the 21th month after treatment, higher than those of control group (57.89%, 22/38) ($P < 0.05$). Side-effects of skin such as skin discolouration, ichthyosis only occurred in 40 patients of clofazimine therapy group. Other side-effects including liver injury and gastrointestinal adverse events, etc., are similar in two groups.

Conclusions: Using clofazimine to treat MDR-TB can significantly improve clinical symptoms, promote lesion absorption and cavity closure, and accelerate sputum negative conversion. Clofazimine can help MDR-TB patients to improve life quality with mild adverse reaction but good drug tolerance.

PC-393-01 Hua-Lien Hospital, Department of Health, Executive Yuan, Hualien, Taiwan, outcome of rifabutin replacing intolerable rifampicin during anti-tuberculosis treatment

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Background: The safety and outcomes of rifabutin (RFB) replacing intolerable rifampicin (RMP) during anti-tuberculosis (TB) treatment are still unknown.
Methods: From June 2006 to June 2010, a total of 2868 newly treated TB patients in a TB referral hospital were screened.
Results: Among them, 221 (8%) non-human-immunodeficiency-virus (HIV) infection patients received RFB due to intolerable RMP-related adverse effects (AEs) were included. Among those, 158 (72%) patients successfully completed anti-TB treatment with RFB, but 47 (21%) and 16 (7%) patients experienced mild and severe RFB-related AEs and needed to discontinue RFB. Multivariate logistic regression analysis shows that females (odds ratio = 3.35, 95%CI 1.06–10.56, $P = 0.04$) and patients with hepatitis B virus (HBV) or hepatitis C virus (HCV) co-infection (odds ratio = 3.72, 95%CI 1.19–11.67, $P = 0.02$) are at a higher risk of RFB-related severe AEs (SAEs, including neutropenia, severe hepatitis and uveitis). Compared to patients intolerance to RFB, patients who tolerated RFB required signifi-

cantly shorter treatment duration for completing anti-TB treatment (316, 389 and 449 days for tolerance, mild AE and severe AE, respectively, $P < 0.01$) and higher 12-month (77.2%, 46.8% and 43.8% for tolerance, mild AE and severe AE, respectively, $P < 0.01$) and 18-month treatment success rate (94.9%, 76.6% and 62.5% for tolerance, mild AE and severe AE, respectively, $P < 0.01$). No relapse of tuberculosis was found during 2 years follow-up.
Conclusions: RFB replacing intolerable RMP was well-tolerated among non-HIV patients and with favorable treatment outcomes. Female and those with HCV or HBV co-infection were more prone to RFB-related SAEs and needed more cautious monitor.

PC-395-01 Immunosuppressive therapy and tuberculosis in a big city

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Background: To know the main differential characteristics of patients with tuberculosis (TB) that have been treated with immunosuppressive therapy (TB-IM), their underlying diseases, treatments and the exhaustivity of TB screening.
Design/methods: Population based cross-sectional study on patients that started TB treatment between 2000 and 2012 in Barcelona, Spain. Clinical charts of TB-IM patients diagnosed in the hospitals of the city were revised. Sociodemographic, clinical and outcome variables related to previous IM were analized by logistic regression calculating the odds ratios (OR) and its 95% confidence intervals (CI).
Results: 5904 patients started TB treatment during the study period and 221 presented IM. The prevalence ranged from 2% in 2002 to 8% in 2010 ($P < 0.001$). Clinical charts from 104 (47%) patients were reviewed. 40 patients (38.4%) presented chronic inflammatory disease, 36 (34.6%) any kind of cancer and 11 (10.6%) organ transplantation. Citotoxic drugs were used in 54 (47.8%), oral corticoids in 41 (36.3%) and biologic therapies in 15 (13.3%). Only 16% of patients were screened for TB before starting IM. A multivariate model identified that patients with TB-IM had increased risk to be older than 64 years (OR 5.4, 95%CI 1.9–15.1), were more frequently born in Spain (OR 1.4, 95%CI 1.0–2.1), received more individualized TB regimes (OR 3.0, 95%CI 1.9–4.6), with longer TB treatment duration (OR 4.3, 95%CI 2.0–9.3) and presented higher lethality (OR 3.2, 95%CI 1.6–6.4).
Conclusion: The prevalence of patients with TB-IM history has increased in last years. They needed a more complex treatment management and the lethality was higher. The coverage of TB screening in TB-IM patients should be improved.

PC-396-01   Effects of high-dose vitamin D in patients with pulmonary tuberculosis in Tbilisi, Georgia

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Background: Patients with tuberculosis (TB) are commonly vitamin D deficient, which may impact immunity. We investigated whether high-dose oral vitamin D3 enhances the efficacy of anti-TB drugs in treatment of pulmonary TB.

Design/methods: Double blind, randomized, controlled, intent-to-treat (ITT) trial in adults with pulmonary TB in Tbilisi. Subjects were randomized to vitamin D3 (1 400 000 IU in divided doses) or placebo for 16 weeks concomitant with standard anti-TB drugs [RIPE] through directly observed therapy. Sputum AFB cultures (LJ) were performed at weeks 0, 2, 4, 6, 8, 12 and 16. Cox proportional analysis was used for the primary outcome (time to culture conversion).

Results: A total of 784 subjects were screened, with 585 excluded (345 met exclusion criteria; 240 declined to participate). Of 199 patients enrolled, 100 were randomized to receive vitamin D3 and 99 to receive placebo. The majority of subjects (>85%) were vitamin D deficient at entry [serum 25-hydroxyvitamin D [25(OH) D] < 50 nmol/L]. Baseline characteristics were similar between groups at entry. With vitamin D3, serum 25(OH) D levels peaked at 250 nmol/L at 8 weeks and decreased to 160 nmol/L by week 16. High-dose vitamin D treatment was safe, with similar adverse events and no differences in serum calcium levels between groups. A total of 192 subjects with sputum culture-confirmed TB were included in modified ITT efficacy analysis. A total of 23 (12%) had confirmed multi-drug resistant TB [MDR-TB; 12 vitamin D, 11 placebo]. Culture conversion rates were similar between vitamin D and placebo groups at 8 weeks and over time (HR = 0.84, 95%CI 0.62–1.15). However, the MDR-TB cohort showed enhanced culture conversion with vitamin D vs. placebo at 8 weeks (vitamin D3 88% vs. placebo 40%; $P = 0.03$) and over time ($P = 0.02$).

Conclusions: This regimen of vitamin D3 treatment was safe, but did not improve TB clearance in the overall cohort of TB patients. However, patients with MDR-TB randomized to vitamin D administration demonstrated a shorter time to culture conversion. Additional trials on the efficacy of high-dose vitamin D in MDR-TB patients are warranted.

PC-397-01   Could the common anti-inflammatories be the new coadjuvant treatment against tuberculosis?

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Background: Trying to discern the transformation of latent TB into cavitation in the lung has let us to the discover of ibuprofen as a clue treatment and prevention against TB. As seen in the minipig model, the lesions in LTBI are characterized by an early encapsulation because of the septae wich structure the lungs in big mammals (GilPLOSOne_2010_TB_minipigs). In this scenario the development of cavitary lesions—which requires a minimal size of 20 mm—appears to be impossible. In this process, the softening of the necrotic tissues appear to be paramount, and that's why—recalling previous experiences with SCID mice model treated with Ab (Guirado, Passive Serum Therapy, MicInfect 2006)—we looked after different necrotic models in mice, as C3HeB/FeJ.

Design/methods: Mice were intravenously infected with 2×10^4 *M. tuberculosis* H37Rv Pasteur. The histopathology, immune response, bacillary load and survival were evaluated. Anti-inflammatory treatments and C3H/HeN mouse strain were used to complete the characterization.

Results: Massive intra-alveolar neutrophilic infiltration related to the peripheric dissemination of infected foamy macrophages lead to the rapid growth of the granulomas. A central necrotic area appeared when they overpassed a certain size. This center evolved towards a progressive cellular destruction, the alveoli cell walls initially being conserved (caseous necrosis) but finally destroyed (liquefactive necrosis). From day 28 and on, lesions tended to coalesce into superlesions. The anti-inflammatory treated and C3H/HeN groups presented better outcome regarding bacillary load, histopathology and survival and an anti-inflammatory immune response profile.

Conclusion: Because of the role of the massive neutrophilic infiltration, inflammation might be a key factor in the progression towards active tuberculosis. These results highly support the idea of the introduction of ibuprofen in the treatment of active TB could be very benefitial to the patients, specially for those
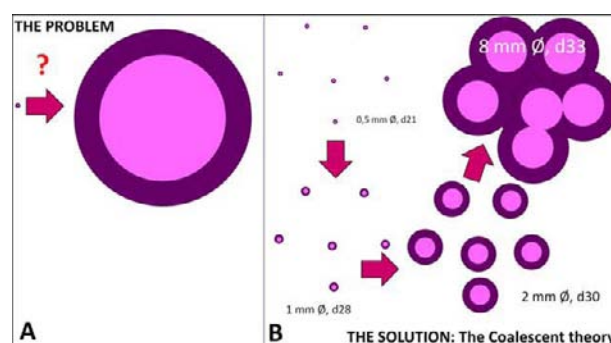
suffering from MDR/XDR, which have no other hope. For all this, we strongly ask for scientists to perform Phase III Clinical Trials able to directly assess this effect in humans. Moreover, observational studies could be also be needed to compare the incidence of TB in different cohorts—currently treated or not with low-dose aspirin, for example patients suffering of diabetis or a cardiac situation requiring anti-aggregation treatment.

PC-398-01 Pyrazinamide-induced hepatoxicity: caution when using recommended daily dosage for body weight bands

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Background and challenges to implementation: World Health organization recommends formulations and fixed dose combinations (FDCs) of anti-TB drugs and proposes standardized daily dosage for body weight bands to facilitate procurement, distribution and administration of treatment to patients. Practices according to available dosage recommendation including National TB Program (NTP) guidelines in Thailand led to pyrazinamide (PZA) dosing in some weights higher than the upper limit of its recommended dose (30 mg/kg/day) (see Table).

Intervention or response: A prospective study was conducted at Phattalung provincial hospital in Thailand comparing the incidence rate of PZA-induced hepatotoxicity (diagnosed by doctor, and confirmed by increased liver enzyme and re-challenge result) among 3 patient groups treated with PZA dosing: A) 15–25 mg/kg/day B) >25–30 mg/kg/day C) >30–40 mg/kg/day. Study subjects were TB cases registered during October 2007–June 2009. All cases with age of ≥15 years old and treated with isoniazid,rifampicin and PZA were included. Cases with renal failure and received PZA according to creatinine clearance were excluded. Data were analysed by survival analysis and multiple Cox regression.

Results and lessons learnt: Among 391 patients with age ranged between 16–103 years, 273 (70%) were male, 89 (23%) had co-morbidity associated with hepatotoxicity including HIV/cirrhosis/alcoholism/hepatitis,and 20 developed PZA-induced hepatotoxicity. Of 84 group A patients, 2 developed PZA-induced hepatotoxicity (2 per 1000 person-weeks [pw]) with incidence rate of 18/1000 pw at 2nd week. Five of 160 group B patients developed PZA-induced hepatotoxicity (4/1000 pw) with incidence rates of 5, 11, 6 and 6/1000 pw-week at 1st, 2nd, 3rd and 4th week, respectively. Thirteen of 147 group C patients developed PZA-induced hepatotoxicity (12/1000 pw) with incidence rates of 7, 29, 23, 24, 10

Table   PZA dosing according to recommended daily dosage for body weight bands

Recommendation	Body weight bands (kg)			
4-FDCs (H75/R150/Z400/E275)	30-37	38-54	55-70	>70
PZA dose (mg/day)	800	1200	1600	2000
PZA dose (mg/kg/day)	21.6-26.7	22.2-31.6	22.8-29.1	28.2
Weights with PZA>30 mg/kg/day		38-39		
NTP 2005	30-39	40-49	≥50	
PZA dose (mg/day)	1000	1500	2000	
PZA dose (mg/kg/day)	25.6-33.3	30.6-37.5	≤40	
Weights with PZA>30 mg/kg/day	30-33	40-49	50-66	
NTP 2008	30-39	40-49	≥50	
PZA dose (mg/day)	1000	1250	1500	
PZA dose (mg/kg/day)	25.6-33.3	25.5-31.3	≤30	
Weights with PZA>30 mg/kg/day	30-33	40-41		

and 16/1000 person-week at 1st, 2nd, 3rd, 4th, 5th, 9th week, respectively. The risk of PZA-induced hepatotoxicity among those with PZA >30–40 mg/kg/day was greater than those with PZA 15–30 mg/kg/day with statistical significance (hazard ratio adjusted by age, sex and co-morbidity = 3.33, 95%CI 1.30–8.50, $P = 0.007$).

Conclusions and key recommendations: Incidence rate of PZA-induced hepatotoxicity was highest with PZA dosing of >30–40 mg/kg/day. Recommended dosage for body weight bands should be used with caution for some weights with PZA dosing of >30 mg/kg/day.

PC-399-01 Level of isoniazid metabolites in tuberculosis patients depending on acetylation genotype

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One is the putative reason of insufficient tuberculosis (TB) chemotherapy is a deficit of data concerning metabolism peculiarities of the most effective agent isoniazid in TB-patients. That's why the aim of the present work was an investigation of acetylisonizid (AcINH) and hydrazine (HZ) concentration in tuberculosis patients with consideration of their acetylation genotype.

NAT2 (N-acetyltransferase 2) polymorphisms C>T 481 NAT2*5A, G>A 590 NAT2*6A, G>A 857 NAT2*7A/B were analyzed with the help of polymerase chain reaction. Isoniazid (INH) and AcINH concentration was detected in venous blood 2, 4, 6 and 24 h. After ingestion of standard dose of INH, recommended by DOTS-strategy (4–6 mg/kg), according to Vollenberg method with modification of Shenderova R. I., 1975 with spectrophotometer. The concentration of HZ was detected by method of Filov V., 1982 with spectrophotometer. The blood samples were obtained from TB-patients with new cases from Odesa Regional Tuberculosis Dispensary in 2012.

Among 84 TB-patients according to NAT2 genotype 39.3% individuals belong to rapid or intermediate acetylators (RA/IA), others—60.7%—to slow acetylators (SA). In RA/IA the INH concentration 4
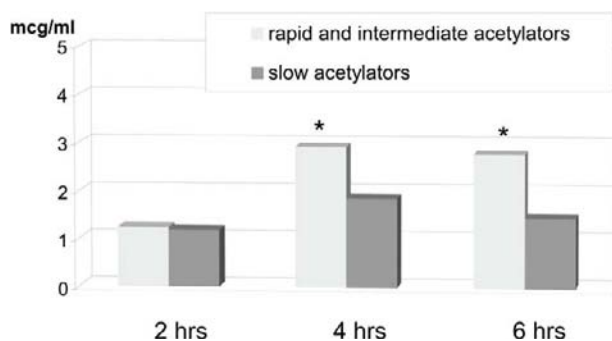
Figure Ration acetylisoniazid/isoniazid in blood of TB-patients in different time intervals after isoniazid intake. *$P < 0.05$ (correspondently to slow acetylators).

and 6 h after INH intake was 20.6% ($P = 0.047$) and 38.0% ($P = 0.044$) correspondently less, than in SA. After 4 h of INH administration in SA the level of AcINH was 20% less than in RA/IA ($P = 0.033$). Also after 4 and 6 h in RA/IA the ratio AcINH/INH was on 57.0% ($P = 0.026$) and 89.1% ($P = 0.005$) higher, than in SA (Figure). The content of HZ in RA/IA 2 and 4 hrs after INH ingestion was on 25.1% ($P = 0.030$) and 21.2% ($P = 0.032$) correspondently lower, than in SA. The obtained data showed that in RA/IA there is higher production of AcINH and less HZ than in SA. It can be explained by the fact that in RA/IA INH biotransformation predominantly occur through production of AcINH, that later transform into acetyl- and diacetylhydrazine. In the same time in SA INH is transformed into HZ that later undergo oxidation in liver. That may determine peculiarity of INH toxicity depending on acetylation genotype.

PC-400-01   What determines initial loss to follow-up in tuberculosis patients at primary health care facilities in South Africa?

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Background: In South Africa TB incidence increases annually. Previous research has indicated 25% of individuals diagnosed with TB do not start treatment in a timely manner at primary healthcare facilities (PHC). These individuals, termed 'initially lost to follow-up' (ILF), may transmit *Mycobacterium tuberculosis* within communities thereby contributing to the epidemic.
Design/methods: In a matched case-control study, 641 individuals (168 cases, 473 controls) were identified at 80 PHC in five provinces of South Africa. Cases (ILF) were smear positive TB patients who did not start treatment within four weeks of diagnosis. Controls were smear positive TB patients who started treatment within four weeks of diagnosis. Conditional logistic regression models were used to investigate determinants associated with ILF. Of the partici-

pants identified, 188 were found in the community (40 cases, 148 controls). Questionnaire data from these individuals were used to populate additional models.
Results: For individuals identified at facilities ($n = 641$), scanty positive smear grade was significantly associated with ILF (OR = 0.35, 95%CI 0.15–0.72, $P = 0.01$) comparing 1+ to scanty (OR = 0.23, 95%CI 0.09–0.56, $P < 0.01$) comparing 2+ to scanty and (OR = 0.36, 95%CI 0.17–0.76, $P = 0.01$) comparing 3+ to scanty. Whether a person was not found in the community was significantly associated with ILF (OR = 1.99, 95%CI 1.17–3.41, $P = 0.01$). For individuals found in the community ($n = 188$), scanty positive smear grade was significantly associated with ILF comparing 1+ to scanty (OR = 0.03, 95%CI 0.00–0.42, $P = 0.01$) and 2+ to scanty (OR = 0.05, 95%CI 0.00–0.96, $P = 0.05$), as was whether an individual made an economic contribution to the household (OR = 5.46, 95%CI 1.27–23.43, $P = 0.02$).
Conclusion: Scanty smear positive individuals may not be as ill as their 1+/2+/3+ counterparts which could influence health-seeking behaviour, or healthcare workers may be less prone to trace scanty positive individuals. Individuals may attend facilities other than their own because of stigma, thereby hindering tracing efforts. Individuals on treatment have to attend facilities daily for DOTS, leading to less employment opportunities thus indicating conflict between the economic demands and the welfare of a household. Interventions ensuring treatment of scanty smear positive TB patients and innovative methods of case finding may be useful to decrease ILF.

PC-401-01   Factors associated with default from tuberculosis treatment in the country of Georgia: a case control study

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Background: Poor adherence to tuberculosis (TB) treatment is one of the main challenges for TB control. It fosters TB transmission in the community and emergence of drug resistance. TB treatment default rate remains above 10% globally. We sought to determine factors associated with default from TB treatment in the country of Georgia.
Design/methods: An unmatched case-control study was conducted in 2008–2010; re-treatment TB cases registered in the Georgian National Tuberculosis Program (NTP) surveillance database between 2007 and 2010 were enrolled in the study. Patients with the TB case definition of 'treatment after default' were

classified as cases and controls were selected from all other re-treatment cases without a history of treatment default. Data on factors potentially associated with TB treatment default was collected by interview. Data on demographic characteristics, socio-economic status, alcohol and drug abuse, and imprisonment were collected.

Results: 60 'treatment after default' and 92 re-treatment cases without any previous episode of defaulting were interviewed. 55% (33) defaulted from the previous TB treatment within the first three months of treatment. Early default from treatment was most likely to happen among patients treated in TB dispensaries, then in the directly observed treatment (DOT) spots, then among those treated by a patronage nurse, with the least likely to default being patients treated in hospitals (adjusted odds ratio [aOR] 2.2 95% confidence interval [CI] 1.0–4.9). Among 60 defaulters interviewed, 41.7% (25) attributed their default to feeling better, 15.0% (9) to travelling away from the treatment site, 15.0% (9) to family problems, 13.3% (8) to side-effects and 15.0% (9) did not report a reason. On multivariate analysis, female gender (aOR 3.8, 95% 1.1–13.2), unsatisfactory living conditions (aOR 3.2, 95%CI 1.1–9.4), and alcohol abuse (aOR 5.8, 95%CI 1.5–22.4) were independently associated with the default.

Conclusion: The rate of defaulting was higher during the initial three months of treatment. Multiple factors were attributed by defaulting patients as cause for abandoning treatment whereas different factors were independently associated with the TB treatment default. Strengthening of outpatient treatment and enhanced psycho-social support to TB patients may reduce default rates.

PC-402-01 Linezolid for the treatment of extensively drug-resistant tuberculosis: a multicenter, randomized controlled study

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Background: Extensively drug-resistant tuberculosis (XDR-TB) has recently emerged as a global public health problem. Linezolid is a new antibiotic with activity against *Mycobacterium tuberculosis* in vitro and in animal studies. To evaluate the clinical efficacy and safety of Linezolid for the treatment of XDR-TB.

Methods: We enrolled 59 patients who had sputum-culture-positive XDR-TB tuberculosis in 5 major tuberculosis specialized hospital in China. Patients were randomly assigned to linezolid therapy group ($n = 30$) and control group ($n = 29$). Patients in two groups were adopted two years of individual-based chemotherapy regimens based on the patient medica-

tion history and drug susceptibility test results. Meanwhile, linezolid therapy group was added to linezolid that started at a dose of 1200 mg per day for 4 to 6 weeks, followed by 300 to 600 mg per day for at least 6 months.

Results: Four patients in linezolid therapy group discontinued therapy because of side effects or other reasons, and three patients in control group discontinued therapy because of side effects or other reasons. In linezolid therapy group, the longest period of applying linezolid for treatment was up to 24 months, the minimum was 6 months with the average of about 12 months. The sputum culture conversion rates in the linezolid therapy group were 73.07% (19/26) in the 12th month after treatment, significantly higher than those of control group (30.76%, 8/26) ($P < 0.001$). The cavity closure or reduced rates in the linezolid therapy group were 57.69% (15/26) in the 12th month after treatment, significantly higher than those of control group (26.92%, 7/26) ($P < 0.001$). Of 20 patients completed therapy in the linezolid therapy group, 14 (70%) had treatment success (cured and treatment completion). Of 21 patients completed therapy in the control group, only 7 (30%) had treatment success. In the linezolid therapy group, 13 (50%) had adverse events such as peripheral neuropathy, leucopenia and anaemia, gastrointestinal reactions, liver injury, etc. However, 10 (38.46%) had adverse events in the control group.

Conclusions: Linezolid containing chemotherapy for treatment of XDR-TB may significantly promote cavity closure, accelerate sputum culture conversion and improve treatment success rates. Meanwhile adverse reaction might be tolerated and resolve after suitable intervention. Therefore, we suggest that linezolid be recommended for the treatment of XDR-TB.

PC-403-01 Effectiveness and toxicity of aminoglycoside use for MDR-TB treatment: a matter of dead or deaf?

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Background: Aminoglycosides (AGs) are considered a critical component on multi-drug resistant tuberculosis (MDR-TB) treatment regimens. Although extensive data and experience supports their efficacy for the treatment of sensitive TB, data focusing specifically on the effect of AGs on clinical outcomes of MDR-TB patients is scarce. Moreover, factors leading to AG-related toxicity in patients receiving MDR-TB treatment are unknown. In this study, we determine the effect of AGs over clinical outcomes of MDR-TB

patients and the risk factors associated with AG-related toxicity.

Methods: All confirmed and presumed MDR-TB cases older than 15 years of age who were initiated on MDR-TB treatment between January 2006 and June 2012 in Botswana were included in the analyses. We used mixed effect models to determine the effect of AGs over clinical outcomes and the risk factors associated with ototoxicity.

Results: 410 MDR-TB patients were included in the analyses. 330 (80%) had good clinical outcomes and 280 (68%) developed ototoxicity. Overall, 272 (66%) were co-infected with HIV. Good clinical outcomes (cure or treatment completion) were independently associated with longer AG treatment (adjusted odds ratio [aOR] 1.42, 95% confidence intervals [CI] 1.27–1.59) and higher AG doses (aOR 1.13, 95%CI 1.01–1.28). In addition, longer duration of AG treatment (aOR 1.98, 95%CI 1.86–2.12) and higher AG dose per weight (aOR 1.04, 95%CI 1.01–1.08) were also strongly associated with development of ototoxicity. Duration of AG treatment modified the effect of AGs dosage over the risk of ototoxicity by increasing it as the time on AGs increased (aOR 1.23, 95%CI 1.11–1.35).

Conclusion: AGs are effective for the treatment of MDR-TB. However, they are associated with high risk of ototoxicity. Duration of AG treatment and AG dosage are associated with improved clinical outcomes. However, these factors are also the most important determinants of ototoxicity.

CLINICAL ISSUES AND TUBERCULOSIS

PC-404-01 Pleural cavity sterilization procedure for the management of complicated pleuro-pulmonary tuberculosis

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Background: Pleuropulmonary tuberculosis and its complications, pneumothorax, hydropneumothorax, empyema thoracic and bronchopleural fistula are relatively frequent conditions in Pakistan. The management of such cases has always been challenging for clinicians as a large number of these (TB) patients are so debilitated that they are unfit for surgery and mortality and morbidity in these patients is significantly high.

Design/methods: We treated all such cases through the technique of cavity sterilization procedure. This technique is not only innovative as all such cases in the literature are being managed by decortication combined with thoracoplasty or thoracomyoplasty, but is also non-invasive as the patients do not require any general anesthesia or any invasive surgery.

The treatment is based on tube thoracostomy through most dependent intercostal space and regular pleural cavity washes with antiseptic solution usually normal saline.

Results: A total of 32 patients, 17 males and 15 females were treated through this method, at the Department of Thoracic Surgery, Ojha Institute of Chest Diseases, Dow University of Health Sciences Karachi, during January 2006 to December 2008. We achieved 100% re-expansion of the diseased lung with almost complete anatomical and functional restoration in 30 patients.

Conclusion: The cavity sterilization procedure comprising of tube thoracostomy with regular pleural cavity wash is a good alternative in the management of complicated pleuropulmonary tuberculosis and conditions like TB empyema and broncho-pleural fistulas as

1 It has least mortality and morbidity
2 It ensures complete anatomical and functional restoration of diseased lung in majority of cases as compared to thoracoplasty and thoracomyoplasty where lung re-expansion cannot be achieved
3 The procedure can also be performed in patients who are not fit for surgery
4 This procedure can be performed in any health facility as it does not require any operation theatre or general anesthesia.

The most significant advantage of this procedure is that the high TB burden countries which are poor and underdeveloped can be greatly benefited with this procedure as it is cost effective and easily applicable in any hospital setup even in remote areas

PC-405-01 Prevalence of non-tuberculous mycobacteria infection in drug-susceptible and drug-resistant tuberculosis patients undergoing treatment in a tuberculosis center in Karachi

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Background: Non-tuberculous mycobacteria (NTM) are commonly encountered as environmental bacteria, some of which may cause lung diseases. The aim of this investigation was to determine distribution of NTM species isolated from clinical specimens of drug-resistant and drug-susceptible patients.

Design/methods: A total of 3760 patients' samples (pulmonary) were cultured. Most were drug-susceptible patients while 322 were drug-resistant. All cultures were grown using MGIT960 and on LJ slopes. Identification of mycobacterial species was performed by using a commercial line-probe assay (GenoType Mycobacterium CM/AS; HainLifescience, Germany).

Results: 1321 (35.13%) specimens were positive for mycobacterial culture, of which 69 (5.2%) cultures were positive for NTM. These positive cultures were

obtained from 44 drug-susceptible patients (%), and 25% from drug-resistant cases. The most common isolates in frequency were *Mycobacterium tuberculosis* complex 23, *M. intracellulare* 13, *M. fortuitum* 11, *M. kansasii* 10, *M. abscessus* 5, *M. gordonae* 3, *M. malmoense* 1, *M. avium* 1, and two mixed cases.
Conclusion: Finding NTM among follow-up cases of MDR patients is a significant finding which may affect treatment regimen. This study also highlights the importance of follow-up cultures in TB treatment cases.

PC-406-01 Utility of the chest X-ray in the era of IGRA testing for latent tuberculous infection prior to anti-TNF therapy

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Background: Anti-TNF therapies are associated with increased risk of reactivation of latent *Mycobacterium tuberculosis* infection (LTBI). Screening for LTBI is recommended prior to commencing anti-TNF therapy. BTS guidelines for screening incorporate epidemiologic risk, clinical examination, Mantoux testing and chest radiography (CXR). Other guidelines recommend the use of interferon gamma release assays (IGRAs). We audited the use of IGRA and CXR as part of screening for LTBI in patients who were being considered for immunosuppressant therapy.
Design/methods: All IGRAs requested from Glasgow Royal Infirmary (GRI) over a 21 month period were retrospectively assessed for the following: patient history, test indication and result, CXR report and patient outcome. GRI serves the most deprived population in the UK. TB incidence in Glasgow was 19.4/100 000 in 2010. A single laboratory provides TB bacteriology for the whole of Glasgow, and is the sole provider of IGRA testing for LTBI utilising T-Spot. *TB* (Oxford Immunotec, Abingdon, UK).
Results: Between August 2010–May 2012, 354 T-Spot®.TB tests were performed. Planned immunosuppressant therapy was the indication in 70% (n = 248); etanercept was the most commonly proposed drug (32%, n = 78), followed by adaluminab (29%, n = 72), anti-TNF not otherwise specified (11%, n = 28) and infliximab (6%, n = 15). Of those for whom immunosuppression was the indication, 80% (n = 199) of T-Spot.TB tests were negative, 17% (n = 41) indeterminate and 3% (n = 8) positive. CXR was performed in all but 6% (n = 11). CXR findings and patient outcomes for patients with negative T-Spot. TB tests are summarised in the Table. Of the 16 abnormal CXRs in keeping with possible previous TB, 81% (n = 13), had evidence of calcified granulomata. All 16 were referred to a TB specialist for review and none had chemoprophylaxis commenced or any alterations in their management recommended.

Table Outcome of a negative T spot test

Negative T spot test	n (199)	Chemo-prophylaxis given	CXR changed management?	Patient outcome (immuno-suppressant)	LTBI reactivation
CXR normal	77.9% (155)	0	No	5.2% (8) not commenced 7.1% (11) patient declined 0.6% (1) stopped (recurrent LRTIs) 0.6% (1) stopped (new renal CA)	0
CXR abnormal (possible previous TB)	8% (16)	0	No	6.25% (1) not commenced (disease activity too low) 6.25% (1) stopped (leg ulcers) 6.25% (1) stopped (wheeze) 6.25% (1) stopped (leucopenia)	0
CXR abnormal (other)	6% (12)	0	No	8.3% (1) patient declined	0
CXR previously normal	2.5% (5)	0	No	20% (1) patient DNA f/u	0
CXR not done	5.5% (11)	0	N/A	9.1% (1) patient declined 45.5% (5) not commenced (disease activity too low)	0

Conclusion: With increasing use of IGRAs, new guidance on screening for LTBI prior to anti-TNF therapy is required. In our cohort of 248 patients, the majority had a negative T spot test reflecting that despite high levels of deprivation, TB prevalence in Glasgow is low. CXR did not alter patient management, TB chemoprophylaxis was not given in any case and there were no cases of LTBI reactivation or de novo TB within the follow-up period (11–32 months). We propose that if IGRA is negative, CXR is not required as part of screening for LTBI prior to anti-TNF therapy.

PC-407-01 Characteristics of sarcoidosis initially misdiagnosed as pulmonary tuberculosis

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Background: Differential diagnosis of pulmonary TB is still difficult. Tuberculosis and sarcoidosis are chronic granulomatous diseases that are similar in many aspects. Sometimes it is difficult to distinguish between these two diseases. We found the tendency to overdiagnosis of pulmonary TB in TB hospital.
Design/methods: Medical reports of 35 patients were analyzed. All patients have been hospitalized in TB hospital with wrong diagnosis 'pulmonary TB'. Males 37%, mean age 44.6 ± 11.8 yrs. Clinical, radiological, laboratory data of all admitted patients were collected. Odds ratios (OR) and nominal 95% confidence intervals were presented.

Results: The period from the disease manifestation up to establishment of final diagnosis was 167.7 ± 131.9 (mean ± SD) days. 26% of patients were previously treated of an assumed pneumonia before hospitalization in TB hospital, 54% of patients up to making a hospital diagnosis received anti-tuberculosis treatment. All patients have been hospitalized with wrong diagnosis 'pulmonary TB', a principal cause—misinterpretation of chest radiogram. In 5.7% of all cases a few acid-fast bacilli were found in sputum by luminescent microscopy (that we suppose as false-positive result). Factors associated with increase of diagnostic delay: male sex (OR 0.32, 95%CI 0.16–0.66, $P = 0.001$), acute disease beginning (OR 0.24, 95%CI 0.08–0.70, $P = 0.005$), low body weight (OR 0.10, 95%CI (0.01–0.73, $P = 0.005$), fever (OR 0.23, 95%CI 0.07–0.78, $P = 0.01$), weakness (OR 0.43, 95%CI 0.21–0.88, $P = 0.018$), productive cough (OR 0.34, 95%CI 0.13–0.91, $P = 0.024$), infiltrative pattern on chest X-ray (OR 0.02, 95%CI 0.00–0.12, $P = 0.000$), cavitary pattern (OR 0.05, 95%CI 0.01–0.39, $P = 0.000$), detection of AFB (OR 0.22, 95%CI 0.05–0.96, $P = 0.026$), not the use of biopsy (OR 0.09, 95%CI 0.01–0.78, $P = 0.000$).

Conclusion: Several reasons for long delays were found, but the main reason was the error of radiologist. It is important to consider a low sensitivity of chest X-ray. Other important reasons for delay were non-typical symptoms. Diagnosis requires histological confirmation. Due to high incidence of tuberculosis in our country there is a tendency to overdiagnose tuberculosis.

PC-408-01   BCG vaccination is associated with decreased severity of tuberculosis in Pakistan

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Background: Pakistan ranks 6th amongst high-burden countries worldwide and has an incidence of 231/100 000 population. Vaccination with Bacille Calmette–Guérin (BCG) is given at birth to protect against tuberculosis (TB) in Pakistan.
Objective: To determine whether BCG has any protective effect against more severe forms of TB in Karachi, Pakistan.
Material and methods: This was a cross-sectional multi-center hospital-based study. TB patients ($n = 218$) with pulmonary (PTB, $n = 120$) or extrapulmonary (ETB, 98) were recruited, and the presence of a BCG vaccination scar was documented. Cases were further classified into minimal, moderate and advanced PTB or less severe (LETB) or severe disseminated (D-ETB) disease. The association of age, gender and severity of TB infections with BCG vaccination of the individual TB cases was investigated.

Results: No difference was found of the BCG vaccination status of PTB and ETB cases, or in relation to age or gender. Patients under 29 years of age comprised the largest group. There were more females with ETB than PTB. The largest group within ETB comprised those with tuberculous lymphadenitis (LNTB, 39%). A significantly greater number of LNTB cases had received BCG vaccinations than had those with pleural (unilateral) TB ($P = 0.004$), and tuberculous meningitis ($P = 0.027$) groups. Also, there were more immunized patients with pulmonary as compared with pleural disease ($P = 0.001$).
Conclusion: LNTB represents localized granulomatous disease and the observation of higher vaccination rates in this group suggests that BCG has protected against more severe forms of TB in this high-burden region.

PC-409-01   Chronic pulmonary aspergillosis may frequently complicate treated tuberculosis

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15–25% of Africans treated appropriately for pulmonary tuberculosis (PTB) die within a few years of completing treatment. Chronic pulmonary aspergillosis (CPA) may be responsible for many of these deaths. CPA is a progressive condition leading to prolonged fatigue and breathlessness over many years and ultimately death from respiratory failure or sudden massive haemoptysis. A recent controlled trial in India, however demonstrated treatment with generic fixed dose Itraconazole is well tolerated and leads to stabilization or improvement in 76% of patients. In 1970, 34% of 544 British patients with residual cavities after treated PTB were found to have precipitating antibodies to Aspergillus. Half of these developed an aspergilloma, a late manifestation of CPA, within a 2 year follow up period. Our group has recently estimated the global annual incidence of CPA at 372 000 cases, with a global 5 year period prevalence of 0.8 to 1.3 million cases and 43 cases per 100 000 in a representative sub-saharan country (DR Congo). This estimate was based on the results of the 1970 survey and current published data on the frequency of residual cavitation after completing PTB treatment. It does not take account of the possibility of either increased susceptibility or reduced chronic inflammation with fibrosis due to HIV/AIDS. We aim

Table Findings from survey of 400 patients previously treated for tuberculosis in Gulu, Uganda

Finding	All patients (n = 400) n (%)	HIV negative (n = 200) n (%)	HIV positive (n = 200) n (%)	P value
Median CD4 count	—	—	415 cells/μL	—
CD4 below 200	—	—	30 (15% of all HIV positives)	—
Mean time since TB treatment	44 months	42 months	46 months	0.55**
Cough	77 (19)	31 (15)	46 (23)	0.057
Haemoptysis	9 (2)	4 (2)	5 (2)	1.000*
Fatigue	150 (37)	75 (37)	75 (37)	1.000
Breathlessness	149 (37)	75 (37)	74 (37)	0.918
Chest pains	166 (41)	76 (37)	90 (45)	0.155
One or more chronic symptoms	238 (59)	115 (57)	123 (61)	0.415
Pleural thickening on CXR	69 (17)	45 (23)	24 (12)	0.006
Cavities on CXR	97 (24)	61 (31)	36 (18)	0.004
Single	22 (6)	11 (5)	11 (6)	0.990
Multiple	75 (19)	50 (25)	25 (13)	0.001
Aspergilloma on CXR	12 (3)	5 (3)	7 (4)	0.507
Possible	9 (2)	5 (3)	4 (2)	1.000*
Probable	3 (1)	0	3 (2)	0.123*
Chronic symptoms and X-ray changes	60 (15)	36 (18)	24 (12)	0.093

Note: P value for difference between HIV positive and negative cases calculated by chi-squared except for rows marked * where Fishers exact test was used and rows marked ** where t-test was used to compare means.

to measure the prevalence of CPA in Gulu, Uganda. Diagnosis requires a combination of 1) chronic respiratory symptoms, 2) radiological changes (either aspergilloma or progressive cavitation/pleural thickening on chest X-ray) and 3) evidence of Aspergillus infection (culture growth from respiratory sample or specific antibodies). We recruited 400 patients who completed PTB treatment within the last 7 years, plus 300 healthy controls, between October 2012 and January 2013. Chronic respiratory symptoms were present in 59%. Chest X-ray demonstrated cavitation in 24%, pleural thickening in 17% and aspergilloma in 3%. Overall 15% of patients had both chronic symptoms and X-ray changes consistent with CPA. These initial results suggest that CPA may well be a common complication of treated pulmonary tuberculosis. Serum has been taken from patients and will be screened for antibodies to Aspergillus. We plan to perform a re-survey of this cohort in 2014 with repeat chest X-ray and serology. This will allow us to identify progression of cavitation. We will then be able to state the frequency of CPA as a complication of PTB in this African population.

PC-410-01 Clinical and immunological manifestation of generalized tuberculosis

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Background: Analysis of clinical course and immune condition in patients with generalized tuberculosis (multiple organs involvement).
Methods: Retrospective analysis of 115 cases with generalized tuberculosis was performed.
Results: The majority (61.3%) of surveyed patients were males, 34.5% of those were aged 18–40 years old. 26.7% of the patients entered the hospital within the period of one year after the first symptoms of the disease occurred. The majority of them were provided with out-patient treatment. The most common form of non-pulmonary tuberculosis, among those surveyed was skeletal tuberculosis (35.8%), the second most common form was genitourinary tuberculosis (20.3%), 10.8% of the patients had polyserositis, in 8.8% of cases lymph node tuberculosis was detected, and in 5.4% miliary tuberculosis was revealed. In 18.9% of patients occasional combinations of generalized tuberculosis were seen. One third of the patients (34.5%) had a combination of 3 and more localizations of tuberculosis. In 34 cases (29.6%) tuberculosis was associated with HIV infection. All patients with tuberculosis and HIV/AIDS co-infection were examined for CD4 cells. The analyze of CD4 lymphocytes quantity has revealed that in the case of decrease of the number CD4-blood cells up to 200 in 1 μl the vast of pulmonary tissue damage with the presence of breakdown and total dissemination were observed in different organs in 88.9% patients. In patients with CD4-blood cells more than 200 in 1 μl the character of such disturbances were revealed only in 42.9% ($P < 0.05$) cases.
Conclusion: Patients with generalized tuberculosis most commonly present with lung damage, skeletal tuberculosis, and genitourinary tuberculosis. Almost in third part of patients generalized tuberculosis develops against immunodeficiency caused by HIV infection. Extensive and widespread damages are seen in the patients with CD4 cell count < 200 in 1 μl.

PC-411-01 Tuberculosis and renal failure, Egypt experience

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Background: the prevalence rate of TB in Egypt is 28/100 000 population and the incidence rate is 17/100 000. There may be interaction between tuberculosis and renal failure, which is a debilitating disease, and therefore, it may be considered one of the predisposing factors.

Objectives:

1 To measure the magnitude of TB problem among patients of renal failure under hemodialysis by measuring the prevalence of TB among those patients.

2 Check for the possibility of any correlation between TB and renal failure as a debilitating disease.

Methodology: A nationwide study included 22 governorates. All the renal dialysis units belonging to MOH were included in the study. The patients attending these centers for dialysis were enlisted and then they were subjected to structured questionnaire through interview. Based on this screening questionnaire, patients who gave suggestive history were subjected to further investigation (X-ray).

Results: Results showed that number of investigated dialysis cases was 3534. Nineteen of them got TB before onset of dialysis and manifestations of renal failure with a rate of 0.5%. Fifteen cases manifested TB during dialysis and after onset of renal failure with a rate of 0.4%. 3 cases manifested TB before dialysis and continued their treatment during the period of dialysis. Males constituted 66.7% of TB patients during dialysis while 78.9% of TB patients before onset of dialysis were males. The mean age of patients who got TB before dialysis was 47.9 years while the mean age of patients who manifested TB during dialysis was 50.5 years. Only 0.3% of all the dialysis patients gave a past history of contact with tuberculosis patients, no history of contact with tuberculosis patients was reported among the patients who developed TB before dialysis and 6.7% of patients who developed TB during dialysis gave history of contact with tuberculosis patients. Pulmonary tuberculosis form contributed to 94.7% of tuberculosis patients before dialysis while extra-pulmonary contributed to 53.3% of tuberculosis after dialysis.

Conclusion: The study concluded that socio-demographic factors were not associated with occurrence of TB among renal failure; history of drug injection in treatment of TB has no role in occurrence of renal failure and TB among patients with renal failure and on hemodialysis is equal to 15 times the prevalence of TB among the general population. Frequent examination of patients under dialysis is recommended. INH chemoprophylaxis may be studies.

PC-412-01 C-reactive protein and serum amiloid A in patients with tuberculosis

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Aim: To study level of serum amyloid A (SAA) in blood serum of patients with active pulmonary tuberculosis (TB) and its comparison with level of C-reactive protein (CRP).

Materials and methods: We studied level of SAA and CRP in blood serum of 93 TB patients in the age from 18 till 55 years (male—38 and female—55). Concentrations of SAA were determined by ELISA and CRP by immunoturbidimetric method.

Results: It was established that the level of SAA increased in 99% of patients, whereas rates of CRP was increased in 80.7% of patients. The degree of increase SAA also was much higher: the levels of SAA over 100 mg/l were observed in 68.8% of patients, but CRP—only 11.1% of cases. The degree of increase SAA was directly related with the manifestation of tuberculosis intoxication, the quantity of *M. tuberculosis* in sputum, the spectrum of drug resistance of *M. tuberculosis*, the extension of the lung process and the presence of destruction in lung tissue. A maximum value of SAA in patients with pulmonary tuberculosis was 247 mg/l. The level of SAA after 3 months of chemotherapy decreased by about half in patients with effective treatment, but remained significantly increased in comparison to the norm. In patients with inefficient of the treatment the level of SAA was not substantially changed.

Conclusion: SAA is a useful marker of activity of the process in patients with pulmonary tuberculosis and its sensitivity is higher than that CRP.

PC-413-01 How well are physicians diagnosing tuberculosis based on chest X-ray in Vizianagaram, South India?

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Background: Under the Revised National TB Control Programme in India, all presumptive Tuberculosis (TB) cases with more than two weeks of cough undergo sputum smear examination and the smear negative presumptive cases are subjected to chest X-ray (CXR) after a trial of broad spectrum antibiotics. All the physicians in the peripheral health institutions are empowered to read and make a diagnosis based on the CXR findings. The low specificity of CXR, used for the diagnosis of smear-negative TB, risks high levels of over diagnosis and there are concerns about varying CXR interpretation skills among treating physicians attending routine health care settings.

Objective: To determine whether the physicians' interpretation of CXR findings among sputum smear negative presumptive TB cases as suggestive of TB under programmatic settings, is as good as Xpert MTB/RIF (Xpert) test results.

Methods: The study was conducted under routine programme settings in the District TB Centre of Vizianagaram (population 0.6 million). All chest symptomatic

attending the centre from February to March 2013 were screened for two weeks cough and all presumptive TB cases subjected to sputum smear microscopy and Xpert testing. The smear negative cases additionally underwent CXR examination. Based on CXR findings suggestive of TB or not, cases were termed as CXR positive or negative.

Results: All the 555 sputum smear negative presumptive TB cases attending the centre were subjected to CXR and Xpert testing. There were 26 (4.7%) CXR positive and Xpert-positive TB cases, 28 (5%) CXR negative and Xpert-positive TB cases and 40 (7.2%) CXR positive and Xpert-negative TB cases. The remaining 461 (83.1%) cases were negative both for CXR and Xpert. CXR based TB diagnosis in this group would have caused 52% false negative and 66% false positive diagnosis of pulmonary TB in comparison with Xpert.

Conclusion: Over and under diagnosis of pulmonary TB with the use of CXR remains a subject of concern. Capacity building of treating physicians in interpreting CXR findings, quality control of CXRs and a standardized scoring system may improve diagnosis. Appropriate diagnosis and treatment of TB cases can be ensured when sputum smear negative presumptive TB cases are subjected to Xpert.

PC-414-01 Selective influence of exogenous pulmonary surfactant on different subpopulations of alveolar macrophages in tuberculosis

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Background: Defective production of pulmonary surfactant (PS) by alveolocytes type 2 results in accumulation of alveolar macrophages (AM) with defective lysosomal compartment without signs of phagocytic activity (I) and AM with incomplete phagocytosis (II), which promotes continuous persistence of *M. tuberculosis*. The aim of our study was to evaluate stimulating influence of exogenous pulmonary surfactant (EPS) on AM subpopulations under TB inflammation and experimental chemotherapy.

Methods: To evaluate influence of EPS on phagocytic activity of macrophages we used different experimental models: 1) bronchoalveolar lavage (BAL) from disseminated TB patients; 2) guinea pigs infected with *M. tuberculosis* strain 37Rv (infected animals received chemotherapy regimens IZN and IZN+EPS); human monocytic leukemia cells THP-1. We used transmission electron microscopy (TEM), light and luminescent microscopy.

Results: Introduction of EPS into BAL of disseminated TB patients induced: decrease in the number of AM (I) from 40% to 25%; emergence of numerous pseudopodia, phagocytosis of PS membranes; emergence of large phagolysosomes in the both subpopulations of AM. In the group of infected guinea pigs we registered decrease in the number of viable AM in BAL and increase in the number of AM (I) (41.52 + 0.91% instead of 13.61 + 0.7% in intact controls). After 3 months of treatment with IZN the number of viable AM was 72.07 ± 0.9%, while in healthy animals the same parameter was 95.87 ± 0.4%, high levels of AM (I) remained—29.72 ± 0.83%. In animals, which received IZN+EPS, BAL macrophages practically did not differ from AM of intact animals. Addition of EPS to THP-1 cells led to emergence of macrophages with long 'arms', elevation of phagocytic index 1.75 time, diffuse distribution of lysosomal compartment vs. perinuclear localization in control cells.

Conclusion: We determined pathways of EPS influence on the heterogeneous macrophage population under TB inflammation. Addition of exogenous surfactant to chemotherapy allowed improving effectiveness of TB treatment vs. chemotherapy alone.

MDR-TB: MANAGEMENT IN SPECIAL POPULATIONS

PC-415-01 Risk factors for primary multidrug-resistant tuberculosis in Vladimir region, Russia

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Background: Anti-TB drug resistance is a major public health problem. Globally, Russia ranks third in terms of estimated numbers of multidrug-resistant tuberculosis (MDR-TB) cases. The objectives of this analysis were to describe the prevalence of, and identify risk factors for, primary MDR-TB among newly diagnosed TB patients in Vladimir region, Russia.

Design/methods: We conducted secondary analysis of data collected from consecutive adults diagnosed with TB in Vladimir Regional TB Dispensary during February–December 2012. All enrolled patients underwent a clinical examination, radiology and bacteriology testing including conventional culture and drug susceptibility testing as well as HIV examination. We used logistic regression model to identify independent predictors of primary MDR-TB that occurs when a person is infected with a strain already resistant to anti-TB drugs.

Results: Of 402 patients diagnosed with TB, 335 (83%) were new cases. Of 402 patients, 60 (15%) had MDR-TB, including 44/335 (13%) with primary MDR-TB and 4/44 (9%) with primary XDR-TB;

23/ 335 (7%) were HIV infected. Of 44 primary MDR-TB cases, 17 (39%) were diagnosed during routine mass screening through the primary healthcare. Of these, 15/17 (88%) did not have symptoms suggestive fior TB. In univariate analysis primary MDR-TB disease was assosiated with positive HIV status (OR = 3.3, CI = 1.3, 8.6), homelessness (OR = 4.0, CI 1.1, 14.4) and cavitary TB disease by chest X-ray (OR = 2.7, CI 1.4, 5.2). Independent predictors of primary MDR-TB included positive HIV status (aOR = 3.6, CI 1.3, 10.0) and cavitary disease (aOR = 2.8, CI 1.4, 5.6).

Conclusion: Among new TB cases, 13% had MDR-TB, including 9% XDR-TB, suggesting ongoing transmission of drug-resistant strains in the community. These numbers are lower than WHO estimated 20% of MDR among new TB cases in Russia. Cavitation on chest X-ray and positive HIV status were independent predictors of primary MDR-TB.

PC-417-01   Treatment outcomes of retreatment Category IV default patients: a Manila-based MDR-TB treatment centre experience, Philippines, 2009–2011

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Background: Completing an 18 to 24 month treatment regimen for patients undergoing Category IV treatment have proven to be daunting for the MDR-TB program since the scaling up of the treatment services in 2009 in the country. Patients still have variously contributed to the increasing default rate, and largely affects case-holding measures for MDR-TB treatment centers. Despite the incidence of defaults, defaulted patients with intentions to be re-treated were readmitted to the program.

Intervention or response: The study involved reviewing records of the defaulted patients from the Category IV treatment, and patients who signified their intentions to be re-enrolled, were re-admitted to the program at the PTSI Tayuman PMDT Treatment Center in Manila from the 2009–2011 cohort. The individual records of these patients were reviewed and tabulated, and analyzing their demographic data, and associated factors contributing to their new treatment outcomes.

Results and lessons learnt: Of the patients from the 2009–2011 cohort that were declared as treatment defaults and were subsequently re-appropriated with revised Category IV regimens on their re-treatments, only one patient (10.0%) successfully completed the re-treatment and was declared as 'completed,' with two patients declared as 'died' (10.0%) and the rest of the patients succumbing to repeat defaults (80.0%).

Conclusions and key recommendations: Despite the

counter measures implemented for treatment defaults by the program for patients under Category IV, a large percentage of patients still succumbed to repeat defaults even after having been re-enrolled to the program. A more thorough review of the program protocols should be initiated to the program to lessen the default rate, key in measures that would make the treatment services accessible to far flung areas in the Philippines, and strengthen case-holding strategies to ensure continuous treatment of the patients under the program.

PC-418-01   Proportion of multidrug-resistant tuberculosis cases in a community representative tuberculosis prevalence survey, Gujarat, India

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Background: To determine the point prevalence of bacteriologically positive tuberculosis cases a community representative survey was undertaken by Gujarat (population of 60 million): a province in western part of India. 85 clusters were randomly selected and 87530 people were screened for TB symptoms and digital X-ray. Two sputum samples from eligible persons were collected for sputum microscopy and culture. Usually DST is not performed on samples designed for tuberculosis prevalence survey. However, it is important to know the proportion of multi-drug resistant TB cases out of all bacteriologically positive TB cases in a community representative sample as the Drug Resistance Surveys (DRS) results are representative of only TB patients diagnosed at the health facilities which may not be representative of community. This study was carried out with an objective to assess the proportion of multi-drug resistant TB cases out of all bacteriologically positive TB cases from community representative prevalence survey.

Methods: Solid media, drug susceptibility testing (DST) was performed on all culture positive TB cases and line probe assay (LPA) was performed on culture negative with smear positive sputum samples.

Results: A total of 335 bacteriologically positive TB cases were detected. DST was performed on samples from all 335 patients. 105 patients had previous history of anti tuberculosis treatment and 230 patients were new. A total of 36 (10.7%) multi-drug resistant TB cases were detected with proportion of 17.1% in previously treated and 7.8% in new cases.

Conclusion: Proportion of MDR (7.8%) amongst the new TB cases diagnosed from community representative sample is relatively higher as compared to

Table   Number of tuberculosis and MDR-TB cases diagnosed during community representative prevalence survey, Gujarat, India, 2011–2012

	Type	Persons	TB	MDR
Past H/o TB	Old	1716	105	18 (17.1%)
Currently on Rx	New	239	56	28 (50%)
Both past history and currently on ATT	Old	77	23	5 (21.7%)
Past h/o TB but currently not on ATT	Old	1639	82	13 (15.9%)
Currently on Rx but no past history	New	162	33	3 (9.1%)
No past history & currently not on ATT	New	85652	197	15 (7.6%)
Total S/C+		87530	335	36 (10.7%)

Type of cases	TB cases diagnosed	MDR TB cases diagnosed	Proportion
Old (Re-treatment)	105	18	17.1%
New	230	18	7.8%
All	335	36	10.7%

the results of previous (DRS) in three states of India including Gujarat in which the proportion was between 2–3%. This is indicative of higher transmission of multidrug resistance in the community. While estimating burden of MDR-TB in the community, methods need to be developed to remove selection bias of patients diagnosed at health facilities as done in DRS. To address higher transmission of drug resistance in the community NTP should consider the strategy like airborne infection control in public transportation, workplace, industries, housing development etc.

PC-419-01   National drug resistance survey: a much awaited experience in Nigeria

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Background and challenges to implementation: For an effective implementation of PMDT, countries need to determine the burden of drug resistant TB. Nigeria was ranked among the 27 high MDR-TB burden countries. In 2012 WHO Global TB report estimated that the MDR-TB rate is 3.1% among new pulmonary notified cases and 10% among previously treated cases.

Objective: To compare the actual DR-TB survey outcome with WHO global estimates for Nigeria.

Methods: A prospective, cross-sectional survey (conducted between October 2009–November 2010) of adult patients with sputum smear positive TB enrolled for care. A modified weighted 30-cluster sampling technique proportional to the size of new smear positive TB cases was used based on 2007 TB case notification. 3 National Reference Labs (NRLs) were engaged for culture using LJ slopes and resistance strains identified by LPA (Hain) method. Isolates were processed for DST through support from a Supra NRL.

Results: 97% participation rate (1723 patients) was achieved. Among the participants, 84.1% (1449) had LPA result. Of this, 2.4% were found to be NTM and 97.1% (1407) were *M. tuberculosis* complex. 1372 (94.7%) of the patients had results for both rifampicin and isoniazid. Of the latter, 1138 (82.9%) were new cases, 230 (16.8%) previously treated cases and 4 (0.3%) with unknown history. The adjusted prevalence of *Mycobacterium tuberculosis* strains resistant to both rifampicin and INH among the new cases was 2.9% (95%CI 2.1–4.0) and among re-treatment cases 14.3% (95%CI 10.2–19.3). The mono-resistance pattern among all cases for rifampicin, INH, ethambutol, pyrazinamide and streptomycin, was 3.1%, 4.8%, 20.0%, 9.1% and 30.6% respectively. The recorded HIV sero-positivity rate among participants was 14.2%.

Conclusions: Nigeria retains a high ranking amongst the MDR-TB burden countries as estimated. Therefore, the need for rapid scale up of PMDT is pertinent.

PC-420-01   Implementación de un sistema automatizado para la gestión de fármacos antituberculosis de segunda línea en México

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Marco de referencia y desafíos: El criterio para la descripción del proceso de abasto de los fármacos antituberculosis de segunda línea en México, basado en un sistema automatizado de gestión, se sustenta como parte fundamental de la gestión de medicamentos y así garantizar en los establecimiento de salud que atienten a las personas afectadas por la tuberculosis resistente: la disponibilidad, uso apropiado, la seguridad, efectividad y calidad de los medicamentos antituberculosis de segunda línea.

Intervención o respuesta: Para dar respuesta al uso racional de fármacos antituberculosis de segunda línea es necesario: una atención especializada para todos los pacientes con TB-DR, métodos diagnósticos confiables y medicamentos de calidad garantizada, así como; la capacidad instalada y capacitación operativa para el almacenaje y distribución cuidadosa de los fármacos. Con la finalidad de garantizar el envío de medicamentos de acuerdo a requerimientos de los servicios de salud en el momento apropiado y en la cantidad necesaria, el Programa Nacional de TB en México realizó un sistema automatizado de cálculo y balance para la solicitud de fármacos llamada 'Sistema para control de fármacos antituberculosis de segunda línea', el cual opera desde los programas estatales.

Resultados y enseñanza: Durante el periodo de 2010 al 2012 el Sistema para control de fármacos

antituberculosis de segunda línea permitió realizar un conteo exhaustivo de todos los fármacos entregados a los estados así como uso del mismo por paciente. Posterior al análisis clínico y diseño del esquema de tratamiento con fármacos de segunda línea a 679 casos con TB-DR, se recibieron en el Programa Nacional 634 (93.3%) solicitudes de medicamentos de segunda línea, las cuales fueron surtidas al 100%, 45 solicitudes (7%) no fueron surtidas debido a que los pacientes fallecieron o tenían criterio de no apto para iniciar esquema de tratamiento hasta asegurar la adherencia terapéutica. Se realizaron 1513 conteos exhaustivos de fármacos por paciente y de acuerdo a la dosis establecida y duración del tratamiento llamado BALANCE DE FÁRMACOS, lo que permitió evitar sobreabasto y pérdidas por caducidad.

Conclusiones y recomendaciones: El uso de herramientas técnicas y automatizadas ofrece un mayor control en la logística y gestión de fármacos necesarios de manera racional para la atención de enfermos con TB-DR.

PC-421-01   Lessons learnt: experience on MDR-TB in prison at a tertiary government hospital in metro Manila, Philippines

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Background and challenges to implementation: The Philippines, one of the high tuberculosis burden countries. It ranks 8 among 27 countries with MDR-TB. The drug resistant survey findings from in 2004 showed the prevalence of MDR-TB was 4% among new cases, 21% among previously treated. In 2011, WHO estimated 10 600 MDR-TB cases; of these, only 2397 were detected and started on treatment, i.e., only 23%. The PhilPACT was developed under the Health Sector reform agenda covering 2010–2016. It includes strategy to address MDR-TB, TB-HIV, and needs of vulnerable populations including inmates, the elderly and children. Since 2005, Lung Center of the Philippines, first tertiary public government facility engaged in screening and treating MDR-TB following the WHO guidelines.

Intervention or response: Starting 2008 referrals of drug resistant suspects from prison camp have been on-going at the LCP-DOTS clinic. Health prison staff are compassionate in accompanying patients for consultation, screening at the DOTS clinic. To sustain efforts, advocacy to management, capacity building of health staff manning the prison DOTS clinic and continuous partnership were done to intensify casefinding activity within the special group.

Results and lessons learnt: Initially, only 3 DRTB suspects were screened, diagnosed as MDR-TB and managed. It gradually increased in 2011 to 27 (87%)

out of 31 diagnosed MDR-TB were started treatment; 2 (6.5%) died before treatment; 2 (6.5%) lost to follow up since the patients are temporarily jailed and awaiting final decision from the lower court. The 2008 cohort of patients showed promising interim and final outcomes while the rest are still on-going treatment inside the jails.

Conclusions and key recommendations: The preliminary results showed a promising outcome among inmates in the prison camp. Partnership and continuous coordination with stakeholders are important in the development of structured policies and guidelines among captive group most especially on the PMDT referral system, infection control, monitoring and supervision once patients are released from the jails.

PC-422-01   Network of MDR-TB management in Indonesian prisons

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Background: Indonesia has 434 prisons and detention centers with 98 625 inmates capacity but the total inmates by December 2012 was 150 768 (50% over capacity). It is a risky environment for inmates to contract TB/MDR-TB. PMDT system in the prison was built in 2012, with the initiation of treatment of 3 first MDR patients. At the beginning, treatment of MDR patients relied only on one prison hospital, and the country was aware that it is not a long term solution.

Responds: TBCARE1/USAID facilitated discussion on the guideline for MDR-TB in the prisons, and drafted the guideline and further finalized by NTP and Directorate General of Correction (DGC). With continuous advocacy, DGC committed to assign 4 prisons and 1 prison hospital as satellites of PMDT hospital. These prisons are located in West Java, Central Java, East Java, and North Sumatra, whereas the hospital is in Jakarta. Prisons staff detect MDR suspects using 9 MDR-TB suspect criteria, sputum of the suspects will be referred to PMDT hospital in each province or the most accessible one from prison. With *Mycobacterium tuberculosis* pos and RMP-resistant, the inmates will be transferred to PMDT satellite prison for treatment under PMDT hospital supervision and coordination. TBCARE1/USAID facilitated preparation of MDR ward in each of PMDT satellite prison, and coordination meetings in the district/province. On the job training for the prisons to PMDT hospital, and routine technical assistance to prisons were delivered as well.

Results: The Guideline of Management MDR-TB in

the prisons was finalized, disseminated and trained to initially 6 provinces (33 prisons) which are accessible to PMDT satellites prisons. The guideline includes 9 MDR suspect criteria, how to pack and send sputum, and related recording and reporting. Before February 2013, 3 MDR patients from 5 suspects were identified from 5 prisons, and treated. During Feb–April 2013, 43 suspects from 18 prisons were identified, 30 had the sputum checked for Xpert, 3 died, 1 released, 1 transferred, 8 were planned for Xpert. Out of the 30 suspects, 2 were *M. tuberculosis* positive and RMP-resistant, both of them are HIV-positive. These two patients are treated for both MDR and HIV.

Conclusion: The possibility of MDR-TB will be detected because of close contact in the prisons. Decentralization is necessary to allow access for diagnosis and treatment, and this is possible only with strong commitment and support from all levels, particularly PMDT network of NTP.

PC-423-01   Intensified DR-TB case finding among previously treated tuberculosis patients in Cross River State, Nigeria

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Background and challenges to implementation: The advent of rapid molecular testing has improved case finding strategy for drug resistant tuberculosis (DR-TB). Though the initial NTP policy of DR-TB diagnosis was focused on Category 2 treatment failures due to inadequate laboratory and treatment capacity for the detected DR-TB patients, routine case finding strategy included all previously treated patients. The TB programme in Cross River state commenced documentation and reporting of DR-TB surveillance activities in 2011. The objective of this study was to evaluate the results of implementation of routine DR-TB surveillance in the state.

Intervention or response: This is a descriptive cross-sectional study. Previously treated TB patients from within and outside the state were referred or reported to the TB treatment centre in Calabar. The case histories of the patients were reviewed by clinic staff to confirm their previous TB treatment outcomes. Identified DR-TB suspects were documented in the national DR-TB suspect register and sputum samples collected and sent to the AFB lab for diagnosis. Sputum samples were also sent to the reference lab for line probe assay (LPA) for rifampicin and INH DST. The test results were collected and analysed.

Results and lessons learnt: Ninety-eight DR-TB suspects (43 males and 27 females) were screened using LPA for diagnosis of rifampicin and INH resistance during the period between 2011 and 2012. All the suspects tested were 15 years and above. The DST results revealed that 17 (17.3%) were rifampicin-IHN resistant indicating MDR-TB diagnosis. Seventeen PLHIV were among the DR-TB suspects evaluated for MDR-TB diagnosis representing 17.3%.

Conclusions and key recommendations: The introduction of molecular techniques has paved the way for rapid diagnosis of DR-TB in implementing National Tuberculosis Control Programmes. This has prompted increased DR-TB case finding activities among the state TB programmes in Nigeria. There is urgent need to build treatment capacities within the state TB programmes to manage the increasing number of DR-TB cases detected.

PC-424-01   Increasing the number of sputum specimens tested for MDR-TB and cases detected using expedited mail service sputum transportation in Tanzania

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Background: MDR-TB is among the most deadly challenges facing TB programs today, especially in Tanzania. A commonly used predictor of the magnitude of a country's MDR-TB burden is the number of failure cases recorded. In Tanzania, this number increased from 96 cases in 2010 to 146 cases in 2011. The CTRL operates as a reference laboratory for diagnosis of TB through microscopy, mycobacterial culture, and drug susceptibility testing (DST) for TB patient management. The laboratory receives samples from all types of health facilities countrywide. Previously, transport of sputum samples was done by public transport and ordinary post office mail; however, many samples were lost and/or significantly delayed en route to the CTRL.

Objective: To improve detection of multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR) -TB by strengthening specimen referral from health facilities to Central TB/Leprosy Reference Laboratory (CTRL).

Intervention: With support from the US Agency for International Development, PATH Tanzania negotiated a contract to support the transport of sputum specimens countrywide to the CTRL using a postpaid service rendered by expedited mail services (EMS). Data for one year prior to using the EMS system (July 2010 to June 2011) and one year after utilizing EMS (July 2011–June 2012) was collected and analyzed to assess the effectiveness of EMS services in transporting sputum specimens.

Results: Before EMS, 1027 samples were received by the CTRL; in the first year of the intervention, 3538 samples were received. Thus there was more than a three-fold increase in the number of samples received at CTRL. The increase in number of samples differed by district. In addition, average transit time was reduced from 11 days to 7 days, a 40% reduction in transit time hence positive effect on the test accuracy. Increasing the number of specimens reaching the laboratory increases the likelihood of detecting drug resistant TB, as more samples are tested. Before EMS, 22 MDR-TB cases were detected by CTRL; however after the intervention, 37 MDR-TB cases were detected.

Conclusions: EMS has contributed to an increase in the number of samples received by the CTRL and reduced transit time, hence increasing the number of MDR-TB cases detected. It is important to understand why the new EMS system is having a more significant impact in some districts vs. others and troubleshoot in those areas with lower sample numbers and longer transit time.

PC-425-01   Previous tuberculosis treatment in MDR-TB patients in Bangladesh and health system factors

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Background: Previous TB treatment is known risk factor for MDR-TB. But there are other health system factors related to the previous TB treatment which is not much known for MDR-TB patients in Bangladesh. In this current study we explored the factors related to previous TB treatment.

Design/methods: As a part of a case-control study of 250 MDR-TB as cases and 750 non-MDR-TB patients as controls we reviewed some characteristics MDR-TB. We included MDR-TB patients from September 2012 to March 2013 from four functional government hospitals of Bangladesh for initiating MDR-TB treatment. Controls are selected based on the site of MDR-TB. Interview and record review were conducted. Data analysis carried out using Stata.

Result: Previous TB treatment in MDR-TB patients for more than once episode was found in 64% and 34% had TB treatment at least once previously. Among the non-MDR patients it was only 6%. Among the MDR-TB patients, 78% reported about supervised treatment but 25% was provided by family member and 12% by the health staff at facility level. Rest is by community level providers, informal providers and neighbors. Those who had a incomplete treatment 5% of the patient said to feel better and 1% had adverse effect. Others due to no improvement

or remain positive and then switched to the MDR-TB diagnosis and treatment. 91% of incomplete treatment was followed up by any providers. 31 percent of the patients had an extension of treatment.

Conclusion: Prevention of MDR-TB is much important for controlling the disease. Factors related to previous TB treatment could be addressed in the programme to control the TB management and thus to prevent further drug resistance. The detail study will provide more information on prevous treatment episode.

PC-426-01   Molecular-genetic analysis of the *M. tuberculosis* isolates circulating in the penitentiary system of Kazakhstan

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Background: A closed penitentiary system (i.e., prisons) represents a special risk of distribution of many infectious diseases, including tuberculosis (TB). A high level of multidrug-resistant (MDR) types of tuberculosis is being observed in the prisons. That is why it is extremely important to study the *M. tuberculosis* DNA mutation spectrum, in order to improve the system of infection control and quality of treatment in these establishments. The study objective is to assess the biological diversity and the mutation features of a set of the *M. tuberculosis* strains extracted from the TB-infected patients in Kazakhstani prisons.

Methods: 33 MDR isolates of *M. tuberculosis* were used for study through DNA sequencing and MIRU-VNTR (Mycobacterium Interspersed Repetitive Unit–Variable Number Tandem Repeat) analysis.

Results: It was found that that the most frequently occurring mutations are identified in the codon 531 of the *rpo*B gene (88% of cases), when replacing serine to leucine (TCG→TTG). The mutations were also detected in the codon 526 codon of the *rpo*B gene (12% of cases) when substituting histidine on leucine (CAC→CTC). Moreover, the mutations were found in the codon 315 of the gene kat*G* in all 33 strains (100% of cases). The MIRU-VNTR analysis was carried out on 24 MIRU-VNTR loci. Based on information received from VNTR-analysis a phylogenetic tree was constructed using the web-source www.miru-vntrplus.org. A low genetic diversity was observed among the *M. tuberculosis* isolates (strains) used for the study. The isolates belonged to the genetic families called Beijing (94% of cases) and LAM (6% of cases) and are associated with MDR, which was confirmed by the DNA sequencing. In other words, all the isolates represent the MDR strains. The

Beijing type of strain was found more often among the patients with a recurrent case of tuberculosis rather than among those who are sick with TB for the first time.

Conclusions: The obtained study results are of a high interest for the industry and should be used for improving and fine-tuning the strategy of the epidemiological control and TB treatment in the penitentiary system of Kazakhstan.

PC-427-01   Prevalence of drug resistance among patients who fail treatment

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Background: Namibia is a sparsely populated country in Southern Africa with a high TB incidence and high HIV prevalence. In 2010, 12 625 cases of tuberculosis were notified of which 46% were bacteriologically confirmed. 35% of all cases were new smear positive; 9% were relapses, while those treated after failure and default were 1% respectively. The national guidelines recommend standard treatment with FLDs for new and retreatment cases in line with WHO guidelines. Treatment success rate was 85% for new smear positive cases and 71% for retreatment cases. Failure rate was 5% for new cases and 10% for retreatment cases. There has not been clear guidance on the best regimen to manage patients who fail initial treatment simply because there is no local data on prevalence of drug resistance among these cases. We hereby present the first preliminary data for Windhoek district.

Methods: A retrospective analysis of the Windhoek district tuberculosis register was made, identifying patients who had been classified as treatment failures after at least 5 months of standard treatment. Failure was defined as smear positivity 5 months or later during treatment.

Results: 93 patients were identified as having failed treatment between 2008 and 2010. 82 patients had traceable mycobacterial culture and DST investigation
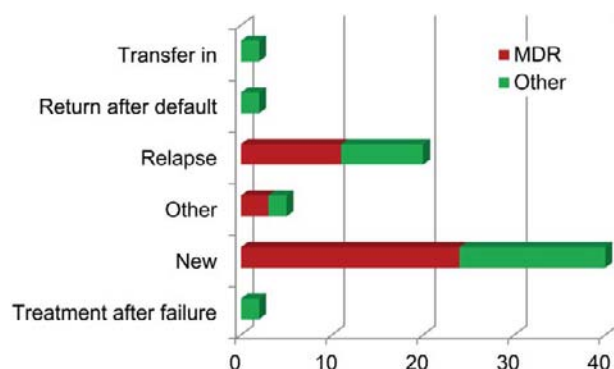
Figure   Occurrence of MDR TB among treatment failures to FLD.

requested at or around the time of treatment failure. Two grew non-tuberculous mycobacteria, while nine had either negative or invalid culture results. 71 had at least one culture result which confirmed tuberculosis. Of these, 40 had been on initial treatment of 2HRZE/4HR, while 29 had been on 2SHRZE/1HRZE/5HRE. Two were recorded as 'transferred in' with no clear regimen. All 100% (71) patients had *Mycobacterium tuberculosis* resistant to at least one of streptomycin, ethambutol, rifampicin or isoniazid. 79% (56) of patients had isoniazid resistance, while 68% (48) patients had rifampicin resistance. 55% of all patients had MDR-TB (60% new, 50% retreatment).

Conclusion: Although these are preliminary data and will need to be confirmed with analysis from other districts, it appears there is a high rate of drug resistance among patients failing FLDs in Namibia. This should be considered when recommending empiric regimens for patients who fail FLD treatment but have no DST results.

PPM, PARTNERSHIPS, COLLABORATION

PC-428-01   A user-friendly, open-source tool to project the impact and cost of diagnostic tests for tuberculosis

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Background: Local and country-level decision-makers have a wide array of options available for improving the diagnosis of tuberculosis (TB). Evidence-based projections of the potential cost and epidemiological impact of each option could inform these decisions, but such projections are generally not available in a fashion that reflects local epidemiological reality.

Design/methods: We constructed a user-friendly, open-source transmission model of TB capable of projecting the impact of various diagnostic strategies in populations defined by user-defined values of TB incidence, multidrug-resistant (MDR-) TB prevalence among new cases, adult HIV prevalence, and per-patient TB treatment costs. We demonstrate utility of this model by evaluating nine alternative diagnostic strategies in four emblematic epidemiological scenarios: high incidence, low incidence, high MDR, and high HIV.

Results: The impact of improved diagnostic testing was greater for mortality and MDR-TB prevalence than TB incidence, and was maximized in high-incidence, low-HIV settings. The ranking of the selected

diagnostic strategies did not vary widely across epidemiological settings (except in long-term costs), but the numerical estimates of cost and impact differed dramatically. In settings with little capacity for up-front investment (<25% of TB program budget), same-day microscopy had greatest impact on TB incidence of the available options and became cost-saving within five years if feasible to deliver at $10/test. In settings where more initial investment was possible, population-level scale-up of either Xpert MTB/RIF or microcolony-based culture offered substantially greater benefits, often averting ten times more TB cases than narrowly-targeted diagnostic strategies but with similar long-term costs. Where containing MDR-TB is the overriding concern, Xpert for smear-positives has reasonable impact on MDR-TB incidence, but at substantial price and very little impact on overall TB incidence and mortality.

Conclusion: This novel, user-friendly modeling framework improves decision-makers' ability to evaluate the impact of TB diagnostic strategies, accounting for local epidemiologic reality.

PC-429-01   Using modelling to explore the potential effectiveness and cost-effectiveness of the national strain-typing service in England

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Background: In 2010, the national TB Strain-Typing Service (TB-STS) was introduced in England with the aim of routinely typing the first *Mycobacterium tuberculosis* isolate from all TB cases using 24-locus MIRU-VNTR. Amongst other benefits, this could reduce the burden of TB by increasing the proportion of latent infections that are detected and shortening the time until active cases are detected through better-targetted cluster investigation.

Methods: We used mathematical modelling to explore the potential effectiveness and cost-effectiveness of the TB-STS in population groups in which the incidence is low (native UK population and declining annual risk of infection (ARI)), medium (similar to the non-white UK-born population) and high (similar to the non-UK-born population). Cost-effectiveness was estimated using outputs from the transmission model, data from questionnaire surveys and routinely-collected data sources.

Results: The results indicate that increasing the pro-

portion of infections that are detected will have a small impact on the TB incidence and the number of cases prevented in the native-born UK population. However, in medium/high incidence settings, detecting even a small proportion (20%) of infections could lead to an approximate 25% reduction in the TB incidence over a 20 year period. In medium incidence settings, reducing diagnostic delay even by a week could potentially lead to large (~33%) reductions in the TB incidence. However, these findings are sensitive to assumptions about the proportion of immigrants who enter the population with TB. The service was not estimated to be cost effective over a 20-year period (£97 311 per quality adjusted life year (QALY).

Conclusions: Whilst the TB-STS provides an invaluable resource for understanding TB epidemiology and ongoing transmission, its effect on TB incidence is likely to have been small in the native UK population. For it to be effective in medium/high incidence groups in England, the rate at which immigrants with TB enter the population would have to be negligible and the TB-STS would have needed to lead to the detection of 20% of infections or reduced diagnostic delay by at least one week. To date, there is no evidence for either having occurred. These findings are relevant for other countries wishing to evaluate their strain-typing service and for identifying potential interventions to control TB incidence.

PC-430-01   Outcomes for intersector actions: strengthening tuberculosis control among vulnerable populations in Brazil

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Background and challenges to implementation: Because tuberculosis (TB) is a disease determined by social and economic factors, it affects intensively more vulnerable populations. Considering this, the Brazilian National Tuberculosis Programme (NTP) has been articulating with other policy agencies from the Brazilian Federal Government in order to develop actions and strategies that consider the needs of those vulnerable populations and to strengthen tuberculosis control. This study aims to analyze the results of joint intersectoral actions in response to the social aspects related to tuberculosis in Brazil.

Intervention or response: Descriptive study from documents and activities between 2011 and 2012, with qualitative focus, containing the analysis of outcomes from the joint actions from the NTP with health sectors, social assistance, food security and the Legislative.

Results and lessons learnt: Among the products, the highlight is the resolution of the National Health Council as deliberative entity for health policy in

Brazil, which established the need for developing intersectoral actions to confront the social vulnerabilities of people living with TB, particularly related to poverty. The creation of the Parliamentary Front against Tuberculosis, allowed to promote the discussion on TB control in the Brazilian parliament. It also allowed a change in the legislation, facilitating the development of activities by civil society organizations. The partnership with food security programme resulted in the inclusion of TB's theme in the training course for health professionals that monitor income transfer programmes beneficiaries. Finally, the dialogue with the Ministry of Social Development described the socioeconomic profile of people living with TB, by crossing the Unified Registry for Social Programmes with the Information System of Disease Notification (SINAN) for TB, which has allowed knowing their social and economic reality.

Conclusions and key recommendations: There was improvement in terms of public policies and programmatic advances at the Federal level, with the involvement of public policies from outside the health sector, specifically through advocacy for health. However, it is necessary to continue the intersectoral actions both at state and municipality levels.

PC-431-01   Using film and involving film celebrities for tuberculosis messaging and creating tuberculosis awareness: a report from Tamilnadu, India

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Background and challenges to implementation: In India, low awareness about TB and community participation for improved care seeking is an important challenge for TB control. In a scenario, where films cut across age, gender and income barriers, media campaigns using film celebrities and documentary films assumes paramount importance in influencing people's health seeking behavior. The following abstract reports the process to create/increase awareness about TB among community, to highlight and increase accessibility to government TB health services using film celebrities and the dissemination process.

Intervention: Celebrities were chosen based on celebrity appeal within the local context, relevance to public health cause, and their willingness to lend support for the initiative. Concepts for documentaries were developed by the non-governmental organization in consultation with film makers and community participation. Key messages were identified following discussions with key stakeholders of TB control program.

Results: Popular cine-stars, film makers and television stars in all totaling to 36 have participated in this initiative on a voluntary basis. About five 15-minute documentaries and four short films of 1–2 minute duration have been conceptualized, developed and produced. More than 2500 copies have been distributed widely to public health system, wherein the films are telecast in primary health centers and district hospitals and to different stakeholders working for TB control. In addition to being uploaded in the social media, the films are also being telecast in theatre halls and cable networks. The films have served as an important teaching video during training session for different target groups such as private practitioners, pharmacists, medical students, etc. The films have revolved around different facets of TB such as mythsand facts of disease, availability of quality health care for TB etc.

Conclusions: To meet public health challenges like TB, celebrity leverage for a public health cause finds an important place. Involving films and celebrities with their promise of trust to the cause that they are associated is an inexpensive way in influencing people to appropriate and timely action taking for their health.

PC-432-01   Tuberculosis prevalence survey, Pakistan: tuberculosis burden higher than estimated

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Background: Pakistan ranks 5th amongst the 22 high TB burden countries. The estimated incidence and prevalence rate of all forms TB is 231 and 364/100 000 populations by WHO. There was a need to conduct a new prevalence survey as more than two decades have passed since the last TB prevalence survey conducted in 1987. WHO Global Task Force on TB Impact Measurement selected Pakistan based on certain eligibility criteria for survey in 2007.

Design/methods: The primary objective of the survey was to estimate the prevalence of bacteriological confirmed pulmonary TB among the adult population ($\geq$15 years) in a nationwide representative survey during 2010–2011. The survey design was household based cross-sectional survey, multistage cluster sampling with sample size of approximately 133 000 adults (15 years or over) in 95 clusters with cluster sample size of 1400 adults. It was conducted from August 2010 to December 2011. The fieldwork of 14 days duration started in six clusters simultaneously with household census followed by symptom screening, X-ray chest and smear microscopy of TB suspects.

Results: The initial results shows the total number of eligible adults were 129 827 and 103 387 participated (79.6%). Eligible females were more likely to participate (86.4%) than eligible males (72.0%). The

participation rate was fairly similar in the different age categories with a participation rate higher than 80% in the age category 25–34 years of age. The preliminary prevalence of bacteriological confirmed cases 255.7 per 100 000 adult population (95%CI 213.6–297.8). The final analysis will be available by May 2013 year to provide more accurate estimate.

Conclusion: The results of Pakistan tuberculosis prevalence survey are crucial and the higher prevalence needs attention to adopt innovative strategies to enhance TB notifications in the country.

PC-433-01 Tuberculosis: spreading information in the communities

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Background and challenges to implementation: Surveys conducted in 2010 showed that 50% of the Brazilian population is unaware of several tuberculosis aspects, which shows that lack of information is still one of the main challenges for disease control. A survey from 2011 showed that there were few insertions of the theme in the media, and that those responsible for what is usually released on TB are international agencies, government and academia, excluding affected communities. With the end of the Global Fund TB Project in Brazil, it became necessary to assist the Metropolitan Committees—created to monitor the actions of this project in states of high TB incidence—to disclose actions through communication tools, creating an information flow between them and their partners, strengthening the social movement and expanding the scope of information.

Intervention and response: The Global Fund TB Project Brazil with the National TB Programme, conducted a workshop with communication activities, reflecting on the materials produced to fight the disease. It focused on the relationship of social actors with the press, through mapping the means of communication available in the communities. An educational approach was chosen to guide the members of eleven committees, composed by one government representative and four civil society representatives. They were selected democratically and committed to share with the community the knowledge acquired. 40 people were trained through theoretical and practical classes with the production of material for radio, TV, Internet and printed media, always considering local specificities.

Results: The tuberculosis: spreading information blog was developed during this workshop, found at the link: www.blogdatuberculose.blogspot.com as well as facebook and twitter profiles were created in order to share actions taken by the metropolitan committees and general information about TB, which are of interest to all the community, promoting greater community engagement.

Conclusion and key recommendations: The blog is recognized by the Brazilian Ministry of Health, state and local governments and civil society organizations as a space to disseminate various actions on the fight against TB. These media tools allow the construction of a collective space for interaction, sharing contents and ideas, as an alternative from the traditional media approach. In other words, the information flow is spontaneous, in a larger scale and it is easy to use.

PC-434-01 Fighting tuberculosis together: a symbol to raise awareness

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Background and challenges to implementation: In 2010, two Brazilian studies showed that 50% of the population does not know about TB. Both the one conducted by the Fluminense Federal University Research Centre (DataUFF) coordinated by the Global Fund Project TB Brazil, as well as the research commissioned by the Pneumology and Phthisiology Brazilian Society (SBPT) to the Datafolha Institute, show that half of the population lacks information on the different aspects of this disease. This proves that even though TB is an ancient disease, considered by WHO as a global emergency since 1993, the lack of information is still one of the main challenges to TB control.

Intervention and response: Aiming the stimulation of common efforts to TB control in the country, the Global Fund TB project in Brazil, in partnership with the National TB Programme from the Ministry of Health, conducted the Contest: Fighting TB Together, in order to create a logo that represents the joint efforts between civil society, health professionals and other sectors involved in this cause.

Results: 47 proposals were received from different audiences such as: health professionals, public school students, prisoners, designers, among others. The first three competitors were awarded in a ceremony on the World TB Day (24 March) theme in the city of Brasilia/DF. The ceremony had the presence of the Health Minister, civil society representatives, health professionals and national and local press.

Conclusion and recommendations: The winner logo proposal is recognized as the symbol for the fight against TB in Brazil by both the Brazilian Ministry of Health and the civil society organizations. The logo is being included in the TB programmes at local, state and national levels. Throughout these insertions, the aim is to consolidate the logo as a reference to the fight against TB in Brazil, for the society as a whole.

PC-435-01   Socio-economic profile of tuberculosis cases in Brazil: linkage between tuberculosis information system and the Unified Register for government social support programme

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Background: The linkage between TB information system (Sinan-TB) and the Unified Register for government social support programs (CadÚnico) aimed to know social economic variables of TB cases among low income families and treatment outcomes between cases under conditional cash transfers program—Bolsa Família (PBF).
Methods: Descriptive study of TB cases diagnosed in 2011. It was calculated the percentages of individuals and social variables as race, diabetes, alcohol abuse, HIV status, education, cash transfer beneficiaries and amount, employment and income in the previous year and treatment outcome.
Results: Of 73 833 new cases of TB diagnosed in 2011, 25.1% (18 509) were registered in Cad Único and 13.9% (10 278) were under PBF. They belong to families who had income below half Brazilian minimum wage per person or up to three times the minimum wage all together. The average money received was 134.00 Brazilian reais (32 912). 53.5% of cases receiving family benefit were black and 23.9% white, while 41.4% and 37.0% were from this races in the remaining cases. Only 22.1% of new TB cases had more than 8 years of study and this percentage drops to 17.4% when it comes to cases receiving family benefit. Out of all cases, 87.1% were at working age and between those under cash transfer programs only 36.1% had any kind of job in the past year and the average amount earned was 1800 reais (14 200). Co-morbidities were slightly lower between cases under cash transfer programs. HIV infection, diabetes and alcohol abuse was 7.7%, 5.6% and 12.3% among them, against 10.1%, 6.7% and 14.5% in the re-maining cases. Regarding treatment follow up, 49.5% of cases receiving family benefit were under DOTS against 44.1% of the rest of the cases. Outcomes were favorable to cases under cash transfer programs, showing a cure rate 6.0% higher among them. Cure and default rates were 77.7% and 7.7% respectively in cases receiving family benefit against 71.8% and 9.5% in the rest of it. Deaths by or with TB were 3.8% and 9.2% respectively, also lower in these families. The proportion of TB cases under family benefit varies between Brazilian states ranging from 26.4% to 7.9%.
Conclusion: Treatment outcomes were favorable to cases under conditional cash transfer programs. Still further analysis is needed on the impact of PBF in tuberculosis control to support the development of more effective responses to socially vulnerable population.

PC-436-01   Engaging rural health care practitioners in India's Revised National Tuberculosis Control Programme through a GF supported civil society tuberculosis project

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Background and challenges to implementation: People living in rural areas of India depend mostly on unqualified Rural Health Care Practitioners (RHCPs) for health services including TB. For many TB patients RHCPs are the first point of contact. Many of those TB cases received incorrect treatment and information from RHCPs and not reported to Revised National TB Control Program (RNTCP) of India and missed. World Vision India and its 6 partners have initiated interventions to engage RHCPs in RNTCP through Project Axshya (Global Fund supported TB project). The project mainly focuses to hard-to-reach, politically unrest and underserved areas within 74 low performing districts of 7 states of India namely Madhya Pradesh, Chhattisgarh, Jharkhand, Bihar, West Bengal, Orissa, Andhra Pradesh.
Intervention or response: Key purposes of RHCPs engagement:
1 RHCPs should refer chest symptomatic to Designated Microscopy Centres (DMCs) of RNTCP for evaluation of TB.
2 RHCPs should function as Community DOT Provider to provide DOT to the TB cases who were diagnosed and enrolled for treatment in RNTCP.
8363 RHCPs were trained from April 2010–September 2012 on TB and RNTCP by the project with specially designed RHCP training modules and materials and by involving RNTCP health staff. Regular quarterly review meetings of District TB Officers and trained RHCPs were facilitated by the project to enhance their engagement with RNTCP. In West Bengal, RHCPs' Registered Unions were sensitized by the project. The project also developed referral tracking mechanism from RHCPs to RNTCP.
Results and lessons learnt: 16 232 chest symptomatic (about 2 chest symptomatic per trained RHCP on an average) were referred by trained RHCPs to the DMCs of RNTCP for TB evaluation; 83% ($n = 13 495$) evaluated for TB through sputum microscopy in DMCs and 9% chest symptomatic ($n = 1233$) were detected with sputum positive pulmonary TB and put under DOT. 351 RHCPs (4.2% of those trained by the project) provided DOT to the TB patients in RNTCP as community DOT providers. For every 100 RHCPs trained by the project, 15 new sputum positive pulmonary TB cases were detected which could have missed by RNTCP without RHCPs engagement. Training on TB and RNTCP and motivation of RHCPs by the project helped in TB case detection in areas where RNTCP had limited reach.

Conclusions and key recommendations: With proper training and motivation, RHCPs can be used as the extended hand of public health system in hard to reach villages to enhance TB case detection.

PC-437-01   Patient and household costs associated with tuberculosis care in Ebonyi State, Nigeria

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Background: Poverty is both a cause and consequence of tuberculosis. The objective of this study is to quantify patient/household costs for an episode of tuberculosis (TB), its relationships with household impoverishment, and the strategies used to cope with the costs by TB patients in a resource-limited high TB-HIV setting.

Design/methods: A cross-sectional study was conducted in three rural hospitals in southeast Nigeria. Consecutive adults with newly diagnosed pulmonary TB were interviewed to determine the costs each incurred in their care-seeking pathway using a standardised questionnaire. We defined direct costs as out-of-pocket payments, and indirect costs as lost income.

Results: Of 452 patients enrolled, majority were male 55% (249), and rural residents 79% (356), with a mean age of 34 ($\pm$11.6) years. Median direct pre-diagnosis/diagnosis cost was \$49 per patient. Median direct treatment cost was \$36 per patient. Indirect pre-diagnostic and treatment costs were \$416, or 79% of total patient costs, \$528. The median total cost of TB care per household was \$592; corresponding to 37% of median annual household income pre-TB. Most patients reported having to borrow money 212 (47%), sell assets 42 (9%), or both 144 (32%) to cope with the cost of care. Following an episode of TB, household income reduced increasing the proportion of households classified as poor from 54% to 79%. Younger age ($P = 0.002$), rural residence ($P = 0.02$), HIV-positive status ($P < 0.001$) and care-seeking at a private facility ($P < 0.001$) were significantly associated with increased household impoverishment before TB. After TB care, younger age ($P < 0.001$), male gender ($P = 0.01$) and HIV-positive status ($P = 0.01$) significantly increased household poverty.

Conclusion: Patient and household costs for TB care are potentially catastrophic even where services are provided free-of-charge. There is an urgent need to implement strategies for TB care that are affordable for the poor.

PC-438-01   Tuberculosis treatment adherence according to patients' knowledge and bond with professionals in Brazilian municipality

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Background: The WHO defines adherence as a dynamic and multifactorial process, which must be achieved throughout all treatment period once it prevents unfavorable outcomes, such as the drop-out, death and drug resistance.

Aim: To analyze adherence to TB treatment according to patients' knowledge and bond with healthcare staff in Ribeirão Preto, Brazil.

Design/methods: Descriptive epidemiological study with quantitative approach, conducted in a large municipality at southeastern Brazil. This study population comprises of 127 TB patients under treatment for at least 3 months from September 2011 to September 2012, aged 18 years and more, residents in the city. Data were collected thought three structured interviews: (I) Adherence Measure to TB Treatment (II) Knowledge of TB patients about the disease and treatment, and (III) Bond with healthcare staff. The questionnaire (I) was analyzed using Cluster Analysis in order to classify treatment adherence in satisfactory or unsatisfactory. Multiple Correspondence Analysis was used to identify association between the clusters, the knowledge of patients and the bond with the healthcare staff.

Results: The cluster of satisfactory adherence was associated with the existence of a reference professional, with enough time to provide an appointment and to evaluate patients' health status, in which he feels understood and allowed to participate in decisions about their proposed treatment. The adherence was associated with the interest in searching information about the disease and with the best knowledge about TB transmission, time of treatment and cure.

Conclusion: The study confirms the importance of TB knowledge and bond as aspects that strengthen adherence to treatment, being fundamental the active communication between professionals and patients, and responsibility of both for treatment completion.

PC-439-01   Involvement of community-based organisations in a TB-HIV collaborative intervention in Oyo State, Nigeria

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Background and challenges to implementation: Tuberculosis (TB) is responsible for most of the deaths in people living with HIV (PLHIV). TB-HIV co-infections need be tackled rigorously to mitigate against its impact and wide-spread. This warranted involvement of Community-Based Organizations (CBOs) for the fact that they are closer to the community populace—men, women, youth and children. Moreover, the CBOs are readily available to provide the needed and essential services to the people at the grassroot level both at urban and rural communities.

Intervention or response: Fifteen CBOs were trained and engaged on TB-HIV collaborative intervention activities in 10 local government areas (LGAs) of Oyo Sate in Nigeria. The CBOs carried out Advocacy, Mobilization, Awareness creation, Community Outreach Education, Capacity Building for staff and volunteers, Focus Group Discussions, Play-let Drama, Distribution of Informative, Educative and Communicative (IEC) materials on TB-HIV, Condom Promotion (for male and female), HIV Counseling and Testing (HCT). Rapid Result Test Kits were used along with effective pre-Test and post-Test Counseling.

Results and lessons learnt: 521 people (male 269, female 252) were referred for TB screening, 421 People (male 214, female 207) showed-up at the TB DOTS Centres, while 100 people could not show up due to distance and poverty. 102 were smear-positive to TB. 25% of TB cases detected in 10 LGAs were from the CBOs during the period of 3 months (January–March 2013). A total of 584 people on TB treatments contributed to 30% of smear-positive TB cases in focused LGAs of Oyo State, Nigeria. TB-clients tested positive to Human Immuno-deficiency Virus (HIV) were referred to nearest the ART Clinics. PLHIV who voluntarily declared theuir status and those newly detected were given drug adherence counseling and referred to TB DOTS Centers for screening.

Conclusions and key recommendations: TB-HIV cases detection were achieved by the CBOs who are members of the Oyo State Chapter TB Network. 10 out of 33 LGAs in Oyo State were reached with TB-HIV intervention activities. The remaining 23 LGAs need to be reached. This gap need to be addressed urgently. More CBOs need to be involved.

PC-440-01   Health and socio-economic inequalities of tuberculosis prevalence in Brazil: analysis of the National Household Sample Survey 2008

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Background: Tuberculosis (TB) is one of the five priority diseases in Brazil and the fourth cause of death for infectious disease. Although the lower socioeconomic condition is a risk factor for infection and disease, there are few studies about health and socioeconomic inequalities among TB patients in Brazil. So the purpose of this study was to analyze health and socioeconomic inequalities among people who had TB and those who did not.

Design/methods: Men and women, over 17 years old, residents in all Brazilian regions were selected from the National Household Sample Survey/2008 (PNAD) ($n = 271\,677$). The dependent variable was the presence or absence of self-reported TB during the whole life. Considering the complex sample design, the TB prevalence by demographic, socioeconomic and morbidity variables was calculated. The prevalence ratio (PR), 95% confidence interval (CI) and P 5% was estimated using Poisson regression considering people without TB as reference category.

Results: TB prevalence was higher among men, 45 years old or more, non caucasian, low education level, low income, unemployed, economically inactive, low self-reported health status and among those with chronic diseases (diabetes, chronic renal failure, bronchitis or asthma). After the model adjustment the following characteristics had significant association to TB: men (PR 1.65, 95%CI 1.34–2.03), non caucasian (PR 1.29, 95%CI 1.05–1.58), unemployment (PR 1.62, 95%CI 1.03–2.55), economically inactive people (PR 1.30, 95%CI 1.04–1.63), worse self-reported health status (PR 2.67, 95%CI 2.06–3.45), physical activity restrictions due to health impairment (PR 2.02, 95%CI 1.58–2.58), diabetes (PR 1.58, 95%CI 1.17–2.14), chronic renal failure (PR 3.54, 95%CI 2.53–4.95) and bronchitis or asthma (PR 3.95, 95%CI 3.07–5.09).

Conclusion: TB control has been a challenge for the country especially when economic adjustments can lead to poverty increasing TB incidence. Considering the observed inequalities, special attention and specific strategies should be developed for TB control among vulnerable groups of low socioeconomic status and those with chronic diseases.

PC-441-01   Determining the minimum tuberculosis incidence risk among adults in the district of Manhiça, Mozambique

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Background: Although the global incidence of TB shows a downward trend in many countries, the incidence in countries with high HIV prevalence remains high. Mozambique, included in the list of 22 high burden countries by WHO, ranks third and sixth in this list in TB incidence and mortality, respectively. In fact, it is one of the few countries whose TB figures have not stagnated or fallen in recent years.

Objective: To estimate to the minimum TB incidence risk among adults (aged 15 or older) in the District of Manhiça during 2012.

Design/methods: This is a retrospective longitudinal study based on routine data already collected by the TB National Program in Manhiça Hospital and Xinavane Hospital, belonging to the District of Manhiça, a rural area in Southern Mozambique. We included relevant variables from all TB patients aged $\geq$ 15 registered in the 2012 National TB Program Registry Books from Manhiça and Xinavane Hospital. Population at risk was calculated using a) population data for the District of Manhiça obtained from the last official census (2007) through the National Statistics Institute and b) estimated 2007–2012 population growth, using annual data from the demographic surveillance system of Manhiça Health Research Center (CISM). TB case, new TB case and retreatment TB case were defined as per WHO guidelines.

Results: During 2012, 889 cases aged 15 or older were diagnosed in the District of Manhiça. Preliminary results show an estimated incidence of 907 cases per 100 000 population aged 15 or older. Fifty-seven per cent of all cases were male. The HIV prevalence in incident TB cases was around 73%. Only 42% of all TB cases were confirmed by microscopy (36% and 55% in HIV positive and negative patients respectively). Eleven per cent of them were classified as retreatment cases with no significant differences depending on HIV status. Among those HIV positive patients, 20% of the cases were extrapulmonary TB, compared to 11% in those HIV negative.

Conclusion: The minimum annual burden of TB in adults aged 15 or older in the district of Manhiça is very high. The proportion of HIV positive TB cases is enormous, higher than country level estimates. Urgent action is needed to reverse this public health threat.

REACHING THE UNREACHABLE: THE ROLE OF CIVIL SOCIETY IN TUBERCULOSIS

PC-442-01   Improving tuberculosis control through service integration and community outreach: experiences from South Sudan

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Background and challenges to implementation: In South Sudan, access to tuberculosis (TB) care is often impeded by political insecurity, geographical obstacles, and stigmatization of TB by both residents and health workers. Furthermore, high staff turnover and poor infrastructure in government facilities has prevented TB service integration into the general health system. Other challenges include low treatment coverage (i.e., TB services are provided in just 6% of health facilities), uneven distribution of health facilities, lack of TB coordination at the county level, inadequately skilled staff, a limited TB laboratory network, lack of a functioning national reference laboratory, and inadequate community involvement in TB control.

Intervention: To improve TB service delivery at all levels of the health system and reach the large population living in remote areas, the MOH began integrating TB services into the Basic Health Package in 2006. As part of this integration process, the Global Fund and USAID-funded TB CARE I project worked with the MOH to train community health workers (CHWs) to support health facilities' TB control efforts through community outreach. Specifically, these partners trained CHWs on TB suspect identification, defaulter tracing, direct observation of TB treatment, and community education. In 2012, TB CARE I and its implementer, Management Sciences for Health, conducted a study to evaluate the impact of TB service integration and CHW training on the nation's TB epidemic. The team analyzed national and state-level data from 2007 to 2012.

Results: From 2006 to 2012, TB case notification in South Sudan increased from 4844 to 8924 and health facilities providing TB services increased from 32 to 72. In 2012, approximately 40% of TB cases were treated in NGO-supported TB sites health facilities and approximately 25% of all smear positive cases were notified through CHWs' community outreach activities. The national treatment success rate remained above 78%, however, the treatment success rate was 95% in health facilities supported by CHWs' community outreach compared to just 54% in facilities not supported by CHWs.

Conclusions and key recommendations: STB service integration and CHWs' community outreach activities contributed to improved TB case detection and treatment success in South Sudan. This strategy should be replicated in similar settings, especially those where there are many barriers to care.

PC-443-01   Grassroots leadership and management to improve the tuberculosis control programme for the urban poor in Quezon City, Philippines

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Background and challenges to implementation: TB prevalence is high in urban poor communities like Payatas in Quezon City. Factors related to access, human resource, finance and governance impede DOTS services for the urban poor. In 2010, Quezon City Health Department (QCHD), with USAID support, aimed to reduce these barriers by strengthening TB program leadership and management at the grassroots (barangay) level using existing structures such as the Barangay TB Management Council (BTBMC). A barangay is the smallest administrative unit in the Philippines headed by a Barangay Captain.

Intervention or response: QCHD revised BTBMC's structure, roles and processes to promote ownership of, and lead the TB program. A BTBMC core team was organized composed of the Barangay Captain, health workers, and other stakeholders, and was tasked to plan, coordinate, monitor and evaluate program activities; align and mobilize stakeholders/resources; and advocate for policy and financial support. The core team adopted MSH's Leading and Managing practices. A secretariat was created and capacitated to manage information, meetings and coordination. Regular meetings were held to monitor achievements, discuss problems and find solutions. QCHD monitored and documented BTBMC activities and results.

Results and lessons learnt: In 2011 and 2012, BTBMC developed and implemented focused action plans. Coordination and collaboration among stakeholders increased and led to sharing of resources such as TB diagnostic committee and medicines, establishment of diagnostic facilities (smearing stations) and increased referrals. Financial support from the Barangay increased and used to remunerate community health workers, fund meetings and other activities. A network of treatment partners was established. In 2012, the number of TB symptomatics examined by microscopy increased by 27% while TB cases treated increased by 23% compared to 2011. Results

suggest that strengthening program leadership and management at grassroots level using a team approach can reduce barriers to service delivery and improve performance.

Conclusions and key recommendations: Community participation in program leadership and management strengthens the TB control program. The leading and managing processes must be applied continuously to strengthen organizational capacity to face program challenges. The Payatas model can be applied to other health programs to improve public health services.

PC-444-01   Room for improvement: looking at quality of care of tuberculosis through the patient's eyes

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Background: DOTS TB program in Indonesia has escalated to exceed global target on CDR and CR, innovation has made through many initiatives to overcome new challenges. Capturing patient perspective is an approach to provide balance information on how patient perceived the quality of care. The objective of the study is to have information on patient perception toward TB services.

Methods: Using a mix of qualitative and quantitative methods by conducting interview with 285 patients and in depth interview with patient, providers and health cadres.

Result: 222 respondents said that they learn about TB in health care facility. 63.2% of respondents also said they went to the health facility after they diagnosed that they got TB. Although TB services are free in Indonesia, the services still perceived as expensives for some patient due to indirect cost caused related with health seeking behaviour to private sector (private practitioner and hospital) this is also related with the fact of socioeconomic condition of TB patient where 38.6% respondent are not working. We also find that most of the patients and HCWs had never heard about patient charter. Soft stigma on TB still exists in the community and preserved by HCWs.

Where did patient learn about TB?
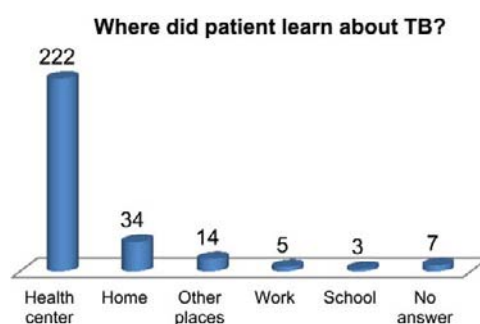
Conclusion: Patient experienced that health care facility as the main source of information about TB. FGD conducted using Quote TB Light tools shows that respondent put patient-provider interaction and counselling, and communication and information as the areas they consider important after provider competence. Strengthening the capacity of health provider in communication is necessary to improve patient-provider interaction. These will also enhanced communication in delivering TB related information. Community should be involved and considered in intervention to create dialogue between patient and health provider to have better understanding on patient charter and to erase the stigma. Intervention need to be made align with the TB health seeking behaviour to private practitioner/hospital to reduce the indirect cost created.

PC-445-01   Patients' perceived barriers to access to and use of public tuberculosis diagnostic services in Viet Nam

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Background: Viet Nam ranks 12th of the 22 high TB burden countries. According to World Health Organization (WHO) estimates, 44% of TB cases remain undetected in Viet Nam. Efforts to understand and overcome barriers to TB diagnosis are critical for improving case detection.
Methods: We conducted a cross-sectional study of 398 smear-positive TB cases selected from district and provincial registers and 1092 people with presumptive TB recruited from provincial and district TB clinics in three provinces representing three regions of Viet Nam. Semi-structured interviews collected information on knowledge, attitudes, and practices around TB; care-seeking behavior; barriers to access and use of public TB diagnostic services; and suggestions for system improvements.
Results: TB patients and persons with presumptive TB had a good understanding of TB symptoms, care, locations of services, and did not report gender bias or stigma related to their TB condition. The most important barrier to diagnosis identified was a lack of risk perception among study participants that they could have TB (87% of cases; 49% of persons with presumptive TB); thus, when symptoms presented, the most common response was to do nothing or self-treat (52% of cases; 44% of persons with presumptive TB) or go to pharmacy (32% of cases; 28% of persons with presumptive TB). Participants reported that they went to public TB facilities for diagnostic services as a third step (41% of cases; 42% of persons with presumptive TB), usually three weeks after TB symptoms began. Other barriers included long time needed to seek care (12% of cases; 17% of persons with presumptive TB), financial expenses (8% of cases; 5% of persons with presumptive TB), complex insurance procedures (4% of cases; 5% of persons with presumptive TB) and the quality of services (6% of cases; 3% of persons with presumptive TB).
Conclusion: Although the participants in this study reported many barriers to accessing public TB diagnostic services, lack of risk perception was identified as the principal reason why TB patients and persons with presumptive TB delay seeking early care. The findings of this study emphasize the need for developing and implementing targeted communication strategies to increase individual awareness of risks for TB and of the need for early access to TB diagnostic services throughout the community for improving TB case detection in Viet Nam.

PC-446-01   Support groups among tuberculosis patients: a suitable framework for the restoration of self-esteem

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Background: The fight against tuberculosis in Burkina Faso is based on the integration of community health system interventions. Since 2005, the PAMAC (support program to association and community based organization NGOs in fight against AIDS, tuberculosis and malaria) through associations conducts outreach activities, the support group of TB patients co-infected TB/HIV is part of the minimum activities Community support package and integrates the psychosocial care of the disease. It is a speaking space for TB patients who share some concerns. They can exchange them thoroughly and share their experience.
Definition and objectives of a support group: The discussion group (support group) is a floor space for TB patients who have common concerns and allows them to share in depth, share their experience, listen to what everyone lives, feels, understands, and to support them in an atmosphere of trust and non-judgment. 1) Offer patients a space of free exchange from various themes proposed by the group itself; 2) promote exchanges of patients about their difficulties and help support mutual psychosocial; 3) break the isolation and help some patients to accept their status to live positively; 4) help TB patients co-infected TB-HIV to observe their treatment?
Intervention strategy: Identification of a theme and planning session, information to potential participants by phone or poster, setting up the group of volunteers (between 5 and 25 people), identification of a moderator, appointment of a facilitator and co-facilitator, identification of a contact person who can be a doctor, a psychologist, a magistrate to provide specific answers to participants.

Results: During January to June 2012—12 groups of words were made by 5 associations—245 TB have benefited from a discussion group. An evaluation through focus groups with these patients showed: 100% of patients are satisfied with support group (discussion group), 80% think the discussion groups helped them to accept the disease, 60% believe they have had some affection despite their disease, 100% had friends with whom they shared their concerns, 100% had the courage to continue the treatment of tuberculosis.

Conclusion: The discussion group is a framework that allows the development of TB patient and promotes good adherence to TB treatment.

PC-447-01   mHealth initiative 'Talk for Life' improves tuberculosis management in remote areas of Botswana

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Context: Ghanzi District in Botswana has the highest TB notification rates in the country. The remote areas remain with challenges of access to health services. Vast distances, sandy terrain, limited electrification, poor communication infrastructure and lack of transport in the remote areas contribute to the challenge of access.

Approach: Kuru Health, a local non-governmental organization established the first mHealth initiative 'Talk for Life' in the district to improve management of TB. A closed mobile cellular network was provided to health workers in the remote areas to communicate with each other from the facility, to the lab and to community health workers on the farms. Before the mHealth initiative, the system relied solely on physical transport for means of communication.

Results: The 'Talk for Life' mHealth initiative has improved TB diagnostic turn around times, enabled early treatment initiation and improved communication in remote health service delivery. Despite vast distances and lack of transport within the health system, the 'Talk for Life' phones enable easy follow up of sputum results and increased access to health care. Health worker perceptions about the initiative are positive and expansion is highly desirable.

Recommendations: mHealth solutions should be integrated with maximum support for sustainable development in remote area health systems. 'Talk for Life' requires extended partnership to enable the basic two way voice communication to transform into a more comprehensive interoperable telemedicine project to improve TB data management and integrated service delivery to the remote areas of Botswana.

PC-448-01   ACSM strategies for early presentation of TB-HIV co-infected patients for care and to improve treatment outcomes in Sedibeng District, Gauteng Province

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Background and challenges to implementation: South Africa continues to face the dual TB-HIV epidemic, with a TB incidence of 993/100 000, with 65% of TB cases co-infected with HIV. The URC TB Project funded through USAID provides TB technical support in Sedibeng District. One of the objectives of the projects is to increase the demand for TB services, through which advocacy, communication and social mobilication (ACSM) strategies are used. Baseline assessments were conducted in 2010 to inform interventions, which were developed, implemented and jointly monitored.

Intervention or response: Data was collected in randomly selected facilities using a baseline assessment tool. Findings indicated that 82.5% of the TB patients were co-infected, 88.3% of the HIV-positive presented with CD4 count less than 350 c/ml. A plan to address the late presentation was developed. The plan included partnerships built with communities of Sedibeng to raise awareness on symptoms of TB and HIV, use of IEC material (pamphlets in local language), integration of Kick TB campaign that integrates theme of football through which TB messages are conveyed to children in schools; as well as a support group forming a community of care and support for both TB and HIV patients.

Results and lessons learnt: The results were compared to 2010 at baseline data collected. Patients presenting with CD4 count less than 350c/ml decreased by 20% to 68.8%, while the recording of the HIV status improved less from 85.4% in 2010 to 93.5% in July–September 2012. The TB treatment cure rate improved from 77% in 2009 to 80.7% in 2011.

Conclusions and key recommendations: Targeted ACSM interventions based on available data are designed to improve and contribute to changes in social norms and creation of social networks that support individual change leading to demand for and timely uptake of appropriate health services. Increasing awareness, health education and the use of information and education material targeted at specific groups is key populations. Community dialogues form an impotant base which informs challenges unique for defined populations. The model can be replicated in other districts where TB patients present late for care.

PC-449-01   The three plus one critical tuberculosis vaccines advocacy priorities in the next decade

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Background and challenges to implementation: Modeling studies have shown that more effective TB vaccines are essential if we are to reach the global goal of eliminating tuberculosis. There is however a complete lack of adequate global awareness about both the urgent need for new better TB vaccines and the tremendous progress that has been made towards that goal. This has made it untenable to build the necessary support for vaccines research and development. We looked at what will constitute the most critical advocacy priorities in order to raise the profile of TB vaccines in the next decade.

Intervention or response: We analyzed the TB vaccines blue print and identified its strategic advocacy choices for the next decade, and also interviewed advocates and researchers in two forums; the 3rd South African TB Conference and the Third TB vaccines forum. Responses were analyzed and compiled and were merged with the blue print choices for the outcome.

Results and lessons learnt: The identified advocacy priorities are: 1) to expand financing to provide sufficient resources to advance and sustain research on TB vaccines; 2) to continue and expand on efforts to raise awareness of the role of new TB vaccines as part of a comprehensive response to the global TB epidemic and build support at all levels; 3) to broaden the base of advocates, allies and champions not only for TB but vaccine research and development, plus one; which is 4) bridging the gap between advocates and researchers to exploit the best of synergy power between the two parties.

Conclusions and key recommendations: There is an urgent need to increase the profile of TB vaccine research at global, national and community levels in order to generate support and political will to increase investment in TB vaccine research, to create an enabling and supportive environment for clinical trials, and to lay the groundwork for acceptance and adoption of new TB vaccines once licensed. To effectively accomplish this, we need to prioritise the three plus one activities.

PC-450-01   Advocacy, communication and social mobilisation to enhance tuberculosis control in Pakistan: an evaluation

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Background: Despite over 20 years of international focus on tuberculosis and the widespread implementation of DOTS strategy in the control of TB, case detection rates (CDR) for tuberculosis remain low. In many countries, CDR do not meet the WHO millennium target of at least 70% detection rates or have plateaued while the estimated incidence has increased. Advocacy, Communication and Social Mobilisation (ACSM) is part of WHO's Stop TB strategy aimed at improving case detection and treatment adherence, combating stigma and discrimination, empowering people affected by TB and mobilising political commitment and resources for TB. Pakistan has the fifth highest tuberculosis disease burden among high burden tuberculosis countries with approximately 420 000 new TB cases identified annually on positive sputum smear results. Pakistan is also estimated to have the fourth highest prevalence of multi-drug resistant tuberculosis worldwide. Pakistanis a large country with many affected populations living in poorly accessed regions. The role of ACSM in vaccine uptake programmes is well documented. Evidence from Viet Nam has indicated an association between an increase in CDR following the introduction of ACSM, however a more robust evaluation of its role in TB control is needed. We assess the effect of ACSM on smear positive CDR in the Punjab Province of Pakistan.

Methods: The Pakistan National Tuberculosis Programme (NTP) collected routine data on smear positive CDR in the Punjab province in 2008. Using a natural experimental design, we assessed the impact of ACSM on smear positive CDR in the Punjab province in 2008 and 2009. We used districts as our unit of analysis and compared CDR in districts where ACSM was implemented to those where it was not.

Results: The Punjab province consists of 36 districts. ACSM was implemented in 19 of these districts and was originally introduced in 2008. An analysis of the smear positive CDR from routine data collected by the NTP in 2008 and 2009 is presented here. In 2008, the smear positive CDR was 81.1% in ACSM districts compared to 67.8% in non-ACSM districts. In 2009, the smear positive CDR was 79.8% compared to 67.8% in ACSM and non-ACSM districts respectively.

Table   Summarising case detection rates (CDR) in ACSM and non-ACSM districts of the Punjab Province of Pakistan in 2008 and 2009

	2008	2009
CDR in ACSM districts	81.1%	79.8%
CDR in Non-ACSM districts	67.83%	67.8%

Conclusion: A crude estimate of CDR for smear positive tuberculosis in Punjab showed that the CDR was higher in ACSM districts compared to non-ACSM districts. An interrupted time series analysis is proposed to detect any causal associations.

PC-451-01 Screening and testing for tuberculosis and HIV in correctional facilities in the Western Cape, South Africa

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Background and challenges to implementation: Overcrowding, poor ventilation, malnutrition, depressed immune status and violence have all been implicated in increased rates of TB and HIV infection in correctional facilities. This is exacerbated by inadequate medical care and contributes to the emergence of resistant strains that infect other prisoners, and the community at large. TB-HIV Care Association in collaboration with Right2Care, the Department of Correctional Services, the National Health Laboratory Services and the Western Cape Department of Health provided intensified screening and testing for TB and HIV in Pollsmor correctional facility in the Western Cape. This service will help determine the prevalence of active tuberculosis and HIV among inmates at the correctional facilities and result in timeous and appropriate treatment for inmates.

Intervention or response: Lay and adherence counsellors were employed within the correctional facility to screen, test and refer for TB and HIV clinical care. The results of the counselling and testing sessions are recorded on a unique consent form which is in line with the stationery used by the Western Cape Department of Health. A GeneXpert machine was installed at Pollsmor prison at the end of February 2013 to speed up the diagnosis and treatment of TB. The data was captured by a data capturer into a database and reports are generated for reporting and analysis.

Results and lessons learnt: The results from March 2013 demonstrate that 1176 inmates were tested for HIV and received the HIV test results. 85 inmates tested HIV positive (7.3%) and 85 (100%) individuals were referred for a CD4 test. Out of those 35 were eligible for ARV's and were started on ARV treatment. 1176 inmates were screened for TB symptoms. The 259 inmates had positive symptoms and had sputum collected for GeneXpert testing, 29 (11%) inmates tested positive for TB and were all rifampicin sensitive. All of them (100%) were started on TB treatment.

Conclusions and key recommendations: The results of this service will give a more accurate picture of the burden of TB disease and HIV infection within correctional facilities and help guide future policy on screening and testing for TB and HIV in correctional facilities in South Africa.

PC-452-01 Tuberculosis in the workplace: achievements and challenges in the garment industries in Bangladesh

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Background and challenges to implementation: The garment sectors of Bangladesh, a tuberculosis (TB) prevalent country, have about three million workers. Volume of workers varies from hundred to ten thousand per factory, of whom 90% are women. Employees often work in crowded situation in poor ventilated housing structures which is favorable for spreading TB and for this they have 2.4 times more chances to be infected with this disease. Workers also conceal TB due to fear of losing job and most of them are treated irregularly by private practitioners which may cause drug resistance. In this situation, a partnership programme was initiated in 2010 through 12 health centers to diagnose and treat TB cases among workers under DOTS strategy. This paper shows the achievements and the challenges of that programme.

Intervention or response: Advocacy and health education campaign has been initiated to raise awareness of owners, medical officers, paramedics, supervisors and workers on TB. Alongside, relevant health staff and supervisors refer workers with TB symptom to nearby DOTS center for sputum microscopy and other requirements for diagnosis. If the suspect is diagnosed as a TB case, doctors provide treatment, paramedics continue DOT and follow up them in the factory premises and keep records.

Results and lessons learnt: Up to December 2012, 414 orientation/advocacy meetings on TB have been organized in different garment industries where 20 638 employees participated. In 2011 and 2012 year 160 and 187 new smear positive cases and overall 292 and 389 TB cases were diagnosed respectively, and gender wise overall case detection ratio was 1:1.25 and 1:1.24 respectively. Yearly case detection data indicates a positive trend but the case detection rate and gender wise case detection ratio is not satisfactory. Conversely, overall treatment success rate was 90.07 which was below national average and the unacceptable outcome was high, at 8.51 percent.

Conclusions and key recommendations: Gender sensitive effective advocacy and social mobilization strategy need to be initiated among factory management and workers to strengthen the TB-control programmes further in garment factories. Quality of microscopy and referral of smear negative suspects need to improve. Moreover, effective follow-up and referral linkage need to be developed to reduce the unacceptable treatment outcomes.

PC-453-01   Reaching the unreached through community strengthening

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Background and challenges to implementation: Rajasthan is the largest state of India, in context to Tuberculosis Control Program, the long distances between the services and communities act as a barrier for the marginalised population in accessing the health services. Engaged in various occupations people like stone crushers, bidi makers, mineworkers, PLHIV, female sex workers, etc. are termed vulnerable as they are more prone towards acquiring or transmiting the infection. Project Axshya supplements the Govt of India's RNTCP objective of reaching the most vulnerable and marginalised population for TB care and control. Project Axshya is being implemented in partnership with MAMTA in 14 districts of Rajasthan.

Intervention or response: In consultation with district level RNTCP staff and other important stakeholders mapping of vulnerable and marginalised area was completed. From each district, 50 community volunteers were identified from vulnerable and marginalised areas and were trained on IPC tool, sputum collection and transport. Sensitization of influential groups like women groups, committee of local self-government, community based organisations, etc. were done through community meetings on issues of tuberculosis. The influential groups and community volunteers helped in identifying the chests symptomatic TB having more than two weeks of cough. Community volunteers collect and transport the sputum of chest symptomatic to DMC for testing.

Results and lessons learnt: In April–June 2012, 205 sputum samples were collected and transported out of which 11 were diagnosed positive and all were put on DOTS. Similarly, in next quarter July–Sept 2012, 1987 sputum samples were transported out of which 229 were diagnosed as smear positive and 225 were put on DOTS. In last quarter of October–December 2012, 2770 TB symptomatic samples were transported and diagnosed, out of which 168 were identified as positive and 165 were put on DOTS. In January–March 2013, the total sputum samples transported were 2151 and out of which 111 tested positive and all were put on DOTS.

Conclusions and key recommendations: Sputum collection and transport through volunteers can be a very effective strategy to reach the people, who are at risk of acquiring infection and could not access the health testing services.

EXPANDING THE STOP TB STRATEGY

PC-454-01   Improving access to tuberculosis diagnosis through establishment of sputum collection centres in Kenyan urban slums

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Background and challenges to implementation: Kenya still faces considerable challenges in its efforts to reduce the burden of TB disease despite the excellent progress in meeting WHO targets over the last few years. Access to TB diagnosis remains uphill task as a result of the high population, its distribution and geographical location of the few available diagnostic centers. There are 1581 AFB microscopy diagnostic sites in the country majority of which are GOK and mission facilities. Establishment of sputum collection canters helps in improving access to diagnosis services by offering the client an alternative to the long journey which is more often than not made on foot. This in turn helps reduce delay in TB diagnosis, contributing to the fight against the burden of TB in the country.

Objective: To improve access to TB diagnostic services and reduce delay in diagnosis hence cut the chain of transmission of TB disease.

Intervention or response: The project was implemented in four urban administrative districts in the country namely; Makadara, Starehe, Kilifi and Msambweni between January and December 2012. Provider mapping of all private and public facilities in these districts was done. The facilities' willingness and capacity for engagement was assessed. 28 facilities accepted to act as sputum collection centers for TB suspects. Staffs in participating facilities were trained on sputum sample collection, handling/transportation and supplied with tools and, commodities for TB screening and sputum collection were provided.

Results and lessons learnt: 3267 sputum specimen were collected and transported to the diagnostic sites for AFB investigation, 3186 (97.5%) specimens were investigated and 188 PTB+ cases were identified. The identification of such high number of TB cases proved that development of sputum collection centers improves access to diagnosis. However, infection prevention control can be a big challenge during the development of sputum collection centers, but can be overcomed by intense training and support.

Conclusions and key recommendations: Access of TB diagnosis services can be improved by developing sputum collection centers which will improve early case detection of TB cases.

PC-455-01   Comparing two years of active case finding results from 11 interventions

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Background: TB REACH is a multi-country initiative focusing on innovative ways to improve TB case notification and treatment. In many case detection interventions, many prevalent cases can be found in a 'mopping up' effort to clean the pool of cases that may be diagnosed late. During a first wave of funding 30 projects were funded and 11 of them in 8 countries were provided a second year of funding based on performance during the first year. We track the performance of projects during the first a second years to compare yields impact on case notification.

Methods: Additional cases are calculated be finding the difference in cases notified to the NTP and placed on treatment during a baseline year and implementation period. We analyzed standard reporting data from 11 TB REACH projects that had at least two years of implementation data for numbers of additional cases over time, the numbers of cases these interventions directly found, and trend data.

Results: Eleven projects covered a total population of 26.6 million people. Additional cases were defined as the difference between the number of cases found during baseline and the intervention period. At baseline, there were 26 494 SS+ cases in the evaluation population. In the first year of the intervention there was a 31% increase in detected SS+ cases (34 772), with projects directly identifying 40% of these cases. 58% of these directly identified cases were additional. In the second year of implementation, there was a 26.7% increase in notified cases from baseline. A larger proportion (57%) of all notified cases was directly identified by the projects; however, only 37% of these directly identified cases were additional.

Conclusions: Active case finding interventions can improve case notifications consistently over a period of 2 years. Although there seem to be a significant number of prevalent TB cases that can be detected as a one off initiative, sustained active case detection interventions can continue to have an impact on overall notifications over time. Active case detection initiatives can identify previously undiagnosed TB in communities and should be prioritized as a lagging global indicator.

PC-456-01   Referral for presumptive tuberculosis in Nigeria: comparison of three models of active case finding by community volunteers

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Background: Emerging evidence suggests that active case finding detects TB earlier than the classical (passive) paradigm. Diverse donors, NGOs, and state actors support community volunteer TB referral efforts in Nigeria via different models. However, rates of referral by the community volunteers vary widely. This study aimed to assess the factors responsible for the differential performance.

Methods: A retrospective comparative qualitative/quantitative cross-sectional study in randomly selected states in SE and SW Nigeria was conducted. Local government areas with the presence of one or more CV referral models were selected. Assessments of recruitment, training, supervision, incentive structures and CV knowledge were conducted. Focus group discussions and key informant interviews complemented numerical comparisons. IBS SPSS version 19 and Atlas ti version 5 were used.

Results: A total of 17 928 persons with presumptive TB were referred by 3722 CVs, an average of 5 TB symptomatic per CV in 9 months, representing 7% of total of 254 794 population referred during Q1–Q3 2012.

Table   Active case finding models engaging community volunteers

State/ LGA	# CVS	Program since	Incentives (Naira)	Partner (funder)	Funder
24 states	3600	2011–2012	N2000	Health Alive Foundation	Global Fund
2 states	72	2012	N500	TB REACH	WHO/ CIDA
1 state	50	2012	N1000	FHI/TB CARE I	USAID

Conclusion: Referral for presumptive TB was modest among all three models. No single factor explains CV performance. Active-case finding efforts must balance level of CV support with need for sustainability. A health systems approach is needed.

PC-457-01 Patients' perspective on perceived quality of service: experiences using TB QUOTE Light in Nigeria

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Background: People's perception of the quality of health services influence their health seeking behaviour and their utilization of health services. Learning from the patient's experiences can inform the improvement of health services to better meet their needs, and increase access and decrease delays in seeking care.

Method: A mixed method approach consisting of a cross-sectional survey and focus group discussions (FGD) with TB patients currently on treatment in Osun, and Ogun states was conducted. Focus group discussions were held to measure an importance score by ranking nine quality dimensions of TB services as perceived by the patients. Structured interviews were conducted to measure the performance score of TB services delivered at health facilities. A combination of the importance and performance scores result makes the quality impact score (QI), an indicator of which dimension of TB services needs improvement. Any QI score >0.75 require improvement.

Results: During the FGDs, 9 quality dimensions were ranked: communication and information; professional competence; availability of TB services; affordability; patient provider interaction and counselling; support; TB-HIV; infrastructure and stigma. FGD participants ranked availability of TB services as most important (97%) and the least important was TB-HIV in both locations (17%). The QI score indicates that support (in cash and kind) received the highest QI score of 5 in Ogun and 6 in Osun State suggesting a need for the TB program to explore patient support issues as a means of improving service. Interestingly TB-HIV and stigma were least important to respondents. Measurement of stigma by friendliness of service provider indicate that it was not an issue in Ogun (0.26) and Osun (0.031); likewise the measure of contempt of provider turning face away was also not an issue (0.33) in Ogun and (0.21) in Osun state. Other areas of quality dimension requiring immediate attention were professional competence which received a score of 4 in both locations specifically the delay between sputum submission and release of results and non-examination of close TB contacts.

Conclusion: While TB program managers have considered stigma a major barrier. This was however not so in the present study. Availability of TB services and competent staff with communication skill were considered most important quality determinants of care by TB patients suggesting the need for TB control programs to concentrate on these areas.

PC-458-01 Comparison of hospitals' performance before and after the CATCH TB cases project

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Background: The CATCH TB cases project aims to detect more TB cases by engaging big public hospitals in Metro Manila. The Department of Health's (DOH) policy states that public hospitals must have TB clinics, where all TB cases seen within the hospital should be referred (internal referral) for registration or referral to peripheral DOTS facilities (external referral). However, only few hospitals were able to comply with the guidelines. Before the project started, we conducted a rapid assessment survey (RAS) in 14 public hospitals. We reviewed the 2008 hospital statistical reports to determine their potential to contribute to TB case finding, and design interventions for the project. Eleven (79%) of the 14 hospitals joined the project in June 2010. We assisted them in improving the TB referral process. The aim of the study is to compare accomplishments of 11 hospitals before and after the project.

Design/methods: A descriptive study was done. Quantitative data obtained during the RAS in 2008 were compared to hospitals' accomplishments in 2012.

Results: In 2008, hospitals detected around 10 408 TB cases mostly from out-patients and wards. However, only 2160 (21%) were seen by TB clinics, and 602 (6%) were notified, either by the hospital or peripheral DOTS facilities. More than nine thousand (94%) of TB patients found by hospitals were lost
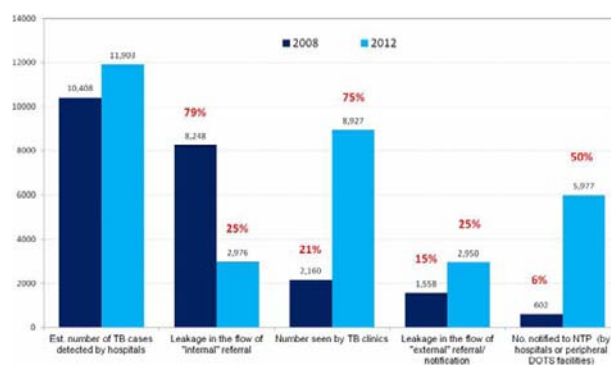
Figure Disposition of TB cases detected by hospitals before and after CATCH TB cases project, 11 public hospitals, Metro Manila, 2008 vs. 2012.

because of the 'leakages' in the flow of internal (79%) and external referral (15%) system. In 2012, almost 12 000 TB patients were detected, 8927 (75%) were referred to TB clinics, and 5977 (50%) were notified. Most (80%) of the notified cases where through successful referrals to peripheral DOTS facilities, mostly health centers. Compared to 2008, the proportion of internal leakage dropped to 25%, but higher (25%) for the external referral. Notification improved almost 10 times (Figure). However, around 6000 (50%) TB patients remain unreported to NTP.

Conclusion: Hospitals could contribute more TB cases if referrals within and outside hospitals are established and strengthened. The cooperation and flexibility of receiving DOTS facilities especially health centers is equally important in the success of the initiative. It took almost three years for the project to improve the system, but more efforts are still needed to reduce leakages, and maximize hospitals' potential. Hospital management and TB teams were committed to sustain the gains beyond project life and continuously improve the system to minimize lost cases.

PC-459-01   Results from a multi-sectorial approach to implementing urban DOTS in Kabul, Afghanistan

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Background: Kabul province, the capital of Afghanistan, has approximately 3 950 000 inhabitants (15.5% of the national population) and consists of 14 rural districts and 22 urban districts. Kabul suffers from overcrowding and poor sanitary conditions at health facilities. In early 2009, the TB case notification rate in Kabul was 26%, the conversion rate was 43%, and TB treatment success rate was 46%. To improve these rates, the USAID-project, TB CAP/TB CARE I, designed an urban DOTS (directly observed treatment, short course) program. From 2009 to 2012, the TB CAP/TB CARE I team, led by MSH, implemented this program using a multi-sectorial approach that included involving public and private health facilities in DOTS, training frontline health workers in DOTS, strengthening coordination among different stakeholders, and conducting regular monitoring and supervision visits to health facilities to ensure effective DOTS implementation. In 2013, the project team worked with Afghanistan's NTP to assess the impact of their urban DOTS program on TB outcomes in Kabul province.

Methods: In 2012, 68 public and private health facilities classified as TB diagnostic-treatment centers offered 83% of the population of Kabul access to free TB-services. From January to March of 2013, the NTP and TB CARE I technical teams reviewed and compared TB data that Kabul's health facilities had recorded between 2009 and 2012. The teams used the standard NTP recording and reporting tools to conduct this assessment and then compared with surveillance data which was available in NTP.

Results: The study identified that number of TB suspects multiplied five times between 2009 and 2012 and the number of TB cases registered increased by 66%. Among these newly registered TB cases, the number of newly identified TB sputum smear positive cases increased by 44% to reach 1176 in 2012 and the conversion rate increased by 33% to reach 76% in 2012. The TB treatment success rate improved by 31% to reach 75% and the number of patients who transferred out of treatment decreased by 31% (from **46%** in 2009 to 15% in 2012). These results reflecting significant improvements TB outcomes are shown in the Table.

Table   Results of multi-sectorial approach of urban DOTS in TB control services, 2009–2012

Year	2009	2010	2011	2012
No. of existing health facilities	106	111	111	111
No. of health facilities covered by DOTS	22	48	53	68
No. of TB suspects identified/ examined	2856	10 150	11 900	14 644
No. of all TB cases notified	1934	2 738	2 728	3 215
No. of new sputum smear positive cases notified	814	1 022	1 082	1 176
Conversion rate of sputum smear positive cases	43%	65%	70%	76%
Treatment success rate of new sputum smear cases	44%	62%	75%	NA
Transferred out rate of new sputum smear positive cases	46%	26%	15%	NA

Conclusion: Urban DOTS contributed to significant improvements in TB outcomes in Kabul including the TB case notification rate, the sputum smear conversion rate, and the treatment success rate. Urban DOTS should be scaled up in Kabul and similar urban settings worldwide.

PC-460-01   Transforming tuberculosis control in Mumbai, India

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Background: Mumbai, India has an urban population of 12 million, 60% resides in slums. Despite >30 000 TB cases detected and treated annually in public sector, Mumbai faces a serious ongoing epidemic

of drug sensitive (DS) and drug-resistant (DR) TB. The challenge of TB control in Mumbai was brought in sharp focus in January 2012 with reports of XDR-TB. Accordingly, MCGM strengthened services and accelerated detection of MDR-TB but lacked a comprehensive vision and plan to address the serious public health challenge of TB control in face of the city.

Response: Since January 2012, Mumbai has decentralized programme management, added human resources, expanded eligibility for MDR-TB screening, and accelerated MDR-TB services expansion. Results showed increased TB case detection, and dramatic rise in MDR-TB case finding (Table). In Feb 2013 a multi-sectorial workshop came up with a comprehensive plan to accelerate TB control and achieve Universal Access (UA) to quality TB diagnosis and treatment. The plan articulates 7 key strategies for achieving universal access to quality TB care including: (1) mission mode active case finding in slums, (2) access to rapid diagnostics including universal DST, (3) improving access to effective treatment, (4) extending services and support to providers and patients in private sector, (5) infection control, (6) building empowered communities and (7) organizational strengthening of Mumbai Districts TB Control Society. Targets include 100% slums covered for intensified case finding, 15 000 additional TB cases (DS and DR), Private Provider Interface Agency identified and functional, and a three-fold increase in budget.

Discussion: Mumbai TB control programme has taken rapid strides in expansion of services with corresponding increase in TB case detection (DS and DR), and is a model for accelerating MDR-TB service deployment in urban areas. While Mumbai's TB response plan provides a roadmap for further transforming urban TB control, the immediate challenge is financing and execution.

	2011	2012	Change %
Districts	1 (6 zones)	24 districts	400
Microscopy Centres	116	145	25
DOT Centres	998	1 631	63
Program Management Units	27	59	118
Persons examined by smear microscopy	97 710	117 234	119
TB Cases Notified	29 212	30 814	5
TB Patients Screened for MDR-TB	345	10 323	2892
MDR-TB Diagnosed	181	2 429	1242

PC-461-01 Comparison of different models for active tuberculosis case finding in Zimbabwe

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Background and challenges to implementation: Zimbabwe is 17th among the 22 high TB burden countries. TB detection rates remain low <50%. In 2005 Population Services International (PSl) introduced TB symptom screening offered to all clients accessing services through their HTC center network. A review of TB suspects referred for diagnosis and treatment from one HTC center in Harare revealed a 50% suspect referral success rate, yielding 5% TB cases identified. To improve on-site TB diagnostics and to reduce referral losses, PSI integrated fluorescence smear microscopy and Xpert MTB/RIF in 4 of the 17 HTC centers. To intensify TB case finding, PSI introduced community based TB screening using mobile vans in the communities surrounding the 4 HCT/TB centers.

Intervention or response: Laboratory facilities at 4 HTC centers were upgraded to accommodate TB diagnostic services. Between October 2011 and March 2013, all clients visiting the 4 HTC centers were screened for TB, regardless of HIV status and services sought. Mobile teams visited urban and peri-urban communities and most-at-risk populations (MARPS) giving health information on TB symptoms, screened and collected sputum of presumptive TB cases for laboratory testing at the HTC sites and returned results the next day. Medical facilities with no or limited TB laboratory diagnostic capacity also submitted sputum samples for free testing. All diagnosed cases were followed up and linked to treatment.

Results and lessons learnt: A total of 104 754 individual were screened for TB symptoms through community mobile outreach yielding 118 (0.1%) TB cases identified, HTC centers screened 133 446 individuals, yielding 596 (0.4%) TB cases and outreach to MARPS screened 4039 individuals, yielding 40

Table Summary of outputs by process indicator

	Process indicators	Totals	Proportions	NNS
TB case finding: community mobile outreach	Total screened for TB symptoms (urban & peri-urban areas)	104,754		888
	Total suspects identified (urban & peri-urban areas)	4,587	4%	
	Total TB cases (SM+ and/or GeneXpert+) confirmed (urban & peri-urban areas)	118	0.1%	
TB case finding: HTC static sites	Total screened for TB symptoms (static site)	133,446		224
	Total suspects identified (static site)	5,535	4%	
	Total TB cases (SM+ and/or GeneXpert+) confirmed (static site)	596	0.4%	
TB case finding: MARPS	Total screened for TB symptoms through HTC mobile teams	4,039		101
	Total suspects identified through HTC mobile teams	763	19%	
	Total TB cases (SM+ and/or GeneXpert+) confirmed through HTC mobile teams	40	1%	
TB case finding: among referrals	Number of suspects referred from other facilities	4,816		
	Number of TB cases (SM+ and/or GeneXpert+) confirmed from referrals	636	13%	
Totals	Number of suspects identified, all interventions	15,701		
	Number of TB cases (SM+ and/or GeneXpert+) confirmed	1,390	9%	

(1%). The number needed to be screened to identify one smear-positive case was 888, 224 and 101 respectively for community outreach, HTC centers and outreach to MARPS. Active TB case finding through community outreach was the least successful model, requiring screening of close to 9 times more individuals to identify one TB case than outreach to MARPS and required screening of 4 times more individuals than TB screening at HCT centers.

Conclusions and key recommendations: Routine TB screening offered to clients accessing HTC services with integrated TB laboratory services is effective in identifying TB cases. It is essential to target areas with populations at high risk of HIV and TB infection if community based active case finding is to be effective.

PC-462-01   Expanding patient-centred tuberculosis care in five regions of Russia

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Background: The patient-centered 'Sputnik' program has been successfully implemented since 2006 in Tomsk City, Russia, by NGO 'Partners in Health' and local TB services for high-risk patients. However, such care is still rare in TB community of Russia. In 2011 PIH launched 'Patient-Centered Accompaniment' project in 5 Russian cities with support from USAID.

Methods: High-risk TB patients who are refused to get treatment, being defaulted or with poor adherence (daily doses intake was less than 70%) were referred to the PCA project by created local adherence committees. Most of the referred patients were already receiving incentives such as food sets, transportation tickets and treatment at home without great effect. PIH created local PCA teams consisting of nurses, driver, TB physician, coordinator and local experts from HIV harm reduction projects. Teams were equipped with car and fuel, cell phones, ancillary medications, food sets and clothes for patients in need. The project model includes intensive psychological support, DOT through treatment at home or at any location chosen by the patient, daily food sets ($1.7/day), complementary side effect management, addiction care, and building provider-patient relationship as co-partners. Teams work was intensively monitored by PIH coordinator on weekly basis. Patients' clinical data was collected, and program effectiveness was measured using adherence rates and treatment outcomes.

Results: Between February 2011 and December 2012, 295 patients were enrolled in PCA project (half of them with MDR-TB). The average rate of medica-

tion intake among all patients increased from 60.4% prior to enrollment (for patients who were on treatment prior to enrollment) to 89.2% after being treated under the project.Among the 166 patients who have treatment outcomes as of March 1, 2013, 83.7% were cured, 8.4% defaulted and 7.8% died.

Conclusion: Preliminary data shows that patient-centered approach is one of the most effective ways to get high-risk patients on treatment, improve their adherence and decrease the overall default rates in the Russian Federation. Expansion of such programs across Russia is urgently needed in order to improve the quality of the provided TB care.

PC-463-01   Successful outcomes of isoniazid preventive therapy among people living with HIV/AIDS in an urban slum setting, Nairobi, East Kenya

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Background: Tuberculosis (TB) is the most frequent life threatening opportunistic disease among people living with HIV/AIDS (PLHIV) and is the leading cause of illness and death. Eastern Deanery AIDS Relief Program (EDARP) begun Isoniazid Preventive Therapy (IPT) implementation to PLHIV in 2004; making it one of the first programs in Kenya to provide IPT. This was in line with the World Health Organization (WHO) guidelines. This abstract aims to demonstrate the effectiveness of IPT intervention on TB prevention among PLHIV at EDARP situated in the Eastern slums of Nairobi, Kenya.

Design/methods: We reviewed retrospective routine program client records for PLHIV enrolled in HIV care aged ≥15 years. We included those started on IPT between 1st January 2008 and 31st May 2009; and they were followed up for two years from the completion of IPT. Completion of IPT was calculated as 168 days of isoniazid refills documented in the medical records. We assessed IPT completion rates, marital status, gender, TB incidence rates by IPT completion status, whether the client was on Highly Active Antiretroviral Therapy (HAART), and HAART initiation time. We conducted multivariate analysis to identify potential factors associated with IPT completion. Odds ratios (OR) and 95% confidence intervals are reported.

Results: Ninety-one percent of 1474 clients assessed completed IPT. The median time on IPT was 181 days (Interquartile Range (IQR) 168–196). HAART initiation before IPT initiation was a positive predictor for IPT completion (OR 0.5, 95%CI 0.3–0.8). Gender and marital status were not associated with IPT completion. The TB incidence among

the IPT completers was 2.6% compared to 4.4% among the non-completers. The median time to development of TB was 592 days (IQR 261–720) among completers and 335.5days (IQR 218–641) among non-completers.

Conclusion: This abstract shows success in IPT implementation among adult PLHIV. There is also low TB incidence following use of IPT. With this, policies to promote IPT in comprehensive HIV care settings are useful and should be advocated for. There is a need to closely monitor clients who have not been initiated on HAART for adherence on IPT to improve IPT completion rates in this group.

PC-464-01 Diagnosis of smear-negative and extra-pulmonary tuberculosis: minimum financial assistance can maximize the detection rate

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Background and challenges to implementation: The sputum smear negative and extra-pulmonary TB are under detected in Bangladesh. The national notification rates of smear negative and EPTB among all cases in 2011 were only 14.5% and 18.1% respectively. Reasons included scarcity of diagnostic facilities in public sector, lack of trained human resource, and poverty and challenges accessing health care. The USAID TB CARE II Bangladesh Project initiated a simple intervention to provide financial support to poor TB symptomatic (who are sputum negative) for X-Ray and FNAC to increase smear-negative and EPTB detection.

Intervention or response: In the rural Sunamgonj district of Bangladesh, the TB CARE II project extended financial support to patients who were identified as poor and bacteriological negative but with persistent symptoms of TB for further investigation (X-ray, FNAC) from the private sector. Graduate and non-graduate health practitioners were trained and linked to the referral network. Following the NTP diagnostic algorithm, the practitioners were trained to refer TB suspects for X-Ray/FNAC to the private diagnostic facilities at the district and divisional (for FNAC) levels. Based on the recommendation of the graduate practitioners, patients eligible for financial support were identified from the DOTS center. Upon submission of the investigation report and receipt from the diagnosis center, the patient receives the money from the DOTS center. Each TB suspect received between 300 and 400 taka for transportation and X-ray costs, or 1200 taka for FNAC.

Results and lessons learnt: The program assisted 290 TB suspects to receive X-Ray and 22 for FNAC testing between July and September 2012. Among them, 133 smear negative cases and 18 EP TB cases were diagnosed. During the same period, 329 smear nega-

tive and 154 EPTB cases were diagnosed in Sunamgonj district; an increase of 34% and 2% in the number of smear negative and EPTB cases detected respectively in the same quarter of the previous year. The system requires the patient to spend the investigation cost from his/her own pocket before being reimbursed by the DOTS center.

Conclusions and key recommendations: The preliminary result of the initiative shows that the intervention can effectively be used to increase detection of smear negative and EPTB cases in resource-limited settings like Bangladesh.

PC-465-01 Effect of supervision and provision of social support on tuberculosis treatment outcomes in rural areas of Tomsk Oblast, Russia

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Background: Irregular medication intake and default from treatment negatively affect treatment efficacy and outcomes. Maintaining high adherence rates is especially challenging in rural areas due to extreme poverty and long distances between health centers and patients' homes. In response to these problems, daily food packages were introduced as a form of incentives for DOT treatment. In addition, the performance of medical personnel and volunteers was closely supervised. The program was managed by collaborative efforts from the Tomsk Division of the Russian Red Cross (RCC), Partners in Health (PIH) and the Tomsk TB services (TOTBS).

Objective: To assess the effect of supervision and food set provision on treatment outcomes for TB patients in the rural population of Tomsk Oblast.

Method: All patients from rural areas who started TB treatment and were enrolled in the social support program between 01/12/2004 and 30/11/2012 were included in the study. Treatment results were assessed according to the initial resistance pattern.

Results: 3150 (88.2%) out of 3569 patients enrolled in rural regions were patients with susceptible TB (S-TB), 324 (9.1%) with multidrug resistant TB (MDR-TB), and 25 (0.7%) with polyresistant TB (PDR-TB). 99.8% (3144) patients with S-TB, 93.8% (304) with MDR-TB and 100% (25) with PDR-TB successfully completed treatment. Only 20 cases with MDR-TB and 6 with S-TB defaulted from treatment.

Conclusion: Collaboration between the TOTBS and non-governmental organizations—PIH and RCC—was successful in reaching high adherence rates. This model of care, which employs social support and regular staff supervision, can be recommended for other rural TB projects in the Russian Federation.

EMPOWERING PATIENTS IN THE FIGHT AGAINST TUBERCULOSIS

PC-466-01   An exploratory study of stigma associated with tuberculosis in a Zambian adult population

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Background: Various studies have demonstrated that stigma related to TB keeps people away from seeking care. Studies suggest that TB patients experience double stigma with TB being considered as a disease of the poor and that all TB patients are HIV positive. The current study aimed to explore tuberculosis related stigma in tuberculosis infected adult patients.
Methods: The study was carried out at one health facility each from three districts in North Western Province in Zambia. Participants in the study included adult TB patients on treatment for a minimum of 3 weeks, as well as health care workers and community members. After obtaining informed consent, a survey questionnaire was administered to 111 TB patients. The survey was translated into local languages and piloted before use. Data was also obtained from health care workers and community members through focus group discussions and in-depth interviews. Smaller groups of TB patients also participated in focus group discussions. The data was subjected to quantitative and qualitative analysis.
Results: More than one quarter of the participants (28%) reported being discriminated against because they had TB and a lesser number (10.8%) agreed that people with TB should be kept out of school or other services to prevent infection spreading. Some participants felt that they themselves were ill and needed to be secluded (self-stigma), for example 31% of the participants reported that TB patients must be kept at a distance from other patients. The main perpetrators of TB related stigma and discrimination were identified as family members (59%), steady boyfriends/
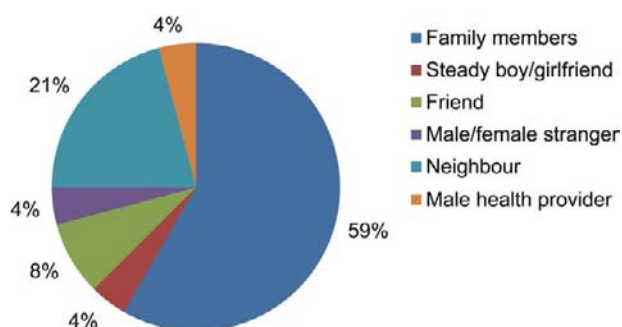
Figure   Main perpetrators of TB stigma.

Table   Behavioural expressions of stigma

Stigma	Percentage of response
I would be willing to share a meal with someone suffering from TB	54 (78.3%)
I would be willing to buy food from a food vender that had TB	54 (78.3%)
I would be willing to move into a home if the neighbor was a TB patient	57 (82.6%)
If someone coughs, I will automatically develop TB	14 (20.3%)
Patients with TB should be kept at a distance from other patients	31 (44.9%)
Clothes and linen, dishes used by TB patients should be disposed of or burned	12 (17.4%)
Providers do not like to treat TB patients because of fear of infection	5 (7.2%)
TB is spreading due to poverty	24 (34.8%)

girlfriends (21%) and friends (8%). Tuberculosis also seemed to be associated with HIV as some participants were reportedly being stigmatized and discriminated against as people thought they were HIV positive. Separation and isolation from family including parents, siblings and spouses were experienced by respondents.
Conclusion: Stigma was prevalent in the study. Participants perceived being stigmatised and discriminated. Increasing awareness in patients and sensitization of the community were identified as a way of reducing stigma.

PC-467-01   Knowledge, attitudes and practice regarding tuberculosis among dislocated North Koreans in South Korea

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Background: Dislocated North Koreans in South Korea have much higher prevalence of active tuberculosis (TB) and latent TB infection (LTBI) compared with South Koreans. A thorough understanding of their knowledge, attitude, and practice concerning TB is vital for TB control among them. The objective of this study was to assess the level of knowledge, attitude, and practice regarding tuberculosis (TB) among dislocated North Koreans in South Korea, and to determine the real condition of TB treatment in North Korea.
Design/methods: North Koreans aged 15 and above were interviewed using a structured questionnaire at Settlement Support Facility for Dislocated North Koreans between April and December 2012. Logistic regression analysis was employed to determine associations between predictor variables and outcome variables.
Results: Of the 1459 respondents, 62 (4.2%) had previously received TB treatment in North Korea.

Only 17 (27.9%) among them had completed standard regimen at health facilities during a six-month period. Of the total, 409 (28.5%) answered 'a bacterium' as cause of TB while 582 (40.6%) mentioned 'heredity'. Those with a previous history of TB were more likely to be aware about TB than those with no history of TB (adjusted OR = 4.76, 95%CI 2.34, 9.69). 921 (63.8%) perceived that they would have a problem with interpersonal relations if they had TB. Those with a higher level of TB knowledge were found to be more likely to have a lower level of stigma compared to those with a lower level of TB knowledge (adjusted OR = 0.60, 95%CI 0.49, 0.74). 887 (62.7%) answered they would talk to health providers about their illnesses and 1203 (82.5%) answered they would go to TB clinic if they had symptoms of TB. Those with a higher level of TB knowledge were more likely to have appropriate health seeking behaviors regarding TB than those with a lower level of TB knowledge (adjusted OR = 1.99 and 2.27, 95%CI 1.50, 2.66 and 1.58, 3.27).

Conclusion: The level of TB knowledge was proved to be associated with the level of TB stigma and the level of appropriate practice regarding TB among dislocated North Koreans in South Korea. Therefore, health education is crucial in minimizing delayed presentation and poor adherence to TB treatment among them. The government should develop regular health education programs about TB at the beginning of their settlement lives.

PC-468-01   Qualitative research permits a better understanding of patient's perception of HIV and tuberculosis in specific populations: the military population in Democratic Republic of Congo

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Setting: The military population of the South-Kivu Province in the Democratic Republic of Congo (DRC) has been identified as a group at high risk for tuberculosis (TB) and HIV. This population lives in camps, with a very intense promiscuity and financial vulnerability. Between 2009 and 2011, the positivity rate among those tested for HIV was 27% (558/2050), compared to 18% in the control group (361/2052). The sociologist E. Goffman defines 'total institutions' as places where people are all treated alike and behavior is regulated. In these closed environments, individuals develop secondary adjustments, or 'abnormal' behaviors as a way to express their remaining capacity of auto-determination. These concepts can be transposed to soldiers living in military camps. Our hypothesis is that they develop 'non-responsible' sexual and social behaviors exposing them to dangerous diseases as HIV and TB.

Design/methods: In our study, in order to allow soldiers to share their own perception on the diseases and their behaviors, we performed semi-structured interviews among 14 individuals belonging to this specific community and 2 interviews among the medical staff. This method is well validated in the domain of social sciences and consists of having a list of prepared themes to be explored, without constraining the discussion to rigid forms. In our study, we questioned soldiers about their knowledge, perception and behaviors regarding HIV and TB.

Results: We observed that, in spite of the fact that information was available, 13/14 (93%) reported unprotected sexual intercourses with multiple partners. Despite free availability of condoms in the military camps, their use is discouraged by various 'mystic' beliefs, doubts about their efficiency or their negative impact on pleasure sensations. 5 (36%) reported to use condoms to light the fire or clean their shoes. 10 (71%) did not consider getting tested for HIV in the future. 3 (21%) believed that HIV testing has a negative impact on health. Regarding TB, 9/14 (64%) reported to know someone who had the disease, and 6 (43%) knew that TB was a curable disease. 7 (50%) considered prolonged cough a sign of TB and 2 (14%) considered that TB was suspected only in presence of hemoptysis.

Conclusion: This qualitative study shows that the military population in Eastern DRC is at very high risk of HIV and TB, but that beliefs and perceptions of these contagious diseases are a major obstacle to early detection, effective treatment and disease control.

PC-469-01   District TB Forum protects the rights and entitlements of tuberculosis patients and acts to remove the barrier during cough to cure

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Background: Global Fund supported Axshya Project is being implemented by The Union through nine subrecipients across 21 states of India covering 300 districts. The project is in operation in 15 districts of Punjab. Voluntary Health Association of India (VHAI) and Catholic Health Association of India (CHAI) are the Sub Recipients (SRs) to The Union in Axshya

Project. As part of the project strategy, district TB Forums have been formed in each district with representatives from various cross-sections of the society, such as social repute opinion leaders, doctors, media persons, retired bureaucrats, business men, philanthropists and more importantly cured TB patients.

Intervention: Axshya Project through its SRs has formed 15 district TB forums in the state of Punjab. The TB forum's mission is to work for ensuring rights and entitlements of TB patients and strengthening the TB control measures as civil society representatives. The forum advocates with TB patient, TB department, other departments for convergence and social protection of TB patients and civil society groups including media. This paper is an outcome of the qualitative analysis of visit and discussion with members of five District TB Forums in Punjab.

Results and lessons learnt: The forums are successful in taking the cause of TB emergency to the higher level and dissemination at the public by advocating for hoardings with TB message in public, sensitising local political representatives, providing nutritional support to TB/MDR-TB cases (from red cross, their own fund and advocate with social welfare, PRI and women child departments) and raising the issues in the media. Quantitatively, in Amritsar, the forum met 12 defaulter cases and retrieve 8. In Gurdaspur, it gives financial support for nutritional supplement to two MDR-TB cases. In Mohali, the TB forum supports for sputum collection and transportation in two centres. Punjab RNTCP taking cognisance of this has proposed to link the TB forums with district TB associations.

Conclusion: The District TB Forum represents a solid body representing civil society for the benefits of the TB patients and equally supports to the TB control measures as well. More representation of TB patients in the forum will further strengthen in taking up gaps and barriers starting from cough to cure.

PC-470-01   Atención integral con planes de cuidados de enfermería en tuberculosis en México

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Marco de referencia y desafías: Los Planes de Cuidado de Enfermería (PLACE) mediante las taxonomías NANDA, NIC NOC para la atención individualizada en los pacientes con TB, marcarán la diferencia en la adherencia terapéutica así como en las tasas de curación para el control de la tuberculosis en México.

Intervención o respuesta: Se realizó a través de la implementación de planes de cuidado enfermero en pacientes con tuberculosis previa prueba piloto en Distrito Federal, Hidalgo México, Morelos y San Luis Potosí. Se utilizó el Proceso de Atención de Enfermería con el Modelo de Virginia Henderson, se elaboraron instrumentos de valoración y planes de cuidado, utilizándose las taxonomías NANDA, NIC, NOC. Se seleccionó al personal de enfermería que atendió enfermos de tuberculosis en unidades de salud para capacitación con seguimiento de la aplicación de los instrumentos y en la identificación de diagnósticos enfermeros para implementar intervenciones específicas de enfermería y evaluación de indicadores del programa de TB.

Resultados y enseñanza: Se realizaron 5 cursos y capacitaron a 200 enfermeras de unidades de salud en el 2011 y se aplicaron planes de cuidado (PLACE) en 141 pacientes con tuberculosis, de los cuales el 90% (127) curaron al mantenerse en edherencia terapéutica en 100%.

Conclusiones y recomendaciones: La atención integral de los pacientes con tuberculosis por el personal de la Red TAES de enfermería, a través de Planes de Cuidado (PLACE) individualizado, mejora la adherencia al tratamiento y la curación de los pacientes, lo que además se ve reflejado en su entorno social y familiar.

PC-471-01   Involving affected people in the fight against tuberculosis in low-incidence countries: UK's TB Action Group

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Background: TB in the UK has been managed overwhelmingly through a clinical model of health, with limited focus on the wider social determinants of health. Little attention has been paid to the role of people affected by the illness in TB care and control. Whilst TB patient advocacy is a relatively new concept in the UK, changes in the National Health Service mean there is opportunity to create meaningful patient advocacy at national and local levels. TB Action Group (TBAG), the only network of People Affected by TB (PATB) in the UK, has been at the forefront of the development of the civil society response.

Intervention: TBAG was established in 2008 by TB Alert, the UK's national TB charity. TBAG's members, who all have personal experience of TB, are active in: contributing to consultations on TB policy and service design and delivery; increasing knowledge of the patient experience amongst health professionals; training community representatives at TB workshops; raising awareness through media advocacy; providing telephone and online peer support to patients. The capacity of TBAG is being built to ensure the independence and sustainability of the group. TBAG is

evolving from a network of PATB engaged in awareness and peer support activities, to become a nationally and internationally recognised patient advocacy organisation.

Results: TBAG is an integral part of TB Alert's awareness programme, The Truth About TB. Members have helped deliver 28 awareness seminars and training workshops for staff of Community-Based Organisations (CBOs) that support people most at risk of TB. Members of TBAG are working towards civil society engagement in TB care and control in England through TB Alert's Local TB Partnerships, which bring together state partners, CBOs and PATB to support local services. TBAG members have become stakeholders in national policy activities, as well as engaging in advocacy and evidence sessions in Parliamentary arenas.

Conclusion: No country can effectively respond to TB without engaging affected individuals, and specific factors relating to the speed and quality of diagnosis and treatment in a low incidence country create motivation for people to be involved. Through TBAG's work, health service and other state partners increasingly value the contribution of PATB. A structured national mechanism is required to recruit, train and build the role of PATB to enable meaningful patient advocacy in TB care and control in the UK.

PC-472-01 Socio-demographic factors and health services associated with knowledge about tuberculosis in families of patients with the disease

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Background: Studies related to tuberculosis (TB), in the social setting, have been the subject of ongoing discussions. In this sense, the importance given to the management of health care has valued the inclusion of the family in the health/disease process. However, only few studies address the knowledge and attitudes about this disease. Thus, this research investigated the sociodemographic and health services factors associated to the knowledge on TB and performed a comparative analysis of family groups with or without knowledge about their attitudes towards the patient with TB, in Ribeirão Preto/SP, Brazil.

Design/methods: A cross-sectional epidemiological study with probabilistic type sampling was constituted by 110 family members and cohabitants of TB patients that were diagnosed between January 1, 2010 and July 31, 2011. The authors conducted a bivariate analysis with variables dichotomization and binary logistic regression to test the factors associated with knowledge. As a compliment, it used the Multiple

Correspondence Analysis (MCA) to identify patterns of correspondence among the variables: education (no education, primary school, high school and university), the level of knowledge about TB (none, low and high) and relatives' attitudes (to feel shame or not for the relative with TB).

Results: The sociodemographic variables: education (OR = 4.39, 95%CI 1.11–17.35), watching television (OR = 3.99, 95%CI 1.20–13.26) and internet access (OR = 5.01, 95%CI 1.29–19.38) showed association to the knowledge of TB. From the ACM, it was possible to verify that families with less education correspond to those with less knowledge and more ashamed of the TB patient. Knowledge about TB is related to factors that transcend the organizational aspects of health services. They are linked to issues of social protection, such as income, education and access to information about the disease. From this research, it was possible to notice that being in directly observed therapy (DOT) or latent treatment was not associated to the knowledge about TB.

Conclusion: The results show that knowledge about TB, within the families, is associated with social opportunities in a territory that requires inclusive public policies to improve the media access. An educational work with the families of TB patients is an investment that should be prioritized by teams of DOT.

PC-473-01 Development and initial testing of messages to encourage tuberculosis testing and treatment among BCG-vaccinated persons

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Background: Misperceptions surrounding the Bacille Calmette-Guérin (BCG) vaccine can lead some vaccinated individuals to initially resist tuberculosis (TB) testing and treatment. Educational messages that would best explain the risk of TB to BCG-vaccinated, foreign-born Hispanic persons in the United States were systematically developed and tested.

Methods: Phase I: 60 TB program staff provided messages they had used to persuade BCG-vaccinated TB suspects and contacts to undergo testing and treatment without delay. Systematic analysis of submitted messages identified 7 thematic message groups that reflected both positive and negative message framing, as well as theoretical constructs from the Health Belief Model and Elaboration Likelihood Model. Phase 2: Message statements within each group were reviewed by TB experts to establish content validity. Message statements that were accurate, representative of similar statements within each group, and strong from a theoretical perspective were presented to 10 previously diagnosed TB patients to

establish face validity. Phase 3: Four semi-structured group interviews were conducted with 43 Hispanic persons who worked with, or sought services from, a community organization for migrant workers. Participants selected the statements they considered most persuasive, and discussed reasons for their choices. Phase 4: Interviewees' preferred statements were used to develop one long and three short comprehensive messages. One-on-one interviews were then conducted with 8 Hispanic persons to assess the saliency of these messages.

Results: Participants expressed preferences for statements that explain the protection from the vaccine wanes, encourages people to draw upon their knowledge of TB prevalence despite the widespread use of the BCG vaccine, and focuses attention on obtaining positive outcomes for the individual and loved ones. Among the 3 short messages presented, participants preferred the message that was primarily positively framed. When asked to report their thoughts while listening to the long message, half the participants indicated they contemplated their own or family member's susceptibility to TB. Others reported increased perceptions of disease severity and the belief that upon immigrating, they had left the problem of TB behind in their birth country.

Conclusion: The messages developed and tested through this project merit further refinement and evaluation to assess their effect on TB program indicators.

PC-474-01   Study on tuberculosis screening in drug rehabilitation centre in people living with HIV/AIDS

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Background: Early detection of TB in HIV/AIDS patients could increase patients' survival time, improve patients' quality of life, and also reduce the spread of TB. The purpose of this study is to determine the TB symptoms screening result and improve the awareness level of TB knowledge in drug rehabilitation center in people living with HIV/AIDS.

Design/methods: Using typical survey method, 605 people living with HIV/AIDS were enrolled from one compulsory drug rehabilitation center in Sichuan province. TB suspicious symptoms were obtained through TB screening questionnaire, and the positives were diagnosed by sputum smear and X-ray examination. Besides, using TB-HIV leaflets to health education, the difference of knowledge before and after one month was compared using the χ^2 test.

Results: Of 605 patients, male accounted for 100%, average age was 31.5 ± 6.7 years old, 99.5% (602/605) only with junior high school education or less.

The TB symptoms positive rate was 10.1% (61/605), the most common symptom was cough lasting more than 2 weeks which accounted for 86.9% (53/61) and 18.0% (11/61) occurred night sweat also. Active TB detection rate among these positives was 21.3% (13/61) and 2.1% (13/605) among people living with HIV/AIDS. The total awareness rate increased from 20.8% to 87.1% ($\chi^2 = 2174.261$, $P = 0.000$), the awareness rate of the first question, do you know anything about TB, increased from 61.7% to 100% ($\chi^2 = 287.035$, $P = 0.000$), the awareness rate of the second question, what causes TB, increased from 14.7% to 98.0% ($\chi^2 = 853.548$, $P = 0.000$), the awareness rate of the third question, what are the symptoms of TB, increased from 0 to 71.7% ($\chi^2 = 676.727$, $P = 0.000$), the awareness rate of the fourth question, what should be pay attention for TB patients, increased from 6.9% to 78.8% ($\chi^2 = 637.910$, $P = 0.000$).

Table   Difference of TB knowledge before and after health education in HIV/AIDS

Questions	Awareness before (%)	Awareness after (%)	χ^2	P value
Do you know anything about TB	373 (61.7)	605 (100)	287.035	0.000
What causes TB	89 (14.7)	593 (98.0)	853.548	0.000
What are the symptoms of TB	0 (0)	434 (71.7)	676.727	0.000
What should be pay attention for TB patients	42 (6.9)	477 (78.8)	637.910	0.000
Total	504 (20.8)	2109 (87.1)	2174.261	0.000

Conclusion and recommendations: Compulsory drug rehabilitation center should become the key place for TB-HIV control, further effort should be focus on standardizing the TB screening procedure and increasing the awareness rate of TB knowledge in people living with HIV/AIDS.

PC-475-01   Poverty and lack of tuberculosis-related knowledge are associated with delayed diagnosis in Peruvian shantytowns

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Background: Tuberculosis (TB) is common among poor and marginalized communities, including shantytowns in Peru. We hypothesized that socio-economic determinants, knowledge and beliefs about the disease might predispose to outcomes such as delayed diagnosis.

Objective: To assess socio-demographics, knowledge and beliefs about TB, and test for an association with diagnostic delay.

Design/methods: Participants were interviewed in their homes in Lima shantytowns. The questionnaire was applied by nurses and characterized knowledge, beliefs, socio-demographic factors and the duration of symptoms suggestive of TB prior to TB being diagnosed. Potential determinants of tuberculosis diagnostic delay were analyzed by stepwise multiple logistic regression.

Results: 1013 newly diagnosed TB patients, 2130 people being tested for TB and 488 randomly selected healthy community controls were recruited. Compared with the controls, TB patients were more likely to be males ($P < 0.001$) and have low income ($P < 0.001$). The TB knowledge score was higher among patients than among controls ($P < 0.001$). Few participants knew that hemoptysis and chest pain were symptoms of TB (13% and 21%, respectively). Sixty-four percent believed that eating more and better food was the most important action to avoid getting TB. Low income ($P = 0.005$), older age ($P < 0.001$) and low knowledge score ($P = 0.018$) were associated with prolonged diagnostic delay (above the median value 60 days, Table).

Table Socio-economic factors, knowledge and diagnostic delay

	Prolonged diagnostic delay*	
	Odds ratio	P value
Age above median	1.67 (1.27–2.19)	<0.001
Wealth: below median US$/person/month	1.46 (1.12–1.91)	0.005
Knowledge: below median score†	1.39 (1.06–1.83)	0.018

* Prolonged diagnostic delay was defined as above the median (60 days). Numbers in brackets are 95% confidence intervals.
†60% correct answers was the median value.

Discussion: Many of the participants lacked knowledge about TB symptoms. Poor knowledge and poverty indicators were associated with delayed diagnosis.

Conclusion: The association between low knowledge, low income and delayed diagnosis imply that educational and economic interventions may facilitate earlier detection of tuberculosis cases.

PC-476-01 Perception of workplace stigma towards tuberculosis in Delhi, India

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Background and challenges to implementation: Besides economic consequences, there are devastating social and psychological effects with workplace stigma towards tuberculosis. These lead to delay in healthcare seeking, social isolation and noncompliance to treatment, which further compounds the burden of TB by feeding the disease cycle.

Intervention or response: A cross-sectional study was conducted in an urban hospital of Central Delhi in 2012. Stigma faced by TB patients at their workplace and from their family member's was assessed through a pre-designed structured questionnaire graded on Likert scale.

Results and lessons learnt: A total of 100 patients on DOTS were interviewed. Out of the 36 employed TB patients, 65.5% ($n = 23$) experienced negative change in the behavior of their colleagues and employers. Nearly one third of patients ($n = 34$; 34%) noted negative changes in the behavior of their family members towards them while 40% were isolated on being diagnosed with the disease. There were 21 patients who reported to have delayed treatment seeking due to stigma. Significantly higher proportion of female TB patients said that they will not disclose the disease status to a family member, neighbour, employers or work colleagues ($P < 0.001$). Workplace stigma was more among employed women ($P < 0.05$) than among employed men.

Conclusions and key recommendations: Perception for workplace stigma towards TB was high; especially among employed women TB patients. Strategies which address the issue of workplace stigma towards TB which include Factsheets on Workplace TB displayed at all offices and Workplace Counseling Sessions with focus on gender sensitive behavior change communication should find adequate weightage in the overall policy framework for urban TB control.

PC-477-01 Programme of health education intervention for improving adherence among migrant tuberculosis patients with good treatment outcomes

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Background and challenges to implementation: The study aimed to investigate the effectiveness of health education programs by using the PRECEDE-PROCEED Model to improve non-Thai migrant TB patient's compliance during treatment.

Intervention or response: This quasi-intervention study was conducted in three targeted hospitals located in two vicinity provinces of Bangkok in Thailand during August 2009–December 2010. The study sample consisted of 100 cases, 50 cases who registered and served as the intervention group and 50 cases who registered and enrolled were the control group.

Results and lessons learnt: At the end of the health education intervention, the intervention group showed significantly improved health-behavior scores in 9 domains—health promotion, health education, predisposing, reinforcing, enabling factors, behavior and lifestyle, environment and health status—which were also significantly higher than the control group ($P <$ 0.001). The percentage of patients achieving successful treatment outcomes was 76% in the intervention group and 62% in the control group.

Conclusions and key recommendations: The tuberculosis treatment and care program thus provided, and the associated health education interventions, would enable migrants to complete the treatment regimen and achieve treatment success. It would also help TB staff develop an appropriate program and clear understanding of TB control among migrants. It is recommended that this type of information and health education program should be used to other hospitals and health care settings providing TB services for migrants throughout the nation.

TUBERCULOSIS CONTROL AMONG VULNERABLE POPULATIONS

PC-478-01   Using tuberculosis services as an instrument for health system strengthening in nomadic communities in northern Nigeria

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Background and challenges to implementation: Health service delivery to Nomadic communities has remained a challenge globally. Adamawa, one of the 36 States of Nigeria, is home to an estimated 450 000 Nomads who are known to be exposed to ill health due to factors which include poor access to health care, low immunization coverage, poor housing and overcrowding, consumption of unpasteurized milk, migration and low level of awareness. With support from WHO through its Wave 2 TB Reach grant in 2011, TB control service was mounted within Nomadic Communities of Adamawa State.

Intervention or response: The aim of the paper is to demonstrate the use of TB Control structures for health system strengthening to deliver other health services to Nomadic communities in Nigeria by other partners

Results and lessons learnt: Within a period 12 months, 180 community volunteers (CVs), 440 health workers and 63 laboratory staff were trained on TB control. 4433 TB suspects were screened by microscopy, 884 all forms of TB cases were notified with 70% be-

ing sputum positive for TB. 36 new leprosy cases were also notified and free consultations for other ailments and mass de-worming was delivered. After evaluation by TB Reach, the project was awarded additional funding for a second year. The success of the project created more opportunities for delivery of other health interventions to the Nomadic people. The mapping done by the TB programme was adopted by WHO to improve immunization coverage in Nomadic communities. The Adamawa State Malaria Control Programme engaged 82 of the CVs used by the TB programme to deliver malaria control services to the Nomads while FHI360 engaged 40 of the CVs to boost CTBC in Nomadic communities of Adamawa State.

Conclusions and key recommendations: Proper planning, stakeholder analysis and result sharing contributes to the successful implementation of other health interventions among the Nomadic communities. A retrospective review of the current achievement of TB Reach project and other services that were made available to the Nomads as a result of the TB Reach success.

PC-479-01   A healthcare evaluation of the London Find and Treat project: an innovative service model for socially complex tuberculosis patients

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Background: The pan-London 'Find and Treat' service addresses TB in hard to reach groups (the homeless, problem drug and alcohol users, prisoners), in whom rates of 788 per 100 000 exist. These high risk groups have difficulty in accessing healthcare, and have disproportionately high rates of infectious and drug resistant TB, with poor adherence and outcomes. Active case finding, with a mobile X-ray unit (MXU), combined with integrated case management and social support, aims to maximise diagnosis and retention on treatment. We evaluated the structure, processes and outcomes of Find and Treat, describing and analysing its cohort of patients between 2008 and 2013.

Design/methods: A healthcare evaluation study describing the Find and Treat service model. Data were obtained from a prospectively-collected database of all patients managed by the service between February 2008 and January 2013 ($n = 1285$). Descriptive analysis was performed in STATA (version 12) to illustrate the characteristics, management and outcomes of patients.

Results: Referrals to Find and Treat came from numerous sources (31.8% MXU, 54.9% NHS TB service), resulting in 686 cases of active TB, with a further

260 suspected unconfirmed. 79.3% were non-UK born and 71.7% had known social risk factors: 50.6% had a history of homelessness, 37.8% drug or alcohol abusers and 21.3% had been imprisoned. 84.7% cases were pulmonary TB, of which 52.2% smear positive and 34.1% drug resistant. At the outset of case management 32.4% were lost to follow up (LFU), with 45.6% LFU at any point during the episode. Find and Treat achieved return to service for 68.1% of active TB LFU patients. 75.9% of those with active TB completed or are retained on treatment, with an LFU rate at the end of data collection of 17.1% and mortality 2.9%. Treatment of MDR-TB (12.7% of active TB) was effective; 86.5% completed, or are continuing treatment, 7.7% LFU and 3.8% died.

Conclusion: London's Find and Treat service combines active case finding and intensive, integrated case management support, achieving improved outcomes for treatment completion and retention on treatment in the most at-risk groups. Awareness-raising, improved adherence, supporting treatment delivery and enhanced social support mechanisms have resulted in high treatment completion and reduced LFU. The Find and Treat model is an effective solution to TB control in hard to reach populations, with far-reaching potential impacts on this public health issue.

PC-480-01 Tobacco smoking and alcohol consumption: major risk factors for pulmonary tuberculosis in a tribal population of Madhya Pradesh, central India

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Background: Tuberculosis (TB) is predominantly a disease of the disadvantaged and marginalized populations, particularly the poor and hard to reach groups. Tobacco smoking and alcohol consumption are important risk factors for TB and are highly prevalent amongst tribal population inJabalpur district of the central Indian state of Madhya Pradesh. This paper attempts to find out whether tobacco smoking and alcohol consumption is associated with the development of pulmonary tuberculosis disease amongst them.

Methods: A community based cross-sectional TB prevalence survey was conducted amongst the tribal population of Kundam Block in Jabalpur district of Madhya Pradesh, central India. Information on tobacco smoking and alcohol consumption was also collected during the survey from all the individuals aged 15 years and above. Data on the prevalence of exposure and disease were obtained by comparing disease occurrence between exposed and non-exposed groups. The prevalence odds ratio (POR) was used as the effect measure. It was obtained by univariate analysis using SPSS 13.0 software.

Results: Of the 4631 individuals screened for chest symptoms, 3903 (84.3%) belonged to tribal population. The prevalence of tobacco smoking and alcohol consumption was significantly higher amongst men compared to women (47.4% and 34.0% vs. 0.2% and 1.5%). The highest prevalence (71.5% and 49.5%) was seen amongst males aged 35 years and above. Overall prevalence of sputum positive pulmonary tuberculosis was found to be 589 per 100 000 population. Persons aged 35 years and above had a 2.1 times higher risk of developing pulmonary TB disease than persons below 35 years and males had a 3.2 times higher risk than females. Smokers and alcohol consumers had a 3.2 times higher risk than non-smokers and alcohol non-consumers.

Conclusion: Age, sex, tobacco smoking and alcohol consumption are significantly associated with pulmonary TB disease in this central Indian tribal population. There is an urgent need to develop and implement culturally appropriate awareness raising activities to target tobacco smoking and alcohol consumption to support the efforts to control TB in this tribal community. There is also a need for further research on the impact of these activities on tobacco smoking, alcohol consumption and tuberculosis situation in this tribal population.

PC-481-01 Intensified outreach activities for tuberculosis case detection among vulnerable and marginalised populations: a field report from Tamilnadu, India

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Background and challenges to implementation: The TB Control Program in India has adopted passive case finding approach for TB case finding because most TB patients are symptomatic and present to health facility. Within the country, there are several pockets with vulnerable and marginalized population who do not have access to quality diagnostic services and lack awareness about TB. In this context, we are reporting the results of intensified outreach activities that were undertaken for increasing TB case detection from these populations.

Intervention or response: A retrospective analysis of the records collected during the process of outreach community activities conducted in a slum population pocket and a refugee camp during September 2013 in 2 districts in Tamilnadu. Following a process of mapping, a house to house visit of slum population and a refugee camp population was undertaken by trained community volunteers. Each site was visited by 4 volunteers over 2 to 3 days period. During this process, the volunteers sensitized each person on basics of TB. They were also enquired about the presence of cough for more than 2 weeks and if found so, were either

referred to the nearest Designated Microscopy Center (DMC) or their sputum was collected and transported to the DMC and those found to be TB were started on DOTS medicines as per the program treatment guidelines.

Results and lessons learnt: Of 1606 slum population and 1420 refugees visited, 43 (2.7%) and 34 (2.4%) were found to have cough for more than 2 weeks. Of them, 38 (88%) and 32(94%) got themselves tested and 4 and 3 sputum positive pulmonary TB were subsequently started on treatment.

Conclusions and key recommendations: The above findings highlight the importance and necessity of conducting periodic outreach activities among the vulnerable (slum) and marginalized (refugees) population. These groups usually have lack/limited access to TB diagnostic services. Seeking diagnosis for their symptoms could receive low priority for these populations who encounter other social challenges, resulting in delayed diagnosis and worsening of the disease. The above activities resulted in early diagnosis among these groups which would help in reducing the transmission in the community. The process served to reach across to these populations with basics of TB and facilitated linkages of these communities with the health system.

PC-482-01   Tuberculosis among the Roma population in Macedonia

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Introduction: The latest data by WHO show that 80% of TB cases in Europe are in the countries which have numerous Roma population. The number of Roma in Macedonia is 53 870 (2.66%).

Aim: To find out what is their participation in the total number of TB patients, what is their incidence and are they a risk group for TB and possible reasons for that.

Patients and methods: For this purpose we analyzed data in latest six (6) years with special accent on Roma population with TB (sex, age, incidence).

Results: We had 563 patients with TB in 2007; the incidence was 27.8/100 000 for general population, but the incidence for Roma people was 74.2/100 000. The next year incidence in Roma population was 59.4/100 000 and in general population 23.8/100 000. In 2009 the incidence in Roma population was 42.6/100 000 and in general population 23.4/100 000. The next year the incidence in Roma people was 70.5/100 000 and in general population 20.8/100 000. In 2011 the incidence in Roma people was 51.9/100 000 and in general population 17.9/100 000. The last year there were 356 regsitrated TB patients in the country with incidence of 17.2/100 000. The incidence of Roma people was 46.4/100 000.

Conclusions: Roma are more vulnerable community. They are risk group for TB because their incidence is three times higher than in general population. Possible reasons for this are: substandard living conditions, lack of education and low rate of employment.

PC-483-01   Association between age and treatment outcomes among tuberculosis patients registered under the Revised National Tuberculosis Control Programme in Uttar Pradesh

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Background: With increasing life expectancy in India, there has been an increase in elderly population. Since elderly population are a vulnerable group for tuberculosis (TB) and there is paucity of data about the manifestation and outcomes of TB among this group, we undertook a study to describe and compare the socio-demographic and clinical characteristics and treatment outcomes of elderly (60 years and above) as compared to younger (15 to 59 years) TB patients registered in Revised National Tuberculosis Control Program (RNTCP) and to identify the risk factors associated with poor treatment outcomes among the elderly.

Design/methods: We conducted a retrospective cohort study involving review of routinely maintained RNTCP records from July to September 2011, in five districts of Western Uttar Pradesh (population: 40 million). World Health Organization (WHO) recommended disease classification and treatment outcome definitions are used by RNTCP. Qualitative data was expressed as proportions, χ^2 test and relative risk along with 95% confidence intervals (CI) were calculated to analyse the association between outcome and potential predictor variables.

Results: Of 2472 TB patients, 821 (33.2%) were elderly, 1656 (67%) were males 81.7% resided in rural areas and 80% were new cases. Among the elderly TB patients, 22% had unsuccessful (death, default, failure and transfer out) outcomes as against 14.5% in the comparison group ($P < 0.001$). Factors significantly associated with unsuccessful outcomes among elderly group were living in an urban area (RR = 2.33, 95%CI 1.77–3.07), history of a previous treatment (RR = 1.7, 95%CI 1.29–2.23) and non-conversion of smear at end of intensive phase (RR = 4.37, 95%CI 2.27–8.42).

Conclusion: Elderly TB patients had poorer treatment outcomes as compared to the younger TB patients. This could be due to associated co-morbidities

in this age group. This study stresses the importance of providing special attention to elderly TB patients, especially those with the identified risk factors with early identification and effective management of co-morbid conditions.

PC-484-01   Supported accommodation for destitute tuberculosis patients

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Background and challenges to implementation: Disadvantaged communities are disproportionately affected by the increase in tuberculosis (TB) rates in London. Destitute TB patients, those with no recourse to public funds (NRPF), are at very high risk of poor treatment outcomes. A review of 100 TB patients with NRPF referred to Find&Treat, a pan-London TB outreach team, found that more than half had become lost to follow up care. Access to suitable accommodation is pre-requisite to TB treatment and recommended by the National Institute for Health and Clinical Excellence. Despite this, in practice many local services are reluctant to fund and support accommodation for destitute TB patients.

Intervention or response: Find&Treat in collaboration with Olallo House, a central-London hostel, established a 5-bedded care facility for destitute TB patients. An individualised support plan ensures both medical and social care needs are met. All residents receive directly observed therapy.

Results and lessons learnt: During the first 64 weeks, the project has supported 10 Eastern European men with histories of rough sleeping, addiction, imprisonment and mental ill-health. Six of the cases had drug resistant TB (1 extensively, 3 multi and 2 mono-resistant). Average length of stay in the unit was 31 weeks and all patients were previously non-adherent. To date 6 have completed treatment and moved onto independent living, 4 are still on treatment with >90% adherence overall. None have been lost to follow-up and none have been admitted to hospital. We are currently formally evaluating the cost-effectiveness of this service model.

Conclusions and key recommendations: Providing appropriate accommodation is a pre-requisite to TB treatment. This supported housing model appears highly effective in engaging and improving the health and social circumstances of destitute TB patients. The service prevents loss to follow up care and unplanned hospital admission and preliminary health economic analysis demonstrates high cost effectiveness.

PC-485-01   Gateway of elderly patients for tuberculosis diagnosis in systems of health in Brazilian cities

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Background: Analyze the factors associated to 'gateway' of health system for the diagnostic of the tuberculosis (TB) in elderly people undertaken in seven municipalities of three Brazilian regions.

Design/methods: Descriptive study, that involved all TB cases in people aged over 60 years ($n = 91$), identified in a sample of 706 TB cases in all ages from seven municipalities: Ribeirao Preto (10), São José do Rio Preto (17) Vitoria (7), Foz do Iguaçu (7), Pelotas (16), Joao Pessoa (13) and Feira de Santana (21). The tool used to data collect was based on the Primary Care Assessment Tool (PCAT) adapted for the attention to TB, with an emphasis on the 'gateway' dimension. The chi-square test was used for proportions and residual analysis of variables were done according to two kinds of health care service: primary health care (PHC) and specialized services (SS).

Results: Specialized services (59.4%) were the health care services most commonly visited by elderly TB patients at the onset of symptoms, followed by primary health care (40.6%). However only in 37.4% of cases, the clinical suspicion of TB was made on the first contact. It was found a statistically significant association ($P = 0.0001$) between the first health service searched and the unit that diagnosed the TB showing better performance of specialized services in the TB diagnosis (68.1%).

Conclusion: The specialized services have been elected by the elderly as the gateway to the health service system, which still show better performance for the diagnosis of tuberculosis. Should develop an evaluative study on the subject nationwide, whose purpose is to innovate the actions to control the disease with specific for the elderly population.

PC-486-01   Drug-resistant tuberculosis in indigenous people with a high prevalence of tuberculosis in Madhya Pradesh, India

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Background: Sahariya is a group of indigenous people in the state of Madhya Pradesh, India. Earlier studies from our centre has shown that the prevalence of tuberculosis is very high in this community (1500 per

100 000 population). Owing to this the present study was undertaken to determine the rate of drug resistance in this population. The objective of the study was to determine profile of drug resistance in *M. tuberculosis* strains isolated from tuberculosis patients registered for treatment.

Design/methods: The study was undertaken in 2 districts; Guna and Gwalior which has this group of indigenous people. Both new and retreatment cases attending the designated microscopy centres for treatment of tuberculosis were included in the study. Two sputum samples were collected from all eligible individuals, transported to the laboratory, and examined by Ziehl-Neelsen smear microscopy and solid media culture methods (Löwenstein Jensen-LJ medium). Drug susceptibility testing (DST) was done for isoniazide, rifampicin, streptomycin and ethambutol by proportion method on LJ medium. Readings were taken as per guidelines.

Results: Total of 102 TB patients were registered for the study. Sputum was collected from these individuals. Of these 88 individuals were culture positive. Fifty-one isolates were susceptible to all the four drugs. Monodrug resistance was seen in 12 isolates with the maximum of 9 (10%) being resistant to streptomycin. Nineteen MDR isolates were detected of which 15 (17%) were in retreatment cases while 4 (4.5%) were from new cases.

Conclusion: In spite of high TB prevalence among this indigenous population of Madhya Pradesh the drug resistance for TB is not different from national figures. This indicates that with continued efforts the tuberculosis situation of the community can be brought under control.

PC-487-01 Does a sputum collection and transportation strategy reduce delays in initiation of treatment? Evidence from tribal districts of India

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Introduction: Collection of sputum from symptomatics (two) with quality smear microscopy (minimum three subsequently in smear positive) forms the backbone of the TB management. Designated Microscopy Centres (DMCs) were established for this specific purpose. However the reach of these facilities is limited due to large geographic areas and population. Expansion of this DMC network is affected due to resource crunch and monitoring of adherence to quality standards. These are leading to delay in sputum collection from symptomatics/patients in tribal/far flung areas, resulting 'delay' in initiating the treatment. Under involvement of NGO/private providers

as per the programme strategies-project Axshya took up sputum collection and transportation to the nearest DMC which improves the convenience to the patients and RNTCP coverage.

Objective: To analyse the impact of project Axshya initiative for early diagnosis and treatment adherence among tribal populations.

Method: Cross-sectional study design is adopted to collect data from identified tribal DMCs in districts where Project Axshya has been implemented. The data is collected from lab registers of DMCs and segregated into TB symptomatics from Tribal areas and non-tribal areas. For this study data pertaining to TB symptomatics from tribal areas were selected. From this data, analysis was done to compare the onset of treatment within 7 days among those tribal symptomatics referred through Project Axshya and from others.

Results: Data source—25 DMCs from 15 Districts of Madhya Pradesh, Jharkhand, Chhattisgarh and Nagaland. Total TB symptomatics where sputum microscopy was done during 1st Quarter of 2013—5252. SC&T done through Axshya—1103 (21%). Out of a total 5252 samples 438 (8.3%) were positive and 132 (12%) of them were through SC&T initiative. 388 (88.5%) of the 438 positives were initiated treatment within 7 days, whereas 131 (99%) were through SC&T.

Conclusion: SC&T is definitely providing access to early diagnosis and subsequent adherence to treatment.

PC-488-01 Assessment of tuberculosis detection and care in congregate settings, Mumbai City

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Setting: Congregate facilities in Mumbai, Maharashtra state, India comprising of old age homes, shelter homes, orphanages, remand and beggar homes.

Objective: To study the practices, policies and infrastructure for management of tuberculosis (TB) in congregate settings.

Design: Data was collected using a semi-structured interview schedule. The questions asked during the interviews focussed on TB treatment and detection approaches, staff capacity to cope with TB infection in inmates, infection control practices, health care worker safety, contact investigation within the residents/staff as well as environmental and administrative controls to prevent TB in inmates and staff.

Results: A total of 35 facilities were randomly selected from the 24 administrative wards of Mumbai and surveyed between the period of January 2013 and June 2013. General health screening was compulsorily conducted before entry in 25 out of the 35 assessed facilities. However, only 15 facilities screened

inmates for TB before entry into the facility, while only 1 performed TB screening for their staff members. Chest X–ray (CXR) followed by sputum examination and tuberculin skin tests (TSTs) were the most frequent screening strategies for TB. While all facilities referred inmates suspected of TB to public health facilities, only 19 facilities maintained accurate record of TB cases from the past 5 years. Only 12 facilities isolated their TB patients from other inmates, while no facility provided health care workers with necessary screening, education and protection during handling of active TB cases. 20 facilities did not have follow-up services for inmates that were released before completing their TB treatment.

Conclusion: The gaps identified highlight the need to setup protocols for comprehensive TB detection, care and follow-up of patients in these settings. It is crucial to build linkages between congregate facilities and public health system, and to advocate the significance of early TB detection and treatment to the managerial staff of congregate settings. It is also paramount to improve the documentation and notification system in order to understand the actual burden of tuberculosis in these set-ups. This would contribute to reduction of disease transmission in the city.

PC-489-01   Adding Xpert® MTB/RIF assay for tuberculosis diagnosis in an active tuberculosis case finding among tuberculosis high risk

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Background: HIV infected and TB multidrug resistance (MDR) suspect are TB high risk people. WHO approves GeneXpert (Xpert) is a new tool for TB detection and TB MDR diagnosis. However, its added value to microscopic smears within active case finding (ACF) is not well documented.

Objective: To describe the results of Xpert and its additional yield to microscopic smears within an ACF program.

Design/methods: We conducted an ACFproject in—poor urban villages in Phnom Penh. A house-to-house TB-symptom screening strategy was implemented by community TB—officers and village health-volunteers. High risk TB-suspects were classified into 1) MDR suspect group (sub-groups: re-treatment and MDR-contact), 2) HIV-group (confirmed/suspect), 3) Smear negative (Sn) in the Non-MDR and non HIV-group with persistent TB-symptoms. All TB-suspects provided sputum for fluorescence microscopy, Xpert, and solid culture. Laboratory results were communicated to field team by phone messaging (SMS), who then referred patients for TB treatment.

Results: From 9 February 2012 to 28 February 2013, 1814 TB suspect among high risk people submitted sputum for smears, Xpert, and cultures. Total sputum smear positive (SS+) and Bacteriologically (Bact.) confirmed were 193/1814 (10.6%). Of these, SS+ were 122/193 (63.2%); these included 71/193 (36.8%) SS+ concordant with Xpert MTB+/RIF−, 8/193 (4.1%) SS+ with Xpert MTB+/RIF+ (MDR), 39/193 (20.2%) SS+ but Xpert MTB−/RIF− which were missed diagnosis if using Xpert alone. Whereas, Xpert provided 130/193 (67.4%) Xpert MTB+/RIF+ and MTB+/RIF−, of which 57/193 (29.5%) were SS− with Xpert MTB+/RIF− additionally yield to SS+ (179 SS+ and Bact. confirmed vs. 122 SS+, 31.8% relative increase). Culture provided 14/193 (7.3%) additionally to SS and Xpert results.

Conclusion: Our results support the benefit of adding GeneXpert to ACF among high risk TB people. Our project found that availability of combining more tests eventually increase more yield in TB diagnosis.

IMPROVED CASE DETECTION USING GENEXPERT® MTB/RIF

PC-490-01   Performance of Xpert® MTB/RIF in adult HIV-clinic enrollees in Zambia

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Background: Xpert® MTB/RIF (Cepheid) is widely hailed as the new tool for TB diagnosis. We evaluated its performance for screening among adult HIV-infected patients seeking care in a primary care setting.

Design/methods: As part of a cohort study in Lusaka, Zambia, we routinely screened antiretroviral therapy-naive, new HIV care enrollees at a Lusaka clinic using history, physical exam, chest X-ray and cultures from two sputum. For this sub-study, we archived a third sputum specimen for Xpert testing. Using a gold standard of liquid and solid culture, we evaluated the performance of the following: (a) a single Xpert test; and (b) the standard of care (SOC) diagnosis in Zambia, based on smear, chest X-ray, history and physical exam. Among patients with culture-confirmed TB, we compared clinical characteristics of Xpert-positive and negative patients. Ethical approval was obtained from the University of Zambia and the University of Alabama at Birmingham.

Results: We screened 400 patients from July 2011–April 2012 and performed retrospective Xpert testing on 353 (88%) sputum. 332 (94%) patients with complete data were included in analyses. Sensitivity of SOC diagnoses was 52% (95%CI 39–65) and specificity 89% (95%CI 85–92). Sensitivity of Xpert

was 64% (95%CI 51–76) and specificity 98% (95%CI 96–99). Three out of 4 Xpert-positive/culture-negative patients who had repeat TB screenings were later diagnosed with culture-confirmed TB. Among culture-confirmed cases, Xpert-positive patients appear to have more advanced disease than Xpert-negative patients (Table).

Characteristic	Xpert positive ($n = 39$)	Xpert negative ($n = 22$)	P value
Age, median [IQR]	34.8 (31.8–42.3)	32.5 (28.7–39.0)	0.14
Male sex, n (%)	28 (72)	14 (64)	0.57
BMI	19.0 (18.0–22.7)	20.8 (19.3–22.7)	0.06
CD4	94 (30–189)	246 (106–380)	0.002
Log10 viral load	5.3 (4.9–5.5)	4.9 (3.7–5.5)	0.19
Hemoglobin	10.1 (8.4–11.8)	11.6 (10.1–13.0)	0.01
Number of symptoms			
0	0 (0%)	2 (9%)	
1–2	2 (5%)	4 (18%)	
3–4	14 (36%)	7 (32%)	
5–8	23 (59%)	9 (41%)	>0.05
CXR consistent with TB	29 (74%)	7 (32%)	0.002
Died within 6 months of screening	6 (15%)	2 (9%)	0.70

Conclusions: With higher sensitivity and specificity than SOC diagnosis, Xpert has potential to increase true positive and reduce false positive diagnoses in our setting. However, it still missed a substantial number of cases, mostly among those with less severe disease. While Xpert is an improvement over available tools, close follow-up of all Xpert-negative TB suspects should be considered.

PC-491-01   Xpert® MTB/RIF pilot roll-out in Brazil: results and lessons learned

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Background: WHO has recommended the use of Xpert MTB/RIF for detection of *Mycobacterium tuberculosis* and rifampicin resistance. Brazil has decided to implement Xpert nationally. Here, we report results and lessons learnt from a pilot roll-out study with Xpert implementation under routine conditions in Brazil.
Design/methods: Xpert implementation was evaluated in Rio de Janeiro and Manaus, cities with high tuberculosis incidence and low drug resistance prevalence, covering an 8 million population. Two smear tests were replaced with one Xp. This stepped-wedge study included 14 laboratories covering over 200 health clinics, from January 30 to October 4

2012. Web-based laboratory and notification information systems and cross-linkage were used to collect data. Primary outcome was the impact on the case detection of pulmonary TB (PTB). Random-effect Poisson regression modeling was used to calculate incidence risk ratios (IRR), comparing the intervention with the baseline period for PTB diagnosis and notification.
Results: Total PTB notification went up from 68.2 to 87.7 per 100 000 population (IRR 1.59, $P = 0.0002$), laboratory confirmed PTB diagnosis went up from 29.2 to 52.4 per 100 000 (IRR 1.46, $P = 0.001$). Notification of PTB without laboratory confirmed diagnosis did not change (37.7 vs. 35.3, IRR 0.92, $P = 0.71$). The proportion of laboratory confirmed patients with >14 day delay between sputum testing and start of treatment decreased from 21% to 12%. Test limitations included 6% of samples with insufficient volume for Xpert, and 7% with indeterminate result or errors. Conversely, sputum samples categorized as saliva did give positive Xpert signals in 10% of cases. Results on MDR-TB diagnosis and start of treatment will be available at the conference.
Conclusion: This pragmatic implementation trial provides a wealth of information critical to successful national scale-up. On the short term, Xpert implementation produced a 59% increase in laboratory confirmation of PTB, and 46% increase in PTB notifications. However, the proportion of clinically diagnosed patients without bacteriological confirmation requested remained high. The dissemination of the incremental yield of laboratory confirmation of PTB by Xpert may have an impact on clinicians' pursuit of confirmation of PTB in the long term.

PC-492-01   Experience after one year of Xpert® MTB/RIF in Nepal

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Background and challenges to implementation: Low case finding is a challenges for the National TB Programme (NTP) in Nepal. With support from the TB REACH initiative, International Organization for Migration in collaboration with NTP implemented Xpert® MTB/RIF technology to TB improve case detection in the Eastern Development Region of Nepal from January to December 2012.
Intervention or response: Xpert was deployed in nine microscopy diagnostic centres. NTP laboratory staff were trained in using the technology. Smear-negative individuals with chest X-ray suggestive of TB were Xpert tested. Testing was extended to MDR suspects. RMP resistant cases were confirmed by National Reference Laboratory using molecular line probe assay and solid culture before second-line treatment. Quarterly Review meetings were conducted with NTP

and other stakeholders to share findings and make recommendations. UPS and generator were installed for power shortages. Information campaign was conducted to increase referral for testing and performance based incentives were provided to resolve additional workload in the laboratories. Monthly monitoring visits were conducted to provide technical support to the Xpert centres. Test failures were analyzed and laboratory staff were trained on how to minimize them.

Results and lessons learnt: Over one year, 7755 tests were performed with 1376 MTB+/RIF−, 108 MTB+/RIF− and 13 cases with RMP indeterminate result. Overall positivity was 19% (range 9% to 30%). RMP resistance among MDR suspects was 24%. There were 899 test failures, 546 errors, 198 no result and 155 invalid. The majority of no results were due to power interruption. Some Xpert centres did not comply with the algorithm due to unavailability of chest X-ray. It was found that chest X-ray before Xpert increased the test yield. There was 24% increment in smear/bacteriological positive cases in the evaluation population. A national algorithm for Xpert is developed and case notification protocol was revised. This technology is accepted by NTP as a diagnostic tool for TB and the country plans to use the technology widely. Coordination mainly with NTP and WHO is crucial for the success of the project including resolving policy related issues. The project encountered numerous test failures (11.6%). Most failures were due to improper processing of specimen, power back up and faulty cartridge and modules. Proper staff training and on time calibration of the machine minimized this. Some staff needed training on basic computer use as they were not computer literate. Despite power back up system, the unstable power supply was one concern that could not be ruled out for high number of test failure. The modules broke down 6 times and almost 50% of the Xpert modules failed with remote calibration kits and needed to be replaced. Maintenance and servicing is important part of the technology. Regular technical support to Xpert centre for fixing machinery problems is very important, a trained technical person at national level should be available to provide on call service. Only 77 RMP-resistant cases were sent for confirmation, 31 were lost to follow up. 64 (94%) were confirmed of 68 valid cases for evaluation. The agreement rate between Xpert test and LPA/culture was satisfactory; however, confirmation was difficult due to the limited culture facility including difficulties in maintaining the cold chain and difficult geographical terrain. Many cases were lost to follow up due to this. Proper follow up for RMP+ cases and well organized transportation should be in place to minimize this. The incentive payment is effective to maximize the test; however, sustainability is a major challenge after the project phase out. Procurement is important, better planning is needed for formalities such as custom clearance. The life of test cartridges is short (one year), ordering cartridge in two shipment can be a option for this.

Conclusions and key recommendations: The MTB/RIF assay can be effectively used to increase TB case detection and detect RMP resistance in resource-limited settings. Power back up, referral mechanisms and staff motivation are among the issues to be considered while planning roll out of this technology in Nepal. Furthermore, sustainability and maintenance are the major issues to be considered for the continuation of the service.

PC-493-01 Evaluation of Xpert® MTB/RIF assay for sputum smear negative patients

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Methods: Six hundred and fifteen sputum smear negative (SN) was obtained at Hospital Vall d'Hebron in Barcelona between June 2009 to December 2012. All specimens were digested and decontaminated using the method described by Kent and Kubica. After decontamination and concentration, the specimens were prepared for: 1) microscopic examination; 2) Xpert MTB/RIF (Cepheid, Inc.) and 3) samples were inoculated in MGIT medium and incubated in Bactec MGIT 960 (Becton Dickinson Diagnostic Instrument System, MD, USA) and 3/GenXpert MTB/RIF (Cepheid, Inc.). Identification was performed with GenoType® MTBDR plus (Hain Lifescience GmbH).

Results: Four hundred ninety-seven (81%) were both SN sputum and Xpert MTB/RIF negative, in 489 (98.4%) of those samples the culture was negative for *M. tuberculosis* and in only eight samples (1.6%) the culture was positive for *M. tuberculosis*. In 118 SN sputum the Xpert MTB/RIF was positive, the culture was negative in 36 (30.5%) of them and positive in 82 (69.5%), the mycobacterium identified were 81 *M. tuberculosis* and 1 *M. abscessus*.

Conclusions: The sensitivity and specificity of Xpert MTB/RIF for sputum smear negative was 91% and 93% respectively. It is important to notice that molecular techniques detect genomic regardless of the viability of mycobacteria. An isolation of *M. abscessus* was Xpert MTB/RIF positive.

PC-494-01   Xpert® MTB/RIF to improve the diagnosis of smear-negative tuberculosis among HIV-positive and -negative patients in Kinshasa, Democratic Republic of Congo

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Background and challenges to implementation: In 2010, the WHO endorsed Xpert® MTB/RIF (Xpert) as initial diagnostic for MDR-TB or HIV-associated TB and as follow-on test to microscopy. Questions remain about its scalability in resource-constrained areas.

Objective: To describe experiences introducing Xpert as follow-on test to microscopy in 40 primary care clinics in Kinshasa, DRC.

Intervention or response: Fifteen clinics were equipped with a 2-modules instrument and power generator. Volunteers were trained to transport samples from 25 satellite clinics to these 15 clinics. TB suspects with positive or unknown HIV status and ≥3 sputum smear-negative results and HIV-negative TB suspects with ≥2 sets of 3 sputum smear-negative results separated by ≥1 week of antibiotic treatment were eligible for assessment by Xpert.

Results and lessons learnt: From July 2012 to January 2013, 3924 tests were performed for 3827 patients. Almost half (45.5%) were collected at the 25 satellite clinics, 6.2% from children (<15 years), 18.0% from HIV positive and 57.7% from, HIV negative TB suspects. The majority (62.8%) were tested on same day the samples were collected, but some (8.5%, mainly samples from satellite clinics) were processed >3 days after collection. Overall, 424 (10.8%) yielded an invalid result, mostly due to unstable electricity. Of the 3539 samples with a valid result, 588 (16.6%) were MTB+. Of these, 41 (7.0%) were rifampicin resistant. The prevalence of MTB+ was lowest among HIV-negative TB suspects (13.6% vs. 20.9% or 21.0% for suspects with unknown or positive HIV status, respectively), and children (6.3%, 9.5%, 17.3% among <5, 5–14, and 15 years or older, respectively). Comparison of notification data of the 22 health zones covered by the project to that of the remaining13 health zones shows that, despite the restrictive eligibility criteria, the use of Xpert increased notification rate of bacteriologically positive cases by 13% in the first 3 months, from baseline.

Conclusions and key recommendations: We demonstrated the feasibility of scaling-up Xpert in highly resource-challenged settings. The yield in smear-negative pulmonary TB was high, particularly among HIV-infected patients.

PC-495-01   Experience with public policy aspects of using GeneXpert to accelerate diagnosis of tuberculosis in high tuberculosis and HIV prevalence settings

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Background: Xpert® MTB/RIF is a new technology with potential to improve case detection for TB and drug resistance. It can also improve accuracy of the diagnosis of smear negative patients and potentially reduce delays to treatment initiation. In Malawi different partners assisted the National TB Program in different aspects of implementation and these early experiences have been documented to provide guidance for national policy for this new diagnostic test.

Methods/intervention: Starting in the last quarter of 2011, Malawi's NTP and Project HOPE secured a TB REACH grant to use Xpert to improve TB case detection. Eight machines were installed in 6 districts at 7 hospitals and 1 health center covering a population of about 3 million, as part of programmatic rollout of Xpert testing. Xpert tests were used for new case detection with a plan to test 24 000 people with suspected TB in line with 2011 WHO guidance using Xpert the primary TB test for all suspects given high TB and HIV prevalence. Other machines in the country planned and used far fewer tests. Corresponding training for health staff was organized in Oct–Dec 2011. Implementation commenced in January 2012 and proceeded through March 2013.

During 2012 the national algorithm was modified to limit Xpert to a follow–on test to microscopy for all TB suspects except for those hospitalized or critically ill, and to detect drug resistance. District staff had to be retrained and challenges in sample testing and reporting procedures arose. Partly as a consequence, 9367 Xpert cartridges were consumed (39% of the planned figure), including invalid/error results (Figure).

Figure   Malawi, 6 districts, Xpert cartridges used (including tests with error results) Jan 2012–March 2013.

Sputum sample transportation was organized to secure more SS− samples and improve Xpert throughput. Results were delayed as a result due to follow up testing, return visits and sputum collection and transportation. Rifampicin resistant cases were rare with 0.14% ($n = 13$) found. Toward the end of 2012, additional restrictions were proposed to further limit Xpert as a follow-on test to microscopy only for HIV+ suspects although currently most people with suspected TB have undocumented HIV status.

Conclusions: Even without restrictions, the eight machines tested an average of 80 samples a month (<25% capacity). Algorithms should balance the savings from fewer tests, against the costs of less case detection, failed treatment and deaths. Early implementer experience should provide evidence to guide national policy on testing algorithms and machine placement.

PC-496-01 Assessment of the effectiveness of Xpert® MTB/RIF in the diagnosis of tuberculosis among smear-negative HIV patients in Nigeria

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Background: TB increases mortality and morbidity of people living with HIV (PLHIV). WHO recommends the routine screening of PLHIV in order to provide opportunity to identify and treat those with TB as well as prevent TB in those that do not have the disease. GeneXpert presents the opportunity to detect TB in HIV smear-negative persons and MTB/RIF resistance cases.

Objectives: To assess the performance of GeneXpert in detecting TB in AFB smear-negative HIV patients and; to assess the prevalence of MTB/RIF resistance among HIV patients.

Method: The study design consists of a retrospective review of routine GeneXpert data submitted quarterly to the National TB and Leprosy control program.

Results: A total of 3725 sputum samples were subjected to GeneXpert test. Of these a total of 463 (12.4%) sputum samples were obtained from PLHIV AFB smears negative suspects and tested using GeneXpert. Three hundred and fifty seven (77%) were MTB negative, while 78 (17%) were MTB positive and 28 (6.0%) were invalid. This indicates an additional diagnostic yield of about 17% over AFB test. Of those that were MTB positive, 5 (6.4%) were diagnosed to be rifampicin resistant.

Conclusion: This study has shown that there is a need to rapidly scale up GeneXpert services to ART centres to aid early diagnosis of TB in PLHIV and MTB/RIF resistance cases as well as prevent transmission or resistance strains of TB.

PC-497-01 Experience with the implementation of Xpert® MTB/RIF assay in Rwanda, a low HIV-MDR-TB burden setting

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Background: Laboratory capacity for diagnosing and monitoring MDR-TB patients varies widely in developing countries with most of them having little or no diagnostic capacity to perform culture. Consequently, sputum smear microscopy for acid-fast bacilli (AFB) is still the most important and widely available diagnostic tool. Xpert® MTB/RIF test was introduced in Rwanda in 2012 to strengthen and sustain accessible, quality assured bio safe molecular TB diagnostic at the point of care to improve case detection of TB, drug-resistant TB and HIV-associated TB.

Intervention: Several meetings were held with national TB Control Program (NTP), National Reference Laboratory (NRL) and partners to discuss on implementation plan. One sub-district and five district health facilities were selected based on high suspicion rate of TB and MDR-TB, high workload, and high TB-HIV co-infection rate. In addition these sites were selected in order to generate experience from urban and rural settings. These sites were visited and assessed and at the same time registers, operating procedures and tools were revised. Central training on the Xpert® MTB/RIF assay was carried out at the NRL with laboratory technicians and clinicians selected sites followed by on-site machines installation.

Results and lessons learnt: Over the first 15 weeks period of this initial implementation phase, a total of 614 Xpert MTB/RIF tests have been processed in all the six sites with an average of 7.6% error rate. Out of the total specimens, overall positivity rate of Xpert MTB/RIF was 23% (135/614), of which two were resistant to rifampicin. Compared to microscopy, Xpert MTB/RIF increased laboratory detection by more than 50%. A major challenge during this initial implementation phase was revealed to be the low utilization rates in almost all the sites. This is being addressed through sensitization of providers and refresher clinical training on diagnostic algorithm. Linking up with health care facilities that refer samples to the sites for cases referral and follow up was challenging. Additional constraints were high rates of error results, which required regularly monitoring with corrective action as well as further on-site trainings.

Conclusion and key recommendations: Our experience with the initial implementation phase provided evidence that Xpert MTB/RIF is a valuable tool to significantly increase TB detection in sputum.

PC-498-01   Assessment of the performance of GeneXpert® MTB/RIF at country level: experiences from Nigeria

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Background: Acid fast bacilli (AFB) microscopy has been the main tool in the diagnosis of TB. However with the recent introduction of GeneXpert technology in 15 sites across Nigeria, it is expected that there would be increased performance in TB diagnosis and detection of MTB/RIF.

Objectives: To assess the performance of the Gene Xpert in the detection of MTB/RIF resistance cases among suspects.

Method: The study design is a retrospective review of TB patients subjected to GeneXpert MTB/RIF test from Q4 2011–Q4 2012 in the states where TB CARE I installed the machines. Eligibility for Gene Xpert test consists of patients classified as DR-TB suspects.

Results: A total of 3725 sputum samples of various categories of TB suspects were obtained and tested using GeneXpert machines over a 5 quarter period (Q4, 2011–Q4, 2012). Of the total sputum samples tested a little over three-fifth was *M. tuberculosis* negative (2378); 1195 were *M. tuberculosis* positive (23%); and 152 (4.1%) were invalid. Of the total cases of *M. tuberculosis* positive 353 (29.5%) were diagnosed to be positive with rifampicin resistance. Higher proportions of males (64%) than females (36%) were diagnosed with rifampicin resistance. Pearson's χ^2 tests indicate that the diagnosis of rifampicin resistance in DR suspects differed significantly in the category of DR suspects tested with GeneXpert MTB/RIF at the sites $P < 0.001$. Prevalence of rifampicin resistance among DR TB suspects was estimated to be 126 per 1000 DR suspects tested using Gene-Xpert MTB/RIF machines in the various sites. The low MTB positivity rate among DR TB suspects was attributed to non-adherence of the diagnostic algorithm by clinician.

Conclusion: There is need to ensure scale up and decentralization of GeneXpert MTB/RIF services; organise training to clinician on diagnostic algorithm and ensure supportive supervision.

PC-499-01   GeneXpert implementation in Malawi: moving toward improved case detection

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Background: Malawi's TB cure rates (88%, 2010) are excellent, while the case notification rate has remained lower than desired (65%, 2010). To improve this, Malawi's NTP and Project HOPE secured a TB REACH grant to use GeneXpert (Xpert) to find improve case finding.

Methods: Xpert platforms were installed in 6 districts at 7 hospitals and 1 health center. Sputum from persons suspected of TB but with SS− results were tested by Xpert. Installation, training and testing for Xpert was done in October–December 2011 (Q1).

Results: From Q2 (1/2012) to Q6 (end 3/2013) suspect identification rates (per 100 000) improved dramatically to >1000 in 2 districts where community involvement had been established under other projects. It remained stagnant (400–500) in 2 districts and just >200 in 2 districts, showing that more efforts are feasible in at least 4. By end Q6, 18 395 persons had smears (1905 SS+, CDR = 10.4%) and 9527 SS− samples (58% of eligible) reached Xpert assay. Xpert added 810 cases (CDR = 8.5%), including 13 MTB+/RIF+. Community sputum collection sites were deemphasized as a priority, as it was evident that too few of the eligible SS− samples reached Xpert. Problems of sputum collection, transportation and challenge about the Xpert algorithm and corresponding responsibilities of health staff, explain the loss rate. Issues of power outages and poor quality of sputum also caused Xpert error results (1097; 11.7%). With myriad efforts the 'loss ratio' of eligible SS− samples failing to reach Xpert testing fell from 51% (Q2) to 37% (Q4) and to 32% (Q6). Microscopy
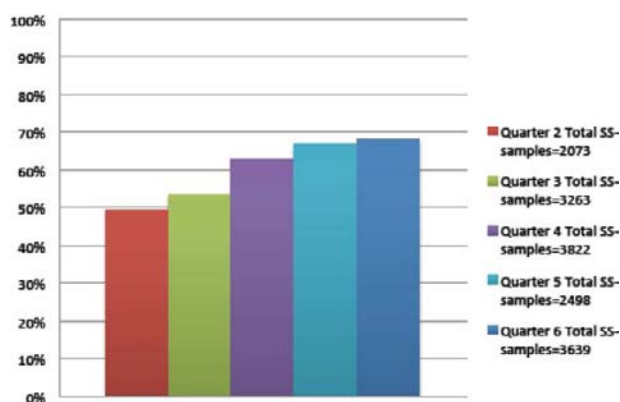
Figure Malawi, % SS− sputum samples successfully reaching Xpert testing by quarter (Q1 data not comparable; only 33 samples tested in Q1).

plus Xpert yielded a robust CDR of 14.8% (Q6) with Xpert increasing all confirmed cases by almost 30%. Had all eligible SS− sputum samples been tested (i.e., loss rate = 0%) an additional 558 MTB+ cases may have been found (hypothetical total CDR of 17.8%, microscopy plus Xpert).

Conclusion: Xpert significantly increases the number and share of confirmed TB cases, thereby bringing more patients into treatment, avoiding misdiagnosis, reducing TB transmission and saving lives. Project experience shows: (i) an Xpert algorithm consistent with WHO guidance and corresponding procedures for staff should be maintained; (ii) good sputum collection and transportation, supported by health worker training on suspect identification and sputum collection/handling is essential; (iii) community education and sputum collection points may appropriately yield more suspects for Xpert testing where loss rates are low.

PC-500-01 Assessment of the performance of GeneXpert MTB/RIF at various levels of health care system in Nigeria

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Background: WHO has recommended that Xpert MTB/RIF machines should be suitable for use at district and sub-district levels, this is the ensure early access by patients at point of care and minimize the logistics challenges of patient or sample movement to reference laboratories.

Objectives: To describe the performance of Xpert machines at various levels of health care.

Methodology: Xpert machines in Nigeria were installed at various levels of health care, secondary, tertiary and private health facilities. Routine quarterly reports obtained from 15 GeneXpert sites from October 2011–December 2012 were reviewed and analysed. Comparisons in utilization/uptake, error rates, invalid/indeterminate results were made across the different levels of care.

Results: Of 15 machines, 6 gene were located in tertiary; 8 in secondary and one at a private hospital. In all 3725 sputum samples of various categories of DR TB suspects were obtained and tested over a 5 quarter period (Q4, 2011–Q4, 2012). Quarterly average sputum test per site was 69.6 which was higher for secondary sites (73.6) than tertiary facilities (63.8). Average quarterly failure per site was 1.7% but was higher among tertiary sites (2.2%) than the secondary site (1.5%). However, FMC Katsina accounted for the highest average quarterly failure rate (7.5). Of total sputum tested, 151 (4.1%) were invalid; however quarterly average invalid rate for all sites was

2.3%; and was also higher for tertiary (4.4%) than secondary levels (0.96%). About 32.1% of total sputum tested were positive for MTB. MTB positivity was generally low, but even lower at the tertiary facilities (32.8%) compared to (36.1%) at secondary levels. Overall 353 RIF resistance cases were diagnosed (29.5%).

Conclusion: The performance of secondary health facilities was relatively better because of adherence to SOP's and national guidelines.

PC-501-01 Evaluation of GeneXpert for detection of *Mycobacterium tuberculosis* in Antananarivo, Madagascar

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Background and challenges to implementation: Gene-Xpert MTB/RiF® (Cepheid) offers rapid detection of *Mycobacterium tuberculosis*. However, little is known about routine use in high TB burden settings.

Intervention or response: To evaluate the performance of GeneXpertMTB/RIF® for the diagnosis of smear-negative tuberculosis in Antananarivo (Madagascar). The detection of *Mycobacterium tuberculosis* by the GeneXpert® MTB/RIF assay was compared with conventional smear microscopy and culture methods. For each individual, one sample was provided for smear microscopy, culture and GeneXpert® assay. A total of 440 (373 respiratory and 67 non-respiratory) specimens received from 440 patients suspected of TB were investigated.

Results and lessons learnt: Four hundred and twenty-nine specimens had interpretable results with Gene-Xpert®, and 44 of them were positive by GeneXpert® assay. Eight samples showed false negative Gene-Xpert® results, which could be explained by the delay in performing the test. Compared with the culture, the GeneXpert® assay had 81.4% (95%CI 67.38–90.26%) sensitivity, and 97.67% (95%CI 95.63–98.77%) specificity. For respiratory specimens, sensitivity was 83.78% (95%CI 68.96–92.35%) and specificity was 97.87% (95%CI 95.66–98.96%), while for non-respiratory specimens, sensitivity was 66.67% (95%CI 30–90.32%) and specificity was 96.55% (95%CI 88.27–99.05%). For smear negative and culture positive respiratory specimens, sensitivity was 78.57% (95%CI 60.46–89.79%).

Conclusions and key recommendations: GeneXpert® assay showed relatively high sensitivity for the detection of *M. tuberculosis* in smear-negative but culture positive microscopy and can therefore be used to increase the tuberculosis detection when culture is not available.

PC-502-01   The impact of Xpert at the point of care in a low-burden country

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Objective: To assess Xpert MTB/RIF (Xpert) at the point-of-care (POC) in a low burden setting for the detection of active tuberculosis (TB) disease. Xpert is an automated real-time PCR test for the detection of *Mycobacterium tuberculosis* and rifampicin resistance that has shown a sensitivity of 68% on smear-negative samples and close to a 100% on smear-positive samples combined with excellent specificity. In addition, the Xpert may provide an impact on the care of patients beyond its improved accuracy over smear through its fast turn-around time of less than two hours.

Methods: We evaluated Xpert sensitivity and specificity for detection of active TB on induced sputum samples compared to TB cultures as the reference standard at the POC in a routine TB clinic setting in Montreal, Canada. We assessed the potential reduction in time-to-TB treatment initiation by using Xpert as compared to the standard of testing with three smears and culture. We plan to enroll 900 patients.

Results: We enrolled thus far 420 consecutive patients that presented to the TB clinic for evaluation of active TB. Twenty-five patients were identified to have active TB. Xpert had a sensitivity of 45.8% (95% confidence interval (CI) 25.6–67.2) and specificity of 99.7 (CI 98.4–100.0). The sensitivity was improved in smear-positive patients (85.7, CI 42.6 to 99.6). Indeterminate results were detected in 10% of samples overall. Two isolates were found to be rifampicin resistant on Xpert testing and only 1 was confirmed by culture based drug susceptibility testing. Overall culture-positive cases were found to have minimal disease: 12 out of 25 patients had no symptoms

Figure   Time to diagnosis and accuracy.

at presentation and seven patients had no radiographic findings. Xpert would have diagnosed smear-negative patients on average 12 days earlier, however time to diagnosis would not have been improved for smear-positive cases.

Conclusions: Our findings suggest limited possible impact of Xpert testing in a low-incidence setting. The reduced sensitivity in smear-negative cases compared to prior studies is likely due to an aggressive active case finding strategy with patients presenting with minimal disease. An impact on time to diagnosis was not observed for smear-positive cases likely due to the good diagnostic performance of the standard diagnostic algorithm, excellent logistics and empiric therapy by experienced physicians.

PC-503-01   Early experiences from 33 implementers of Xpert® MTB/RIF testing in 18 countries

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Background: The Xpert MTB/RIF assay, endorsed by WHO in 2010, has garnered significant interest as a sensitive and rapid diagnostic tool to improve detection of sensitive and drug resistant tuberculosis (TB). However, most literature has described the performance of Xpert testing in study conditions, and little information is available on its use in routine case finding or its impact in programmatic settings. TB REACH is a multi-country initiative focusing on innovative ways to improve case notification and treatment.

Methods: We analyzed reporting data from 33 implementers of Xpert testing in 18 countries as part of TB REACH grants. Projects reported on types and placement of machines, screening and algorithms used, test results and error data.

Results: A total of 145 (2 and 4 module) machines and 243 740 Xpert cartridges were ordered through TB REACH and the Global Drug Facility. Most projects began testing in Q2 2012 while some began as early as Q4 2011. All implementers used algorithms for detection of new cases as opposed to drug resistance. Machines were placed in a variety of settings including mobile clinics, temporary chest camps, health centers, hospitals, and private labs. Testing algorithms varied, including Xpert as a follow on test to microscopy, direct Xpert testing of all individuals with symptoms or an abnormal chest X-ray, testing only in HIV+ populations, and among other groups including migrants and children. As of December 31, 2012 all projects used a total of 121 778 Xpert tests. Overall, projects detected 16 169 (13.2%) individuals with MTB+ results including 1935 (0.7%) with
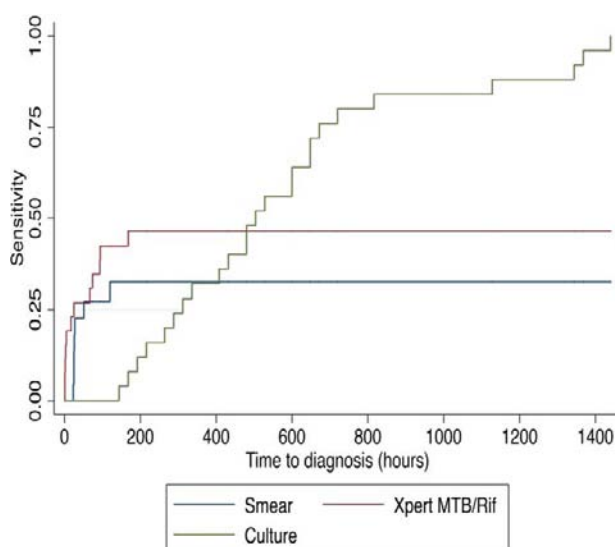
rifampicin resistant results. Error rates were 8.4% overall and ranged from 2.4–16.5%. During the first quarter of implementation errors averaged 12.4%, of which irregular electric supply accounted for a large proportion. During the first quarter of implementation projects used an average of 394 tests, and over the next two quarters projects more than quadrupled testing to an average of 1799 tests per quarter.

Conclusions: A significant proportion of bacteriologically positive TB is not being diagnosed using conventional testing methods. There are many challenges to rolling out Xpert testing in high burden, low income countries, but these challenges can be addressed through local innovation. Xpert testing can be successfully conducted across a wide range of settings, using different approaches. Further documentation of costs and impact on a larger population level is needed.

PC-504-01   Introduction of Xpert® MTB/RIF for tuberculosis diagnosis among person living with HIV/AIDS in Hasan Sadikin Hospital, Bandung

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Background: Since April 2012, Xpert® MTB/RIF (Xpert) was introduced as routine test to diagnose TB among persons living with HIV/AIDS (PLWHA) in a provincial referral hospital in Bandung, West-Java, Indonesia. Xpert is expected to give increased diagnostic yield and faster treatment initiation among PLWHA suspected of having TB. This study aimed to evaluate its implementation impact.

Intervention: Xpert has been implemented in Hasan Sadikin Hospital Bandung in April 2012 as one of 5 pilot sites in Indonesia. The test is used to detect rifampicin (RMP) resistance in presumptive MDR-TB cases and diagnose pulmonary TB among PLWHA. This report is limited to its impact among PLWHA. Comparison of diagnosis yield, time to diagnosis and time to treatment initiation was done between conventional diagnosis with smear microscopy and TB culture before Xpert introduction (April 2011–January 2012) with diagnosis by Xpert after introduction (April 2012–January 2013)

Results: During ten months before Xpert implementation, 309 PLWHA attended the HIV clinic and among them, 146 (47%) were suspected of TB. A total of 44 sputum was submitted for smear microscopy where 19 of them (13% of suspected) were positive for TB. During 10 months after Xpert implementa-

tion, 356 PLWHA attended the clinic, 118 were suspected of TB and sputum was submitted by 95 (81%) for Xpert and microscopy. Xpert gave positive TB result in 18 (16% of suspected) and microsopy detected 6 (5% of suspected), none were RMP resistant. In comparison with microscopy of the same samples, Xpert increased TB positivity yield by 9% (7/78 smear negative). Time to diagnosis before Xpert implementation was median of 11 (range 0–104) days, while after implementation it was reduced to 2 (range 0 to 27) days ($P < 0.005$).

Conclusion: Xpert has been implemented in a provincial hospital in Bandung, Indonesia to detect TB among PLWHA. It has shown benefit with increasing sensitivity of TB diagnostic, although the numbers are not quite substantial. Impact of Xpert implementation has been mostly shown in the reduced time to initiate diagnosis.

DRUG RESISTANCE: GENES AND SURVEYS

PC-505-01   High proportion of fluoroquinolone monoresistant *Mycobacterium tuberculosis* strains in Pakistan, 2010–2012

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Background: The prospect of using fluoroquinolones (FQ) as a first line therapy for TB has been challenged due to the concern of increased FQ resistance in countries with high FQ usage. Increased FQ resistance in multidrug-resistant (MDR) *Mycobacterium tuberculosis* strains has already been reported from Pakistan. In this study we have analyzed trend of FQ resistance in non-MDR-TB strains over a 3-year period (2010–2012).

Design/methods: Study was conducted at the Aga Khan University laboratory that is designated as a technical partner of Pakistan National TB Program. *M. tuberculosis* susceptibility is also periodically validated by the WHO Supra-National Reference Laboratory network. The laboratory receives specimens across the country through its peripheral collection units. *M. tuberculosis* was isolated using standard methods. Susceptibility testing was performed using agar proportion method with drug concentrations as recommended by Clinical Laboratory Institute Standards (CLSI). FQ susceptibilities were determined using ofloxacin 2 μg/ml. *M. tuberculosis* H37Rv was used as control with each batch of susceptibility testing. MDR was defined as resistance to both isoniazid (0.2 μg/ml) and rifampicin.

Results: During the study period 8170 *M. tuberculosis* strains were isolated. Of these 3321 (40.6%) were

MDR and 4849 were non-MDR. FQ resistance in MDR strains increased from 691/1266 (54.6%) in 2010 to 436/763 (57.4%) in 2012. In non-MDR *M. tuberculosis* strains FQ resistance increased from 214/2059 (10.3%) in 2010 to 184/953 (19.3%) in 2012. The proportion of FQ mono-resistant TB strains increased from 125/2059 (6%) in 2010 to 108/953 (11.3%) in 2012.

Conclusion: Increasing trend of FQ resistance in non MDR *M. tuberculosis* strains with high proportion of FQ mono-resistant strains in Pakistan is alarming. Our data highlight limited potential of empirical FQ usage for TB treatment in both MDR and non-MDR cases.

PC-506-01   Whole genome sequencing reveals novel putative compensatory mutations in drug-resistant *Mycobacterium tuberculosis* strains in a Peruvian population

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Background: Identifying mutations associated with drug resistance in *Mycobacterium tuberculosis* improves our understanding of the mechanism of drug resistance, increases the sensitivity of diagnostic tests and may also lead to the development of novel treatments.

Design/methods: Here we investigate the differences at the level of the whole genome between 28 multidrug-resistant tuberculosis (MDR-TB) strains, 11 rifampicin mono-resistant strains, 21 isoniazid mono-resistant strains and 10 drug sensitive strains collected from patients in Lima, Peru. Following DNA extraction, the strains were sequenced on an Illumina HiSeq 2000 platform with paired-end 101 bp reads, and genomic variants characterised using both de-novo assembly and direct mapping of quality trimmed reads to the H37Rv reference genome.

Results: By comparing the variation between drug resistant phenotypes, we were able to confirm mutations in rpo*B*, kat*G*, rps*L*, emb*B* and rpo*C*, and identified a set of novel non-synonymous mutations that occurred in drug resistant strains and not in any drug sensitive strains.

Conclusion: Many of the genes in which the polymorphisms are found, particularly those in the polyketide synthase gene cluster and the mammalian cell entry operon, are associated with *M. tuberculosis* virulence and could compensate for the fitness costs of becoming drug resistant.

PC-507-01   Trend of anti-tuberculosis drug resistance in Karachi, Pakistan: a five-year study

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Background: Facilities of drug susceptibility testing especially for second-line TB drugs are not available in most of the testing labs and there are very few reports on the extent of drug resistance particularly MDR and XDR among tuberculosis (TB) patients. This study was conducted to establish the drug resistance pattern among newly diagnosed and treated TB patients in Karachi.

Design/methods: Clinical specimens from suspected pulmonary and extra pulmonary cases were processed by NaOH-NALC method and inoculated in BACTEC MGIT 960 as well as LJ medium for primary isolation and DST was performed by MGIT 960.

Results: From November 2007 to December 2012, 3731 suspected TB patient's specimens were processed in the laboratory of The Indus Hospital, Karachi. During this period we found 1729 new/treated cases. Among these 49.2% were sensitive to all drugs while 50.8% had some level of drug resistance. There were 31.2% were found to be MDR and 1.5% were XDR. Among 540 MDR cases 11% were additionally resistant to streptomycin (SM), 4% to ethambutol (EMB), 14% to PZA, 9% to EMB/PZA, 6% to STR/EMB, 15% to SM/PZA, and 27% to SM/EMB/PZA. Resistance to INH was the highest 50%, while resistance to STR was 41%, RIF 5.4%, EMB 1.6% and PZA was 2%. For the second-line drug resistance among MDR cases, there were 20.3% resistant to fluoroquinolones (FQ), 10.6% to ethionamide (ETH), 0.5% to capreomycin (CM), 0.2% to amikacin (AK), 8.3% to FQ, ETH, 1.0% to FQ, AK and 0.3% to FQ, CM.

Conclusion: Among the first-line drugs about 50% of cases showed resistance to INH. In general drug resistance especially MDR/XDR is high which indicates that the second-line drug susceptibility testing is critical in this setting to treat TB patients effectively. More availability of drug susceptibility testing facilities would help in TB control and spread of drug resistance in Pakistan.

PC-508-01   Detection of mutations beyond the hot-spot regions of drug resistance genes of XDR-TB isolates using whole genome sequencing

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Background and objectives: Molecular detection of drug resistance in *Mycobacterium tuberculosis* is based on identification of common mutations in drug resistance conferring genes. Whole genome sequencing (WGS) has facilitated the identification of synonymous and non-synonymous single nucleotide polymorphisms (SNPs), as well as indels and large deletions in *M. tuberculosis*. Geographical variations in SNPs highlight the importance of understanding region-wise variations.

Methods: We performed WGS of extensively drug-resistant (XDR) ($n = 37$) and susceptible ($n = 5$) *M. tuberculosis* isolates from Pakistan. Thirty-seven genes conferring resistance to first and second line drugs were analyzed.

Results: Over 150 SNPs (>60% previously unreported) were identified, including 79 in genes resulting in resistance to; rifampicin (rpo*B*), isoniazid (kat*G*, fpb*C*, Rv1592C, ndh, Rv2242, fab*D*, kas*A*, acc*D*, oxy*R*, fadE24, and nat), streptomycin (rrs (500 region), and gid*B*), pyrazimamide (pnc*A*), ethambutol (emb*A*, emb*B*, emb*C*, emb*R*, Rv3124, rml*D*, ini*A*, ini*B*, ini*C*, and man*B*) and 22 SNPs associated with genes conferring resistance to second line drugs; ofloxacin (gyr*A* and gyr*B*), aminoglycosides (rrs and tly*A*) and ethionamide (eth*A* and fabG1).

Conclusions: Not all of the above gene targets are included in commercially available molecular diagnostic assays for detection of drug resistance in *M. tuberculosis* (i.e., GeneXpert MTB/RIF assay, Haines line probe assays; MTBDR*plus* and MTB-DR*sl*). Based on our data of these XDR-TB strains we observe that the commercial assays would have missed isoniazid resistance in 11%, fluoroquinolone resistance in 22% and aminoglycoside resistance in 19% of *M. tuberculosis* isolates. Therefore, inclusion of additional SNPs for drug resistance conferring genes are required to improve molecular methods for *M. tuberculosis* resistance detection.

PC-509-01   Global transcriptional profiling of longitudinal clinical isolates of *Mycobacterium tuberculosis* exhibiting rapid accumulation of drug resistance

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Background: The identification of multidrug-resistant (MDR), extensively and totally drug resistant *Mycobacterium tuberculosis*, in vulnerable sites such as Mumbai, is a grave threat to the control of tuberculosis. The 'ominous progression from MDR to XDR to TDR' in endemic regions like Mumbai, indicate differential evolution of drug resistance in such locales. The current study aimed at explaining the rapid expression of MDR in DOTS-compliant patients, represents the first study comparing global transcriptional profiles of 3 pairs of clinical *M. tuberculosis* isolates, collected longitudinally at initiation and completion of DOTS. While the isolates were drug-susceptible (DS) at onset and MDR at completion of DOTS, they exhibited identical DNA fingerprints at both points of collection.

Design/methods: The whole genome transcriptional analysis was performed using TBv3 micro-array chip (BuGS, St George's University, London) on clinical isolates belonging to the 3 locally predominant spoligotypes viz. MANU1, CAS and Beijing. The total RNA from these 3 pairs of clinical isolates, and H37Rv was hybridized on the TBv3 microarray glass slide consisting of 8 quadrants.

Results: Global transcriptional profile yielded 36, 98 and 45 differentially expressed genes in MDR MANU1, CAS and Beijing isolates respectively as compared to their drug susceptible pretreatment isolates. Genes encoding transcription factors (sig, rpo*B*), cell wall biosynthesis (emb genes), protein synthesis (rpl) and additional central metabolic pathways (ppdK, pknH, pfkB) were found to be down regulated in the MDR isolates as compared to the DS isolate of the same genotype. Up regulation of drug efflux pumps, ABC transporters, trans-membrane proteins and stress response transcriptional factors (whiB) in the MDR isolates was observed.

Conclusion: The data indicated that *M. tuberculosis*, without specific mutations in drug target genes may persist in the host due to additional mechanisms like drug efflux pumps and lowered rate of metabolism. Furthermore this population of *M. tuberculosis*, which also showed reduced DNA repair activity, would result in selection and stabilization of spontaneous mutations in drug target genes, causing selection of a MDR strain in the presence of drug pressures. Efflux pump such as drrA may play a significant role in increasing fitness of low level drug resistant cells and assist in survival of *M. tuberculosis* till acquisition of drug resistant mutations with least fitness cost.

PC-510-01   Competitive fitness costs of genotypically identical *M. tuberculosis* strains acquiring drug resistance during first-line treatment in adherent patients

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Background: The increasing levels of multidrug-resistant tuberculosis (MDR-TB) in endemic regions are a cause of concern. Mumbai in Western India is endemic for TB, characterized by high levels of MDR, strain heterogeneity and amplification of drug resistance in patients undertaking compliant DOTS therapy. Such MDR strains with no fitness costs, threaten global tuberculosis control. Evaluation of factors other than the particular non-synonymous substitutions, such as epistasis that contribute to the fitness of strains may have an important bearing on understanding the spread of MDR-TB. The aim of the study was to determine the fitness of MDR-TB strains from Mumbai, which have acquired drug resistance during DOTS. The role of epistatic interactions in *Mycobacterium tuberculosis* as a plausible mechanism of enhancing and stabilizing drug resistance mutations was also reviewed to support the findings of the laboratory study.

Design/methods: Paired isolates of different lineages (one that was drug resistant and one that was drug susceptible) from 5 patients (with no past history of treatment), which acquired resistance during antibiotic treatment (DOTS) and bearing drug resistance mutations in the rpo*B* and kat*G*/inh*A* regions were mixed axenically. Fitness of *M. tuberculosis* strains was evaluated using the difference in generation times of drug resistant and susceptible population obtained by enumeration of CFU. The rise in the levels of drug resistance mutations in two independent loci, i.e., rpo*B* and kat*G*/inh*A* but specific allele combinations over a considerably long time period (1985–2007) from various regions of TB outbreak were analysed using the TBDReaM database.

Results and conclusion: The drug resistant strains bore no significant fitness cost. The selection of specific allelic combinations (epistasis) in multiple drug resistance governing loci may attribute the enhanced/retained fitness of the drug resistant strains. The rise of 'fit' drug resistant *M. tuberculosis* strains due to selective environmental forces resulting in genetic alterations may replace drug susceptible strains allowing an impending drug resistant outbreak of TB in an endemic setting.

PC-511-01   Drug-resistance tuberculosis in Macedonia, 2007–2012

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Background: Anti-tuberculosis (TB) drug resistance is a major public health problem that threatens progress made in TB care and control worldwide. Drug resistance arises due to improper use of antibiotics in chemotherapy of drug-susceptible TB patients. Macedonia belongs to the countries with low TB incidence. TB notification rate from 2002 is decreased slowly and continually and in 2012 was 17.2/100 000 population (355 new and retreatment cases).

Design/methods: The aim of this study was to present the overall TB resistance strains in Macedonia from 2007 to 2012. The data were obtained from the National TB Laboratory Register from the Institute for lung diseases and Tuberculosis, Skopje.

Results: From 2007 to 2012 drug susceptibility tests (DSTs) were performed in 88.8%, 73.2%, 92.0%, 89.16%, 91.76% and 97.83% of positive cultures, separately. In 2007 the total resistance was seen in 33 cases or 16.5%. The total resistance continually declined to 2011 when was seen in 11 cases or 7.05%. In 2012 we noticed slightly increasing in the total resistance of 8.83% or in 16 cases. Among the resistant cases, MDR-TB cases were present in the range of 5.88 till 54.54%, or in this 6-year period 23 cases were registered with MDR-TB of which only one is with XDR-TB. 20 patients with MDR-TB (87%) had acquired and only 3 or 13% had primary drug resistance. In this work the distribution of drug resistnace toward all tested drugs will be shown.

Conclusion: Anti TB drug-resistance in Macedonia is not a big problem, but it is sufficient to require serious and systematic approuch in improvement of management of laboratory network and TB diagnosis.

PC-512-01   *Mycobacterium tuberculosis drug resistance prevalence in tuberculosis spondylitis patients*

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Background: Tuberculosis spondylitis (TS) makes 60% of all bone-joint tuberculosis in Russia. It is characterized by malignant clinical course often resulting in a patient disability. Adequate chemotherapy based on the causing agent (MTB) drug susceptibility (DS) spectrums may have higher efficiency. However there is little knowledge on prevailing DS spectrums. The aim of the study was to develop an algorithm to isolate the culture or DNA MTB and to estimate the prevalence of drug-resistant (DR).

Design/methods: 673 samples extracted surgically from 584 patients with infectious spondylitis in 2007–2011. 359 had TS and 225—osteomyelitis. Diagnoses were confirmed by pathomorphological analysis. Microbiological tests included culturing on solid medium (Löwenstein-Jensen and Finn II) (SM), liquid medium Middlebrook 7H9 (LM) utilizing BACTEC MGIT 960, real-time PCR (RT-PCR, SINTOL LTD). DS was tested by indirect absolute concentration method and by microarray DNA test (TB-BIOCHIP) MBT or DNA from clinical samples.

Results: The sensitivity of the two SM summarily was 44.8% (197/440), of LM—38.3% (111/290), of

RT-PCR—87.1% (125/272) with 100% specificity for all three tests. Proportion of cultures isolated on SM was statistically higher than on LM: 86.8% and 77.1% correspondingly ($\chi^2 = 3.966$, $P = 0.046$). LM was beneficial in turn-over time: average growth time on LM was $23+2.3$ days compared with $40.6+3.2$ days on SM. 24.7% of the isolated strains were sensitive, 17.8% mono- and poly-resistant, 57.5%—MDR/XDR. Streptomycin resistance was in 78.2%, Isoniazid in 68.5%, rifampicin in 63.5%, pyrazinamide—51.2%, ethambutol in 44.8%, ethionamide—38.8%, kanamicin—38.7%, capreomicin—26.3%, amikacin—22.1%, ofloxacin—9.7%, PAS—9.3%, cycloserine—0% of isolated cultures. 80% MDR/XDR strains carried combination of rpo*B* (Ser531→Leu) and kat*G* (Ser315→Thr) mutations.

Conclusion: Efficiency of microbiological and molecular-genetic methods in TS was 89.1%. DR prevalence in TS patients in Russia is high. Using a complex of methods offers the potential to quickly verify the diagnosis, to determine the correct DS and to prescribe adequate chemotherapy of TS patients.

PC-513-01   Molecular characterization of rpo*B* mutations in multidrug-resistant *Mycobacterium tuberculosis*

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Background: Multidrug resistant tuberculosis (MDR-TB) is an important global health problem due to limited treatment options. Resistance to rifampicin develops due to mutation in the gene encoding the beta subunit of the RNA polymerase (*rpo*B) of *Mycobacterium tuberculosis*. Mutation in *rpo*B gene is considered as marker for MDR-TB. The pattern and frequency of mutations in the *rpo*B gene has variable geographical distribution, and limited data is available on specific *rpo*B mutational patterns in Pakistan.

Design/methods: This current study was undertaken to detect and characterize the *rpo*B gene mutations among rifampicin resistant *M. tuberculosis* isolates from Punjab, Pakistan. A total 1080 suspected TB patients were included in the study. PCR based molecular detection of *rpo*B gene followed by DNA sequencing was performed.

Results: Among 1080 referred TB cases, 63 (6%) were resistant against at least one of the four first line TB drugs. Out of these 63 resistant isolates, 24 isolates (38%) were found to be resistant against isoniazid and rifampicin. Sequence analysis of MDR-TB isolates detected single mutation in the *rpo*B gene at codon 512 (11%), 516 (21%), 528 (5%), 531 (58%)

and 533 (5%); however a double mutation was observed in one MDR-TB sample on codon 512 and 516. Moreover five MDR-TB isolates lack any mutation in the target sequence.

Conclusion: *rpo*B gene mutations in drug-resistant *M. tuberculosis* were analyzed. Further study about these mutations might be helpful in the development of diagnostic tools for rapid detection of *M. tuberculosis* in high TB endemic area like ours.

PC-514-01   Association of low-level isoniazid resistance with ethionamide resistance in *Mycobacterium tuberculosis* strains from Pakistan

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Background: Pakistan ranks fifth highest in tuberculosis and the third in multidrug-resistant tuberculosis (MDR-TB) prevalence. Susceptibility testing for second-line anti-tuberculous therapy (ATT) is not widely available. Ethionamide is an integral part of second-line ATT. An association has been described between low-level isoniazid resistance gene inhA and ethionamide resistance. It will be valuable to know if phenotypic resistance to isoniazid, especially low-level isoniazid, can predict ethionamide resistance. Thus we performed data analysis to determine the association of low-level isoniazid resistance with ethionamide resistance.

Design/methods: Aga Khan Clinical Laboratory data retrieved from 2011–2012 was retrospectively analyzed. All culture positive *Mycobacterium tuberculosis* isolates with susceptibilities to isoniazid and ethionamide available were included. Isoniazid (1 and 2 µ/ml) and ethionamide (5 µ/ml) susceptibility was performed using agar proportion method on Middlebrook 7H10 agar. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of isoniazid resistance for determining ethionamide resistance were calculated.

Results: A total of 6099 isolates were included in the study. The sensitivity, specificity, PPV and NPV of isoniazid resistance as a marker of ethionamide resistance were found to be 92.5%, 51.2%, 11.1% and 99.1%. However, low level resistance had sensitivity, specificity, PPV and PPV of 88.1%, 95.3%, 59.3% and 99.1%.

Conclusion: Low-level isoniazid resistance may predict ethionamide resistance thus guiding choice of ethionamide for second-line ATT. Additional studies involving detection of inhA gene and its correlation with both isoniazid and ethionamide resistance are needed before a definitive conclusion can be drawn.

ENSURING QUALITY OF TUBERCULOSIS LABORATORY SERVICES

PC-515-01   Blinded rechecking of AFB smear microscopy in PHC laboratories in Kazakhstan: results of the first year of implementation

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Background and challenges to implementation: There has been an ongoing effort to strengthen the acid-fast bacilli (AFB) diagnostic laboratory network in the East Region of Kazakhstan, and quality control of microscopy has been initiated as part of this effort.
Aim: To evaluate the impact of external quality assessment to improve diagnostic laboratory network through the implementation of blinded rechecking method.
Intervention or response: Routine slides were collected from the 10 peripheral diagnostic laboratories of Eastern region in 2012 on a quarterly basis by rechecking representative sample of slides, according to the LQAS method. LQAS allows determination of optimum sample size, needed to assess if laboratory meets a certain standard. The assessment is primarily focused on smear quality determined by six characteristics of smears to evaluate the overall performance standard of individual/lab technicians in performing routine sputum microscopy.
Results and lessons learnt: Two thousand six hundred and seventy four slides were collected from the peripheral diagnostic centers. During the year, six of the 10 labs have improved the quality of smears, in the other four laboratories partial success to improve the quality of smears was observed. The analysis showed that in the first six labs there is at least one trained specialist, in other laboratories specialists are changed several times during the year.
Total discrepant results found: 10 false positive, 2 false negative, 7 quantification errors. Quarter 1 found 5 false positive, 1 false negative, 1 quantification errors; Quarter 2 found 4 false positive, 1 false negative, 3 quantification errors.; Quarter 3 found 1 false positive, 3 quantification errors; and Quarter 4 did not result in any discrepancy between the results of smears.
Conclusions and key recommendations: High agreement rate was recorded in the readings of AFB among the peripheral and reference laboratories. Optimal results in quality improvement can be achieved through regular analysis of rechecking results and feedback provided to laboratories. Discrepancies in smear microscopy results and low quality of smears are more likely to occur among newly hired and untrained staff. Regular on the job training of the peripheral laboratory staff together with supportive supervision help improve laboratory performance.

PC-516-01   Implementation of an external quality assurance system in the tuberculosis control system in Ukraine

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Background and challenges to implementation: The national Primary Health Care System (PHC) system has been implementing EQA of microscopic sputum tests since 2006. This activity is supported mostly by USAID-funded projects, since the relevant state regulations are still evolving. Initial efforts were mostly targeted at the organization of microscopy points and establishment of EQA linkages. Separate methods of EQA were used, and the approaches were not standardized. During a 2012 baseline assessment, a number of systematic shortcomings were detected, i.e., the test scoring system did not conform to WHO standards; panel batches consisted of a different number of slides and often contained highly positive stained slides only, and the recording and reporting (R&R) forms were not maintained correctly so measuring change over time was obscured. The study objective was to analyze the preliminary results of different approaches towards EQA of tuberculosis diagnostics used in Ukraine's PHC and address shortcomings.
Intervention: The USAID Strengthening Tuberculosis Control in Ukraine Projectteamed with partners to standardize comprehensive WHO-recommended EQA procedures, which embrace panel testing, blinded rechecking, and on-the-job training. The Project demonstrated the benefit of using panel batches containing at least 10 unstained slides and some scanty smears, simultaneous on-the-job training, and blinded rechecking. Special attention was paid to the proper implementation of WHO-recommended R&R forms.
Results and lessons learnt: In Kharkiv oblast, one of the target regions, WHO-recommended EQA activity has now become routine with all regional PHC. In 2012, the USAID Project supported 13 mentoring visits to PHC laboratories and 51 blinded rechecking sessions. No diagnostic discordances were detected, faults in smear thickness and staining occurred in only 1.6% (95%CI 1.4–1.7%) and 0.8% (0.7–0.9%) respectively, and 38 out of 45 laboratories underwent panel testing without mistakes, the rest received a 95% score. R&R forms have been introduced in the oblast. At the same time, the frequency of saliva samples was 26.5% (95%CI 25.3–26.8%), indicating insufficient rate of patients' selection and instructing in sputum sample collection. The feedback was given to fields and discussed in the facilities.
Conclusion: A standardized EQA procedure augmented by immediate on-the-job training can improve diagnostics in the short run, as evidenced by the Kharkiv example.

PC-517-01   Integration of international standard practices for the strengthening of local capacity in tuberculosis reference laboratories in Viet Nam

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Background: Laboratory practice per Quality Management System (QMS) is globally recommended. QMS concept is standard; however, the practice and implementation may vary between countries, based on available resources and infrastructure. Viet Nam Ministry of Health (MOH) has implemented QMS for clinical laboratories since 2010, with funding and technical assistance (TA) from CDC/Presidents Emergency Plan for AIDS Relief. The approach includes different formats matched to a site level and includes: basic QMS education, Strengthening of Laboratory Management Towards Accreditations (SLMTA), and Accreditation per International Organization for Standardization (ISO) requirements. In line with these efforts, in January 2013, MOH issued guidance for Implementation of Lab Quality Management at health care facilities including TB testing services.
Methods: CDC and FHI360 support to participating labs for accreditation (ISO 15189) included: 1 basic training on technical and management requirements to all department staff; 4 trainings on each quality component to Lab management, ISO committee and Quality Assurance Manager; weekly mentoring by FHI360 staff on implementation of each requirement; funding through CDC-FHI360 cooperative agreement.
Results: TB laboratories at Pham Ngoc Thach Hospital and the National Lung Hospital participated in this project starting in 2010. Both facilities performed all the practices and management per ISO 15189:2007 requirements for all pre-examination, examination and post-examination phases in their labs. The facilities use Lab Information Systems (LIS) to manage workflow/data, and participate in External Quality Assessment (EQA) programs organized by Supranational Mycobacteria Reference Laboratory (SRL) in Adelaide, Australia for smear microscopy and drug susceptibility testing. The SRL also provides yearly supervision to the facilities for culture and molecular testing. Both labs were assessed and accredited by Viet Nam Bureau of Accreditation in 2012.
Discussion: Daily practices and improvements toward international standards such as ISO 15189 is an effective and comprehensive approach to build capacity for the national TB lab system, especially in the areas of test standardization and quality assurance. This meets the strategic objective of the National TB Program master plan 2011–2015 on Strengthening QMS to ensure the TB lab network operates according to national and international standards.

PC-518-01   External quality assessment for tuberculosis smear microscopy: creation of a comprehensive national network in Viet Nam

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Background: Smear microscopy remains a practical method for TB diagnosis due to low cost, simplicity of testing and accessibility. Strengthening Quality Assurance (QA) for smear at all levels is part of the Viet Nam NTP strategic plan for 2015. Slide rechecking using Lot QA System method (Rechecking), one component of the external quality assessment (EQA) program ensuring the quality of smear testing, has been harmonized in Viet Nam since 2009 at district but not provincial level labs due to lack of funding.
Methods: Government funding allows provincial TB labs to perform rechecking for all district TB units. Slides are collected at districts and sent to provinces monthly for 2nd reading and corrective action site supervision. In 2012, NTP organized an EQA dissemination workshop to share 2009–2011 district rechecking results. Since 2013, financial support from the CDC/President's Emergency Plan for AIDS Relief allowed for the creation of an EQA program linking the National TB Reference Lab (NRL) to provincial labs. NRL now performs Rechecking for 62 provinces which conduct smear testing for TB suspects. Slides have been collected at provinces in 2 consecutive quarters and sent to NRL for 2nd reading and feedback. The program focuses on technician training/retraining on a recently updated national rechecking training package.
Results: The district results showed 181 of 785 microscopy sites had major discrepancies (i.e., major quantification errors, high false negatives, and high false positives). Suggested corrective actions included retraining technicians on slide preparation and/or slide reading and replacement or regular maintenance of microscopes. To date, rechecking from 5 provinces showed no major discordant results out of 292 slides sent to NRL in the first quarter of 2013. However, most slides did not pass the NTP regulations for quality. NRL's feedback with corrective actions included retraining of provincial technicians and on-site observation on sputum collection and slide preparation.
Discussion: Rechecking is an effective, sustainable method in Viet Nam to assure quality for smear testing. The link between NRL and provincial labs is critical for creating a national network. Despite high staff turnover at districts and provinces, adequate

supervision and quick feedback from rechecking centers led to improved testing quality. Participation in the EQA program may also help the labs be classified per national standards.

PC-519-01   Tuberculosis microscopy laboratory mapping in Manila: a validation study

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Background: A laboratory mapping survey was conducted in Manila, from November 21 to December 19, 2012. The purpose of the said activity was to validate the actual number of microscopy laboratory performing the Direct Sputum Smear Microscopy in public, private, non-governmental organizations and other settings and come up with a verified list of TB microscopy laboratories not included in the original list of the National TB Reference Laboratory. We used the mapping tool prepared by the NTRL and conducted an occular survey of the actual laboratory set-up. We also asked the microscopist to show us the smears that they have prepared and the result form and look into the manner of reporting the AFB.

Design/methods: 57 laboratories were visited by the two NTP QA controllers from the Public Health Laboratory and found out that only 31 (54%) of them perform DSSM while the rest refer AFB examination to other laboratories. Only 10 (32%) out of 31 were trained on basic DSSM, 19 (61.3%) has no training but perform DSSM and 2 (6.5%) were trained on flourescence microscopy. The 8 (26%) microscopists who perfomed DSSM based their knowledge from previous experience and taught by their immediate supervisor. Sixteen (57.6%) microscopists do not follow the six criteria of good smear preparation like specimen quality, staining, evenness, size, thickess and cleanness while only 17 (55%) of them used the standard scale of reporting the AFB. Fifteen (48%) microscopists read 2 horizontal lines or 300 visual fields while 16 (52%) read the whole smear under the oil immersion field.

Table   Profile of the 31 microscopists

	n (%)
Trained microscopists on DSSM	10 (32)
Untrained micrcopists	19 (61)
Followed the criteria of good smear preparation	15 (48)
Reads two horizontal lines 300 VF	15 (48)
Reads the whole smear	16 (52)
Uses the standard scale of reporting	17 (55)
Other scale used	14 (45)

Conclusion: Based from our findings, we have identified the major gaps in EQA implementation and we have validated the existing number of TB microscopy laboratories in Manila which will be used for targeting the NTP indicators on quality assured TB micros-

copy laboratory. Although the microscopist were able to identify corectly the AFB there is an urgent need for them to undergo basic DSSM training in order to attain a standardized smear preparation, staining and microscopic examination. The output of this mapping activity will guide the NTP and the NTRL in future planning activities for the TB laboratory network. The consolidated data will be developed into a directory of TB laboratories. Gathered information can also be use for further verification of the functionality of the TB microscopy laboratories and will provide basic information to facilitate implementation of major gaps in external quality assessment.

PC-520-01   On-site staff mentoring and assessments improve laboratory service quality and microscopy diagnostic accuracy in Ethiopia

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Background: Acid fast bacilli (AFB) microscopy is the main tuberculosis (TB) diagnostic tool in Ethiopia. Ethiopia has external quality assurance (EQA) guidelines for AFB microscopy, adopted from the World Health Organization's (WHO) guidelines. Although the WHO recommends quarterly EQA for all diagnostic facilities, this has not been possible in Ethiopia due to resource limitations. In response, the PEPFAR-funded, USAID-implemented Help Ethiopia Address the Low TB Performance project (HEAL TB) and its implementer, Management Sciences for Health, designed an on-site mentoring and assessment system and implemented it in 659 health facilities. The system was based on the national EQA guidelines and designed to help ensure that laboratory professionals follow the correct AFB procedures and have internal quality measures in place.

Implementation: From October 2011 to September 2012, 15 of HEAL TB's laboratory experts conducted quarterly, on-site mentoring at 659 health facilities in Ethiopia. During these visits, the experts distributed job aids, provided staff training, and checked that staff were properly registering all TB suspects, correctly labeling all slides, and safely storing the slides. They also checked that staff was implementing internal quality measures. To assess the accuracy of AFB diagnosis, the experts selected and examined five slides that the staff had diagnosed as negative and five that they had diagnosed as positive. The experts then tailored their staff mentoring and technical assistance, based on the identified gaps. HEAL TB had collected performance data from all the 691 health facilities and the results of 129 are presented for this abstract.

Results: At baseline, 111 (86%) of the health facilities' slides had a concordance rate of 90% or above with the HEAL TB experts' slide reading. At the end of the fourth quarter, 121 (94%) of the health facilities' slides had a concordance rate of 90% or above with the HEAL TB experts' slide (see graph). The health facilities did not have fully-implemented internal quality measures at baseline but, by the end of the implementation period, 100% of the 129 health facilities' had fully implemented internal quality measures. At baseline the staining quality was 70% and at the end of December 2012 it reached to above 85%. For the rest of the internal quality indicators see the figure.
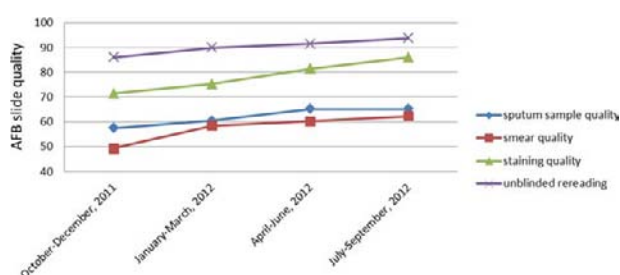
Figure Trend in AFB microscopy diagnostic quality at 129 Ethiopian health facilities, October 2011 to September 2012.

Conclusion and recommendations: Quarterly on-site assessments and staff mentoring contributed to improved AFB slide accuracy. This approach should be implemented at all AFB diagnostic facilities in Ethiopia to further improve the quality of laboratory services and the accuracy of AFB microscopy.

PC-521-01 Building sustained quality assured tuberculosis diagnosis services: the Taiwan experience

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Background: Tuberculosis (TB) is a notifiable disease in Taiwan. A TB laboratory service network was established to process estimated 700 000–800 000 specimens annually. Laboratory diagnosis has to be performed in the National Reference Laboratory (NRL) or Department of Health authorized clinical mycobacteriological laboratories. Authorized laboratories are capable of performing at least smear microscopy, culture, identification and drug susceptibility testing (DST).
Methods: To ensure the quality of the services, Taiwan Centers for Disease Control (TCDC) developed a stepwise external quality assessment (EQA) program for clinical TB laboratories in 2006. The EQA program included proficiency testing (PT), rechecking, on-site visit, training and quality management.

An on-line reporting system was used to timely monitor quality indicators, time for specimen transportation and turnaround time of each test. TCDC implemented a laboratory authorization policy in 2008. Authorized laboratories have been required to be accredited by Taiwan accreditation foundation or College of American Pathologists since 2011.
Results: As of December 2012, 32 clinical laboratories were authorized and 31 (96.9%) were accredited with implementation of the ISO 15189 quality management system. Even though laboratories performed well in smear PT, major errors including 0.8% (1/126) high false-positive, and 0.8% (25/2979) high false-negative still observed during blinded smear rechecking. For DST PT, 16.7% (5/30), 85.7% (30/35), 86.1% (31/36), 82.4% (28/34), 96.8% (30/31) and 96.9% (31/32) of laboratories fulfilled the competency criteria for four first-line drugs in 2007, 2008, 2009, 2010, 2011 and 2012, respectively. Furthermore, the NRL has rechecked all multidrug-resistant *Mycobacterium tuberculosis* strains isolated from clinical laboratories since 2007. Accuracy was improved from 84.1% in 2007 to 91.2% in 2011. In addition, time for specimen transportation within 3 days was improved from 75.9% in 2008 to 99.2% in 2011.
Conclusion: Diligent implementing both laboratory EQA programs and management systems can significantly enhance quality of TB laboratory services.

PC-522-01 Improvement of tuberculosis detection in Uganda and reduction of diagnostic errors made by peripheral laboratories through external quality assurance

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Background: The reduction of tuberculosis (TB) diagnostic errors in microscopy made by laboratory technicians in peripheral laboratories is achieved through external quality assurance (EQA), and improves TB detection rates. The Ugandan National Tuberculosis and Leprosy Program (NTLP) appointed in 2006 Nsambya Hospital as the First Controller of the activities in Kampala Zone under the supervision of AISPO.
Design/methods: Nsambya Hospital and AISPO carried out quarterly on-site supervision of TB microscopy on 53 enrolled private and public laboratories, collection of sputum samples for blinded rechecking

to correct the discordant results, and performing workshops and training of staff, assessing the quality of reagents, microscopes and personnel working at the peripheral laboratories. Ziehl Neelsen (ZN) staining procedure was performed; the analysis of statistical data was also included to evaluate the diagnostic accuracy of each enrolled laboratory.

Results: 450 lab technicians were successfully trained in laboratory management and in TB detection through ZN microscopy examination, in order to properly handle and store slides, reporting and filling results in the NTLP register. During the period 2006–2012, 8758 smears from 53 laboratory in 28 quarters were collected. Considering the laboratory that continuously have participated to EQA, the historical trend was divided into two parts, in order to compare the accuracy achieved in the first period (2006–2009), with the second period (2010–2012). The comparisons made on 29 laboratories, allowed to verify that 19 laboratories have improved significantly their accuracy, 3 were unchanged and only 7 have worsened. Of these, however, no one has dropped below an accuracy of 90%. All erroneous units were followed up and feedback reports issued to them. Focusing on 2012 the data highlighted the lowest error rates compared to the previous years in detecting TB cases.

Conclusion: A steady rise in laboratory performance was observed since when the activities started. This work allowed improving the overall quality of smear microscopy performed in the peripheral laboratories, increasing the effectiveness of reliable output results to the patients, and reducing the workload of the National Tuberculosis Reference Laboratory.

PC-523-01   Expansion of microscopic services, staff training and supportive supervision improves smear microscopy follow-up of smear-positive tuberculosis patients

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Background and challenges to implementation: Help Ethiopia Address Low Tuberculosis Performance (HEAL TB) is a five-year, PEPFAR-funded, USAID project designed to improve TB outcomes in the Amhara and Oromia regions. Through its implementer, Management Sciences for Health, HEAL TB is working to improve TB case detection and treatment outcomes, mitigate the emergence of multidrug-resistant TB (MDR–TB), improve TB-HIV collaborative activities, and strengthen the health system. In 2011 the project team conducted a baseline assessment in the project zones that revealed a need to increase the number of microscopic centers and build health worker. The target facilities in the project zones are 691.

Intervention or response: In response to the assessment findings, HEAL TB supplied 188 microscopes to health centers and hospitals in Amhara and Oromia and trained 1414 laboratory professionals in acid fast bacilli (AFB) microscopy and internal and external quality assurance activities. The project also supported in training staff from 691 health facilities in TB program management and clinical skills. Concurrently, HEAL TB mentors provided quarterly, onsite supportive supervision and mentoring to the target health facilities.

Results and lessons learnt: HEAL TB's microscope donations and staff trainings contributed to increased TB service provision in Amhara and Oromia. The coverage of facilities providing TB microscopy services increased from 65% at baseline to 91% after the intervention. Furthermore, the percentage of smear positive TB cases examined in the targeted health facilities increased by 10% between January 2012 and March 2013. This increase was consistent and statistically significant (χ^2 trend^{Cal} = 119, P = 0.000) (See Figure).
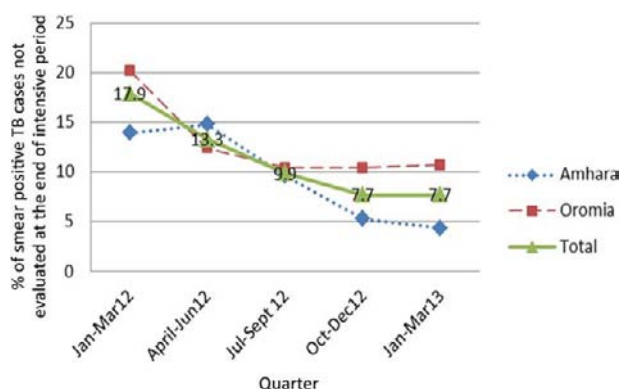
Figure   Proportion of smear positive TB cases not examined at end of intensive period of treatment decreased during the HEAL TB project intervention period.

Conclusions and key recommendations: The microscopic centers, in combination with improve health worker capacity and regular supportive supervision, contributed to an increased number of smear positive TB case examined in the participating health facilities. Improvement in patient follow up will contribute to the overall improvement of TB treatment outcomes and these interventions should be expanded in Ethiopia. Furthermore, training health workers on sputum smear follow up improve TB cure rates and over all treatment outcomes in Ethiopia.

PC-524-01   Contribution of performance indicators in monitoring a microscopy network for tuberculosis: the case of Benin

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Background: In many countries with a high prevalence of tuberculosis (TB), direct smear microscopy for acid-fast bacilli remains the most available tool for TB diagnosis and for monitoring the treatment. A high quality of microscopy is therefore necessary for the control of the disease in these settings. This quality is assessed with performance indicators that can be collected through supervision and external quality control. Using these indicators may help in improving the global performance of the TB diagnostic in the country.

Setting: The microscopy laboratory network for TB in Benin.

Objective: To assess the performance of the TB microscopy laboratories in Benin.

Methods: A longitudinal prospective study was conducted from 1 January 2008 to 31 December 2012, in all the laboratories of the network. Data were collected during quarterly supervisions of laboratories.

Results: The workload varied from one laboratory to another: 1 to 88 slides/day. The average rate of positive patients among suspects was stable at around 17, 4% over the time. From 2008 to 2010, the percentage of errors after slides rechecking was about 1% and for over 80% of laboratories, sensitivity relative to controllers was more than 80%. In 2011, the positivity rate among samples at 2nd/3rd month of treatment decreased in some laboratories followed by a decrease of sensitivity in these laboratories. Thus, only 53% laboratories had reached a sensitivity of 80% and beyond. After several investigations/corrective actions, this percentage increased to 75% in 2012. There was a clear proportional relationship between the sensitivity relative to controllers and the positivity rate among samples at 2nd/3rd month of treatment.

Conclusion: These results highlighted the benefits in following indicators to monitor performances of microscopy network.

ADVANCES IN TUBERCULOSIS CULTURE METHODS

PC-525-01   Comparison between real time PCR and immunochromatographic assays for rapid identification of *Mycobacterium tuberculosis* complex

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Background: Tuberculosis is a disease of major public health concern worldwide. With human immunodeficiency virus (HIV) epidemic, there is increased incidence of non-tuberculous mycobacteria (NTM). Accurate, rapid and simple laboratory methods for differentiation of *Mycobacterium tuberculosis* complex from NTM are greatly needed for appropriate TB diagnosis and management. In this study, we evaluated the performance of protein (MPB64) based immune chromatographic assay methods against Roche light cycler mycobacterium detection assay (Real time PCR).

Design/methods: A total of 102 sputum samples that were MGIT culture and Ziehl-Neelsen (ZN) stain-positive were tested using the three immuno chromatographic assays. These methods included: standard diagnostics (SD), BD MGIT TBc identification test (TBc ID), Capilia TB (TAUNS). The results from these were compared with those for real time PCR.

Results: Compared to real time PCR, Capilia and BD MPB64 based immuno chromatographic assays showed a slightly greater potential for identification of *M. tuberculosis* complex and NTM with a specificity of 97.4% and 94.9% respectively than SD kit (92.3%). All the three immuno chromatographic assays had the same sensitivity of 95.3%. The kappa statistic for Capilia, BD and SD were 0.96, 0.90 and 0.87 respectively. There was no statistical significant difference ($P = 0.089$) in results of the SD and BD identification tests but there was a statistical significant difference between the results of SD/BD and Capilia TB with P values equal to 0.029 and 0.047 respectively.

Conclusion: Capilia is a better alternative for rapid identification of *M. tuberculosis* complex compared to the others investigated. It can however be used interchangeably with BD especially in resource limited settings because it performed better than SD assay.

PC-526-01   Diagnostic yield and detected bacillary load of induced sputum for ambulatory adult and adolescent tuberculosis suspects in a South African community

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Background: Sputum induction (SI) by nebulised saline may increase yield of mycobacterial diagnosis of TB. Our objective was to compare diagnostic yield of sputum induction to routine sputum collection methods.

Method: HIV negative and positive adult and adolescent TB suspects were enrolled from community clinics prior to final diagnosis and treatment. Subjects provided a routine 'spot' sputum sample; a SI sample; and an early morning routine sputum sample. SI was performed by hypertonic (5%) saline nebulization with high-flow oxygen. Sputum smear and culture diagnostic yield (denominator all subjects with a positive *Mycobacterium tuberculosis* culture) and time-to-positivity of MGIT culture (a proxy measure of sample bacillary load), were compared between SI and routine sputum collection methods. Differences in proportions of positive mycobacterial diagnosis were reported with 95% confidence intervals (CI) and McNemar's test for paired samples.

Results: Of 600 enrolled subjects, 41 (7%) were considered unfit for the procedure. In those who completed SI (559), the procedure was stopped early

Table Comparative yield for productive sputum samples, diagnosis by smear, and diagnosis by culture, in HIV positive and negative participants

	Yield by SI, proportion %*	Yield by comparator specimen, proportion %*	Difference in yield % (95% CI)	P value
Productive of sputum				
SI vs spot	98	97	0.3 (−2.3 +1.6)	0.85
SI vs EM	98	97	1.4 (−3.2 +0.3)	0.13
Smear				
SI vs spot	63	58	5 (−4.0 +14)	0.29
SI vs EM	61	53	7 (−0.1 +15)	0.08
Spot vs EM	57 (spot)	56 (EM)	1 (−9.0 +7.0)	0.9
Culture				
SI vs spot	90	87	3 (−6 1 +3.0)	0.56
SI vs EM	89	83	6 (−4.0 +16)	0.30
Spot vs EM	88 (spot)	86 (EM)	2 (−9.0 +12)	0.9

*In case of productivity of sputum, yield is proportion attempts that produced sputum, denominator all participants who completed the SI procedure. For smear and culture yield is proportion positive, denominator culture positive by any collection method in that analysis.
SI = sputum induction; EM = early morning.

in 4 due to adverse events (1%). Of subjects who completed IS (555) 90 (16%) subjects' results were unavailable for analysis (80 contaminated specimens, 10 lost). 125 of 465 (26%) subjects with all results available had a positive *M. tuberculosis* culture on ⩾1 of 3 samples (spot, SI, or early morning sputum). 132/559 subjects (24%) were HIV infected. Sputum was obtained in 97% of spot, 98% of SI, and 97% of early morning collection attempts. There was no difference in diagnostic yield by MGIT culture between SI and spot sputum (+3%; CI −6 to +13%, *P* = 0.56), or SI and early morning sputum (+6%; CI −4 to +16%, *P* = 0.3) for all subjects; or for HIV infected subjects (data not shown). Time-to-positivity on MGIT culture was lowest for early morning sputum, compared to spot sputum (difference −2 days, *P* = 0.02); and compared to SI (difference −1 day, *P* = 0.06). No SAEs were reported and only 11 (2%) minor adverse events.

Conclusion: SI was safe and well tolerated, but did not increase (1) rate of successful sample collection; (2) diagnostic yield of *Mycobacterium tuberculosis* culture; or (3) detected sample bacillary load, compared to routine sputum collection. SI cannot be recommended as a first-line sample collection method for sputum productive ambulatory TB suspects in communities with high HIV and TB burden.

PC-527-01   Comparison of centrifugation and bead-based method to isolate *Mycobacterium tuberculosis*

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Background: The centrifugation is recommended to obtain bacteria from specimens. Several bead-based bacterial collection techniques have been recently developed to recover *Mycobacterium tuberculosis* from clinical specimens without centrifugation. We evaluated the efficiency of centrifugation and magnetic bead method (TB-Beads; Microsens, UK) to isolate *M. tuberculosis*.

Method: The original *M. tuberculosis* suspension was diluted by saline to prepare 3 sets of 4 specimens of different concentrations confirmed as 6.5×10^3, 8.1×10^4, 7.9×10^5, and 6.4×10^6 cfu/mL and named as Specimen A, B, C, and D, respectively. We added 5×10^4 of THP-1 cells (RIKEN BRC, Japan) to another series of specimens. These specimens were subjected to centrifugation and TB-Beads. For the centrifugation method, the specimen was centrifuged at 3 different relative centrifugal forces (RCF), 2000, 3000, and 4000× *g*, for 15 min. The TB-Beads were used according to the manufacturer's instruction.

These experiments were performed in triplicate. The final density (cfu/mL) of bacteria in each treated specimen was calculated from the colony counts after 3 weeks of culture. The concentration ratio was calculated by dividing the final density with the original density. The number of collected bacteria was divided by its original total to determine the recovery rate.

Results: The specimens containing higher number of bacteria and THP-1 cells had a tendency to yield higher concentration ratio and recovery rate than the specimens containing lower number of bacteria by centrifugation ($P = 0.001$–0.21). *M. tuberculosis* could be isolated more effectively from specimen A with THP-1 cells than without THP-1 cells by using centrifugation ($P \leqslant 0.01$). The concentration ratio and recovery rate among specimens from the same bacterial suspension were not significantly different at centrifugation speeds of 2000 to $4000\times g$ except specimen C with THP-1 cells after centrifugation at $3000\times g$. We obtained 24.7–54.4% of *M. tuberculosis* with THP-1 cells after centrifugation at $3000\times g$ for 15 min, while the efficiency of recovery using magnetic beads was a maximum of 12.7%. Compared to centrifugation, TB-beads were more efficient in isolating *M. tuberculosis* at a low concentration with THP-1 cells.

Conclusion: The efficiency of centrifugation depends on the bacterial density, and the efficiency was low in the paucibacillary specimen. A carrier that forms a complex with *M. tuberculosis* will help to concentrate the specimen. The efficacy of capturing bacteria by TB-Beads should be improved.

PC-528-01 Cost and cost-effectiveness of Ogawa and MGIT media with increased supplemental PANTA for mycobacterial culture for tuberculosis diagnosis

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Background: The lack of accurate, rapid and cost-effective diagnostic tests for TB is a major obstacle to global TB control. To assure optimal use of limited human and program resources, it is important that diagnostic tests are introduced for widespread use only after careful assessment of their utility and cost-effectiveness in real world settings. Although many reports address the accuracy of new tests for TB, few studies have focused on cost and cost-effectiveness. The aim of this study was to evaluate of the cost and cost-effectiveness of Ogawa solid and MGIT liquid media for mycobacterial culture in Espirito Santo state, Brazil.

Design/methods: Two-hundred and sixteen sputum specimens from 216 persons with suspected pulmonary TB were cultured at the Mycobacteriology Laboratory, Vitoria, Brazil. We identified the materials and reagents used in all steps during the culture process for each culture method. We differentiated between culture-specific costs that were related to at least one step of the culture and overhead costs that were not a specific part of culture. We estimated the cost per culture and the incremental cost per additional case of TB diagnosed using MGIT culture supplemented with standard and two-fold supplemental antibiotics ($1\times$ and $2\times$ PANTA) to decrease contamination.

Results: Ninety-three (43%) of the patients had at least one sputum culture positive for *M. tuberculosis*. The percentage of cultures positive for *M. tuberculosis* was approximately 10% greater in MGIT media compared to traditional Ogawa media. The contamination rates were 9, 13 and 5.5% for Ogawa, MGIT PANTA $1\times$ and MGIT PANTA $2\times$ media, respectively. The cost per culture was US$20.50 for Ogawa medium and US$35.10 for MGIT media. The total culture cost per patient diagnosed with TB was US$22.60 on Ogawa, US$39.90 MGIT/PANTA $1\times$ and US$37.10 on PANTA $2\times$. The incremental costs per additional case of TB identified by MGIT/PANTA $1\times$ and PANTA $2\times$ compared with OGAWA was US$2.10 and $1.80 respectively.

Conclusion: Our findings suggest that the use of MGIT liquid culture with two-fold PANTA was cost-effective compared to traditional solid media, making it a viable alternative for incorporation in public health laboratories as a new tool for the diagnosis of TB. In areas where contamination rates are high, the addition of two-fold PANTA concentration could improve diagnosis and save time culturing multiple specimens or recalling patients for repeat cultures.

PC-529-01 Comparison of MODS and conventional methods for first-line DST under programme conditions in Lima, Peru

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Background: Drug resistance is a serious problem for TB control in Peru. Rapid methods are important for the initiation of appropriate treatment for resistant TB. Culture-based methods, especially in solid medium; are notoriously slow, especially in patients with low bacillary loads. The microscopic-observation drug-susceptibility (MODS) assay represents an alternative diagnostic that may shorten time to detection of resistance in TB patients with sputum smear

negative. We implemented MODS for smear-negative specimens collected from TB patients enrolled in a cohort study on the transmission of drug-resistant TB in Lima, Peru. We compared results from MODS for susceptibility to rifampin (RIF) and isoniazid (INH) with conventional testing.

Design/methods: Proportion method in LJ media and MODS assay were performed to detect INH and RIF resistance in smear-negative baseline sputum samples from index patients diagnosed with TB between May and August 2012, in 50 health centers in Lima.

Results: Among 159 smear-negative sputum samples, 73 (45.9%) had positive cultures by MODS while 72 (45.3) had positive cultures on LJ. Contamination occurred in 3 (1.9%) of specimens tested by MODS and one for LJ. Results concordant for the presence or absence of *M. tuberculosis* were recorded in 129 (83.2%) of the 155 non-missing results. Discordant results were found in 26: 15 (9.7%) were positive by MODS and negative on LJ while 11 (7.1%) were LJ positive and MODS negative. Among the 73 specimens positive by MODS, all had susceptibility results for INH and RIF while 59 of 72 (81.9%) positive on LJ had susceptibility results by this method. Concordance for INH was observed in 45 of 59 (76.3%) samples tested using both methods and in 51 (86.4%) samples for RIF. For INH, resistance detected by LJ was not found by MODS in 6 (10.2%) specimens while 3 (5.1%) INH-resistant specimens according to MODS were recorded as susceptible in LJ. Discordant results for RIF were found in 3 samples: 2 (3.4%) were resistant by MODS and not by LJ; 1 (1.7%) was resistant in LJ but not by MODS. Classification of presence or absence of MDR-TB was concordant in 152 (95.6%) specimens; 4 MDR specimens (2.5) were detected by both methods.

Conclusion: This analysis reveals a high level of concordance between MODS assay and the proportion method for TB diagnosis and susceptibility testing of INH and RIF, in a cohort study carried out under routine program conditions in Lima, Peru.

PC-530-01   Prospective evaluation of automated liquid culture system for drug susceptibility testing compared with the Löwenstein-Jensen absolute concentration method

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Background: Drug susceptibility testing (DST) is critical for programmatic management of drug resistant tuberculosis (TB). Nowadays, automated liquid culture system is widely used for DST in many coun-

tries, because it is more standardized and rapid than conventional methods using solid medium. This study aimed to evaluate automated liquid culture system through two-year prospective comparison with Löwenstein-Jensen (LJ) absolute concentration method.

Methods: A total of 954 of *Mycobacterium tuberculosis* isolates were collected from January 2011 through December 2012 at a tertiary teaching hospital in Korea. DST for rifampicin (RMP) and isoniazid (INH) was done by BACTEC MGIT 960 system at the same hospital and LJ absolute concentration method at the Korean Institute of Tuberculosis. The critical concentrations of RMP and INH were 1.0 μg/ml and 0.1 μg/ml for MGIT and 40.0 μg/ml and 0.2 μg/ml for LJ.

Results: Concordance rates for RMP and INH between two methods were 99.7% and 94.5%, respectively. There were 25 discrepant results in total. Among 165 isolates resistant to INH in MGIT system, 21 (12.7%) were susceptible to INH in LJ. Three RMP-susceptible isolates with MGIT were resistant to RMP with LJ. Statistical analysis with McNemar's test revealed that INH DST results of MGIT were significantly different from LJ absolute concentration method ($P = 0.000$).

Conclusions: Correlation of MGIT and LJ method for RMP was very high. However, it was shown that MGIT system apparently detects more INH resistance than LJ method. Therefore, further study for discrepant isolates is necessary to find causes of systemic difference between MGIT system and DST using LJ.

PC-531-01   Manual MGIT system for the detection of *Mycobacterium tuberculosis* in a developing contry

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Background: Bacteriological confirmation and diagnosis of *M. tuberculosis* is important for tuberculosis (TB) control. Manual Mycobacteria Growth Indicator Tube (MGIT) has been implemented in developing countries. We evaluate the performance of manual MGIT (mMGIT) compare with traditional Löwenstein-Jensen (LJ) solid media and clinical diagnosis.

Methods: Data from respiratory symptomatic TB suspects enrolled in parallel diagnostic trials during 2007–20011 were included. After less that 48 hours of store at 4°C, samples were decontaminated with NALC-NaOH method and inoculated in LJ and MGIT media. Lectures for culture where done daily

for mMGIT, using BD BACTEC MicroMGIT Fluorescence Reader; and twice per week for LJ. All isolates were tested for *M. tuberculosis* complex using Capilia. Negative cultures were reported after 8 weeks. Two sputum samples were process for each patient, each sample was tested using smear, LJ and mMGIT. Assessment of sensitivity, specificity, PPV, NPV, increase yield of a second mMGIT and time to detection (TTD) in days for both cultures was performed. A composite gold standard was based on LJ culture and onset of TB treatment as clinical diagnosis.

Results: We evaluated 1514 patients and 4228 samples. Samples assessment: 52 (1.2%) samples (18 non *M. tuberculosis*, 32 insufficient data) were not included. Contamination was observed in 57 (1.36%) samples using mMGIT. Sensitivity, specificity, PPV and NPV of mMGIT culture were 99.2%, 99.5%, 99.4%, 99.3%, respectively. TTD was 11.8 ± 6.9 for mMGIT and 22.9 ± 8.1, ($P < 0.05$). Patient assessment: a first mMGIT culture has sensitivity 90.5% (95%CI 88.3–92.3), specificity 98.5% (95%CI 97.1–99.3), PPV 99.8% (95%CI 99.1–99.9) and NPV 87.2% (95%CI 84.4–89.7). A second mMGIT culture had an increased yield in sensitivity of 1.7%, performance of both mMGIT was sensitivity 92.2% (95%CI 90.2–93.8), specificity 96.9% (95%CI 95.2–98.2), PPV 99.4% (95%CI 98.6–99.8) and NPV 89.1% (95%CI 86.1–91.4).

Conclusion: Manual MGIT shows a good performance, and is a good alternative to implement liquid cultures in low income restrictive setting. Low contamination rate, higher sensitivity and shorter TTD after implementation will offer rapid and reliable tools for *M. tuberculosis* detection and susceptibility testing.

PC-532-01   MODS assay for primary diagnosis of tuberculous meningitis and HIV-associated pulmonary tuberculosis in Indonesia

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Background: Bacteriological confirmation of HIV-associated pulmonary tuberculosis (TB) and tuberculous (TB) meningitis is difficult, and mortality is very high. Microscopy is insensitive, standard solid culture is slow, and molecular methods and liquid-culture are often too expensive to be implemented routinely. The recently developed MODS assay may be a good alternative. We compared MODS culture with microscopy and solid culture for diagnosis of HIV-associated pulmonary TB and TB meningitis in an Indonesian setting.

Design/methods: Two groups of patients over a two-year period in a referral hospital in Indonesia were included. The first group consisted of 167 consecutive HIV-infected patients presenting with suspected pulmonary TB. The second group consisted of 88 patients with clinical suspicion of TB meningitis. Sputum samples from HIV-associated pulmonary TB patients and cerebrospinal fluid (CSF) from patients with TB meningitis were analyzed using Ziehl-Neelsen (ZN) microscopy, culture on solid medium (Ogawa), and MODS culture.

Results: MODS showed the highest detection rate in both patient groups. Among HIV-associated pulmonary TB patients, positivity of MODS was 31.2% compared with 26.9% for Ogawa and 20.6% for ZN. Among TB meningitis patients, positivity of MODS was 41.2% compared with 38.8% for Ogawa and 8.3% for ZN. The median time to culture positivity was significantly shorter for MODS compared to Ogawa, both for sputum (median 11 vs. 21 days) and CSF (14 vs. 33 days) (see Figure). In 14 days, MODS detected significantly more cases compared with Ogawa in both patients group (79.2% vs. 2.4% and 68.6% vs. 0%, respectively). Laboratory staff readily used MODS after two weeks of training.

Conclusion: We were able to implement MODS culture as a robust, sensitive, and rapid method for diagnosis of HIV-associated pulmonary TB and TB meningitis in a hospital setting in Indonesia. Further studies may be needed to assess the feasibility of MODS culture in other settings and assess its impact on case detection and timely treatment of both forms of TB.
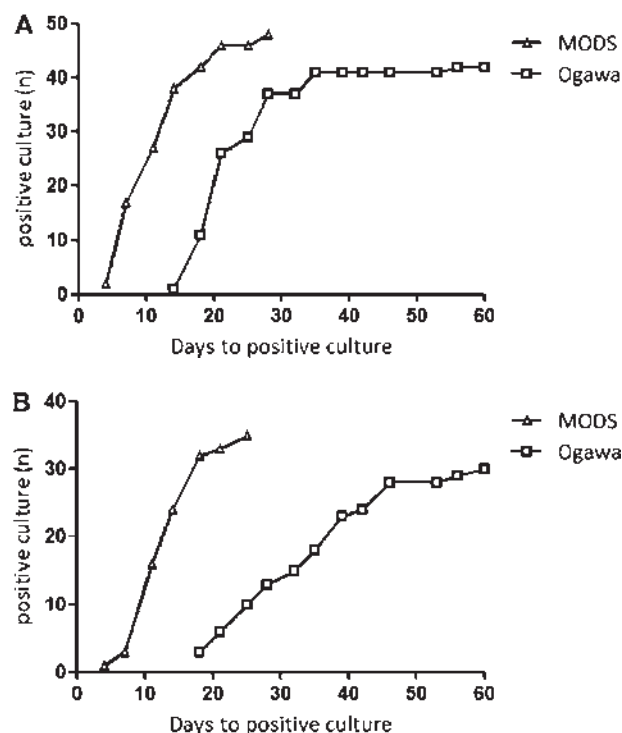
Figure   Positive culture results (*n*) in time for MODS (Δ) and Ogawa ($\square$) among patients with suspected HIV-associated pulmonary TB (**A**) and suspected TB meningitis (**B**).

PC-533-01   Blood agar as a suitable media for *Mycobacterium tuberculosis*

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Background: A comparative study was carried out to check the growth rate and colony morphology of *Mycobacterium tuberculosis* between LJ media, blood agar and chocolate agar.

Design/methods: 50 sputum smear positive samples including 10 multidrug-resistant samples were collected and processed according to Nalc-NaOH concentration method. These were then inoculated in parallel on LJ medium, blood agar, chocolate agar in slants as well as on plates and incubated at 37°C. Growth rate was checked on daily basis.

Results: All isolates recovered on LJ medium slants (100%) as well as on blood agar slants (100%) while 44 on chocolate agar (88%). Growth rate of *M. tuberculosis* on blood agar slants were 12 ± 4.5 as compared to 18 ± 5 on LJ medium slants.

Conclusion: Blood agar also appeared suitable medium for culturing of *M. tuberculosis* because of more colonies on it as compared to LJ medium. This study indicates that in resource limited setting blood agar can also be used for the isolation of *M. tuberculosis*.

TOBACCO BURDEN, SURVEILLANCE AND PROGRAMME IMPLEMENTATION

PC-534-01   Gender roles in tobacco expenses in Pakistan

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Background: Several studies suggest that limited household resources may not deter tobacco use. Gender roles may explain this anomaly, e.g., a male household member who is the breadwinner can prioritize tobacco purchase over other consumables; relationships rarely investigated before. This study assessed associations between tobacco expenses and gender role in household purchases in a low-income country.

Design/methods: Study setting was Pakistan. Data on monthly household expenses and on tobacco were extracted from a nationally representative sample ($n = 15\,512$ households) interviewed in 2005–06. Tobacco products were either cigarettes or raw tobacco (smoked or chewed). Two logistic regression models were constructed where outcome variables were the proportion of tobacco expense in overall monthly household expenses; it was coded as '0' if they were <3% and '1' if ≥3% on either cigarettes or raw tobacco. The main independent variable was a four category response about who decides the household purchases: a) women herself, b) male head of family, c) male with other women, d) male with other members during last year. Analyses were adjusted for household factors such as persons per household, male-female ratio, room occupancy, monthly income, and access to healthcare workers.

Results: Nearly one third (35.2%) of all households spent on cigarettes and one in five (17.7%) spent on raw tobacco. Tobacco expenses accounted for 3–6% of average monthly expenses in 15.4% (95% Confidence Interval [95%CI] 14.5–16.3) of all households. In 9.8% (95%CI 8.8–10.7) of all households, tobacco-related expenses were over 6% of the monthly expenses. Tobacco expenses were likely to be higher than ≥3% of the household expenses where male head of the family made decisions on household purchases including cigarettes (adjusted odds ratio [OR] 1.30, 95%CI 1.06–1.59) or raw tobacco (OR 1.72, 95%CI 1.11–2.65) compared to households where females made decisions.

Conclusion: Gender inequalities might be contributing to high tobacco use in Pakistani households. Our findings need to be carefully accounted in efforts for reducing inequalities as female empowerment itself could be a risk factor for tobacco use.

PC-535-01   Smoke free pilot district headquarters: results of a compliance survey in Tamilnadu, India

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Background: State of Tamilnadu presents an out standing model for tobacco control in India. Article 8 of FCTC and section 4 of COTPA, 2003 prohibits smoking in public places in India in order to protect non-smokers. The law mandates that signages inform people that public places are smoke free. In Tamilnadu, enforcement squad has been formed at various levels to monitor the implementation of COTPA, 2003. Any one found smoking can be fined by a notified officer, including the person in charge of the premises. The Department of Health, Government of Tamilnadu in the last one year carried out capacity building and traning of enforcers; sensitised and created public awareness through various forms of media, and enforcers have fined violators both individuals and premises managers with more than 5000 challans. Present study was conducted to assess the compliance of smoke free rules and assess the respective district head quarters (Kancheepuram, Vellore and Thiruvallur) for preparedness of smoke free declaration.

Design/method: An   unobstructive   cross-sectional

study was done in 1101 public places across 3 intervention district head quarters. Sampled public places were evaluated for five core criteria, i.e., absence of active smoking, presence of signage, absence of tobacco odour and cigarette and bidi stubs, and no sale of tobacco within 100 yards and tobacco free educational institutions. The bench mark of 80% was kept for smoke free declaration.

Results: In 3 district head quarters, compliance to signage was observed in more than 80% public places. 100 per cent of compliance to no sale of tobacco products around 100 yards. More than half of the public places denote absence of cigarette and bidi butts. Over 75% of public places were found free of tobacco smell.

Conclusion and recommendation: The implementation of Sec 6 of COTPA, 2003 provides way for declaration of all educational institutions in three districts to make 100% compliance to the above specified criteria. One of the effective criteria used in Tamilnadu is including 'Tobacco Free Policy' in issuing sanitory certificate to the educational institutions. And enforcement squad is the specific model in Tamilnadu used for monitoring the implementation of COTPA, 2003.

PC-536-01   Tobacco control

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Background and challenges to implementation: The National Program on Tobacco Control was officially launched in January 2000 with the drafting and approval of the National Policy on Tobacco Control and Plan of Action. The National Tobacco Control Committee was formed in March 2002. Enforcement and Implementation are major challenges that require a clear, pragmatic and action oriented approach. The program needs regulations with priority on: implementing pictorial health warnings on all tobacco products; all indoor public places 100% smokefree; ban on all forms of tobacco advertising and promotion; education, communication, training and public awareness to support the strengthened legislation and enforcement measures; setting appropriate price and tax policies; and identification and mobilization of financial and human resources.

Intervention or response: Key strategies of national tobacco control program are as follows:

- Strengthening national laws and regulations on tobacco control
- Establishing a Tobacco Control Section under Public Health Division and expanding infra-structure at national and sub-national level
- Building partnership with related ministries and stakeholders
- Building public awareness on harmful of tobacco use and exposure to secondhand smoke and

strengthening policy advocacy for tobacco control measures.

Results and lessons learnt: With the 2006 Tobacco Control Law and multisectoral efforts towards effective enforcement, there has been some decline in tobacco use. However, tobacco use is still unacceptably high, with 45% of men and 8% of women smoking. Equally alarming is high smokeless tobacco use (51% men; 16% women) including by youth. Exposure to second-hand smoke (SHS) remains high. Continued support with improved strategy is essential in the struggle against tobacco epidemic.

Conclusions and key recommendations: Myanmar Tobacco Control Program needs to set in place mechanisms to strengthen implementation and enforcement of existing tobacco control laws in Myanmar and to develop new regulations needed on key tobacco control policies to bring them in line with WHO FCTC provisions and best practices. The program is also required to build Myanmar's capacity for tobacco control in the long-term.

PC-537-01   Fining and shaming: a two-pronged approach to ensure rapid compliance with tobacco control law in Jodhpur

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Background: Many jurisdictions in India have been declared Smoke Free on the basis of evaluation framework and criteria developed by experts in 2009. One of the key criteria for declaration of a jurisdiction as 'Smoke Free' is installation of signages in more than 90% of surveyed public places whether it is private or government owned. Additionally, the criteria included the initiation of enforcement mechanism to curb and fine violators of the law. Traditional approach has relied on persuasion of private establishments to put up the signage at their own cost and centralized procurement at the district level and subsequent installation in government owned public places. However; this process is time consuming and initial smoke free campaigns in India had duration of 2–3 years based on the size of the city or the district.

Intervention: A review of the progress of 'Smoke Free Jodhpur' in Oct 2012 by the new District Collector led to setting a timeline of 15 days for installation of signage's in all government offices of Jodhpur city. Written orders were issued to all district level departmental heads and verbal orders were conveyed during the review meeting chaired by the district collector. Signage designs were uploaded on www.jodhpur.nic.in. After the expiry of 15 day period, the Distric Nodal Officer commenced observing compliance by visiting offices housing the district level officers who headed that particular department. If the mandated signage was not found, the DNO fined the senior most departmental official with the maximum

fine permitted by the law (Rs 200). In the evening, list of officials fined were compiled and released to journalists for press coverage.

Result: The unorthodox measures introduced by the District Administration were successful in meeting the short term objectives of ensuring installation of 'No Smoking' signages in all government offices. Independent observations indicate that these measures have prompted the private sector to make efforts to comply with the law.

Conclusions: By setting an example of adherence with the government sector, the credibility and public support for Smoke Free campaigns launched by district administration is enhanced. High profile fining of senior government officials serves as a deterrent to violations of the national law and enables rapid compliance. This has a ripple effect on the private sector. Overall, this approach shows promising signs of expediting the smoke free campaign.

PC-538-01   Medical students in Sudan: smoking cigarette despite knowing the hazards

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Background: Cigarette smoking is a leading cause of preventable death worldwide. Smoking is responsible for 30% of deaths of people aged between 30–50 years and 12% of total deaths worldwide (1). The objectives of this study were to determine the prevalence of cigarette smoking among medical students of the National Ribat University and to determine social factors related to smoking.

Design/methods: A cross-sectional, community-based study conducted in the National Ribat University, Sudan. Systematic sampling was considered, size of the sample was calculated as 500. Data was collected by a pre-coded and pre-tested questionnaire and analyzed by SPSS version 16. A written informed consent was obtained from all participants.

Results: The prevalence of smoking among medical students was 19.1%, male female ratio was 7:2. Results showed that 72.3% of the smoker used to smoke on daily bases. The majority of smokers 68% acquired this habit after entering the university. The study showed that 57% of the smokers tried to quit smoking, while 43% of them never tried but 57.5% of them had the desire to quit. Among the smokers in our study group, 26.7% had a family member(s) who smokes whereas for those who had never tried smoking only 23.3% had a smoker family member(s).

Conclusion: The study concluded that the prevalence of smoking in the universities in Sudan is high. Universities became areas for promotion of smoking rather than preventing it. The ability of smokers to quit is advised to be taken as opportunity for serious cigarette cessation programs.

Reference
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PC-539-01   Four years of a National Tobacco Control Programme in India: a critical review

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Background: India launched its National Tobacco Control Programme (NTCP) in 2007–08 in 9 states (18 districts) and 12 states (24 districts) in 2008–09 with the objectives to create public awareness about the harms of tobacco use and institutionalise enforcement through effective implementation of national legislation. The present study was conducted with the objectives to review the programme critically and identify the challenges.

Design/methods: Secondary data analysis and interviews of NTCP staff on semi-structured questionnaire was done in 2010 and 2011.

Results: Mass media campaigns, capacity building, GATS India survey and establishment of toll free helpline number were few of key activities done at national level. All states except one has established state tobacco control cell and steering committees at state and district steering committees. Enforcement mechanism established in 17 states (80%). 29 out of 42 districts have tobacco cessation facilities in district hospitals. Few objectives are yet to achieve, the product testing labs could not be established. Operational guidelines are in a draft stage. NTCP is still a vertical program. Competitive inter-ministerial interests, large workforce employed in tobacco sector and plethora of tobacco products keep posing challenges to NTCP.

Conclusion: Despite all constraints, NTCP has resulted considerable rise in public awareness about harms due to tobacco use. Key stakeholders have been sensitized to take the issue further.

PC-540-01   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 Cigarettes and Other Tobacco Products Act (COTPA) exists since 2005 and aims at protecting all the people in our country; people still smoke in public places.

Aims: To explore perceptions about smoking and in turn about COTPA (smoke-free law) among people residing in Mohali district.

Materials and methods: 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: We estimated proportions and tested for significant differences by residence, smoking status, literacy level and employment level by means of the chi-square statistics. Statistical software SPSS for Windows version 20 was used for analysing data.

Results: The overall prevalence of current smoking among study participants was 25%. Around 96% were aware of the fact that smoking is harmful to health, 45% viewed second-hand smoke to be equally dangerous as active smoking, 84.2% knew that smoking is banned in public places and 88.3% wanted the government to take strict actions to control the menace of smoking. Multivariate logistic regression analysis showed that people aged 20 years and above, unemployed, urban, literate and non-smokers had significantly better perception towards harms of smoking. The knowledge about smoke-free law was significantly better among males, employed individuals, urban residents, and literate people.

Conclusions: There was high knowledge about deleterious multi-dimensional effects of smoking among residents and a high support for implementation of COTPA. Efforts should be taken to make Mohali a 'smoke-free district'.

PC-541-01   Assessing compliance with tobacco control legislation at point of sale: results of a subnational survey in India

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Background: Section-5 of Indian tobacco control legislation (COTPA) prohibits advertisements of tobacco products in all kinds of media (print, electronic, television and cinema and outdoors etc.) However, the law permits advertisements of tobacco products at the point of sales (PoS) but under certain conditions. Tobacco companies have been violating the law by displaying the oversized advertisement boards, using promotional messages, also backliting the display boards. The Point of sales tobacco advertisements violations has been significantly increased in recent years. The present study was conducted to measure the compliance of prohibition of advertisement at 'point of sale' as defined under Section-5 of COTPA 2003 and subsequent rules.

Design/methods: The study was done in February–March, 2013 across three different Jurisdictions in India (District Mohali in Punjab, District Vadodara in Gujarat and District Chennai in Tamil Nadu). Total 1324 tobacco vendors were randomly selected according to PPS in all the three jurisdictions and assessed according to the pretested observational checklist by the trained field investigators.

Results: Near all tobacco vendors (94%) displayed tobacco products advertments in some or other form at the Point of Sale (PoS). Display boards were present in more than two third of PoS (66%). Besides display boards, there were other types of advertments such as posters (34%), stickers (27%) dangles (22%), promotional gifts (17%), product showcases (14%). Gross violations were observed across three jurisdictions; display boards were backlit/illuminated (56%), depicted brand name/pack shot (92%), displayed promotional message (34%) and 92% exceeded the allowable size of 60×45 cm. Health warning was displayed on display board (86%), however, in 34% boards; warning did not comply with the specification (text, design, color and size).

Conclusions: The point of sale (PoS) has become the strategic locations for the tobacco industries to advertise their products. Provision under law to permit the PoS advertisement with certain restriction is looked as a loophole and a major menace now. This is a time for the policy makers to remove this loophole from the existing law and enforce the provision in its true letter and spirit.

PC-542-01   Bottom up approach ensure sustainability of smoke free environment in public places

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Setting: GATS says around 40 percent people use tobacco in one or other forms in the state of Madhya Pradesh, India. 34% in public transport, 32% in workplaces and 40% people in public places suffer from passive smoking. Smoking, entertainment of guest by providing bidi/cigarette is an old practices, senior citizens are not been asked to stop out of respect, imposition of law through government machinery in rural periphery is not easy. People are also not aware about ill effect of passive smoking.

Why bottom up approach? Elected public representatives at village level have greater control and impact on emotions and behaviour of people. Recognized body at village level are headed by people from different background such as religious leader, elected representative, government servants. Directives from top can provide legal provision to government machinaries but can not ensure behavioural changes or effective implementation of the provisions of law unless people are involved and convinced. The traditionally and formally elected heads are the role model, their practices and announcements have greater impact on peoples behaviour and practices. Also helpful in providing conducive environment to bureaucrats and

politicians to implement the law without any bias and mass resistance.

Methodology: Formation of state and district level tobacco control committees, formation of monitoring team, capacity building of enforcers, campaign, involvement of civil societies, use of right to information tool, compliance study, advocacy with top bureaucrats and policy makers, inter departmental coordination and community monitoring etc.

Efforts and results: Orientation of public representatives, members of village level committees including religious leaders helped in declaring public places of 6400 villages of six district/city smoke free. The biggest achievement is not that the places have been declared smoke free but is being sustained, the local community and elected representatives feel responsible and accountable. The self-regulatory mechanism by local community do not need much financial and administrative support.

Conclusion: Bottom-up approach is a positive process, ensures active involvement of community and local heads in planning, implementation, monitoring and providing ownership, therefore results into self sustainability of the process.

PC-543-01   Media advocacy for implementation of stronger pictorial health warnings on all tobacco packs in India

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Background and challenges to implementation: Pictorial health warnings are an effective measure to warn tobacco users of the harm of tobacco use. Pictorial warnings on packaging of tobacco products is legally mandated as per India's national tobacco control legislation Cigarettes and Other Tobacco Products Act (COTPA 2003).

Intervention or response: Using earned media to create pressure on policymakers and to put indirect pressure on the government to maintain compliance of pictorial health warnings. The strategy was to ensure that news items or stories come out to attract the attention of the government and the public. To do so, VHAI decided to increase consumer awareness about the issue of pictorial warnings in the news through a sustained strategy of media engagement. We increased our interactions with the media, both on a one-to-one basis and through Press Meets and Media Sensitization Workshops from January–December 2010. Brief yet accurate press releases were also issued to the print media as templates for stories.

Results and lessons learnt: A total of 20 press meets were held on pack warnings in Delhi and 15 states of India. To sustain the media's engagement with the issue, over the course of a year, about 25 to 30 press releases were shared with journalists on the pack warn-ing in Delhi and 15 states. This strategy of media advocacy resulted in nearly 150 stories in National and Vernacular Media.

Conclusions and key recommendations: The government notified a completely new set of visuals to serve as pack warnings from December 1, 2010. The media was sensitized and in the process, a personal rapport began was developed with journalists. VHAI's state level network, tobacco control partners and linkages with vernacular media helped to make the pack warning issue an all-India campaign.

PC-544-01   Baseline survey about tobacco consumption among PLHIV in Bangladesh

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Background and challenges to implementation: Tobacco consumption is a well known contributor to excess morbidity and mortality. The prevalence of tobacco consumption among PLHIV is significantly higher than the national average in some developed countries. Tobacco consumption is associated with an increased risk of respiratory disease, cardiovascular disease and malignancies. As survival improves, interventions targeting tobacco cessation are increasingly important in reducing morbidity and mortality. To establish tobacco control interventions for PLHIV, baseline survey about tobacco consumption is needed. Estimated figure of PLHIV in Bangladesh is around 7500. Cumulative number of reported PLHIV in Bangladesh as of 1 December 2012 is 2871. Of them 1390 is registered with Ashar Alo Society (AAS), a self help group registered in 2002 as a community based organization. It has 3 centers (Dhaka, Chittagong and Sylhet).

Intervention or response: A questionnaire was administered to PLHIV in 3 service center during November–December 2012. A total 425 respondent participated in the study. 61% was male and 39% was female. Average age was around 38 years. 85% was married, 6% unmarried and rest 9% was widow/widower. 66% was from rural area, 18% from sub-urban area and rest 16% was from urban area. 40% was illiterate, 34% was below 10-grade schooling and rest 26% was above 10-grade schooling. 15% has ever diagnosed as having tuberculosis (8% pulmonary and around 7% extra-pulmonary). 75% is currently receiving anti-retroviral therapy (ART) for their HIV status.

Results and lessons learnt: 20% (86) of respondent is currently consuming tobacco through smoking only, 22% (93) consume smokeless tobacco and 8% (33) consume tobacco in both smoke and smokeless form. 25% (106) is not consuming tobacco in any form and they are not exposed to second hand smoke (SHS), 7% doesn't know about their SHS status but

18% (76) is exposed to the SHS either at their home or at workplace. 45% is exposed to second-hand smoke in public places and 55% is exposed to SHS at workplace (46% male and 9% female). 45% is exposed to SHS at home (9% male and 36% female). The entire current smokeless tobacco consumer consumes chewing tobacco (zarda, sada pata, gul, khoinee) only but no snuffing tobacco.

Conclusions and key recommendations: This cross-sectional study reveals that tobacco consumption among PLHIV in Bangladesh is higher (50%) than national.

PC-545-01 Second-hand smoking in households and pulmonary tuberculosis: a systematic review and meta-analysis

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Background: The exposure to second-hand smoke (SHS) in households has been implicated as a risk factor for acquiring tuberculosis (TB) and worsening of its treatment outcomes. We undertook a systematic review and meta-analysis to assess the association between SHS in households on (i); non-smoking people of all age groups and the risk of acquiring TB infection and disease and (ii); non-smoking TB patients on their disease outcomes (including sputum conversion, treatment success both cured and completed, death, relapse, and recurrence). Although tuberculosis and exposure to SHS exposure is common in several countries, this review is likely to be relevant to those where both TB and tobacco use is high.

Design/methods: We conducted a systematic review and meta-analysis of comparative epidemiological studies (case-control, cohort and cross-sectional designs) reporting effect estimates and 95% confidence intervals on the association between SHS and TB acquisition, disease and outcomes during January 1991 to March 2013. MEDLINE, EMBASE, PsychINFO, reference lists of the included studies, citations in the Journal of International Union against TB and Lung Diseases, Tobacco Control, Nicotine and Tobacco Research, Addiction, and the Conference Proceedings Citation Index: Science (ISI) on Web of Knowledge were searched for a final inclusion of 33 abstracts for data extraction. No language restrictions were applied.

Results: Despite the limitations in the data available, moderate to strong association was observed between SHS and TB disease. However, there was limited evidence to support an association between SHS exposure in households and TB infection or TB disease outcomes in non-smoking TB patients.

Conclusion: Similar to active tobacco smoking, exposure to second-hand smoking in the households also predisposes to the development of TB disease.

Increased emphasis should therefore be given to tobacco control in national TB programs of the countries with dual burden of both tobacco use and TB. There is need for larger epidemiological studies to establish the causal association between SHS and TB acquisition as well as the effects of SHS exposure on TB outcomes in non-smoking TB patients.

PC-546-01 Strategic communication can make a big difference in the quality of life of PLHIV in Bangladesh

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Background and challenges to implementation: Baseline survey of Tobacco consumption among PLHIV in Bangladesh reveals that it is highly prevalent among people living with HIV (PLHIV). Ashar Alo Society (www.aas.org.bd) has been working for care and treatment services to the PLHIV in Bangladesh. Estimated figure of PLHIV in Bangladesh is around 7500. Cumulative number of reported PLHIV in Bangladesh as of 1 December 2012 is 2871. Of them 1390 was registered with Ashar Alo Society (AAS).

Intervention or response: During baseline survey total 425 respondents participated in 3 service center of AAS during November–December 2012. 61% was male and 39% was female. Average age was around 38 years. 85% was married, 6% unmarried and rest 9% was widow/widower. 66% was from rural area, 18% from sub-urban area and rest 16% was from urban area. 40% was illiterate, 34% was below 10-grade schooling and rest 26% was above 10-grade schooling. 15% has ever diagnosed as having TB. 75% is currently receiving antiretroviral therapy (ART).

Results and lessons learnt: This cross-sectional study reveals that tobacco consumption among PLHIV in Bangladesh is higher (50%). 18% of the respondents are exposed to SHS though they are not tobacco consumer in any form. Among the respondent who are exposed to SHS, 55% are exposed at workplace (46% male and 9% female) and rest 45% are exposed at home (9% male and 36% female). Exposure to SHS has no association with educational level of the respondent but 82% of them know that exposure to SHS will hamper their HIV treatment. The study also tried to explore respondent's knowledge regarding association between tobacco consumption and treatment interference of HIV, tuberculosis, other respiratory disease (RTI) and other disease. In multiple response 23% mention about HIV, 27% mentioned about tuberculosis, 7% mention about other respiratory disease, 19% mentioned about other disease, 65% of the respondent mentioned about all these disease and 2% mention that they have no idea about this association.

Conclusions and key recommendations: A multi-facet tobacco control endeavor including extensive family counseling and awareness building for the employer and workmate could save the non-consumer PLHIV from devastating impact of tobacco consumption and thus improve the quality of life of PLHIV.

PC-547-01 Socio-demographic determinants of smoking among women in Romania: implications for public health

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Background: After the change in 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 women. The present study aim was to explore the profile of Romanian women who smoke and to outline the tobacco control interventions needed to specifically address them.

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, using a standard core questionnaire, sample design, data collection and data management procedures. 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 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 health care providers were less likely to ask and advise patients with high educational levels about tobacco use. The proportion of 'heavy smokers' was largest among those less educated (46.8%). Despite the fact that 63.7% of Romanian women who are daily smokers are nicotine addicted, of those who attempted to quit only 8.2% used nicotine replacement therapy and 1.2% prescription medication.

Conclusion: We identified the main characteristics of Romanian women who are current smokers. This will offer support to both tobacco control experts and health professionals to tailor tobacco control policy and health education approach in Romania to specifically address women.

PC-548-01 Social marketing as a tool for increasing compliance with national tobacco control laws in rural Rajasthan of India

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Background: Tobacco causes nearly one million annual deaths in India. With the aim of reducing exposure to second hand smoke and to regulate tobacco sales near educational institutions, the Cigarette and Other Tobacco Products Act (COTPA) was enacted in 2003. Awareness about the specific provisions of COTPA amongst government officials and local elected representatives is low, leading to poor law enforcement at the district and sub-district level. One specific challenge is COTPA's requirement to display signs prohibiting smoking in public places and selling tobacco products to minors. This was worsened by poor access to the signage prescribed under COTPA.

Intervention: In response to this, Population Services International produced signage per COTPA specifications, retailing for Rs 20 each. To create demand for the signage in 960 project villages, PSI rolled out a 'Smoke Free Road Show' (Chetna Yatra). Using job aids developed by PSI, village headmen were detailed about the provisions of the law and were told that as per government law, they have the power to enforce COTPA by fining violators. PSI also educated key officials and tobacco retailers about different provisions of COTPA.

The campaign stressed the adherence to laws prohibiting smoking in public places and the installation of mandatory signage. Citizens were told that if universal adherence is achieved, the district could be officially declared as 'Smoke Free' by the government.

Results: Within a period of 2.5 months, the 'Chetna Yatra' campaign created a buzz in favour of 'Smoke Free' declarations. One hundred and eighty-eight elected village heads declared their villages as being 'Smoke Free' and 'Compliant with Section 6(a)' after verifying installation of COTPA mandated signage in all public places and tobacco selling shops. The social marketing approach involving selling of signage can accelerate compliance with national laws and possibly aid in discouraging public smoking or selling tobacco to minors.

Conclusion: 'Chetna Yatra' is a novel social marketing approach for creating awareness among key stakeholders and increasing enforcement of tobacco control legislation. By publicizing the law provisions and providing an opportunity for applying the learning by facilitating and checking installation of signage, the yatra offers a new way of building local capacity, specifically around knowledge and applications of the law. It seals the learning transfer between NGOs and to key influencers.

PC-549-01 Acute effect of hookah smoking on Ankle Brachial Index

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Background: According to increase of hookah consumption in Iran we evaluated effect of hookah smoking on ankle brachial index. This index is a non invasive measure of peripheral artery disease.
Design/methods: This descriptive cross-sectional study was done on 29 participants. Ankle brachial index was measured before and after of hookah smoking by using an automatic device. Data were analyzed using SPSS software.
Results: 29 persons participated in this study. All of them experienced hookah. The mean age of them was 32.2 ± 9.09. The mean of ABI before hookah smoking was 1.06 ± 0.1 whereas it was 0.88 ± 0.1 after hookah consumption ($P = 0.001$).
Conclusion: Hookah smoking had acute effect on ankle brachial index. This index reduced after hookah consumption significantly. Therefore this type of tobacco product could be associated with the possibility of coronary artery disease.

PC-550-01 A Global Youth Tobacco Study among 7th, 8th, 9th and 10th grade students in Myanmar, 2011

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Background: The study aims to reassess the health, knowledge and practice of students, (7th, 8th, 9th and 10th Standards) after the introduction of National Tobacco Control program for 10 years. This study includes data on prevalence of cigarette, cheroots, other tobacco and betel quid with tobacco use as well as information on five determinants of tobacco use: access, exposure to secondhand smoke (SHS), cessation, media and advertising, and school curriculum. The study under the Global Tobacco Surveillance System provides a good opportunity to monitor the implementation of National Tobacco Control program activities in line with MPOWER package.
Design/methods: A multi-stage, school-based, two-cluster survey ($n = 1652$, 7th, 8th, 9th and 10th Standard) was conducted in 25 basic education middle and high schools of Myanmar in 2011, using a pre-tested modified questionnaire based on the Global Youth Tobacco Survey questionnaire developed by CDC, USA. A total of 1652 students ages 13–15 participated in the study.

Results: Between 2001 and 2011, a significant reduction in the proportion of students currently smoked cigarettes is observed (a fall from overall prevalence among 13–15 year olds of 10.2% to 6.8%) but reported use of other tobacco products had increased during the period from 5.7% to 9.8%. The ability to purchase cigarettes in a store had reduced significantly from 72.9% to 39.2%. There is no change in percent of students receiving education on dangers of tobacco. One-third of the students live in homes where others smoke, and one-third of the students are exposed to smoke around others and outdoor public spaces.
Conclusion: Myanmar Youth Tobacco program should strengthen in all schools to be 100% tobacco-free and also incorporate training of school personnel on tobacco control, specifically youth-focused programs as joint efforts between Ministry of Health and Ministry of Education in collaboration with related ministries. Enforcement of the national legislation on tobacco control needs to be strengthened, and the National Tobacco Control Program needs to be more comprehensive incorporating measures to reduce smokeless tobacco use and other non-cigarette tobacco products.

ABSTRACT PRESENTATIONS SATURDAY 2 NOVEMBER 2013

ORAL PRESENTATION SESSIONS

MDR-TB: CLINICAL COURSE, REVERSIONS, ACQUIRED DRUG RESISTANCE

OP-175-02   Predictors and significance of sputum smear and culture reversion in MDR-TB in Karakalpakstan Republic, Uzbekistan

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Background: Médecins Sans Frontières and the Ministry of Health has treated tuberculosis (TB) in the low-HIV, high second-line drug (SLD) -exposure setting of Karakalpakstan since 1998. The management of cases of multidrug-resistant (MDR) -TB who 'culture convert' then 'revert' to positive again is challenging: current practice requires performance of repeat cultures and drug-sensitivity testing (DST) (as well as adherence optimisation), and failing patients may wait up to four months before their treatment is modified. Conversely, some patients have intermittent positive cultures of ambiguous clinical significance and achieve subsequent cure without treatment adjustment. The ability to better predict which patients are failing treatment may facilitate early appropriate therapy modification. We estimated the association of smear reversion with culture reversion, the predictors of culture reversion and described treatment outcomes according to culture reversion.

Methods: This is a retrospective analysis on culture-positive, pulmonary, DST-confirmed MDR-TB patients, enrolled on treatment between 01/01/08 and 31/07/11 from the MSF database (Epi Info 6 (Epi 6) and analysed in STATA v.9). Culture reversion was defined as positive cultures in two consecutive months after culture conversion; smear reversion as positive smears in two consecutive months after smear conversion. Unsuccessful outcomes were defined as death, failure or defaulter; successful outcomes as cure and treatment complete.

Results: Of the 807 MDR-TB patients who culture converted, 69 (8.6%) subsequently culture reverted.

Smear reversion occurred before or simultaneously to culture reversion in 10/69 cases (14.5%). Smear reversion was more likely to occur in patients who culture reverted than those who did not (OR 18.1, $P = 0.00$). No significant association between adherence and reversion was found (OR 0.95, $P = 0.61$). Of the 69 patients who reverted, 32 (46.4%) had adherence 90% during treatment. Of the patients who reverted, 80.0% had an unsuccessful outcome compared with 21.2% of patients who did not revert (OR 14.8, $P = 0.00$).

Conclusion: Smear reversion does not precede culture reversion consistently to make it a useful clinical indicator. The association of culture reversion with unsuccessful outcomes in MDR-TB necessitates prompt clinical response, without awaiting DST evidence of amplification. Until novel TB drugs become available, culture reversion should be managed with empirical treatment reinforcement.

OP-176-02   Final 120-week results of a Phase II randomised, double-blind, placebo-controlled study of 24-weeks bedaquiline treatment for MDR-TB (C208)

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Background: Bedaquiline (TMC207, BDQ) is a diarylquinoline with a novel mechanism of antituberculosis action. In a Phase II randomised, double-blind study (NCT00449644 Stage 2), BDQ accelerated sputum culture conversion in patients with multidrug-resistant tuberculosis (MDR-TB) vs. placebo (median time to conversion: 83 vs. 125 days, respectively) when added to a background MDR-TB regimen (BR) over 24 weeks (IUATLD 2010). We report the final 120-week results.

Methods: Patients with smear-positive MDR-TB received 400 mg BDQ once daily for 2 weeks, followed by 200 mg 3 times a week for 22 weeks (79 patients) or placebo (81 patients) with a BR. The primary efficacy endpoint was confirmed sputum culture conversion in liquid broth. Sputum culture, adverse events, biochemical parameters and electrocardiography were

monitored at regular intervals. Patients were followed for a total of 120 weeks from baseline.

Results: Patients were predominantly male (63%) with a median age of 34 years. Cavitary TB was present in 80%, and 15% were HIV-positive with a median CD4 count of 454.5 cells/mm^3. The most frequent background antibiotics used were pyrazinamide, ethambutol, ethionamide, kanamycin/amikacin and ofloxacin. BDQ increased the culture conversion rate compared with placebo at 120 weeks from 43.9% to 62.1% ($P = 0.035$). The overall incidence of adverse events was similar in both groups. In the BDQ group, mean absolute QTcF values generally increased vs. reference over 24 weeks. Changes were apparent by Week 1, with mean increases >10 ms from Week 5 onwards and decreased after Week 24. The largest mean increase was 16.2 ms. No patient in the BDQ group and 6 patients in the placebo group developed pre-XDR-TB or XDR-TB during the study. Overall, 10 patients in the BDQ group and 2 patients in the placebo group died; 1/10 BDQ patients died in the first 24 weeks and 9/10 died after 24 weeks (median 344 days after last BDQ intake; range 89–911 days). No discernible pattern of deaths was observed, and no death was considered related to study treatment by the investigator. The main cause of death was TB (5 patients in the BDQ group and 1 in the placebo group).

Conclusion: The addition of BDQ to a BR resulted in a higher culture conversion rate over 120 weeks, indicating that response at 24 weeks may be a reliable predictor of durable cure at 120 weeks. BDQ was generally well tolerated. Efficacy and safety of 9 months BDQ dosing will be further evaluated in a phase 3 study.

OP-177-02 Impact of treatment interruption patterns on MDR-TB treatment outcomes in Armenia and Abkhazia

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Background: Success rate of current regimen recommended by World Health Organization (WHO) for treatment of multidrug-resistant tuberculosis (MDR-TB) patients is poor. One of the main reasons is the high frequency of patients who default from treatment (>2 consecutive months of interruption). Many studies explored predictors of poor outcome, but very few assessed the impact of treatment interruptions other than those defining defaulter. We propose here to explore the effect of patterns of interruptions on treatment outcomes of MDR-TB patients.

Design/methods: We conducted a retrospective anal-ysis of routinely collected data in two MSF supported TB programmes in Armeniaand Abkhazia. Patients were included in the study if they were MDR-TB confirmed and enrolled before July 2010. Treatment outcomes followed the WHO 2008 definitions and were defined as successful if patient was cured or completed treatment, and unsuccessful if patient died, failed or defaulted from treatment. Univariate and multivariate logistic regression were fitted to explore the link between different patterns of interruption (frequency, duration and time between interruptions) and patient outcome.

Results: A total of 323 MDR-TB patients were included in the study. Among them, 141 (43.6%) had successful outcome and 182 (56.4%) had unsuccessful outcome: 28 (8.7%) died, 50 (15.5%) failed and 104 (32.2%) defaulted. For patients with unsuccessful (respectively successful) outcome, median number of interruptions was 7 [IQR 4–12] (7 [IQR 2–12]), median duration was 4 days [IQR 2–9] (3 days [IQR 2–5]) and median time between two consecutive interruptions was 10 days [IQR 4–28] (19 days [IQR 7–49]). First interruption occurred earlier for patients with unsuccessful outcome (65 days [IQR 29–148] vs. 143 days [64–336], $P < 0.001$). After adjustment for gender, history of TB treatment, baseline sputum smear-microscopy and drug resistance profile, adherence, incidence of side-effects and incidence of treatment interruption during treatment, having long (>3 days) interruptions duration (aOR 3.88, 95%CI 1.52–9.92) and short (<10 days) gaps between interruptions (aOR 5.68, 95%CI 2.32–13.90) remained independently associated with an unsuccessful treatment outcome. These results were consistent when defaulters were excluded from the analysis.

Conclusion: This study shows that even relatively short, repetitive, and at short intervals interruptions have a negative impact on the treatment outcome in particular when they start early in the treatment course.

OP-178-02 MDR-TB treatment success rate in a low-income country: Rwanda's PMDT experience, 2005–2012

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Background: Rwanda started managing multidrug-resistant tuberculosis (MDR-TB) in July 2005. This has been a quick response to the 2005 drug resistance survey done country wide which revealed that 3.9% and 9.4% of respectively newly diagnosed and retreatment cases are MDR-TB.

Methods: Patients bacteriological diagnosed with MDR-TB or approved by Rwanda's national second-line selection committee were treated under directly observed therapy with a standardized 20-month regimen of Km-Lfx (Ofx) -Cs-Pto-Z. All patients were provided with close follow-up care and monthly nutrition and transport support for the duration of treatment.

Results: From July 2005 to December 2012, 557 MDR-TB cases were enrolled on second-line TB treatment, giving on average 70 new cases per year. In 2006, 15.6% of enrolled patients died before initiating treatment; by 2011, this proportion had dropped to 6.2% and to 0% in 2012. Mean turnaround time for drug susceptibility tests decreased from 86 days in 2006 to 13.5 days in 2009 and to 3 days in 2011. Over the same period, mean duration of hospital admission decreased from 6.8 months to 3.3 months. Treatment success rate of 88.3% was achieved in the 2005–2010 cohorts (83% in 2005 and 89% in 2010).

Conclusion: In Rwanda, MDR-TB program was successful. This was a result of a strong political commitment, to overcome the problem. Due to challenges in cases detection and follow-up in ambulatory phase, decentralized MDR-TB units at provincial level are installed and new diagnostic tests are introduced in the referral and peripheral laboratories. The second drug resistance survey is being conducted. Given the experience gained, Rwanda hosts the East African Regional Center of Excellence in the Programmatic Management of MDR-TB.

OP-179-02   Bedaquiline as part of a multidrug-resistant tuberculosis therapy regimen: interim and final results of a single-arm, phase II trial (C209)

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Background: TMC207-TiDP13-C209 (NCT00910871) is a Phase II, open-label, single-arm trial of bedaquiline (BDQ, TMC207) as part of an individualized MDR-TB treatment regimen.

Design/methods: Patients $\geq$18 years with confirmed sputum-smear positive pulmonary MDR-TB (either newly diagnosed or previously treated) were enrolled. Patients with extensively drug-resistant TB (XDR-TB) were enrolled if their *M. tuberculosis* isolate was likely susceptible to $\geq$3 drugs for inclusion in the background regimen (BR). All patients received BDQ for 24 wks (400 mg qd for 2 wks, 200 mg tiw for 22 wks) with an individualized BR. BR only was continued for up to 18 more months. Patients were assessed for 96 wks after completion of BDQ. Results included here are from the interim analysis when all patients completed week 24 or discontinued earlier.

Results: 233 patients from 11 countries started BDQ. The modified intent-to-treat (mITT) population excluded 28 patients with drug-susceptible TB or negative MGIT cultures at baseline. The mITT population was 64.4% male, mean 34.9 years, 5.1% HIV+; 86.3% had previously received second-line drugs. Pre-treatment, 45.4% had MDR-TB, 21.5% pre-XDR-TB and 17.6% XDR-TB; 78.5% were resistant to pyrazinamide (mITT population). 89.7% of patients used fluoroquinolones as part of the BR, 52.8% ofloxacin and 33.9% levofloxacin (ITT population). During the BDQ administration period, 88.8% patients reported $\geq$1 AE (ITT population). The most frequent AEs (>10%) were hyperuricemia (13.7%), arthralgia (11.6%) and nausea (10.7%). Serious AEs (SAEs) were reported in 14 patients whilst on BDQ (6.0%); one SAE was related to BDQ (ECG QT prolonged). Two patients (0.9%) died during the BDQ investigational period; neither were considered possibly related to BDQ or had antecedent QTcF values >500 ms. Mean increases in QTcF at week 24 were larger in the 17 patients using clofazimine (31.94 ms) vs. those not (12.28 ms). At week 24, 79.5% had MGIT sputum culture conversion with a median time to conversion of 57 days. Conversion rates were 87.1%, 77.3% and 55.6% in patients with MDR-TB, pre-XDR-TB and XDR-TB, respectively. Conversion rates in patients with no lung cavitations, cavitations $\geq$2 cm in one lung, and cavitations $\geq$2 cm in both lungs were 88.6%, 75.2% and 73.1%, respectively.

Conclusion: Addition of BDQ to an MDR-TB regimen in a heavily pre-treated population was well tolerated and resulted in high sputum culture conversion rates after 24 wks of therapy. Final outcomes, 120 wks after starting BDQ, will be presented.

OP-180-02   Treatment outcomes from a collaborative multidrug-resistant tuberculosis treatment program in Ethiopia

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Background: Ethiopia is among the world's high-burden MDR-TB countries with the 2nd largest population in sub-Saharan Africa. Since February 2009, the Global Health Committee (GHC), in partnership with the Ethiopian Federal Ministry of Health (FMOH), has delivered and scaled up MDR-TB treatment using a community-based model adapted from the GHC's prior program implementation of MDR-TB and HIV and TB care in Cambodia. This is the main mechanism for MDR-TB treatment for the entire country.

Methods: We reviewed clinical characteristics and outcomes from the first cohort of patients to receive second-line drugs (SLD) for MDR-TB in Ethiopia. We included all patients with confirmed or suspected MDR-TB (based upon multiple previous treatment failures despite adherence). A standardized regimen containing capreomycin, levofloxacin, ethionamide, cycloserine and pyrazinamide was used for most patients. Food parcels were provided for all and in addition to monthly evaluation at the OPD, monthly home visits were performed. We examined outcomes for patients with at least 24 months of follow up.

Results: Since February 2009, 720 patients have been initiated on SLD for treatment of MDR-TB in Ethiopia in the GHC/FMOH program with 82 (11.3%) initiating treatment as an outpatient. As of April 2013, 194 patients had at least 24 months of follow-up. One hundred and eighty four (94.8%) had confirmed MDR-TB and 10 (5.2%) were suspected MDR-TB cases, 50.0% were women, and the median number of prior treatments was 2 (interquartile range: 2–3). 75.0% of patients had a body mass index (BMI) under 18.5 and 26.7% had BMI under 15.0. HIV screening was performed upon enrollment, and 46 patients (26.0%) were HIV-infected (median CD4: 217). Overall, 78.4% of patients were successfully treated (cured or completed treatment), 15.5% of patients died, 2.6% failed and 3.1% defaulted. Among the 46 HIV co-infected patients, 67.4% were successfully treated and 26.1% died.

Conclusions: Successful treatment implementation and scale-up of MDR-TB care in a moderate HIV burden setting such as Ethiopia can be achieved using a multidisciplinary model of care. Rapid expansion of MDR-TB access to care is underway throughout the country with plans to adapt this program to other resource-limited settings with growing MDR-TB epidemics.

THE PROMISE OF LIFE: INITIATING HIV TREATMENT

OP-181-02   Timing of antiretroviral therapy for HIV-TB co-infected patients and effects on tuberculosis treatment outcome in Zambia

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Background: Zambia is one of the high TB burdened countries and HIV/AIDS remains an important cause of death among TB patients. However the data is lacking in Zambia with regarding to the timing for initiation of antiretroviral therapy (ART) in relation to the start of anti-tuberculosis therapy.

Methods: This is a retrospective cohort study involving a record review of HIV-TB co-infected patients registered from 1st April 2010 to 30th June 2012. The data was collected from 9 facilities offering both TB and ART services in the three districts of Mazabuka, Livingstone and Monze in Southern province of Zambia. The data collection tool was sent to the TB program focal person in these districts, who transferred the data from treatment registers, treatment cards and ART patient files. The analysis looked at the time taken to initiate ART after commencement of anti-tuberculosis treatment by clinicians in the facilities and the treatment outcomes for those that started ART within 8 weeks (early initiation) and those that started ART 8 weeks (late initiation) after starting TB treatment.

Results: A total of 206 antiretroviral-naive HIV-TB co-infected patients were included in the study. 147 patients started ART within 8 weeks of anti-tuberculosis treatment while 59 started ART later. There is no significant difference in the average of baseline CD4 count between the group of early (177 cells/μl, 95% confidence interval (CI) 140–214) and late (162 cells/μl, 95%CI 55–270) initiation ($P < 0.735$). TB treatment success rate for the patients with early ART initiation was 91.1% (95%CI 86.5–95.8) and compared to the patients with late ART initiation (96.6%, 95%CI 91.9–100), there was no significant difference ($P < 0.173$). The mortality rate in patients with baseline CD4 counts <50 cells/μl

(14.8%, 95%CI 0.5–29.1) was significantly higher than in patients with CD4 counts > 50 cells/μl (3.6%, 95%CI 0.0–7.7; $P = 0.038$).

Conclusions: This is the first study in Zambia to investigate the effect of different timing of ART initiation for HIV-TB co-infected patients. However this study can not show that early ART initiation was associated with better TB treatment outcomes. Further investigation is required especially focusing not only on timing of ART initiation but also the client's status like CD4 count and longer range outcome as well.

OP-182-02   Effects of HAART on mortality of HIV-associated tuberculosis when CD4+ T cell counts are above 350 cells/mm³

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Background: Tuberculosis (TB) is a leading cause of mortality among HIV-infected individuals in the developing world. The World Health Organization recommends the use of HAART for all HIV-infected persons with TB, regardless of the CD4+ T cell count. Although there is abundant information on the benefit of HAART in HIV-infected TB patients with advanced immunosuppression, optimal management is uncertain for TB patients with CD4+ T cell counts > 350 cells/mm³.

Aim: To determine the effect of HAART on HIV-infected TB patients with preserved immunity, we compared survival distributions among HIV-infected patients with CD4+ count ≥ 350 cells/mm³ according to whether HAART was initiated or not during the treatment of TB.

Method: We enrolled 345 subjects with CD4+ count ≥ 350 cells/mm³ in a retrospective cohort study of HIV-infected patients with TB accessing anti-TB therapy between 2006 and 2012 in southern province, Zambia. The survival distributions were compared between patients who were started on HAART during TB therapy and patients not started on HAART. The primary end point was death from any cause. Mortality rates were estimated and compared using Kaplan-Meier methods; Cox proportional hazards analysis was used to control for potential confounders (e.g., age, sex, co-trimoxazole use, performance status).

Results: The patients started on HAART ($N = 252$) were similar to patients not started on HAART ($N = 82$) except for proportion women (59% vs. 47%), CD4+ count 350–499 cells (59% vs. 47%), and co-trimoxizole use (71% vs. 22%). Of patients on HAART, 21 died (8%) and 18 (7%) were lost to follow-up; the mortality rate in this group was 0.076

per 1000 person years. Of patients not on HAART, 20 died (25%) and 20 (25%) were lost to follow-up; the mortality rate in this group was 0.569 per 1000 person years. Patients receiving HAART had a dramatically better 2-year survival compared with those not started on HAART (92% vs. 75%; $P = 0.000$, log-rank test). In a proportional hazard regression model, the risk of death was reduced with HAART by 62% (HR = 0.38; 95%CI 0.16, 0.89) controlling for sex, CD4+ count, and cotrimoxazole use. A sensitivity analysis showed that the study findings are not negated or reversed when assuming all loss to follow-up was due to death from HIV.

Conclusion: In HIV-infected patients with TB and CD4+ count ≥ 350 cells/mm³, starting HAART during TB therapy was associated with improved survival over 2 years.

OP-183-02   Delayed tuberculosis diagnosis is associated with high mortality among HIV-infected patients in Zambia

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Background: Though TB is a leading cause of morbidity and mortality in HIV-infected persons, evidence for TB as an independent risk factor for mortality is conflicting; probably due to differing TB case definitions. We evaluated this association in a well-characterized cohort in Zambia.

Design/methods: We recruited antiretroviral therapy (ART) naïve, HIV-infected patients with no recent history of TB. Patients were screened for TB at enrollment and every three months for a year by history, physical exam, X-ray, smear microscopy, sputum, and blood and urine cultures. TB was diagnosed at time of screening with an algorithm incorporating smear, X-ray and clinical criteria; patients identified only by positive culture were traced to inform them of their TB status. Patients were grouped into 4 categories based on clinical and culture-based diagnoses: (1) 'confirmed-detected' (culture positive and diagnosed by the clinical algorithm); (2) 'confirmed-undetected' (culture positive but not diagnosed clinically); (3) 'culture negative' (culture negative but diagnosed by the clinical algorithm); and (4) 'No TB' (culture negative and not diagnosed clinically). TB treatment and ART were provided according to Zambian guidelines. We evaluated the association between TB exposure group and mortality using Cox proportional hazards models with TB as a time-varying exposure. Ethics approval was obtained.

Results: From July 2011 to April 2012 we enrolled 400 patients; 389 with at least one post-enrollment

encounter are included in analyses. We diagnosed 105 (27%) prevalent and 32 (8.2%) incident TB cases. 17 patients died in 314 years follow-up (5.4/100 person-years). Deaths were distributed as follows: 2/41 (4.9%) confirmed-detected; 9/53 (17.0%) confirmed-undetected; 2/43 (4.7%) culture-negative; and 4/252 (1.6%) no TB. Patients with confirmed-undetected TB had an adjusted hazard ratio (aHR) for dying of 15.1 ($P < 0.0001$) compared to patients with no TB. Patients with confirmed-detected and culture negative TB had elevated but not statistically significant aHRs (2.29, $P = 0.37$; and 3.40, $P = 0.19$, respectively).

Conclusions: While we observed increased mortality among all TB groups, risk appeared substantially higher in patients whose diagnosis was delayed until receipt of culture results. Although our study was limited by the number of mortality events, these results nevertheless underscore the urgent need for rapid, accurate TB diagnostics to facilitate early treatment.

OP-184-02 Timing and predictors of delayed ART initiation among patients receiving integrated treatment for tuberculosis and HIV in a limited-resource setting

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Background: Lack of integration of antiretroviral therapy (ART) services at tuberculosis (TB) diagnosis and treatment facilities is a major barrier to timely ART initiation among HIV-infected individuals diagnosed with TB. Little is known about patient characteristics associated with delayed ART initiation in patients with TB.

Methods: In the Integrated Tuberculosis and ART (ITART) study, Kinshasa, Democratic Republic of Congo, nurses at the TB clinic initiated ART. Per study protocol, expected timing of ART initiation was at 1 month of TB treatment if CD4 count <100 cells/mm³ or clinical stage 4 other than extrapulmonary TB, at 2 months of TB treatment if CD4 100–349 cells/mm³, or at end of TB treatment if CD4 dropped below 350 cells/mm³ between start and end of TB treatment. We assessed actual timing of ART initiation and used logistic regression with backward stepwise elimination to determine patient-level predictors of delayed ART initiation.

Results: Of the 492 adult participants, 29.1% were ART eligible at 1 month, 51.2% at 2 months, and 13.5% at completion of TB treatment. Only 6.3% were ineligible for ART based on a CD4 count >350 cells/mm³ at both baseline and end of TB treatment. About half (46.3%) initiated ART when eligible; (34.8%) after a median delay of 12 days (inter-

quartile range 4–27), and 18.9% never initiated ART during TB treatment. Only two patients refused ART. Participants with smear-negative pulmonary TB (adjusted-OR 1.66, 95%CI 1.07–2.56), extrapulmonary TB (adjusted-OR 1.74, 95%CI 1.03–2.94), contraindication to an antiretroviral drug (adjusted-OR 2.75, 95%CI 1.19–6.34), lower baseline CD4 count (adjusted-OR 1.18, 95%CI 1.06–1.31 per 100 cell/mm³), TB drug intolerance (adjusted-OR 5.12, 95%CI 3.06–8.56), and non-disclosure of HIV status (adjusted-OR 1.55, 95%CI 1.05–2.30) were more likely to experience delayed ART initiation.

Conclusion: Despite fully integrated TB/ART treatment, approximately half of all eligible HIV-infected TB patients did not initiate ART when eligible. Several patient-level factors predicted delayed ART initiation. Pragmatic approaches to ensure timely ART initiation, especially in patients identified as at-risk of delayed ART initiation, are needed.

OP-185-02 Empirical tuberculosis treatment in patients initiating antiretroviral therapy: a simulation study

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Background: Empirical treatment (ET) for tuberculosis (TB) in those initiating antiretroviral therapy (ART) is a novel approach to reduce early mortality in severely immunosuppressed (CD4 count <50 cells/mm³) individuals. Two randomized trials (REMEMBER and PROMPT) are ongoing to assess the efficacy of ET.

Design/methods: To assess the impact at clinic level, we simulated ET implementation per REMEMBER and PrOMPT protocol in an ART clinic in Johannesburg, South Africa. Baseline and 6-month follow-up data from a cohort of adults (≥18 years) initiating ART between 2004 and 2011 was used to simulate the impact of the ET on incident TB and death in the first 6 months of ART. We assumed that ET would prevent all incident TB and 50% of all deaths in the first 6 months of ART.

Results: Of the 16 913 people starting ART, 2856 (17%) were on already on TB treatment before ART initiation and thus ineligible for ET. In the absence of an ET program, 821 deaths and 1194 incident TB cases occurred in the first 6 months of ART in the remaining 14 057 individuals.

The REMEMBER algorithm would initiate ET in 3205 (23%). Among these, 346 deaths and 431 incident TB cases occurred in the absence of an ET program (47 individuals experienced both and are counted in both groups). For every 100 people receiving ET, we estimate that 5 deaths and 13 incident TB cases

are prevented. Overall, REMEMBER would prevent 21% of all deaths and 36% of all incident TB by the 14057 individuals not on TB treatment at time of ART initiation.

The PROMPT algorithm would initiate ET in 736 (5%). Among these, 112 deaths and 130 incident TB cases (18 both) occurred in the first 6 months of ART in the absence of an ET program. For every 100 people given ET per PROMPT, we estimate 8 deaths and 18 incident TB cases are prevented. Overall, PROMPT would prevent 7% of all deaths and 11% of incident TB experienced by the 14057 individuals initiating ART at the clinic.

Conclusion: ET is estimated to prevent 7–21% of all deaths and 11–31% of all incident TB in the first 6 months of ART. ET results in provision of TB treatment to a large number of individuals who would not experience TB or death in the first 6 months of ART in the absence of ET. If the RCTs demonstrate high efficacy, then any decision to implement an ET policy would also need to weigh the effects of potential unnecessary exposure to TB drugs in a substantial proportion of the ART clinic population and the impact this may have on the health care system.

OP-186-02   The effect of prevalent tuberculosis on virologic and immunologic response to combination antiretroviral therapy among South African children

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Background: Tuberculosis (TB) is common among HIV-infected children, but limited options are available for effective concomitant treatment. We investigated the effect of prevalent TB on virologic and immunologic response to combination antiretroviral therapy (cART) among young children initiating cART.

Methods: Between September 2009 and March 2012, 283 cART-naïve HIV-infected children aged 0–8 years were enrolled in a prospective cohort study in Soweto, South Africa. Children initiated efavirenz-based cART ($\geq$3 years or $\geq$10 kg) or protease-based cART (<3 years or <10 kg; ritonavir-boosted if on TB treatment). Virologic suppression (HIV-RNA <50 copies/mL), virologic rebound (HIV-RNA >1000 copies/mL after suppression <50), and median increase in CD4 percentage were assessed over 24 months of follow-up. Prevalent TB was defined as receiving TB treatment at the time of cART initiation.

Results: Of the 283 children initiating cART, 122 (43%) had prevalent TB, 53% were male, and median age was 2.1 years (interquartile range [IQR] 0.8–4.8). Baseline median HIV-RNA levels among those with vs. without prevalent TB were 5.5 (IQR 4.9–6.1) and 5.5 (4.9–6.2) log10 copies/mL. Baseline median CD4 cell percentages in the 2 groups were 15.7% (IQR 9.8–22.0) and 19.6% (14.7–26.5), respectively. Only two children died during follow-up. Similar proportions of children with and without prevalent TB experienced virologic suppression, with Kaplan-Meier suppression estimates of 9% vs. 10% by 3 months, 36% vs. 32% by 6 months, 64% vs. 72% by 12 months, 93% vs. 95% by 24 months (logrank $P = 0.3$). Median time to virologic suppression was 187 days (IQR 126–365) in those with prevalent TB and 188 days (106–338) in those without prevalent TB ($P = 0.6$). Prevalent TB was not associated with virologic rebound (19% vs. 21%, $P = 0.7$). Those with prevalent TB also had a similar median increase in CD4 percentage at 6 months (9.8% IQR [5.1–13.6] vs. 10.0% [5.5–14.3], $P = 0.7$), 12 months (13.6% IQR [8.2–19.0] vs. 11.8% [6.2–16.3], $P = 0.08$) and 24 months (13.5% IQR [9.1–18.8] vs. 13.2% [7.8–19.7], $P = 0.9$) to children without prevalent TB at cART initiation.

Conclusion: Our findings add to the sparse literature regarding the effect of TB on response to cART in children. In our cohort, children with and without prevalent TB experienced similar virologic and immunologic responses to cART, suggesting that the presence of TB should not delay ART initiation in young children.

OP-187-02   The influence of ART on adherence to tuberculosis treatment

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Background: Based on findings from randomized controlled trials, the WHO recommends initiation of antiretroviral therapy (ART) immediately in patients with tuberculosis (TB) with CD4 count <50 cells/mm^3 and as soon as possible after the start of TB treatment in those with less severe immunodeficiency. Health care workers are often reluctant to start ART in patients on TB treatment due to fear of reduced adherence in response to the high pill burden and increased risk of immune reconstitution inflammatory syndrome and side effects. Little is known about the impact of ART initiation on adherence to TB drugs. We aimed to quantify changes in adherence to TB drugs following initiation of ART.

Design/methods: Sixty-five adults (>18 years) with CD4 counts between 50 and 350 cells/mm^3 diagnosed with drug-sensitive pulmonary TB at a primary care

clinic in Johannesburg, South Africa were enrolled. Of these, 46 were included in the analysis; 19 were excluded as they were transferred out ($n = 7$) or defaulted ($n = 6$) prior to start ART, withdrew consent ($n = 1$), refused ART initiation ($n = 1$), had an erroneous prescription ($n = 1$), was hospitalized and changed drug regimen ($n = 1$) or failed to follow study procedures ($n = 2$). Participants were followed from the start of TB treatment until the end of the first month of ART. Adherence to TB drugs was measured using an electronic Medication Event Monitoring System (MEMS), pill count and patient self-report.

Results: Among the 46 participants included in the analysis, median CD4 count was 148 cells/mm^{3} (range 52–344), average time between start TB treatment and ART initiation was 33 days (range 9–104). Adherence by pill count was high, both before and after initiation of ART: 97.4% (95%CI 94.6–100.2) and 95.8 (95%CI 92.9–98.6) after ($P = 0.3$). Self reported adherence was even higher (99.9% before and after). Adherence measured by MEMS was lower, but also similar before and after ART initiation: 65.0% (95%CI 47.9–82.0) before and 58.5 (95%CI 42.7–74.4) after. Reasons for lower adherence by MEMS were unclear, but included technical errors and misunderstandings by pharmacists and patients, suggesting that reliable use of MEMS in resource poor settings may be difficult.

Conclusion: In this pilot study, initiation of ART did not impact adherence to TB-medication. These findings lend further support to the recommendation to avoid delaying ART initiation until completion of TB treatment and instead start ART during TB treatment in all patients with active TB.

OP-188-02 The effect of prevalent tuberculosis on virologic response to combination antiretroviral therapy: systematic review and meta-analysis

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Background: Tuberculosis (TB) is a common presenting condition leading to HIV diagnosis. To determine the impact of prevalent TB on virologic response to combination antiretroviral therapy (cART) among HIV-infected adults, we performed a systematic review and meta-analysis.

Methods: Prevalent TB was defined as receiving TB treatment at cART initiation. We systematically searched PubMed, EMBASE and selected conference proceedings for studies that reported adult HIV-RNA response following cART initiation, stratified by prevalent TB status. Heterogeneity among virologic

response outcome measures was described. Stratified random-effects and meta-regression analyses were used to summarize virologic suppression.

Results: 18 eligible studies provided data on 42 088 (range 42 to 15 646) individuals, of whom 6788 (16%) had prevalent TB at cART initiation. Data on virologic suppression, defined as <50 or <400 copies/mL, was either directly available or could be calculated for 16 studies. Follow-up times ranged from 1 to 48 months following cART initiation. Overall, the summarized random-effects relative risk (RRRE) of suppression in those with vs. without prevalent TB was 0.96 (95%CI 0.89–1.05). When estimates were categorized according to follow-up time, the RRRE for suppression was 1.06 (0.86–1.29) at 1–4 months, 0.91 (0.83–1.00) at 6 months, 0.93 (0.79–1.09) at 11–12 months, and 1.07 (0.86–1.33) at 38–48 months after cART initiation. In meta-regression analysis, whether studies used a lower limit of detection of 50 or 400 copies/mL did not substantially influence the summary relative risks. The lowest relative risks were found among patients receiving nevirapine-based cART. However, half of the nevirapine-specific
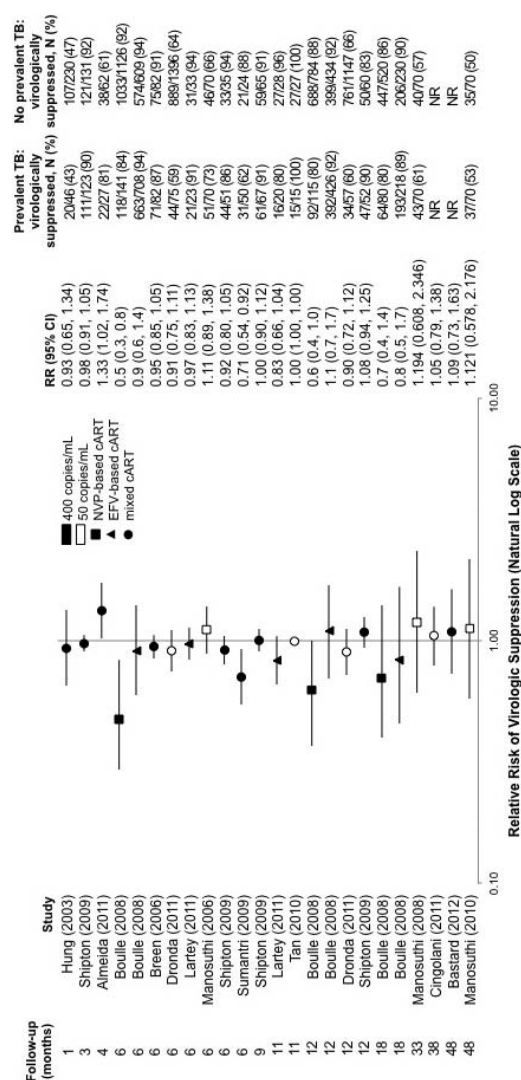
estimates were from one study, thereby confounding the ability to attribute this effect solely to cART regimen. The reported measures of virologic failure ($n = 13$) were much less standardized than virologic suppression, using a variety of definitions and HIV-RNA cut points. While this heterogeneity impaired between-study comparisons, 8 of the 13 estimates indicated no significant effect of prevalent TB on virologic failure.

Conclusion: Patients receiving treatment for prevalent TB at cART initiation do not experience significantly decreased virologic suppression as compared to those without prevalent TB. Virologic response measures are heterogeneous and between-study comparisons could be facilitated by methodological standardization.

INEXTRICABLY LINKED: INTEGRATING TUBERCULOSIS AND HIV CARE

OP-189-02   The potential effects of changing HIV treatment policy on tuberculosis outcomes in South Africa: results from three TB-HIV transmission models

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Background: Many countries are considering expanding HIV treatment following recent findings emphasizing the effects of ART on reducing HIV transmission in addition to already established survival benefits. Given the close interaction of TB and HIV epidemics, ART expansion could have important ramifications for TB burden. Previous studies suggest a wide range of possible TB impacts following ART expansion. We used three independently developed TB-HIV models to estimate the TB-related impact of expanding ART in South Africa.

Design/methods: We considered two dimensions of ART expansion—improving treatment coverage amongst those already ART-eligible, and expanding CD4-based ART eligibility criteria (from CD4 < 350 to CD4 < 500 or all HIV-positive). Three independent mathematical models were calibrated to the same data pertaining to the South African HIV-TB epidemic, and used to assess standardized ART policy changes. Key TB impact indictors were projected from 2014 to 2033.

Results: Compared to current eligibility and coverage, TB incidence was projected to decline by 10–30% by 2033 if ART eligibility were expanded to all HIV positive individuals, and by 28–37% if effective ART coverage were additionally increased to 80%. Overall, expanding ART was estimated to avert 1 TB case for each 10–13 additional person-years of ART. All models showed that TB incidence and mortality reductions would grow over time, but would stabilize towards the end of the projection period.

Conclusion: ART expansion could substantially reduce TB incidence and mortality in South Africa and could provide a platform for collaborative HIV-TB programs to effectively halt HIV-associated TB.

OP-190-02   Implementation of HIV and tuberculosis care service package can reduce HIV-associated tuberculosis under programmatic conditions: Namibia's experience

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Background: Namibia has a high HIV and TB prevalence, with TB notification rates peaking at 822/100 000 in 2004 and antenatal HIV prevalence peaking at 22% in 2002. HIV testing rate among TB patients was low at 16% in 2005 with ART coverage of 42% and 17% among TB patients and eligible HIV positive patients respectively. 58% and 67% of TB patients tested for HIV in 2005 and 2006 respectively were HIV positive.

Intervention: Namibia implemented a multi-pronged HIV prevention strategy since the early 2000s. A TB-HIV technical working group was formed to spearhead implementation of TB-HIV collaborative activities. Guidelines to address TB-HIV were incorporated in both TB and ART strategic plans and guidelines. IPT was adopted as a national policy, with the number of patients commenced on IPT increasing. 14 000 people living with HIV (PLHIV) were commenced on IPT in 2012. Guidelines for starting ART were changed from a threshold CD4 count of 200 to 350 in 2010, and ART for TB-HIV patients was emphasised in TB and ART clinics, with strengthening of referral systems between TB and HIV care clinics. TB infection control guidelines were developed with development and implementation of TBIC plans in district hospitals since 2010.

Results and lessons learnt: Estimated HIV incidence decreased from 2.39% in 2001 to 0.77% in 2011 (a decline of 68%). HIV testing among TB patients has increased from 16% in 2005 to 89% in 2012. ART coverage among TB-HIV patients has increased from 42% in 2010 to 72% in 2012; while ART coverage among eligible PLHIV was estimated at 83% in 2012. HIV prevalence among TB patients has progressively declined from 67% in 2006 to 47% in
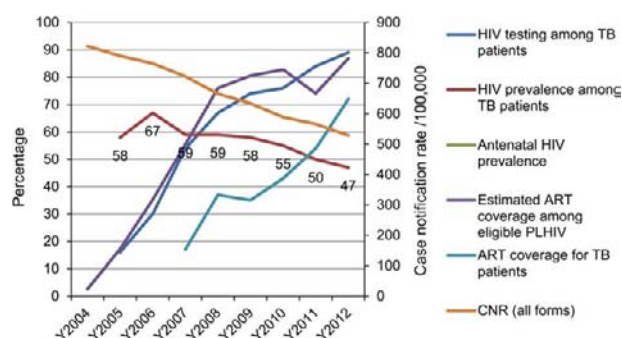
Figure Trends in key TB and HIV indicators, 2004–2012, Namibia.

2012, suggesting possible decline in incidence of HIV-associated TB. There has been an associated decline in the notification rates of TB (all forms) from 822/100 000 in 2004 to 529/100 000 in 2012 (Figure).

Conclusions and key recommendations: Implementation of a package of TB and HIV prevention and care services is associated with a decline in HIV-associated TB. This has the potential to have a long-term impact on the overall TB epidemic. Expansion of HIV and TB-HIV services should be promoted in high HIV incidence countries. Further research is required to identify which of these interventions have the greatest impact on overall TB incidence. Raising the threshold for ART initiation can potentially result in further reductions in TB incidence.

OP-191-02 Integrating HIV services for tuberculosis patients in western Kenya. How well are we doing?

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Background: TB-HIV co-infected patients are known to have a high mortality. The traditional vertical and parallel structure of the two care systems is thought to contribute to this high mortality. We integrated TB and HIV services in the Academic Model Providing Access To Healthcare (AMPATH) health facilities in Kenya in 2011. This study assesses the uptake of HIV services (HIV testing, co-trimoxazole preventive therapy and ART initiation) among tuberculosis patients before and after introducing a 'one-stop shop' model of TB-HIV care.

Design/methods: TB-HIV integration (care for both TB and HIV performed by the same team) started in mid-2011. The pre-integration cohort was enrolled between March–October, 2010 while the post-integration cohort between March–October, 2012.

Study population: Records of 2282 TB patients were reviewed. 1126 were HIV negative, 81 not HIV tested, 386 had previously known HIV positive status. 689 newly diagnosed TB-HIV patients comprised the study population. Time to HIV testing post TB treatment initiation, subsequent linkage to HIV care, and initiation of CPT/ART represented measureable outcomes between pre-integration (57% of study population) and post integration cohorts. Data sources: TB registers and HIV medical charts in 14 health facilities. EpiData 3.1 was used for double data entry and analysis. 95% confidence intervals are used for inferential statistics.

Results: The two cohorts were statistically similar in all measured characteristics (sex, age, BMI, marital status, distance to clinic, type of TB, WHO stage) except TB outcomes (0.81 RR of good outcome in post-integration (95%CI 0.72–0.90, $P < 0.001$). Overall HIV testing rates were 98.1% and 94.8% among all TB patients in the post and pre-integration periods respectively (RR 1.03, 95%CI 1.02–1.05, $P < 0.001$). There was a 2.37 times higher chance of successful linkage to HIV care (at least one documented clinical review by HIV provider) during the post-integration period for TB patients (95%CI 1.87–3.01, $P < 0.001$). CPT and ART uptake were higher in the post-integration cohort (RR = 2.19 (95%CI 1.77–2.71, $P < 0.001$) and RR = 1.68 (95%CI 1.42–1.98, $P < 0.001$) respectively.

Variable	Pre-integration (days) median [IQR]	Post-integration (days) median [IQR]	P value
Time to HIV testing	0 [0, 17.0]	0 [0, 16.0]	0.2
Time to linkage to HIV care	6.0 [0, 33.0]	4.0 [0, 30.5]	0.6
Time to CPT initiation	13.0 [0, 56.0]	1.0 [0, 17.3]	0.002
Time to ART initiation	42.5 [26.8, 82.5]	31.5 [19, 64.8]	0.006

Conclusion: Integration of TB and HIV care services leads to increased uptake of HIV care services among co-infected TB patients. Impact on TB outcomes requires further study.

OP-192-02 Integration and task-shifting for TB-HIV care and treatment in highly resource-scarce settings: one size may not fit all

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Background: Limited human resources and lack of on-site antiretroviral therapy (ART) services are

obstacles to timely ART initiation among HIV-infected patients diagnosed with TB at the primary care level in a highly resource-scare setting. We assessed the effectiveness of nurse-centered, integrated TB-HIV care and treatment in a prospective cohort study of HIV-infected patients receiving care at five primary care clinics in Kinshasa, Democratic Republic of Congo.

Methods: ART was initiated at 1 month of TB treatment if CD4 count <100 cells/mm³ or clinical stage 4 other than extrapulmonary TB, at 2 months of TB treatment if CD4 100–349 cells/mm³, or at end of TB treatment if CD4 dropped below 350 cells/mm³ between start and end of TB treatment. A before-after design was used to assess the effect of ART initiation by primary care nurses ($n = 513$ patients) as compared to referral to a centralized ART clinic ($n = 373$ patients) on ART uptake and mortality during TB treatment.

Results: Overall ART uptake increased (from 17% to 69%; $P < 0.0001$) and mortality during TB treatment decreased following implementation of ART initiation by nurses at the primary care clinic (from 20.1 to 9.8%; $P < 0.0003$). Mortality among patients with CD4 count >100 cells/mm³ approached that of 3577 HIV-negative TB patients (5.6 vs. 6.3%; $P = 0.65$). In contrast, mortality among those with CD4 count <100 cells/mm³ remained high (18.8%). Cumulative mortality during TB treatment was strongly determined by baseline CD4 count: 21.0% in CD4 stratum <50 cells/mm³, 16.0% in CD4 50–99, 4.7% in CD4 100–199, 6.7% in CD4 200–350 and 5.4% in CD4 stratum >350 cells/mm³. While almost all (96.1%) patients reported at least one side effect of TB or ART medications, severe side effects were rare with grade 3 side effects in 23 (4.5%) patients and no grade 4 side effects. Most patients had a successful TB treatment outcome (79.5%) and those who initiated ART experienced a median CD4 count increase of 101 cells/mm³ (interquartile range 46–167).

Conclusion: Nurse-centered, CD4-stratified ART initiation at primary care level is effective in increasing ART uptake and reducing mortality among TB patients, but may not be adequate to prevent mortality among TB patients presenting with severe immunosuppression. Further research is needed to determine the optimal management of TB patients presenting at primary care level with CD4 counts <100 cells/mm³.

OP-193-02   HIV services uptake among pediatric tuberculosis patients in Kenya, 2009–2011

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Background: HIV-infected children are at a higher risk of developing tuberculosis (TB) disease and have higher mortality than HIV-uninfected children. The true burden of HIV among children with TB is unknown, but estimated to range from 11%–64%. HIV testing and counseling for children with TB disease is recommended by Kenya's Ministry of Health (MOH). We reviewed national TB surveillance data to describe the trends in HIV testing and prevalence among children registered for TB treatment in Kenya.

Design/methods: We analyzed data collected from five of twelve regions in Kenya that account for approximately half of all reported TB cases and where district level staff utilize personal digital assistants for routine reporting of TB data. We reviewed data for all children aged 0–14 years who were registered for TB treatment between 2009 and 2011.

Results: Children represented an average of 4.7% (6518/139 420) of all reported TB cases between 2009 and 2011.Trends in reporting of pediatric TB were similar each year, with a median age of 6 years (IQR 3.11). HIV testing of pediatric TB patients increased by 17.2% over the 3 years [2009; 70.2% (1766/2516), 2010; 82.5% (1551/1881), 2011; 87.2% (1849/2121) $P = 0.001$] while HIV prevalence decreased by 5.6% [2009; 41.4% (732/1766), 2010; 34% (527/1551), 2011; 35.8% (662/1849) $P = 0.001$]. ART uptake among HIV-infected children increased dramatically from 37.3% (273/732) in 2009 to 63% (417/662) in 2011. ART uptake varied across the age groups being very low in the 0–2 years and slightly higher among the 11–14 years age group years [2009; 33.6% (49/146) vs. 36% (51/141), 2010; vs. 39% (43/110), 2011; 56.4% (70/124) vs. 67% (112/166)]. On average over the 3 years 98% (1826/1921) of HIV-infected received cotrimoxazole [2009; 91.7% (671/732), 2010; 96.8% (510/527), 2011; 97.4% (645/662)].

Conclusion: HIV testing rates and ART uptake has increased since 2009, but there are still substantial gaps in ART provision for children with TB. HIV-infected children represent a priority group for ART initiation and special interventions are needed to close the treatment gap for these children.

OP-194-02   Scale-up of TB-HIV collaborative activities in Guyana, 2005–2010

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Background: Guyana has been severely impacted by the tuberculosis (TB) and HIV syndemic. In 2012, Guyana had the third highest TB incidence in the

Americas and 29% of patients with TB were HIV-infected. We conducted an evaluation to 1) measure scale-up of HIV testing and care for patients with TB and TB-HIV since 2005, and 2) evaluate provision of isoniazid preventive therapy (IPT) for persons living with HIV (PLHIV).

Design/methods: We conducted a retrospective study at nine TB clinics and 10 HIV clinics. At TB clinics, we collected data on HIV status and initiation of co-trimoxazole preventive therapy (CPT) and antiretroviral therapy (ART) for patients with both TB disease and HIV infection (TB-HIV). We compared HIV status, CPT, and ART indicators in 2010 with data from a 2005 evaluation. At HIV clinics, we collected data on placement and interpretation of tuberculin skin tests (TST), and provision of IPT during the year 2010 only. We conducted semi-structured interviews with staff from HIV and TB clinics and administered questionnaires to PLHIV attending HIV clinics to assess barriers and enablers regarding IPT.

Results: From nine TB clinics, 461 people were diagnosed with TB, and 121 (29%) were reported HIV-infected. Between 2005–2010, we documented increases in the percentage of patients with known HIV status (73% to 91%), prescription of CPT (80% vs. 89%), and initiation of ART (33% vs. 52%). From 10 HIV clinics, we reviewed the charts of 127 PLHIV who were eligible for a TST by national guidelines. In 2010, 87 (69%) PLHIV received at least one TST, 61 (76%) had a documented TST result, 7 (11%) had a newly positive TST, and 4 (57%) were prescribed IPT. Among 37 HIV clinic staff interviewed, 75% thought reminders in patient charts would improve TST practices. Interviews with 44 PLHIV at HIV clinics revealed 94% would be more likely to return for a TST interpretation if staff members took more time to explain the meaning of the test.

Conclusion: Between 2005–2010, the Ministry of Health made substantial progress in increasing HIV testing for people with TB as well as HIV care for people with TB-HIV. Continued scale-up of ART for people with TB-HIV is needed. Targeted provision of IPT to PLHIV might be further expanded with the use of TST clinic reminders for staff and by placing a greater emphasis on explaining to patients the purpose of the TST.

OP-195-02　Evidence of a successful TB-HIV integration in Rwanda: 2005–2012 trends of case TB-HIV care and treatment

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Background: Rwanda has a high burden of HIV and tuberculosis (TB). In 2005, the Ministry of Health (MOH) in collaboration with key stakeholders drafted and approved a national policy on TB/HIV This policy was reviewed in 2011. We describe the Rwandan experience in scaling TB-HIV policy at the nationwide.

Methods: At the initiation in 2005, the MOH in collaboration with the International Centre for HIV Care and Treatment Programs in Rwanda establish two model centers were implemented TB-HIV integration activities included systematic HIV testing for all TB cases and enrollment of those with HIV infection, into HIV care within the TB service. They were also benefiting from a CD4 cells count, provision of cotrimoxazole preventive therapy (CPT) and antiretroviral therapy (ART) under direct observation. After completion of TB treatment, those HIV infected TB cases are transferred to the HIV clinic for further follow up. The 2 models centers functioned as practical trainings sites. Health care workers from TB services nationwide attended 2 days on the job training after receiving theoretical training on HIV care and treatment. The MOH in collaboration with partner institutions ensured regular supervision and site support to assure quality of the TB-HIV integrated services. In the last semester of 2009, HIV testing was extended to all persons with TB symptoms seeking for TB care at health.

Results: During the last three years (2008–2012), HIV testing in TB cases was always ≥99% and >26.1% were HIV infected. CPT provision increased from 87% to 99%. The proportion of those under ART progressed from 39% to 74%. In 2012, 99% of TB suspects with unknown HIV status were tested for HIV infection, and 8% were found to be infected. By 2012, 188 of 198 TB diagnostic and treatment centers fully implemented the one-stop TB-HIV service.

Conclusion: The Rwandan experience demonstrates that it is feasible to achieve rapid and successful implementation of TB-HIV collaborative activities.

OP-196-02　Cost-effectiveness of ART and the Three I's for HIV-TB to prevent tuberculosis in people with HIV

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Background: Antiretroviral therapy (ART) and the Three I's for HIV-TB (intensified TB case finding (ICF), isoniazid preventive treatment (IPT), and TB infection control (IC)) are key interventions to prevent TB in people living with HIV. This study evaluates the cost-effectiveness of different TB prevention strategies that reduce the risk of developing active TB among people living with HIV.

Design/methods: Using a decision-analytic model, we estimated the incremental cost-effectiveness of strategies for reducing TB cases in a cohort of 10 000 HIV-positive persons over 3 years in a setting with active TB prevalence of 5% among people with HIV. The base case (ART coverage of 55% at CD4 count ⩽350 cells/mm³ and TB screening using cough) was compared with nine other strategies that included one or more of the following interventions: 1) increased access to ART, i.e., ART coverage of 90% at CD4 count ⩽350 cells/mm³; 2) IC measures in healthcare facilities which included administrative measures, respirators, surgical masks and natural ventilation; and 3) ICF using the WHO-recommended four-symptom screening algorithm and IPT (for 6- or 36-months) for those without active TB. Those with one or more symptoms were offered further TB diagnosis using 1) sputum smear microscopy and chest radiography or 2) Gene-Xpert. Model inputs were taken from published literature. For different willingness-to-pay (WTP) thresholds, we generated tornado diagrams of univariate analyses for all parameters except those that were common across all policy alternatives.

Results: The 'base scenario' was the least costly, but also the least effective of all the strategies. The cost-effective strategies included 90% ART coverage, IC, and ICF/IPT for 36 months. After eliminating the less effective strategies, the strategy with 90% ART coverage, IC, ICF/IPT for 36 months, and Gene-Xpert laboratory diagnosis for TB case finding averted the most TB cases at the lowest cost (incremental cost-effectiveness ratio of US$5547 per TB case averted compared with the base case). These findings remained consistent in the sensitivity analyses.
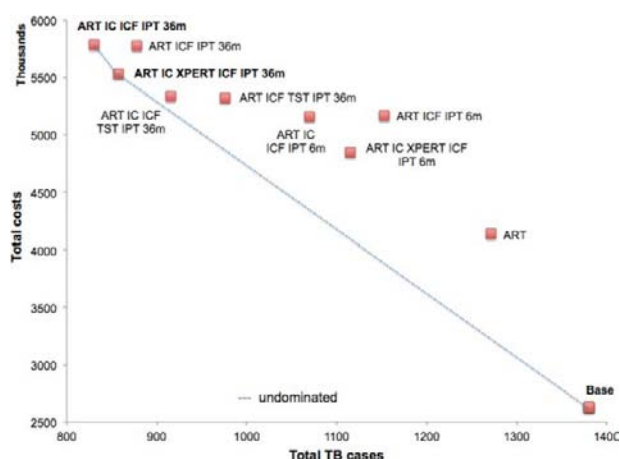
Figure Expected costs and TB cases under the strategies in consideration. Costs are in 2010 US$.

Conclusion: Our findings suggest that strategies including ART, TB infection control interventions and ICF/IPT for 36-months averted more TB cases than other strategies with shorter duration of IPT or ART

alone. These findings provide further rationale for scale-up of ART and the Three I's for HIV-TB in communities with high HIV and TB prevalence.

PARTS OF A WHOLE: DRUGS, DOSING AND MORBIDITY IN TB-HIV

OP-197-02   Adverse effects and risk factors associated with antiretroviral therapy and MDR-TB treatment in Botswana

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Background: Adverse events (AEs) in individuals on first line anti-tuberculosis treatment and anti-retroviral therapy (ART) have been well documented but little is established in those on second and third line anti-tuberculosis treatment and ART. We determined the AEs, their associated risk factors and their association to a poor clinical outcome in patients receiving MDR-TB and ART treatment.

Design and setting: A retrospective study on all confirmed and presumed MDR-TB cases initiated on MDR-TB treatment from January 2006 to June 2012 were included in the analysis. Data was retrieved and collected electronically and from medical charts.

Results: 395 patients were initiated on treatment with majority 327 (83%) as confirmed MDR-TB cases and 68 (17%) suspects. The median age was 37 (IQR 16–82) years, with 220 (56%) males and 175 (44%) females. 268 (69%) were HIV infected and 127 (32%) were not infected. The median CD4 cell count at initiation of MDR-TB treatment was 233.5 (IQR 4–1033) cell/mm³ and 190 (72%) were on ART at initiation of MDR-TB treatment. Of the 73 (28%) who were not on ART at initiation, 56 (77%) were started at a median time of 4.17 (IQR 0.07–33.57) months after MDR-TB treatment initiation. 144 (54%) had received tenofovir, 27 (10%) stavudine or didanosine, 166 (67%) efavirenz and 114 (43%) zidovudine. Diarrhoea ($P = 0.008$), vomiting ($P = 0.018$), anaemia ($P = 0.00$), hypokalemia ($P = 0.026$) and neuropathy ($P = 0.03$) were mostly observed in HIV infected on ART. Zidovudine (AOR 5.09, 95%CI 1.24–20.98, $P = 0.024$), stavudine/didinasone (AOR 5.46, $P = 0.047$, 95%CI 1.02–29.06), and tenofovir (AOR 4.78, $P = 0.031$, 95%CI 1.16–19.73) were associated with neuropathy and diarrhoea was associated with PAS (9.48, $P = 0.037$, 95%CI 1.15–78.40) and ciprofloxacin (17.66, $P = 0.037$, 95%CI 1.19–260.87). Confusion was associated with efavirenz (AOR 0.10, 0.04–0.21, $P = 0.000$), levofloxacin

(AOR 0.10, 0.04–0.21, $P = 0.000$) and depression (AOR 0.10, 0.04–0.21, $P = 0.000$). The only adverse events associated with a poor outcome was depression (AOR 33.7, 95%CI 1.95–581.83, $P = 0.015$).

Conclusion: MDR-TB and ART can be given concurrently with timely and intensive monitoring and management of AEs caused by MDR-TB treatment and ART.

OP-198-02   Isoniazid, rifampicin and pyrazinamide pharmacokinetics in Ghanaian HIV-TB co-infected patients

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Background: Low concentrations of anti-tuberculosis drugs have been reported to occur frequently in tuberculosis (TB) patients with HIV but few of these studies were performed in sub-Saharan Africa, where over 79% of co-infected patients live. We investigated pharmacokinetic profile of isoniazid, rifampin, and pyrazinamide in co-infected patients on concurrent anti-TB and antiretroviral therapy.

Design/methods: 28 (20 males) Ghanaian HIV-TB co-infected patients on self-adminstered standard 4-drug TB therapy and efavirenz-containing antiretroviral therapy had blood samples collected at 0, 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12 and 24 hours post-dosing. The median time from starting anti-TB therapy to blood sampling was 48 days. Drug levels were determined by a validated HPLC with UV detection and pharmacokinetic parameters calculated using noncompartmental analysis.

Results: Of the 28 patients, 8 had undetectable rifampin concentrations and 5 each had undetectable isoniazid and pyrazinamide concentrations. The median (IQR) Cmax and AUC0-last of isoniazid was 1.57 (1.00–1.99) μg/mL and 4.65 (2.62–6.72) μg × hr/mL, respectively. The median (IQR) Cmax and AUC0-last of rifampin was 0.86 (0.62–1.19) μg/mL and 3.12 (2.14–5.40) μg × hr/mL, respectively. The median (IQR) Cmax and AUC0-last of pyrazinamide was 44.65 (36.56–52.21) μg/mL and 349.19 (293.44–443.85) μg × hr/mL, respectively. Compared with published therapeutic range, 22/23 patients had low isoniazid Cmax, 20/20 patients had low rifampin Cmax and none of patients had low pyrazinamide Cmax but 7/23 had pyrazinamide Cmax > upper end of the normal range. Age, sex, body weight, BMI, and baseline CD4 had no significant relationship with the anti-TB drugs pharmacokinetics. All the 11 patients with smear-positive pulmonary TB had sputum smear conversion on

treatment and were considered cured. We could not assess the patients for relapse. Given, the very low rifampin concentrations, we investigated the content of rifampin in the tablets, as well as the stability of rifampin in frozen samples. The content of rifampin was adequate in the tablets but there was a 35% loss of rifampin in frozen samples over 5 years.

Conclusion: While low plasma concentration of isoniazid and rifampin was common in HIV-TB co-infected Ghanaian patients, it did not appear to lead to poor treatment outcome. The relationship between plasma anti-TB drug pharmacokinetics and treatment outcome requires further investigation.

OP-199-02   Concurrent drug-susceptible tuberculosis in HIV-infected patients co-infected with MDR-TB is associated with inferior clinical outcomes

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Background: In endemic settings, patients with multidrug-resistant tuberculosis (MDR-TB) may be co-infected with drug-susceptible isolates. However, the impact of 'mixed' *M. tuberculosis* infections on clinical outcomes among patients being treated for MDR-TB is unknown.

Methods: This study included all culture-positive patients treated for MDR-TB in Botswana during a 7 year period. We used mixed-effect logistic regression to determine the association between mixed *M. tuberculosis* infection and clinical outcome. Mixed *M. tuberculosis* infection was defined as at least one *M. tuberculosis* isolate susceptible to rifampicin and isoniazid and at least one isolate resistant to at least rifampicin and isoniazid collected >3 months from MDR-TB treatment initiation. Clinical outcome was defined as good (cure or completion of treatment) or poor (failure to complete treatment or death). Kaplan-Meier curves were used to compare time-to-culture-conversion among patients with and with HIV and mixed TB infection.

Results: Mixed *M. tuberculosis* infection was identified in 31 of 475 (6.5%) eligible MDR-TB patients. Poor clinical outcome occurred in 123 (25.9%) patients. MDR-TB patients who had mixed infections and were co-infected with HIV were at increased risk of poor clinical outcomes compared to those HIV patients without mixed TB infections (adjusted odds ratio [aOR] 7.84, 95% confidence interval [95%CI]
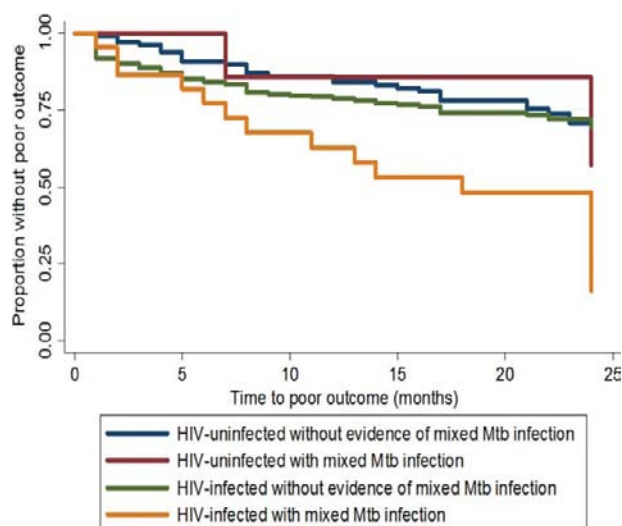
Figure Kaplan-Meyer curves for poor outcome by mixed TB infection and HIV status.

2.75–22.33), whereas MDR-TB patients without HIV who had mixed infections were not (aOR 1.16, 95%CI 0.24–5.56). HIV-infected MDR-TB patients with mixed infections also had longer time-to-culture-conversion when compared with HIV-infected MDR-TB patients without mixed infections (hazard ratio 1.51, 95%CI 1.17–1.85).

Conclusion: Co-infection with drug-susceptible TB isolates is strongly associated with worse clinical outcomes and longer time-to-culture-conversion in HIV-infected patients co-infected with MDR-TB. Studies of treatments that target drug-susceptible TB isolates in cases of MDR-TB with mixed drug-sensitive infection are warranted.

OP-200-02 Determinants of tuberculosis case fatality for HIV-positive adult patients in primary health care tuberculosis clinics in Cape Town, South Africa, 2009–2011

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Aim: To determine annual HIV prevalence in adults starting TB treatment in primary care TB clinics in Cape Town and identify determinants of case fatality in HIV-positive patients.
Methods: A retrospective analysis of the electronic TB register (2009–2011) identified the HIV status of newly registered patients ≥15 yrs. A multivariate logistic regression analysis quantified risk factors for TB case fatality in HIV-positive patients.
Results: The number of newly registered adult TB patients treated in 100 primary health care clinics was 25 841 in 2009, 26 104 in 2010 and 25 554 in 2011. HIV status was determined for 94.6%, 97.1% and

98.0% of patients of which 49.7%, 50.4% and 50.9% were HIV-positive in 2009, 2010 and 2011 respectively ($P = 0.09$). The median baseline CD4 count [IQR] for the HIV-positive patients was 152 cell/mm^3 [69–278] in 2009, 159 cell/mm^3 [73–284] in 2010 and 173 cell/mm^3 [78–305] in 2011 ($P < 0.001$). 5285 (6.8%) were on ART at start of TB treatment and 10 128 (37.9%) started ART during treatment. Case fatality for the HIV-positive patients was 7.0%, 6.4% and 5.8% in 2009, 2010 and 2011 ($P < 0.001$). Determinants of case fatality are shown below.

Variable	OR (95%CI)	P value
Year of treatment	0.99 (0.93–1.05)	0.70
Age	1.03 (1.03–1.04)	<0.001
Female	1.12 (1.02–1.23)	0.02
New patients	1.00	
Retreatment patients	1.43 (1.30–1.58)	<0.001
PTB	1.00	
EPTB	1.11 (0.99–1.24)	0.07
Both PTB and EPTB	1.28 (1.02–1.60)	0.03
CD4 categories (cells/mm^3)		
0–50	1	
51–100	0.63 (0.55–0.71)	<0.001
101–150	0.45 (0.39–0.53)	<0.001
151–200	0.38 (0.32–0.45)	<0.001
>200	0.31 (0.28–0.35)	<0.001
Not on ART	1	
On ART at start of TB	0.53 (0.46–0.61)	<0.001
Started ART during TB	0.43 (0.39–0.48)	<0.001

Conclusion: Retreatment TB, increasing age and patients with low CD4s had the highest mortality risk. Case fatality was substantially lower in patients on ART. Median CD4 counts increased over the years but over a quarter of patients still presented in 2011 with CD4 counts below 78 cells/mm^3 indicating that late presentation remained a problem.

OP-201-02 Pharmacokinetics of rifabutin when coadministered with lopinavir/ritonavir in HIV-TB patients in Viet Nam: ANRS12150b cross-over clinical trial

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Background: Rifabutin (RBT), an alternative to rifampin, can be used with protease inhibitors (PIs). As the doses of RBT are not well established when used with ritonavir boosted PIs, we compared pharmacokinetic parameters of two different doses of RBT in HIV-infected patients with pulmonary tuberculosis receiving ritonavir boosted lopinavir (LPV/r) -containing antiretroviral therapy (ART) in Ho Chi Minh City.
Design/methods: Adult patients aged 18–65 years,

HIV-positive, with a CD4 count ≤250 cells/μL, with newly diagnosed TB and having given written informed consent initiated RBT 300 mg OD in combination with isoniazid (H), pyrazinamde (Z) and ethambutol (E), followed two weeks later by LPV/r containing ART. In a randomized cross over design each patient received either RBT 150 mg 3 times per week (TPW) or RBT 150 mg once daily (OD) during three weeks, and RBT doses then interchanged for a further 3 weeks. Pharmacokinetics (PK) of RBT were evaluated during a dosing interval after 2 weeks of RBT 300 mg daily, after 3 weeks of RBT 150 mg OD with LPV/r, and after 3 weeks of RBT 150 mg TPW with LPV/r. RBT and 25-O-desacetyl Rifabutin (daRBT) concentrations were measured by validated HPLC assay. PK parameters were estimated by the non-compartmental method. Geometric mean ratios (GMR) and 90% confidence interval (90%CI) of AUC of RBT and daRBT with LPV/r vs. alone were calculated. Patients were then referred to national TB and HIV programs and a final evaluation visit took place after another 16 weeks.

Results: Of 33 enrolled patients, 25 completed the 3 PK and 24 all clinical visits. Nine patients terminated the trial early: 1 early consent withdrawal, 4 following SAEs (1 crypto meningitis, 2 hepatitis, 1 severe anaemia), 1 lost to follow-up after PK3—3 secondary exclusions. There were no significant sequence effects. RBT AUC GMR (90%CI) for TPW/alone and OD/alone were 1.12 (0.92; 1.37) and 1.32 (1.16; 1.51) respectively. An average 5-fold increase in daRBT AUC was observed when RBT was coadministered with LPV/r whatever the dose. At the end of the 6-month follow up, average CD4 gain was 120/μL, 19/22 patients had undetectable viral load (<250 cp/mL) and 22/24 patients had TB negative cultures.

Table Pharmacokinetic parameters of RBT and daRBT as median and range

	RBT			daRBT		
		RBT+LPV/r			RBT+LPV/r	
	RBT alone	RBT TPW	RBT OD	RBT alone	RBT TPW	RBT OD
C_{min}, ng/mL (range)	61 (13–152)	62 (13–120)	170 (81–310)	6 (6–329)	46 (11–118)	129 (48–334)
C_{max}, ng/mL (range)	792 (344–1105)	544 (55–964)	671 (246–1146)	80 (25–595)	142 (31–308)	216 (94–535)
T_{max}, h (range)	3 (2–4)	3 (0–5)	3 (2–5)	3 (0–5)	4 (2–6)	4 (2–8)
AUC, ng.h/mL (range)	5640 (2715–8876)	7344 (1426–10896)	7292 (3524–12514)	697 (245–10250)	3807 (872–7628)	4127 (1769–8616)

Conclusion: RBT OD regimen combined with LPV/r led to 32% higher exposure (AUC) than RBT 300 mg alone but to a large increase in daRBT and this could be a suitable dose in combination with PIs.

OP-202-02 Clinical effectiveness of a strategy to manage GeneXpert-negative HIV-infected patients with presumptive tuberculosis in Uganda

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Background and challenges to implementation: The World Health Organization recommends the use of the GeneXpert MTB/RIF® test as the initial diagnostic test in individuals suspected of having HIV-associated tuberculosis (TB). However, how to best manage HIV-infected patients with presumptive TB who test GeneXpert-negative remains unclear.

Intervention or response: The Makerere University Joint AIDS program in Uganda provides comprehensive HIV/AIDS services including routine TB screening and treatment to over 42 000 patients. GeneXpert is used to test smear-negative TB suspects. Patients with persistent symptoms of TB despite a negative GeneXpert test are treated with broad spectrum antibiotics, prior to empiric anti-TB treatment. We sought to describe the clinical practice and outcomes of HIV-infected patients with presumptive TB and a negative GeneXpert test at Mulago AIDS clinic. We retrospectively examined patients' clinical records at baseline and at 6 months to determine vital status and clinical response to treatment following a negative GeneXpert test.

Results and lessons learnt: Of 189 consecutive smear-negative adults with a positive WHO TB symptom screen seen between August 2011 and July 2012, 27 (14%) were GeneXpert-positive, and 162 (86%) were GeneXpert-negative. The majority (115 of 189) were women, with a mean age of 38 years (SD ± 10.0). The Median CD4 count was 293 (IQR 129, 449) and 129 (68%) were taking ART. After treatment with broad spectrum antibiotics, 141/162 (87%) improved and remained symptom-free throughout the 6-month follow-up period. Nineteen (12%) patients did not improve in two weeks, while 2 were lost to follow up. Of the 19 patients who did not improve, 7 had another diagnosis made (1 Kaposi sarcoma, 1 bronchial-alveolar carcinoma, 5 COPD), while 12 patients with persistent symptoms and no alternative diagnosis were treated with anti-TB medications. Of these 12, 11 (92%) patients responded to TB therapy and became symptom-free while 1 was lost to follow up. Thus, 6.8% of GeneXpert negative patients undergoing evaluation in our HIV clinic received empiric TB therapy.

Conclusions and key recommendations: The majority of patients with negative GeneXpert test improved

on empiric antibiotic treatment. A strategy of Gene-Xpert-testing of smear-negative patients followed by an antibiotic trial and empiric anti-TB treatment if there was no improvement on antibiotics, was safe and effective.

OP-203-02   HIV-associated hypothyroidism in patients on multidrug-resistant tuberculosis treatment in Namibia

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Background: In Namibia, HIV co-infection among patients with multidrug-resistant (MDR) TB is about 50% and HIV/MDR-TB co-infected patients may suffer from more adverse events compared to those infected with only MDR-TB. We sought to determine the incidence of elevated ($\geqslant 5.0$ mIU/L) thyroid-stimulating hormone (TSH) in patients treated for MDR-TB and explored the association between HIV infection, treatment with ethionamide-containing MDR-TB regimens and the occurrence of elevated TSH levels (hypothyroidism).
Design/methods: We performed a retrospective review of clinical records of patients admitted and treated for MDR-TB in a tertiary hospital from 1 Jan 2009 to 28 Feb 2012. The patients were followed up for up to 8 months during the intensive phase of MDR-TB treatment. Patients were treated according to Namibia's guidelines for MDR-TB treatment, which are aligned to the World Health Organization guidelines. About half of the patients received a standard MDR-TB regimen containing kanamycin, levofloxacin, ethionamide, cycloserine and pyrazinamide, while the rest received other regimens that were individualized according to the patient's antimycobacterial drug sensitivity profile. Data on patient demographics, HIV status MDR-TB treatment and TSH serum levels was extracted from the treatment records using a structured form and analyzed in Epi Info version 3.5.3. Descriptive and time-to-event analyses, i.e., Kaplan Meier (KM) and Cox proportional hazard (Cox PH) were performed using SPSS version 12.0.1. After confirming the validity of assumptions for Cox PH from KM plots, the resulting hazard ratios (HR, 95%CI) were used to assess the association between HIV infection, ethionamide use and elevated TSH. A P value of <0.05 was considered statistically significant.
Results: Of the 86 patients in the study, 43 (50%) were HIV co-infected and 72 (83.7%) used ethionamide-containing MDR-TB regimens. The mean patient age was 32.8 years $\pm$ 9.8, mean body weight 50.4 kilograms $\pm$ 11.7 and 51.2% were male. The cumulative
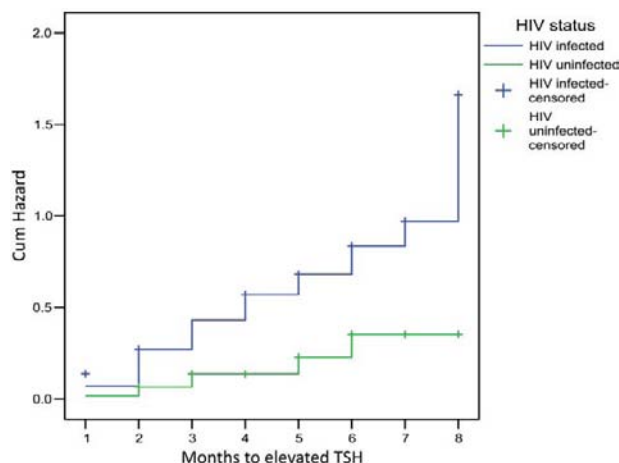
Figure   A Kaplan Meier chart of HIV status and elevated TSH levels.

incidence of elevated TSH was 36 per 100 persons (31/86). In a multivariate Cox PH regression model that combined HIV and ethionamide exposure, being infected with HIV was significantly associated with a three-fold risk of elevated TSH levels (HR = 2.9; 95%CI 1.3–6.5, P = 0.01), while ethionamide use wasn't (HR = 1.2; 95%CI 0.4–3.2, P = 0.76).
Conclusion: HIV infection rather than ethionamide use was associated with elevation of TSH levels in patients treated for MDR-TB in Namibia. Clinicians should closely monitor thyroid function in patients on MDR-TB therapy, especially among those co-infected with HIV, in order to detect and manage asymptomatic hypothyroidism in good time.

OP-204-02   High rate of hypothyroidism in multidrug-resistant tuberculosis patients co-infected with HIV in Mumbai, India

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Background: Adverse events (AEs) occur frequently in multidrug-resistant tuberculosis (MDR-TB) patients on treatment. However, there is still little data on AEs among HIV-infected patients receiving both second-line TB and antiretroviral treatments (ART). Hypothyroidism is reportedly a common AE related to the use of ethionamide, PAS, and stavudine, however there is limited access to laboratory monitoring and lack of prospective data in many programmatic settings. The aim of this study was to determine the frequency of and risk factors associated with hypothyroidism in a cohort of co-infected patients.
Design/methods: This was a prospective, observational cohort study, using routine laboratory data

from HIV/MDR-TB patients followed in a Médecins Sans Frontières clinic in collaboration with Sewri TB Hospital, Mumbai, India. Hypothyroidism was defined as TSH > 10 mIU/L at least once during the course of treatment. TSH was measured in a laboratory at baseline and every 3 months thereafter. Analysis was performed at separate time points in 2011 and 2013.

Results: Between October 2006 and March 2013, 116 co-infected patients were enrolled in the clinic, 74 of whom had at least two TSH values during the follow-up. Four of these patients had elevated TSH at baseline and were excluded. The median (IQR) age was 38 years (34–43) and 61% were male. By September 2011 and March 2013, (21/67) 31% and (37/70) 53% of patients had hypothyroidism after a median of 112 and 90 days respectively. Age, sex, baseline CD4-count, body mass index and stavudine-based ART were not associated with the occurrence of hypothyroidism in bivariate and multivariate models. The co-administration of PAS and ethionamide was found to double the risk of hypothyroidism (RR 2.01, 95%CI 1.09–3.71).

Conclusion: Increasing rate of hypothyroidism was recorded in a Mumbai cohort of co-infected patients on treatment. This is a treatable and reversible AE, however, without regular monitoring it may go undiagnosed. Care providers should not wait until the condition becomes symptomatic with the risk of compromising treatment adherence. Simple, affordable, and reliable point-of-care tools for measuring TSH are needed, especially in high burden MDR-TB countries. Our findings suggest frequent TSH monitoring while awaiting for newer safer and more efficacious MDR-TB regimens.

NOVEL CONCEPT IN THE DIAGNOSIS AND TREATMENT OF TUBERCULOSIS AND CHILDREN

OP-205-02   Opportunities to detect tuberculosis among severely acute malnourished children admitted to nutritional rehabilitation centres in Bihar, India, 2012

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Background: In India, approximately 86 000 new paediatric tuberculosis (TB) cases occur each year. In 2011, the state of Bihar notified 74 TB cases per 100 000 population, and 4.2 paediatric cases per 100 000. However, TB diagnosis among children is difficult, especially those that are immunocompromised. Recent statistics show that, among children less than 3 years old in Bihar, about 58% were underweight and about 4% were severely acutely malnourished (SAM) and are at the highest risk of mortality. Nutritional Rehabilitation Centres (NRCs) treat SAM children less than 60 months old and provide an opportunity to detect and manage TB cases in one of the most vulnerable groups of children in India.

Methods: At 7 selected NRCs in Bihar, medical officers and nursing staff used the Revised National Tuberculosis Control Programme (RNTCP) paediatric guidelines to evaluate and treat TB among SAM children during July–December 2012. SAM children were screened for TB based upon clinical history, household contact exposure to TB, chest radiograph, Mantoux tuberculin skin testing and sputum smear microscopy, when available. Identified TB cases were provided medical and nutritional support at the NRCs for 21 days and received post-discharge follow up on a fortnightly basis for two months. To evaluate TB reporting to RNTCP for treatment and follow-up management, we compared NRC registers and cross-matched all SAM children names and ages with RNTCP TB treatment registers.

Results: Of 440 SAM children evaluated and screened for TB at the NRCs, 39 (8.9%) were diagnosed with TB, including 35 (90%) based upon 2 or more diagnostic criteria. Among SAM children, there was no statistical difference between TB cases and non-TB cases by age and gender; however the majority of TB cases were 13–36 months of age (69%). Among 34 children treated for TB, only 18 (46%) were reported to and treated by the RNTCP.

Conclusion: While NRCs identified approximately 89 TB cases per 1000 children screened, less than half were not reported or treated by the national TB program. NRCs may be an important location for early TB case detection and treatment, however, more effort is needed to link this vulnerable population to RNCTP services.

OP-206-02   Xpert® MTB/RIF in the diagnosis of childhood tuberculosis: the experience of Pakistan

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Background: The Xpert MTB/RIF assay (Cepheid) is the WHO recommended initial diagnostic test for diagnosis of TB and simultaneous detection of rifampicin resistance. We investigated to determine the performance of the MTB/RIF assay in diagnosis of tuberculosis in children and additional diagnostic yield of MTB/RIF assay over sputum smear in different

types and quality of pediatric clinical specimen including raw sputum specimens, gastric lavages and extra-pulmonary specimen.

Design/methods: All clinical specimen of paediatric cases refered for AFB smear microscopy were also tested for Xpert MTB/RIF. DATA was collected between May 2011 and December 2012. Both pulmonary specimen and extrapulmonary specimen were used for testing.

Results: Data collected till May 2012 showed that a total of 469 children were referred for testing 60.2% of children referred were ten or more than ten years of age.

AFB smear positivity ranged 1% in youngest age group (0–4 yrs) to 21.3% in older children (10–14 yrs) able to expectorate. In smear negative children *Mycobacterium tuberculosis* was detected in 10.4% of children tested. 64 cases were AFB smear positive and additional 49 were diagnosed using Xpert MTB/RIF and RMP resistance was detected in 28 cases.

Table Xpert MTB /RIF assay results in children

	M	F	Total	AFB sm+ve		AFB−ve/ UK MTB+ve		Rif resistance
	n	n	n	n	%	n	%	
0–4 yrs	54	47	101	1	1.0	5	5.0	1
5–9 yrs	41	45	86	3	3.5	6	7.0	1
10–14 yrs	99	183	282	60	21.3	38	13.5	26
	194	275	469	64	13.6	49	10.4	28

Conclusion: Xpert MTB/RIF assay more sensitive then AFB smear microscopy in diagnosis of TB in children with additional diagnostic yield of 77%.

OP-207-02   Xpert® MTB/RIF for the diagnosis of tuberculosis in children: systematic review and meta-analysis

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Background: Smear microscopy, the most widely used test for TB in low/middle-income countries, is of limited value in children and therefore rarely done. This leads to under-diagnosis and under-reporting of childhood TB. In 2011, the WHO recommended Xpert MTB/RIF for the diagnosis of tuberculosis (TB) and multidrug-resistant TB in all age groups despite a lack of pediatric data at that time. We conducted a systematic review to assess the diagnostic accuracy of Xpert MTB/RIF for pulmonary TB (PTB) and common forms of extrapulmonary TB (EPTB) in children.

Design/methods: We performed database searches for relevant studies in all languages through April 2013. We included randomized-controlled, cross-sectional, and cohort studies involving children (<15 years) with presumed TB. For PTB, we extracted data separately for expectorated sputum (ES), induced sputum (IS), nasopharyngeal aspirates (NPA), and gastric aspirates (GA). For EPTB, we extracted data for fine needle aspirates and biopsies for peripheral lymphnode TB and cerebrospinal fluid for TB meningitis (TBM). We used two reference standards: culture (studies could perform > 1 culture to confirm TB) and, in addition for PTB, a clinical definition of TB/ Not TB when cultures were negative. We performed meta-analysis to determine pooled sensitivity and specificity when possible using a bivariate random-effects model and investigated heterogeneity in subgroups classified by HIV and age.

Results: We included 12 studies and data from 2760 children: PTB (10 studies), lymph node TB (4) and TBM (5). Five studies (41.7%) were conducted in low or lower middle-income countries. Against a reference standard of culture, pooled sensitivities were 69% (95% Credible Interval 55–81) for Xpert MTB/RIF performed on ES and IS combined (7 studies) and 75% (59–90) for GA (5 studies). In HIV-infected children, sensitivity was 77% (60–89) in ES/IS vs. 59% (44–72) in HIV-uninfected children. There was insufficient data to assess accuracy in HIV-infected using GA. Sensitivity in ES/IS in children aged 0–4 was 57% (36–74) vs. 83% (68–92) in children aged 5–15. Pooled specificity was >95% in all subgroups assessed using culture as a reference standard.

Conclusion: As Xpert MTB/RIF is being rolled out in many TB high burden settings it becomes available for children as an alternative to smear microscopy. Xpert MTB/RIF is highly specific for TB in children. However, sensitivity estimates are estimated with poor precision due to the sparse data available. There is a greater need for pediatric studies of Xpert to support guidelines for use in this population.

OP-208-02   Xpert® MTB/RIF contribution to the diagnosis of tuberculosis in children

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Diagnosis of tuberculosis (TB) in children is challenged by the absence of reliable diagnostic tools and the difficulty to obtain good quality diagnostic

samples. In addition to clinical and radiological evaluation, microscopy, Xpert®MTB/RIF (Xpert) and cultures when available, are combined to enhance TB diagnosis. We analysed routine results from two MSF projects: in Kenya, high HIV prevalence and in Cambodia, low HIV prevalence, to describe the contribution of laboratory testing to the diagnosis of TB in children as a supplement to clinical evaluation. Both projects have Xpert and culture capacity, Löwenstein-Jensen plus thin layer agar or MGIT respectively. Each patient submitted at least one sample. Microscopy and culture were performed on two samples when available, while Xpert was performed on the best quality one. Testing results from children with all three tests were collected from 2012 project registers, during 7 months in Kenya and 12 in Cambodia. In Kenya 74 children were investigated: 21 submitted gastric aspirates and 53 sputum samples. Overall, 5 (6.2%) children were positive by microscopy (4 sputum and 1 gastric aspirate), all confirmed by Xpert and culture. Of 69 (93.2%) microscopy negative, Xpert detected 1 case (1.4%) using a gastric aspirate, confirmed by culture, while culture detected 4 additional children (5.5%) using sputum. As well as the 10 laboratory confirmed cases, another 29 were started on treatment on clinical grounds. In Cambodia 72 children were tested: 19 children submitted sputum, 37 induced sputum and 15 extrapulmonary samples. Of the 72, 1 (1.4%) child was microscopy positive on sputum, confirmed by Xpert and culture. All 71 with negative microscopy results were either negative or inconclusive by Xpert. In addition, 1 (1.4%) child was found positive by sputum culture and 5 (7%) were positive for non-tuberculous mycobacteria. As well as the 2 laboratory confirmed cases, another 14 were started on TB treatment on clinical grounds. Xpert and cultures confirmed all smear positive cases, however among microscopy negative cases, Xpert and cultures contributed to the detection of only 1 and 5 additional cases respectively. Our experience shows that laboratory confirmation has a limited contribution to TB diagnosis in children with only 22% (12/55) of cases started on treatment being confirmed. Clinical evaluation remains the key in the medical decision to start treatment. A new test for TB adapted to children is essential.

OP-209-02   Multidrug-resistant tuberculosis in children in Botswana

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Background: Diagnosis and treatment of multidrug resistant tuberculosis (MDR-TB) in children is challenging. Data on the subject remains notoriously scarce and current practices remain highly dependent on knowledge acquired from adults. In this study, we report the experience of the Botswana National Tuberculosis Programme on the diagnoses and treatment of children with MDR-TB.
Design: This was a retrospective cohort including all patients <16 years of age, who were initiated on MDR-TB treatment between January 2006 and June 2012.
Results: A total of 41 children were diagnosed with MDR-TB during the study period. Their median age was 9.0 (interquartile range [IQR], 0.6 to 15.8) years and 22 (54%) were male. Thirty (73%) children had known probable index cases and 24 (80%) of the index cases were confirmed MDR-TB. Twelve (29%) children were HIV infected, and of these, 7 (58%) were on anti-retroviral therapy (ART) before MDR-TB treatment initiation whilst 4 (33%) started during treatment. Overall, 15 (37%) children had bacteriological confirmation of MDR-TB at treatment initiation. Twenty four (59%) children initiated treatment empirically based mainly on cough 22 (92%), weight loss 17 (71%), abnormal CXR 21 (88%) and household contact 21 (88%). Of the 21 who had a household contact, 18 (86%) were initiated on treatment based on the contact's drug susceptibility testing (DST). Treatment initiation delay after GenXpert MTB/RIF ® was 6.4 (range, 0 to 16) days and after culture confirmation was a median of 26 (IQR 5–223) days. Thirty-one out of thirty-five (89%) children completed treatment successfully with a median treatment duration of 18.8 (IQR 11.9 to 24.1) months.
Conclusion: Children with MDR-TB do well on treatment even in programmatic conditions. The main challenges are delay in diagnoses and initiation of appropriate TB treatment. A lower threshold of initiating empiric MDR-TB treatment whilst awaiting DST in children with exposure should be considered.

OP-210-02   String test: a new tool to collect respiratory specimens for diagnosis of tuberculosis in children

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Background: Childhood tuberculosis (TB) diagnosis is complicated by the difficulty of children to produce sputum. The intra-gastric string test (ST) a gelatine capsule containing a 90 cm coiled nylon string, might be a good alternative to sputum induction (SI) and

gastric aspiration to collect respiratory specimen in children. We compared the TB detection rate of the ST and SI in children with TB suspicion at the Mbarara Regional Referral Hospital in Uganda.

Design/methods: Two ST and SI were performed in children aged between 3 to 14 years with clinical suspicion of TB and at least one of the following criteria: history of TB contact; positive tuberculin skin test; TB suggestive chest X-ray or absence of clinical improvement after 1 week of antibiotics. The paediatric Entero-test® (HDC corporation, USA) was swallowed after a 2 hour fast and retrieved after 2 hours of intra-gastric down time. The SI was performed after the ST with 5% saline for 20 minutes and was combined with nasopharyngal suction in young children. LED-fluorescence microscopy, Löwenstein-Jensen and MGIT TB cultures were performed in all specimens.

Results: From 19 July 2010 to 05 Sept 2012, 120 pulmonary TB suspects were enrolled. The median age was 8 years, 52.5% were females and 36.6% HIV infected. There were 12 (10%) ST and 10 (8.3%) SI procedure failures. Of the 91 children with at least one ST and one SI result, 5 (5.5%) and 4 (4.4%) were smear positive by ST and SI respectively, (McNemar's $P = 1.00$). Using combined LJ and MGIT cultures, TB was detected in 10/91 (11%) patients using ST compared to 12/91 (13.2%) with SI (McNemar's $P = 0.69$). Combination of ST and SI increased the TB detection yield to 18/118 (15.3%). The agreement for culture detection between ST and SI was high (Kappa = 0.69, $P < 0.001$). No severe adverse events were reported.

Conclusion: TB detection using ST was comparable to SI. The ST procedure is more feasible with less nosocomial risk compared to SI and is well adapted to low resource settings.

OP-211-02 Validation of 19 diagnostic algorithms for the diagnosis of childhood tuberculosis in a prospective study in Warao Amerindian communities in Venezuela

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Background: Different algorithm/scoring systems (ASS) for the diagnosis of childhood tuberculosis (TB) have been created in order to establish practical solutions for the diagnosis of this disease. However, few of them have been validated in other studies or populations.

Design/methods: We selected 207 Warao Amerindian children aged <15 years, from 28 villages in the Orinoco Delta in Venezuela, who were household or village contacts of culture-confirmed TB patients. All children underwent clinical, radiological and bacteriological investigation, and were prospectively followed up for 12 months. To identify commonly used ASS for the diagnosis of childhood TB, a literature search was conducted using Pubmed and Embase. All studies examining ASS used in the diagnosis of pediatric TB were reviewed. Nineteen ASS were identified and all children were scored by each method. Children who had a positive response to treatment or died due to TB during 12 months of follow up were regarded as TB positive, and those who remained asymptomatic were regarded as TB negative. Using these data, sensitivity and specificity of each ASS were calculated. Differences between case frequencies identified by different ASS were calculated using the McNemar's test. Cohen's kappa (κ) values were calculated for all 171 possible pair-wise comparisons (PWC) using the 19 ASS.

Results: Childhood TB case frequency using different ASS varied from 3 to 70%. Sensitivity and specificity values ranged between 38–100% and 32–99% respectively. A significant difference in case frequency ($P < 0.05$) occurred in 140 of 171 (82%) PWC between different ASS. General median P value was 0.27. Median P values per score ranged from 0.091 to 0.46. Most of the PWC (70%) showed slight or fair agreement ($P \leqslant 0.4$); only 2% showed almost perfect agreement (k $\geqslant$ 0.8). When analyses were performed including only household contacs, 131 of 171 (77%) PWC showed significant differences, but κ values did not show increased agreement (median $P = 0.27$). Cundall and Theart ASS, which had perfect agreement, also showed the highest median P values (0.46), and a high sensitivity (85%) and specificity (77%). Three ASS showed 100% sensitivity, but their specificity values ranged from 32 to 62%. The two ASS that showed the highest specificity (99.5%), Marais and MASA, showed a fair agreement ($P = 0.24$).
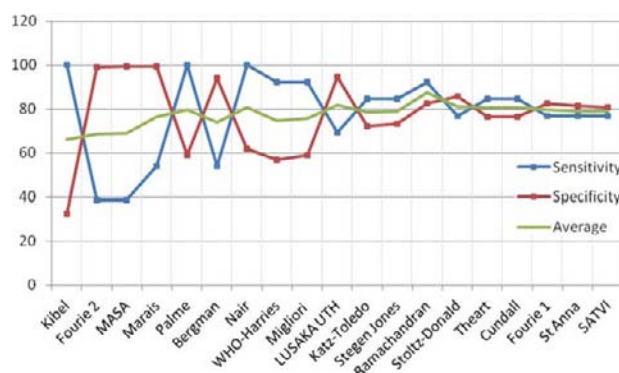
Figure Sensitivity and specificity values among 19 algorithm/scoring systems for the diagnosis of childhood TB.

Conclusion: Sensitivity and specificity values showed a high variability between the different ASS in a Warao Amerindian population. In line with previously published studies, agreement between different diagnostic systems is generally slight or fair, which severely limits the potential to apply them interchangeably over multiple studies.

OP-212-02 Pharmacokinetics of ofloxacin and levofloxacin in children with multidrug-resistant tuberculosis

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Introduction: The fluoroquinoles ofloxacin (Ofx) and levofloxacin (Lfx) are frequently used for MDR-TB. Information on pharmacokinetics and cardiotoxicity data of these agents in children with TB are limited.
Aim: To document the pharmacokinetics (PK) and cardiotoxicity of ofloxacin (Ofx) and levofloxacin (Lfx) in children with MDR-TB.
Methods: Serum concentrations were prospectively assessed in children aged 0–8 years on a MDR-TB regimen including a fluoroquinolone. Each child had PK sampling done on Ofx (20 mg/kg) and, after switching, on Lfx (15 mg/kg). Serum samples were collected prior to (t0), and at 1, 2, 4, 6 and 8 hours post dose and assayed using high-performance liquid chromatography. Maximum serum concentration (Cmax), time to Cmax (tmax) and area under the time-concentration curve from 0–8 hours (AUC0–8) were calculated. To assess cardiotoxicity, a 12-lead electrocardiogram (ECG) was done 3 hours post-dose on both PK assessment days.
Results: 23 children were enrolled; 4 were HIV-infected (all of them older than 6 years of age) and 6 were underweight-for-age (z-score < -2). The median Cmax [μg/ml], median AUC (0–8) [μg × h/ml] and mean tmax [h] for Ofx were: 9.67 (IQR 7.09–10.90), 43.34 (IQR 36.73–54.46) and 1.61 (SD 0.72); for Lfx: 6.71 (IQR 4.69–8.06), 29.89 (IQR 23.81–36.39) and 1.44 (SD 0.51), respectively. For Ofx, age was associated with Cmax and tmax ($P = 0.019$ and $P = 0.008$, respectively), while no association was found with AUC (0–8) ($P = 0.536$). No age-related differences were detected for Lfx. Underweight (weight-for-age z-score < -2) was associated with lower Cmax ($P = 0.041$) and lower AUC ($P = 0.033$) for Ofx, but not for Lfx ($P = 0.906$). Mean QTc was 361.4 ms (SD 37.4) for Ofx and 369.1 ms (SD 21.9) for Lfx, respectively.
Conclusion: Children seem to eliminate Ofx and Lfx faster than adults, leading to a drug exposure about half of that in adults following a standard oral dose (Ofx 800 mg, Lfx 750 mg). Higher or twice daily dosing of Ofx and Lfx might be needed to provide compatible exposures associated with clinical efficacy in adults. No QTc prolongation (QTc $>$ 450 ms) occurred.

DETERMINANTS OF LUNG HEALTH AND DISEASE

OP-213-02 Association of household air pollution and lung function in adolescent girls in rural India

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Background: Numerous studies have reported the disease burden from household air pollution (HAP) is a consequence of exposure to the extremely toxic pollutants produced by solid fuels burned in open fires or stoves in the home for cooking or heating. Currently, about 70% of India's population lives in rural areas and most of the households use solid fuels for domestic energy, resulting in widespread exposure to HAP. Despite the high burden of disease from HAP, it has not received the same attention as other disease risk factors in India. The study was undertaken to assess the effects of household air pollution exposure on lung function in adolescent girls in rural India.
Design/methods: A cross-sectional study was performed in a population exposed to HAP ($n = 785$) and a non-exposed population ($n = 743$) of adolescent girls aged 10–15 years in rural India. Basic socio-demographic and respiratory symptoms data were collected by using standard questionnaire and lung function was measured by spirometric tests. Indoor and outdoor PM_{10} and $PM_{2.5}$ concentrations were measured using portable air samplers. Associations between HAP and respiratory symptoms and lung function were assessed by multiple regression models, controlling for the effects of age, height, weight, and exposure to tobacco smoke.
Results: Most of the study subjects (83.5%) that used biomass as a household energy, had experienced symptoms of respiratory illness in the 30 days preceding the survey. In multivariate analysis, subjects living in homes that use biomass fuel had lower peak expiratory flow (PEF), forced vital capacity (FVC) and lower forced expiratory volume in 1 s (FEV_1) ($P < 0.05$). The study finds a high correlation between indoor $PM_{2.5}$ levels and FEV_1.
Conclusion: Results of the study demonstrate the harmful effects of HAP from solid fuel combustion on the lung function of adolescent girls and highlight the need for public health interventions.

OP-214-02   Association between ambient air pollution and active tuberculosis: prospective cohort study

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Background: Several respiratory risk factors have been report to be possibly associated with tuberculosis (TB). There was no study on the association between ambient air pollution and risk of TB. Since the problem of air pollution is serious in developing countries where TB burden is high, there is a need to understand the association between ambient air pollution and TB.

Design/methods: We included 104 196 participants ($\geqslant$30 years of age) who were enrolled in community integrated health screening service in Taipei County from 2005–2008. All participants were followed up to the end of 2011. Baseline demographic and clinical data were collected by questionnaire and physical examination during health screening. Using the home address of participants, we estimated the individual-level of ambient air pollution by two methods. In the nearest station method, the level of pollutant for each participant was assigned based on the pollution level in the monitoring station that was closest to the individual's address. Secondly, we applied the land use regression model that was developed and validated in the European Study of Cohorts for Air Pollution Effects (ESCAPE) project to estimate the level of pollutant. The occurrence of TB disease during follow-up was ascertained by linking the health screening database to national TB registry of Taiwan Centers for Disease Control. Cox proportional hazards model was used to estimate the association between ambient air pollution and active TB, adjusting for potential confounders.

Results: After a median follow-up of 5.4 years, 284 cases of incident TB occurred among 104 196 participants (incidence rate: 53/100 000). The range of estimated level of $PM_{2.5}$ and PM_{10} was 13.54–50.56 and 18.62–74.78 in the nearest station method, and 21.89–37.96 and 39.39–68.35 in the land use regression model. After adjusting for potential confounders, there was a trend of increasing TB risk with higher level of $PM_{2.5}$ and PM_{10} in the land use regression model, and $PM_{2.5}$, NO_2, and NO_x in the nearest station method (Table). However, the tests for linear trend for all pollutants were not significant.

Conclusion: In the first cohort study on ambient air pollution and TB, we did not find a significant effect of ambient air pollution, probably because the statistical power was too low to identify a weak association. Further studies of larger sample size and longer follow-up will help clarify the impact of air pollution on TB.

Table 1. Multivariate Cox Proportional Hazards Analysis of Hazard Ratio for Active Tuberculosis

OP-215-02   High asthma prevalence in Warao Amerindian children in Venezuela is significantly associated with open-fire cooking

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Background: The International Study on Asthma and Allergies in Childhood (ISAAC) reported a prevalence of asthma in 17 centres in nine Latin American countries that was similar to prevalence rates reported in non-tropical countries. It has been proposed that the continuous exposure to infectious diseases in rural populations residing tropical areas leads to a relatively low asthma prevalence. As almost a quarter of Latin American people live in rural tropical areas, the encountered high asthma prevalence is remarkable. Wood smoke exposure and environmental tobacco smoke have been identified as possible risk factors for the subsequent development of asthma.

Methods: We preformed a cross-sectional observational study from June 1, 2012 to September 30, 2012 in which we interviewed parents and guardians of Warao Amerindian children from Venezuela. Asthma was defined according to the ISAAC definition as self-reported wheezing in the last 12 months. The associations between wood smoke exposure and environmental tobacco smoke and asthma prevalence rates were calculated by means of univariate and multivariate logistic regression analyses.

Results: We included 630 children aged 2 to 10 years. Asthma was recorded in 164 of these children (26%). The prevalence of asthma was associated with cooking method. Children exposed to the smoke produced

by cooking on open wood fires were at higher risk of having asthma compared to children exposed to cooking on gas (OR 2.43, 95%CI 1.30–4.55). Four percent of the children live in a household where more than ten cigarettes are smoked per day and have a higher risk of developing asthma compared to children that are not being exposed to cigarette smoke (OR 2.79, 95%CI 1.13–6.87).

Conclusion: Our findings suggest that children living in rural settings in a household where wood is used for cooking or more than ten cigarettes are smoked daily are at a high risk of developing asthma.

OP-216-02   Morbidité respiratoire et exposition au dioxyde de soufre à Cotonou, Bénin

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Objectif : Mesurer les niveaux de pollution de SO_2 générés par le trafic routier à Cotonou en corrélation avec la fonction respiratoire des personnes exposées.
Méthodes : Etude prospective transversale descriptive et analytique menée du 5 février au 5 juillet 2006. Le SO_2 a été mesuré à l'intérieur et à l'extérieur de 60 maisons situées au voisinage d'une voie à haut trafic et d'une voie à faible trafic. Les résidants ont été interrogés à la recherche de symptômes respiratoires (toux chronique, bronchorrhée, dyspnée à l'effort et rhinorrhée) et une spirométrie de dépistage leur a été réalisée.
Résultats : Plus le trafic est élevé, plus le niveau intérieur du SO_2 est élevé: (4,3 ppm contre 0,83 ppm) vs. (2,8 ppm contre 0,49 ppm). La présence d'une source de combustion à l'intérieur a une influence significative sur le niveau du SO_2. Les fréquences des symptômes respiratoires et des troubles ventilatoires sont plus élevés dans le haut trafic que dans le bas trafic: (78,3% vs. 43,3%, $P = 0,000$) et (23,3% vs. 5%, $P = 0,004$). Pour des niveaux de SO_2 inférieur à 1 ppm le haut trafic multiplie le risque de survenue d'un symptôme respiratoire par 3,70 IC [1,61–8,52] et celui du trouble ventilatoire par OR = 4,0 [0,88–20,49] $P = 0,038$.
Conclusion : Les niveaux de concentration de SO_2 observés dans le haut trafic à Cotonou sont élevés. Il s'en suit une élévation du niveau à l'intérieur des maisons. Ces taux élevés sont corrélés à une fréquence élevée de morbidité respiratoire.

OP-217-02   Clinical characteristics of silicosis in denim sandblasting workers in Turkey

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Background: Sandblasting method has been widely used in textile industry in Turkey. As a result of using this metod in poor working conditions, the epidemic of silicosis were occurred in thousands of workers for the first time in the textile industry in world history.
Design/methods: Denim-sandblasters who admitted to our clinic were included. The characteristics of sandblasters with or without silicosis were compared. Demographics and information on working conditions were obtained by questionnaire and interview. Chest X-rays were evaluated according to ILO classification. Spirometry was performed to patients with silicosis.
Results: The study included 264 sandblasters (184 with silicosis, 80 without silicosis). All of them were male. ILO scores were higher than 2 in 76% of the silicosis patients. Most of them (69%) had respiratory symptoms, especially exercise dyspnoea (91%), cough (23%) and chest pain (12%). Spirometry was performed to 71 silicosis patients (mean FEV1 73%, FVC 68%). The ages of the sandblasters with or without silicosis were similar (30.97 ± 6.38 yr, 31.5 ± 7.67 yr, $P = 0.565$). Also the mean age at onset of work did not differ between them (21.35 ± 5.94 yr, 22.28 ± 7.8 yr, $P = 0.305$). Working duration was significantly longer in patients with silicosis (48.02 ± 29.31 m, 26.02 ± 18.59 m, $P < 0.001$). Most of the silicosis patients have been working mean 12 hours/day for subcontractor small and medium sized firms without insurance.
Conclusion: As a result of the fight, sandblasting method was forbidden in textile sector at 2009 in Turkey. If urgent international precautions are not taken, this risky business will cause new disasters in developing countries in which textile industry is often.

OP-218-02   At what costs do children with asthma benefit from educational interventions? A meta-analysis

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Background: The increased prevalence of asthma among children and its associated burden of disease urges the evaluation and implementation of strategies that might reduce the impact of disease in children. The aims of this review were to establish the costs and effectiveness of asthma educational interventions among children.
Design/methods: Comprehensive literature searches were conducted in Medline, Embase, and the Cochrane central register of clinical trials. A search strategy was built under these mesh terms: Patient Education as Topic OR Intervention Studies AND Asthma AND Child AND Cost-Benefit Analysis. Studies selected were randomized control trials or control trials,

a study population of children from 2 to 18 years old with clinical diagnosis of asthma, a cost-effectiveness or cost-benefit analysis on asthma educational intervention was carried out. The review focused on clinical outcomes such us emergency department visit (ED) and hospitalization (Hosp) due to asthma. The results on the separate outcomes were pooled in a meta-analysis using software RevManager 5.1.

Results: The final selection resulted in 10 studies with in total 3082 patients. Nine out 13 strategies showed a reduction in ED per child of 0.80 (-1.19, -0.41), Heterogeneity: $\chi^2 = 1.87$, df = 2 ($P = 0.39$); $I^2 = 0\%$, Test for overall effect: Z = 4.05 ($P < 0.0001$). Hosp overall mean difference 0.01 (-0.05, 0.04), Heterogeneity: $\chi^2 = 18.03$, df = 4 ($P = 0.001$); $I^2 = 78\%$, Test for overall effect: Z = 0.37 ($P = 0.71$). Higher reductions in expenditure were observed in studies in which simple educational session were compared to multiple educational sessions; these reductions varied from \$41 to \$1.167 per child. The cost-effectiveness ratios (ICER'S), showing low money expenditure to prevent ED visits, spending between \$88 to \$174 to prevent 0.31 to 1.41 mean visit per child.

Conclusion: When two different strategies (simple and multiple sessions) were evaluated, more intensive and large interventions with a closer follow up, demonstrated better results in reducing clinical outcomes. Substantial reductions in asthma related health care utilization were demonstrate looking at direct medical cost at the end of follow comparing intervention to control groups. However this impact was expected to be greater when comparing usual care to interventions. Nonetheless, in multi-factorial diseases bigger efforts have to be made to get significant positive outcomes, projecting asthma education as a tool for reducing the burden of asthma, having into account the inclusion of asthma under 'respiratory chronic diseases' in the global non-communicable diseases agenda.

OP-219-02   Environmental exposure to pesticides in French rural setting and short-term respiratory symptoms (Phytoriv Study)

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Background: Respiratory risks for populations living near agricultural areas where pesticides are spread remain insufficiently known.

Objective: To study respiratory symptoms during treatment season in people living near agricultural areas in Gironde, France.

Methods: Phytoriv study has been performed in two rural places in Gironde, France. Socio-demographic, lifestyle and respiratory health data have been collected by self-administered questionnaire and face to face interview during treatment season in vineyards (14 June to 10 August 2010). During the same period, seven-days atmospheric measurements of 40 pesticides have been performed on a site representative of the population exposure. Associations between measured ambient pesticides and respiratory symptoms have been studied by a logistic regression taking into account potential confounders (age, sex, smoking, residence, educational level).

Results: Among the 814 participants (52.6% women, mean age 43.8 ± 23.9 yrs), 22.9% ($n = 187$) reported at least one symptom concerning the lower respiratory tract (cough, breathing difficulty, wheezing, asthma attack) and 36.0% ($n = 293$) mentioned at least one symptom concerning the upper respiratory tract (sore throat, blocked or runny nose) during the study period. Smoking was significantly associated to cough [OR (95%CI): 1.68 (1.10–2.57); $n = 164$], breathing difficulty [2.45 (1.28–4.68); $n = 47$] and wheezing [2.62 (1.08–6.37); $n = 24$]. Among the nine pesticides quantified in ambient air, three were fungicides, detected during at least five weeks in the study area: folpet, chlorothalonil and cyprodinyl while the 6 others were quantified only one week at very low level. Chlorothalonil concentrations were significantly associated to an elevated risk of sore throat [12.47 (3.40–45.74); $n = 104$] and blocked nose [6.94 (2.24–21.46); $n = 149$]. Folpet concentrations were associated to an elevated risk of sore throat [1.11 (1.04–1.19)]. Cyprodinil concentrations were inversely associated with sore throat risk [0.27 (0.11–0.62)]. There were no associations between pesticide levels and symptoms of the lower respiratory tract.

Conclusion: This study, the first in France dealing with populations living in the neighborhood of spreading areas, showed that exposure to fungicides (folpet and chlorothalonil) could be associated with symptoms of the upper respiratory tract (sore throat and blocked nose).

OP-220-02   Management of adult asthma: a randomized, double-blind, placebo-controlled parallel trial of *Ziziphus spina-christi* extract

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Background: Asthma is characterized by frequent episodes of shortness of breath wheezing and coughing. The management of asthma is based on avoidance of the trigger oral inhaled medications albeit some herbals. *Ziziphus spina-christi* (L.) grows in Africa and

Asia and used for bronchitis and coughing. Although, this agent is proposed to have a safe profile with adequate benefits, it had never investigated in clinical trials to evaluate the efficacy in asthmatic patients. To evaluate the effect of *Z. spina-christi* leaf extract in adult asthmatic patients.

Methods: A randomized, double blind, placebo control, parallel clinical trail to compare the extract with placebo in moderate to severe asthmatic patients. 50 previously diagnosed asthmatic patients and stable on current therapies were randomly divided in 2 arms. 25 patients (Arm A) on regular repeat medications plus placebo. 25 patients (Arm B), the extract was used instead of placebo. Placebo or extract were used twice a day on alternate days as a steam inhalation. The pulmonary function test (PFT) and ST George's questionnaire were completed at base line. Follow up weekly for a period of 2 month.

Results: Spirometry analysis revealed that treatment with *Z. spina-christi* extract may result in some improvement of PFTs and PEFRs with *P* value of less than 0.05 when compared with arm A. In contrast no changes were observed in arm A. Overall, patients in arm B had best improvement in their Quality Of Life (QOL), PFTs and frequency of symptoms.

Conclusion: The extract of *Z. spina-christi* investigated further and has shown some promising result when QOL, PFT and physical symptoms were considered.

IMPROVING THE MANAGEMENT OF TUBERCULOSIS: DRUG TOOLS, X-RAYS AND SURGERY

OP-221-02   Inter-observer concordance on tuberculosis-related chest X-ray changes

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Background: Chest X-ray (CXR) is an important diagnostic test for pulmonary disease investigation. It is frequently used to rule pulmonary tuberculosis (PTB) when latent TB infection (LTBI) is diagnosed. Because it is a reader-dependent test, it requires knowledge and observance for interpretation of possible different lesions. Thus, CXR interpretation can be a challenge for young radiologists. In the present study, we assessed the inter-observer agreement of two junior radiologists using the senior radiologist interpretation as the golden standard in a general teaching hospital in Rio de Janeiro, Brazil.

Design and methods: Selected CXR films from patients with PTB and LTBI were interpreted using a standardized questionnaire. CXR technique details, the presence of parenchymal and pleural abnormalities, lymph node enlargement, and their final impression were analyzed. Radiologists were blinded to their counterparts' readings. Sensitivity, specificity and their 95% confidence interval were calculated for each abnormality, and considered fairy good if over 80%. The agreement between the two young raters was considered moderate if Kappa statistics was over 0.40 and substantial if kappa was over 0.60.

Results: Twenty-nine CXR films were analyzed. Of those, 15 had a final diagnosis of PTB by the senior radiologist. Overall, regarding the technique, both radiologists had good sensitivity but poor specificity. Sensitive and specificity were high for major parenchymal findings such as cavities, with substantial agreement. Radiologist I had a good accuracy for calcification and poor accuracy to identify lymphadenopathy and atelectasis. The opposite was observed with Radiologist II. Sensitivity and specificity for final impression of TB was for good both junior radiologists, with moderate agreement. Sensitivity for bronchiectasis and pleural abnormalities were not assessed, since the senior radiologist did not describe these lesions (Table).

	Radiologist I		Radiologist II		Interobserver concordance (kappa, CI)
	Sensitivity* (% CI)	Specificity* (% CI)	Sensitivity* (% CI)	Specificity* (% CI)	
Radiograph technique					
Adequate penetration (yes/no)	89 (67; 98)	60 (23; 88)	80 (58; 93)	40 (12; 77)	0.7 (0.3; 1.0)
Scapula in lung fields (yes/no)	100 (60; 100)	56 (33; 75)	40 (12; 77)	95 (75; 99)	0.1 (−0.1; 0.4)
Adequate insufflation (yes/no)	95 (76; 100)	50 (10; 90)	100 (87; 100)	50 (10; 90)	−0.05 (−0.1; 0.02)
Centered (yes/no)	89 (66; 98)	50 (15; 85)	75 (53; 89)	100 (23; 88)	0.4 (0.06; 0.7)
Lympha-denopathy	0 (0; 88)	75 (56; 88)	100 (90; 100)	100 (22; 100)	−0.06 (−0.2; 0.05)
Parenchymal abnormalities (yes/no)					
Calcification	100 (37; 100)	81 (63; 92)	0 (0; 63)	96 (80; 100)	−0.06 (−0.18; 0.05)
Bronchiectasis	—	100 (90; 100)	—	93 (77; 99)	—
Atelectasis	0 (0; 78)	96 (81; 100)	100 (22; 100)	96 (81; 99)	−0.05 (−0.12; 0.02)
Cavities	100 (64; 100)	83 (62; 94)	83 (87; 100)	96 (48; 99)	0.6 (0.3; 0.9)
Infiltrates	78 (44; 95)	60 (39; 78)	100 (73; 100)	50 (30; 70)	0.3 (−0.03; 0.63)
Pleural abnormalities					
Pleural thickening	—	86 (69; 95)	—	90 (73; 97)	0.5 (0.04; 1.0)
Pleural effusion	—	100 (89; 100)	—	100 (89; 100)	—
Final impression					
Tuberculosis	80 (48; 95)	84 (62; 95)	79 (56; 92)	90 (57; 100)	0.4 (0.1;0.8)

*Gold standard = senior radiologist.

Conclusion: Although the junior radiologists may need training for refining their image descriptions, they were reasonably accurate regarding final diagnosis of PTB. In settings where PTB diagnosis is carried out in healthcare units with radiologic facilities, this information may be useful. However, because the radiologists in our study were aware that they were participating in a study and they work in a teaching hospital, under supervision, the findings cannot be generalized to all settings.

OP-223-02 Using QUOTE tuberculosis light tools to improve the quality of tuberculosis service in Cambodia

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Patient Centered Approach (PCA) is an important underlying component of the global Stop TB Strategy. TB CARE I introduced a PCA package, which QUOTE TB Light is one among five tools. NTP Cambodia conducted a pilot implementation of QUOTE TB Light to assess and improve quality of TB services and to make them patient-friendly. The pilot study was implemented in communities of four rural health facilities. We recruited all smear positive TB patients who (1) were registered for treatment at those health facilities (2) had a history of at least three weeks of visiting the facility for both TB diagnosis and treatment and (3) were available and willing to participate in the study. In each health facility, the tool was applied using focus group discussions (FGD) with TB patients to identify the importance scores for the nine quality dimensions of TB services. These were combined with the performance score that we obtained from patient interviews assessing the facility. The combination of importance rank score and performance score was used to judge the quality of TB service. A total of 111 smear positive TB patients participated. Of them, 79 patients participated in the face-to-face interviews (for the performance score) and 32 patients participated in focus group discussions (for the importance rank score). All participants were from the rural areas. 59.5% of them were males. The average age of participants was 52 years. 87.3% of participants were famers. More than half of the participants had attended primary school and 30.4% had attended secondary school. 45.6%, 45.5% and 8.9% of them received TB treatment within two days, in more than two days but within one week, and in more than one week after diagnosis as TB, respectively. From the patients' perspective, the dimensions that were ranked as most important were communication and information and the least important were TB-HIV and patient support. Based on the quality impact score with a cut-off point of over 0.75, we found that current TB services were poor in performance on communication and information, information on TB-HIV relationship, infrastructure, professional competence and patient support. Then, the research team provided feedback to the health center staff. Most of the health staff accepted the patients' comments and were happy and willing to change their performance. We conclude that QUOTE TB Light is a good tool to improve TB care.

Table Quality impact for two districts health facility in Kampong Speu

Quality of TB services	Perfor-mance score	Impor-tant rank	Quality impact score	Need Improve-ment
A Socio demographic				
B-1 Availability of TB service				No
B-2 Communication and Information				
• Do the health providers in this facility tell you when you <u>stop spreading TB to others</u>?	0.23	89%	2.0	Yes
• Do the health providers in this facility tell you about the importance of <u>observed treatment</u>?	0.18	89%	1.6	Yes
• Do the health providers in this facility tell you about the need for <u>sputum tests</u> at given points during your treatment schedule?	0.28	89%	2.5	Yes
• During your visits to this facility, do health providers tell you about how to <u>store your drugs</u> obtained for your treatment?	0.14	89%	1.2	Yes
B-3 Patients provider interaction and counseling				No
B-4 TB/HIV relationship				
• Did health providers in the facility inform you about the <u>link between TB and HIV</u>?	0.57	14%	0.79	Yes
• After being diagnosed with TB, were you advised to <u>take an HIV test</u>?	0.70	14%	0.97	Yes
B-5 Infrastructure				
• Is there <u>safe drinking water</u> in this facility?	0.37	39%	1.43	Yes
• How often are the <u>toilets</u> in this facility usable?	0.37	39%	1.43	Yes
• Are people who come in with a <u>cough given priority by the health providers</u>?	0.3	39%	1.18	Yes
B-6 Professional competence				
• Does this facility offer <u>home based TB treatment</u>?	0.16	75%	1.23	Yes
• Were you <u>physically examined</u> during your first visit to this facility?	0.29	75%	2.18	Yes
• How many <u>working days</u> were there between your first sputum submission and the time you got your results?	0.88	75%	6.65	Yes
• In case of germs in your sputum that cause TB, were your close <u>contacts examined</u> by the TB facility?	0.45	75%	3.42	Yes
• How often is there a <u>treatment</u> observer checking on your daily intake of TB drugs?	0.4	75%	3.04	Yes
B-7 Affordability				No
B-8 Support				
• How often do you receive <u>transport</u> support from the health facility?	1	31%	3.06	Yes
• How often do you receive <u>food</u> support from the health facility?	0.9	31%	2.78	Yes
• How often do you receive <u>money</u> support from the health facility?	1	31%	3.06	Yes
B-9 Stigma				

OP-224-02   Vitamin D accelerates clinical recovery from tuberculosis: results of the SUCCINCT Study

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Background: Vitamin D enhances host protective immune responses to *Mycobacterium tuberculosis* by suppressing interferon-gamma (IFN-g) and reducing disease-associated inflammation in the host. The objectives of this study were to determine whether vitamin D supplementation to patients with tuberculosis (TB) could influence recovery.

Methods: Two hundred and fifty-nine patients with pulmonary TB were randomized to receive either 600 000 IU of intramuscular vitamin D3 or placebo for 2 doses. Assessments were performed at 4, 8 and 12 weeks. Early secreted and T cell activated 6 kDa (ESAT6) and *Mycobacterium tuberculosis* sonicate (MTBs) antigen induced whole blood stimulated IFN-g responses were measured at 0 and 12 weeks. Statistical comparisons between outcome variables at 0 and 12 weeks were performed using Student's *t*-test and χ^2 tests.

Results: After 12 weeks, the vitamin D supplemented arm demonstrated significantly greater mean weight gain (kg) + 3.75, (3.16–4.34) vs. + 2.61 (95%CI 1.99–3.23) $P = 0.009$ and lesser residual disease by chest radiograph; number of zones involved 1.35 vs. 1.82, $P = 0.004$ (95%CI 0.15–0.79) and 50% or greater reduction in cavity size 106 (89.8%) vs. 111 (94.8%), $P = 0.035$. Vitamin D supplementation led to significant increase in MTBs-induced IFN-γ secretion in patients with baseline 'Deficient' 25-hydroxyvitamin D serum levels ($P = 0.021$).

Conclusion: Supplementation with high doses of vitamin D accelerated clinical, radiographic improvement in all TB patients and increased host immune activation in patients with baseline 'Deficient' serum vitamin D levels. These results suggest a therapeutic role for vitamin D in the treatment of TB.

Trial registration: ClinicalTrials.gov; no. NCT01130311; URL: clinicaltrials.gov

OP-225-02   Improving the percentage of pulmonary tuberculosis patients who were appropriately managed in Kuala Langat health clinics

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Background: To improve the percentage of pulmonary tuberculosis (PTB) patient who were appropriately managed during their follow up in Kuala Langat health clinics.

Design/methods: A cross-sectional study was conducted among the PTB cases seen in Kuala Langat health clinics. All the PTB smear positive cards were audited and analysed. After the problems in recording and management were identified, intervention stategies were formulated and the remedial actions were carried out. then, the effectiveness of the remedial actions were evaluated.

Results: At the pre-intervention, a total of 68 PTB cases were evaluated. Among the cases, only 23.4% were notified within 24 hours; 44.7% cases have their disease documentation completed and sent to the district officer within 1 week and 42.6% of the cases were register as PTB cases. For their PTB management, we found that there was no cases who has done all the baseline investigations. During their follow up at 2, 4 and 6 months, only 62% of cases had their weight and treatment documented and 57.5% of cases had documentation of their outcome at 6 months. Overall during our audit, we found none of the PTB case were appropriately managed. Availability of the tools in all health clinic was 0% where tools were not properly kept in the right places. the knowledge of the health care workers on PTB were below standard where only 2 doctors and none of the assistant medical officer and nurses scored >80% in the questionnaires. Intervention done were CME and innovations. After the intervention, re-evaluation were carried out after 7 months and then yearly. The results obtained have proven that there was an improvement in the management of PTB cases. PTB were notified on time in 58.1%, 82.8% and 83.3% at 1st, 2nd and 3rd cycles respectively. Baseline investigations were taken in 32.3%, 82.8% and 86.1% at 1st, 2nd and 3rd cycles. The patients weight and treatment were documented at their follow up visit at 2, 4 and 6 months were improved to 55.6%, 57.7% and 88.9% at 1st, 2nd and 3rd cycles. The knowledge of the health care workers also improved with 90% of the doctors, 67% of the assistant medical officers and 48% of the nurses had scored >80% in their questionnaires.

Conclusion: With proper intervention and management, PTB cases can be improved tremendously.

OP-226-02   Isoniazid, rifampicin and pyrazinamide plasma concentrations in relation to treatment response in Indonesian pulmonary tuberculosis patients

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Background: Numerous studies have reported low concentrations of antituberculosis drugs in tuberculosis (TB) patients, but few studies have examined whether low drug concentrations affect TB treatment response.

Design/methods: We conducted a prospective cohort study among 181 patients with pulmonary TB who visited the Persahabatan Hospital, Jakarta, for treatment between March 2010 and March 2011. This was a practical field pharmacokinetic study conducted under routine conditions. Patients were included if they had a positive acid fast bacilli smear and were starting treatment with TB drugs according to the direct observed treatment short course strategy. Among patients with a positive culture at week 0, we examined plasma concentrations of isoniazid, rifampicin, and pyrazinamide at two hours after drug administration (C2h), in relation to culture results at week 4, 8, or 24/32 during treatment. Drug sampling took place at 4 weeks after inclusion in the study, because of the expected steady state in the pharmacokinetics of the TB drugs at that time. Univariate and multivariate logistic regression analyses were used to detect determinants of poor treatment response, defined as a positive culture at week 8 (primary analysis), or any positive culture at 4, 8 or 24/32 weeks of treatment (post-hoc analysis).

Results: Marked interindividual variability was observed in the C2h plasma concentrations of the TB drugs. C2h values below reference values for either isoniazid, rifampicin, or pyrazinamide were found in 91% of patients; 60% had at least two low C2h concentrations. At the end of treatment, 82% of the patients were cured, while 30 patients (17%) had dropped out during the study, and 2 patients (1%) failed treatment. No association was found between C2h concentrations and culture results at 4 or 8 weeks of treatment (Table). Post-hoc analysis showed that patients with low pyrazinamide C2h ($P = 0.01$) and patients with large extensive lung lesions ($P = 0.01$) were at risk of a positive culture at week 4, 8 or 24/32. Concentrations of the other TB drugs used were not associated with treatment response.

Table Relation between antituberculosis drug plasma concentrations and culture results at week 4 and week 8

Characteristic	Negative culture at week 4 ($n = 108$)	Positive culture at week 4 ($n = 56$)	OR (95% CI)
Isoniazid C_{2h} (mg/L)	1.5 (1.0–2.2)	1.3 (0.9–2.2)	0.76 (0.49–1.18)*
Rifampicin C_{2h} (mg/L)	6.7 (4.8–11.8)	6.5 (5.1–10.8)	0.95 (0.66–1.36)*
Pyrazinamide C_{2h} (mg/L)	37.0 (33.2–41.5)	35.4 (31.8–40.9)	0.80 (0.55–1.15)*
	Negative culture at week 8 ($n = 142$)	Positive culture at week 8 ($n = 11$)	
Isoniazid C_{2h} (mg/L)	1.4 (0.9–2.2)	1.3 (0.9–2.4)	0.88 (0.39–1.96)*
Rifampicin C_{2h} (mg/L)	6.8 (5.0–11.7)	6.5 (6.1–12.1)	0.95 (0.47–1.90)*
Pyrazinamide C_{2h} (mg/L)	36.5 (32.4–41.0)	38.5 (34.0–44.6)	1.38 (0.65–2.93)*
Low plasma concentrations of: †			
No drug‡	11 (85)	2 (15)	1.00
One drug	46 (94)	3 (6)	0.36 (0.05–2.41)
Two drugs	50 (93)	4 (7)	0.44 (0.07–2.71)
All three drugs	35 (95)	2 (5)	0.31 (0.04–2.50)
Very low plasma concentrations of: #			
No drug‡	65 (93)	5 (7)	1.00
One drug	64 (94)	4 (6)	0.81 (0.21–3.16)
Two drugs	12 (86)	2 (14)	2.17 (0.38–12.49)
All three drugs	1 (100)	0	n.a.

Note. Data are presented as geometric mean (IQR) or number (percentage) unless stated otherwise. PK parameters were ln transformed. OR, odds ratio; CI, confidence interval; C_{max}, maximum observed plasma concentration; n.a., not assessed.
* Interquartile OR calculated for 75th percentile vs. 25th percentile, based on continuous drug concentration data.
†Isoniazid C_{2h} < 3 mg/L, rifampicin C_{2h} < 8 mg/L and pyrazinamide C_{2h} < 35 mg/L were considered low.
‡Served as reference category.
#Isoniazid C_{2h} < 1.5 mg/L, rifampicin C_{2h} < 4 mg/L and pyrazinamide C_{2h} < 20 mg/L were considered very low.

Conclusion: TB drug concentrations were often low, but treatment response was nevertheless good. No association was found between drug concentrations and 8 weeks culture conversion, but low pyrazinamide drug concentrations may be associated with a less favourable bacteriological response. The use of higher doses of pyrazinamide warrants further investigation.

OP-227-02   Prevalence and severity of adverse drug reactions to clofazimine in the Western Cape province of South Africa

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Background: Clofazimine, a phenazine derivative, was first approved by the Food and Drug Administration (FDA) in 1986 for treatment of leprosy. Although this drug has not been approved for use in tuberculosis (TB) it has shown promising results in murine tests and in a systematic review looking at 12 studies in 10 countries, where overall, 62% of TB patients who received it as part of a multi-drug regimen achieved a successful treatment outcome. Clofazimine fell out of favour due to its lower efficacy but has gained renewed interest as the range of available drugs to offer for drug-resistant patients are limited. Our objective was to report on occurrence and severity of adverse drug event (ADEs) experienced by patients receiving

clofazimine as part of their multi-drug resistant TB (MDR-TB).

Design/methods: We retrospectively reviewed all clinical records of MDR-TB cases diagnosed between 1989–2006 for the occurrence of ADEs due to clofazimine. These patients originated the West Coast/ Wineland districts of the Western Cape Province, South Africa. Patients were included if they had a bacteriological confirmed diagnosis, and were started on a regimen with 3 or more second-line anti-TB drugs (SLD,) one of which was clofazimine. We excluded patients who received clofazimine for one month or less.

Results: In total 1472 patients were enrolled for MDR-TB treatment, among which 86 (5.8%) received clofazimine, 17 (19.8%) as part of their initial MDR-TB regimen while the remaining patients received the drug as part of a salvage regimen. 54/86 (62.8%) were male, median age was 34 (IQR 30–45). HIV information was absent. 5/86 (5.8%) patients experienced a total of 6 clofazimine related ADEs, which were skin hyperpigmentation and/or nausea and vomiting (N+V). 4 patients had hyperpigmentation, and the drug was stopped in 3. One of these patients also experienced N+V from clofazimine, and another stopped the drug due to N+V. Skin hyperpigmentation appeared after 10 (9–14) months of use in the 4 individuals.

Conclusion: Occurrence of side effects to clofazimine were passively monitored and relied on individual patient subjectivity. The prevalence of side effects was very low and demonstrates that clofazimine is a safe and a potentially useful drug for inclusion in regimens for XDR-TB patients.

OP-228-02   What proportion of follow-up smear-positives among new smear-positive pulmonary tuberculosis patients on treatment are culture-negative?

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Background: World Health Organization (WHO) guidelines recommend that tuberculosis (TB) patients whose treatment has failed (based on positive smear results at 5 months or later) should be started on an empirical multi-drug resistant (MDR) TB regimen. There have been concerns around this recommendation as many of the smear positives during follow-up may be culture negative. We aimed to assess the extent of the 'smear positive culture negative' (S+C−) phenomenon in patients receiving regimens with rifampicin throughout the course of treatment.

Methods: Subjects included in this analysis were culture-confirmed new smear positive pulmonary TB patients participating in randomized controlled trials and initiated on a six month rifampicin-containing, thrice weekly intermittent regimen (Category I, 2E3H3R3Z3/4H3R3; H-Isoniazid; R-Rifampicin; Z-Pyrazinamide; E-Ethambutol) at the National Institute for Research in Tuberculosis clinic from January 2000 to August 2012. We reviewed their records and extracted follow-up smear (using fluorescent microscopy) and culture (using Löwenstein-Jensen media) results. The proportion of follow-up smear positives that were culture negative was calculated, disaggregated by month of follow-up examination, pre-treatment drug susceptibility status, HIV status and pre-treatment smear grading. Entry and analysis was done using EpiData software.

Results: Of 520 patients (176 HIV infected), 199, 81, 47 and 43 were smear positive at months 2, 4, 5 and 6 respectively. Of the smear positives, 138 (69%), 62 (75%), 32 (68%) and 27 (63%) were culture negative respectively. S+C− pattern did not vary by HIV status. S+C− phenomenon was more likely among patients whose pretreatment smear grading was 1+ as compared to 2+ or 3+ and more pronounced in patients with bacilli sensitive to all first line drugs (80%, 91%, 78% and 70% at 2, 4, 5 and 6 months) as compared to those with any resistance (39%, 18%, 50% and 33%).
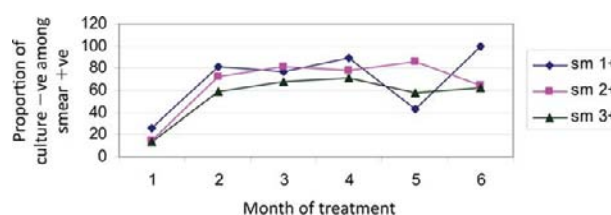
Figure Smear +ve, culture −ve results by month of treatment.

Conclusion: Nearly two thirds of the follow-up smear positives at months 5 and 6 were culture negative. Starting MDR-TB treatment empirically, based on smear results, even in resource limited settings, is incorrect, and can have hazardous consequences including unnecessary treatment with toxic, less potent, expensive and longer duration regimens with unwarranted inconvenience to patients and their families. There is an urgent need to revisit the WHO recommendation.

OP-229-02   Rapid urine lipoarabinomannan testing after two months of tuberculosis treatment independently predicts mortality in a resource-limited setting

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Background: A point-of-care test as a biological marker of tuberculosis (TB) treatment response would be valuable. Our objective was to evaluate a rapid urinary lipoarabinomannan (LAM) test during TB treatment as a prognostic marker for mortality among TB suspects in Durban, South Africa.
Design/methods: We enrolled adults (≥18 years) with ≥2 TB symptoms for ≥2 weeks, either with ≥2 negative sputum smear microscopy (AFB) results or a non-productive cough, and not taking anti-TB medications between Oct 2007–Nov 2009 in Durban, South Africa. We obtained one baseline nebulized sputum sample for AFB and mycobacterial culture on liquid and solid media, and performed rapid urine LAM (Determine™ LAM TB, Alere Inc.) testing on frozen urine samples collected at baseline and 2-months, scoring positive results from 1 (low) to 5 (high). All participants received TB medications for 6 months, and were followed for ≥3 years to assess all-cause mortality reported to the national death registry. We used Cox proportional hazards and regression models adjusted for age, gender, baseline Karnofsky score, and HIV-status to assess associations between rapid urine LAM results and mortality.
Results: Among 90 participants, mean age was 36.9 years; 44 (49%) were female. Eighty-two of 88 (93%) participants tested were HIV-infected; mean CD4 count was 193/mm³. Twenty-nine (32%) participants tested urine LAM-positive at baseline, while 12 of 73 (16%) were urine LAM-positive at 2-months into TB therapy. Twenty-one (23%) participants died during the follow-up period. In univariate age-adjusted analyses, urine LAM-positivity at the 2-month follow-up visit had a trend for greater risk of death ($P = 0.09$), while a LAM score ≥2 had 4.77-fold (95%CI 1.38–16.5) greater risk of death ($P = 0.01$). In multivariate analyses, a LAM score ≥2 at the 2-month follow-up visit was associated with a 7.07-fold (95%CI 1.28–39.2) greater risk of death ($P = 0.03$). During follow-up visits, only a minority of participants could produce sputum, while >90% were able to provide a urine sample. The baseline urine LAM score ≥2 was not significantly associated with mortality.
Conclusion: A strongly positive rapid urine LAM test after 2 months of TB therapy independently predicts mortality in a resource-limited setting. HIV and TB co-infected patients who remain urine LAM positive after 2 months of TB therapy may warrant closer follow-up visits or more intensive medical care.

OP-230-02   A dose-ranging study of daily rifapentine-containing regimens for intensive phase treatment of pulmonary tuberculosis: Tuberculosis Trials Consortium Study 29X

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Background: Rifapentine administered daily has potent activity in a mouse model of TB chemotherapy, but in a phase 2 clinical trial rifapentine 10 mg/kg/dose administered 5 days/week without food was not more active than the conventional rifampin-containing regimen based on the surrogate endpoint of proportion of participants with negative cultures after 8 weeks of treatment. We assessed the safety, tolerability, and antimicrobial activity of regimens containing higher doses of daily rifapentine during the first 8 weeks of combination therapy for pulmonary TB.
Design/methods: Adults with smear–positive pulmonary TB were randomly assigned to rifapentine 10, 15, or 20 mg/kg/dose or rifampin 10 mg/kg/dose, administered 7 days/week for 8 weeks, with isoniazid, pyrazinamide, and ethambutol. Doses were observed and administered with food; rifapentine dose was double-blind. Sputum was collected every 2 weeks for culture on LJ and MGIT media. Outcomes were treatment discontinuations, adverse events, and stable conversion at 8 weeks (2 consecutive culture-negative sputa not followed by a culture-positive specimen). Kaplan-Meier estimates were used to obtain probabilities and confidence intervals of stable conversion by 8 weeks.
Results: 334 participants were enrolled (69% male, 77% with cavitation on chest X-ray); 331 received ≥1 dose of study drugs and were included in safety/tolerability analyses; 290 with drug-susceptible *M. tuberculosis* were included in efficacy analyses. Proportions of participants who discontinued assigned treatment for any reason were 11/83 (13.3%; 90% 1-sided confidence interval [CI] 0, 19) in the rifampin group and 5/86 (5.8%; CI 0, 11), 5/81 (6.2%; CI 0, 11), and 9/81 (11.1%; CI 0, 17) in the rifapentine 10, 15, and 20 mg/kg/dose groups, respectively. Discontinuations due to toxicity were 3/83 (3.6%) in the rifampin group and 0/86 (0%), 1/81 (1.2%), and 2/81 (2.5%) in the rifapentine 10, 15, and 20 mg/kg/dose groups, respectively. Gastrointestinal, hepatic, and hematological toxicity did not differ between study arms. The probabilities of stable culture conversion by week 8 on solid and on liquid media are shown in the Table.

Table Stable culture conversion by week 8, by treatment arm, on Löwenstein Jensen solid medium and on MGIT liquid medium; results expressed as % (95% 2-sided confidence intervals)

	Rifampin 10 mg/ kg/dose	Rifapentine 10 mg/ kg/dose	Rifapentine 15 mg/ kg/dose	Rifapentine 20 mg/ kg/dose
LJ solid medium	83% (71, 90)	94% (86, 98)	91% (80, 96)	98% (87, 100)
MGIT liquid medium	60% (47, 70)	75% (63, 83)	72% (59, 81)	76% (62, 85)

Conclusion: All regimens were well-tolerated and safe. The rifapentine regimens were substantially more active than the rifampin regimen based on the surrogate endpoint of stable conversion at week 8. These results support further evaluation of high dose rifapentine regimens for TB treatment shortening.

PEOPLE LIVING WITHOUT LIBERTY: CASE FINDING AND HOLDING IN PRISONS

OP-231-02   Participación de internos como promotores TAES, en la Prisión de Acapulco, Guerrero México

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Objetivo: Formar internos como promotores TAES, para incidir en el control de la tuberculosis en la prisión de Acapulco, Guerrero.
Justificación: Debido a la tasa de 880 casos de TB por 100 000 habitantes en la prisión de Acapulco, superior a la nacional 16, con 96 veces más de riesgo en PPL, de desarrollar TB, aunado al VIH/SIDA y ante la escasa participación de autoridades penitenciarias, se considera pertinente capacitar a internos para incidir en la transmisión de la enfermedad en ese penal.
Metodologia: Se presentó plan de acción a autoridades penitenciarias, se seleccionaron 24 internos, impartición del curso taller sobre TB, otorgándoles constancia y un chaleco que los acreditó como promotores TAES, se integró el comité y plan de trabajo; en coordinación con el área médica del penal realizaron pláticas celda por celda, en festividades desarrollaron actividades de detección, notificando al servicio médico los sospechosos, recabaron fondos económicos para ayuda alimenticia a enfermos de TB.
Resultados: De agosto 2012 a marzo 2013, identificaron 77 sintomáticos respiratorios, diagnosticándose, 15 casos de TB, 11TBP, 8 con positividad de: 75% +, 12.5% ++ y +++, respectivamente, por; RX (6), TAC (1), 26.7% curó, 20% falleció (SIDA/meníngea), 53.3% continua en TAES. El aporte económico fue de $400.00.

Conclusiones: La estrategia logró empoderar a los promotores TAES, para difundir la existencia de TB en la prisión, favoreciendo la detección, entre PPL y la sensibilización de autoridades penitenciarias del penal de Acapulco.

OP-232-02   Empowering inmates as cough officers: a promising method of active case finding in Cipinang detention centre

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Background and challenges to implementation: Management of TB in detention centre (DC) is one of the key health concerns in Indonesia. According to the National Action Plan of TB Control in Prison and DC in Indonesia, TB is the fourth illness of inmates, and the second cause of deaths in 2011. This suggests TB is still a major health problem in prisons and DC. Inmates represent dynamic, low socioeconomic, low education, productive age, and undiscipline behaviour in a setting that exacerbates TB transmission. Over capacity is also a risk to accelerate TB transmission in DC. Cipinang DC has capacity for 1136 inmates but now occupied by 2939 inmates. In 2012 we have found 29 TB patients with 15 sputum smear positive. In addition to TB screening of new inmates and mass screening, Cipinang DC improved active TB detection by conducting cough surveillance.
Intervention or response: Thirty inmates were trained to be cough officers and were assigned to 4 blocks in the DC and divided into 3 shifts. Their tasks were to identify coughing inmates, to give masks and to refer them to polyclinic for further TB investigation. In addition, the DC also provided masks at the outlets in every block and clinic.
Results and lessons learnt: Between December 2012 to March 2013, a total 261 inmates were given masks and referred to clinic for further TB investigation and 93 suspects were identified. Of 93 pulmonary tuberculosis (PTB) suspects identified from cough surveillance, 17 (18.3%) were identified as smear positive PTB and put on treatment.
Conclusions and key recommendations: Cough surveillance is one of promising method to do active case finding in prison/detention center. Early detection/ prompt treatment and using mask are expected to decrease TB transmission in congregate setting like Cipinang Detention Centre.

OP-233-02   Intensified case-finding for tuberculosis in prison settings in Palawan, Philippines

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Background: It is well proved that TB case rates found in prisons were the highest among any population ever recorded. The Stop TB Strategy expands and enhances the basic components of DOTS and includes TB control strategies to address multidrug-resistant TB and other challenged populations like prisoners. The PhilPACT (Philippines Plan of Action to Control TB, 2010–2016) also addresses TB in prison as one of eight strategies and expands DOTS programme in prison settings. In this context, KOFIH (Korea Foundation of International Health care) supported project covers three (one subnational penitentiary, one provincial and one city level) prisons/jails as parts of 19 project sites located in Palawan, Philippines.

Intervention: A mobile clinic equipped with a digital X-ray, a LED-FM and three Xperts (four modular type) visited prisons/jails to detect TB cases among inmates systematically in collaboration with NTP, CHD4B and LGU (local government unit) authorities in Palawan. All inmates were screened by a digital X-ray and interviewed by health workers with the standardized questionnaire. Anyone who has suspicious symptoms and signs and/or abnormalities for TB on chest radiography was considered TB suspect and subjected to LED-FM and Xpert MTB/RIF testing. Results of testing were informed on the same day and laboratory confirmed cases started treatment on the same day as well at DOTS clinic in prison or were managed with supports from PHO (Provincial Health Office) and CHO (City Health Office). Rifampicin resistant cases identified by Xpert were referred to PMDT center in the Regional hospital in Palawan.

Results and lesson learned: During the first quarter of 2013, 880 TB suspects were identified out of 2294 subjects screened. 127 laboratory confirmed TB cases were detected from 880 TB suspects: 116 RIF susceptible cases, 9 RIF resistant cases and 2 LED-FM positive but Xpert negative cases. Xpert was able to detect 34 TB cases including one RIF resistant case that were missed by LED-FM. All TB cases were registered for treatment at DOTS facilities and 9 RIF-resistant cases were referred to regional PMDT centre for treatment but one case refused treatment. In comparison, these three prisons/jails reported 45 smear-positive TB cases to NTP during the one year period of 2012. Same day same diagnosis is possible with new technologies such as digital X-ray and Xpert MTB/RIF test. And prison authorities recognized the importance of TB control including MDR-TB in prison settings, building up capacities of TB control within its prison facility, and strengthening partnership and referral system with NTP.

Conclusion: New technologies such as digital X-ray and Xpert MTB/RIF enables NTP to diagnose more TB and RIF-resistant TB on the same day in a very effective way, and make it possible to cut transmission as early as possible especially in a crowded setting like prison. Intensified case-finding with focus on high-risk groups such as inmates and coupled with the usage of new tools is a combined strategy that will help NTP in finding more and finding fast TB cases.

OP-234-02   High prevalence of latent tuberculous infection and risk factors associated with a positive TST in Colombian jails

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Background: To determine the prevalence of positive tuberculin skin test (TST) in prisoners and to identify risk factors associated with a positive result.

Design/methods: Cross-sectional study. Male inmates from two jails in Medellín and Itagüí, Colombia, were included if: time of reclusion ≥ 1 year, and agreed to participate in the study and signed the consent form. They were excluded if: prior or active tuberculosis (TB); prior TST administration; immunosuppressive treatment; and administration of live vaccines (MMR, varicella or LAIV) in the 4 weeks prior to the TST application. The TST was administered according to CDC guidelines. Reading was conducted within 48 to 72 hours of administration by two trained nurses and measured and recorded in millimeters of induration. A positive result was considered as an induration of ≥ 10 mm diameter for non-HIV infected people, and ≥ 5 mm for HIV-infected subjects. If the first TST result was positive, the person was considered infected. If the first test result was negative, the TST was repeated in 2–3 weeks. If the second test was positive, the person was considered infected, if it was negative, the person was considered uninfected. Results were expressed as percentages, median and odds ratio (OR) with 95% confidence interval (CI). The outcome was a positive TST result. Bivariate and multivariate analysis was done.

Results: We screened 1006 persons, with 868 TST administrations. Among them, four were not available for reading of the first TST and 25 missed a second TST. The prevalence of positive TST at first administration was 63.9% (552/864), and for the second TST was 36.4% (104/286). The prevalence of positive TST by two-step method was 78.2% (656/839), and stratified by jails were 80.5% and 64.4%. The median age was 32 years and time of reclusion was 13 months. History of contact with TB case was elicited in 30.3% (76.4% were inmates and 21.7% were contacts outside the jail). The percentage of BCG scar was 51.6%, actual drug users 40.2%, prior reclusion 25.3%, diabetes mellitus 6.2% and HIV 0.8%. The risk factor associated with a positive TST was prior reclusion (OR = 1.7; 95%CI 1.1–2.7).

Conclusions: The prevalence of TST in prisoners was higher compared to the general population (42.7%), and it differed between jails. High rates of TB contact in jail may be contributing to the greater prevalence observed in this study. It is important to apply the second TST in order to avoid a misinterpretation during follow-up.

OP-235-02   Prevalence of pulmonary tuberculosis and related factors associated with tuberculosis suspicion among prisoners in Khartoum, Sudan

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Background: A cross-sectional study design was used to determine the prevalence of smear positive pulmonary tuberculosis (SPPTB) among prisoners, and factors associated with TB suspicion.

Design/methods: A total of 382 prisoners were selected from 2647 prison population to include in the study from all five prisons in Khartoum state according to their population proportions. Data were collected by face to face interview using a structured questionnaire. Three sputum samples (spot, morning and spot) were collected by directly observed sputum methods. Sputum specimens were examined for acid fast bacilli (AFB) in Khartoum TB reference laboratory. Multivariable logistic regression was used to explore the factors associated with TB suspicion among prisoners.

Results: Out of 382 prisoners recruited in the study, 21% were TB suspected. Two prisoners were diagnosed as SPPTB; estimated prevalence of SPPTB was 524 per 100 000 prison population. Study participants were predominantly male (75%), and showed a mean age of 33 ± 0.64 years ranging from 16 to 68 years. Educational level of prisoners was low; about 68% did not complete primary school. Only 29% of prisoners had BCG scar. More than half (52%) of prisoners were smokers, while 29% of them took alcohol.

Overcrowding (adjusted OR 2.10, 95%CI 1.14–3.89), contact history with family member diagnosed as pulmonary TB (adjusted OR 3.65, 95%CI 1.30–10.26) and alcohol intake (adjusted OR 1.94, 95%CI 1.01–3.73) were found to be independent risk factors for TB suspicion.

Conclusion: Prevalence of SPPTB was clearly higher among prisoners compared to general population by 5.8 folds. Introducing and integration of National Tuberculosis Program (NTP) activities in prison health services is an important preventive strategy for TB control in prisons and the community.

OP-236-02   Strengthening post-prison tuberculosis patients' treatment follow-up in Azerbaijan by means of geographical information systems

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Background and challenges to implementation: The core reason for the Geographic Information database development is to simplify TB patients' follow up and thus, to improve treatment adherence and success rate among released TB patients. This electronic software enables TB program managers to store and spatially analise treatment related and DOT related information (a line list of all TB patients, DOT care givers; addresses, DOT facilities location; social support [incentives, transport fee]) from one source.

Intervention or response: This database has been designed on MySQL. The PHP programing language has been used on the back-end. Javascript, Ajax and Flash technologies were used on the client side (front-end). Information collected from the field is placed in database by the operator. The access to the database is via internet from the www.prisonhealth.az TB project website. Loginning to the database according to the hierachiral access makes reporting, editing, and utilising database features for various time periods secured. Database generates weekly/monthly/quarterly reports available to the public. Being internet-based, the database is easily accessible everywhere and serves DOT supporters in patients' contact or medical data search.

Results and lessons learnt: Samples of generated spatial GIS data is presented on the picture. 171 DS-TB patients (Figure 1) and 118 DR-TB patients (Figure 2) were released from prison and continued their treatment at DOT centres located spead in the country. There were 13 (11%) cases with HIV (Figure 3) and 81 (47%) cases with HCV (Figure 4). DR-TB patients with HCV and HIV co-infections mainly live in south part of the country. More than 40% of all released

TB patients resided in the capital of Azerbaijan. They were knowingly excluded from visualisation above. **Conclusions and key recommendations:** Analyses and further managerial decision-making becomes easier
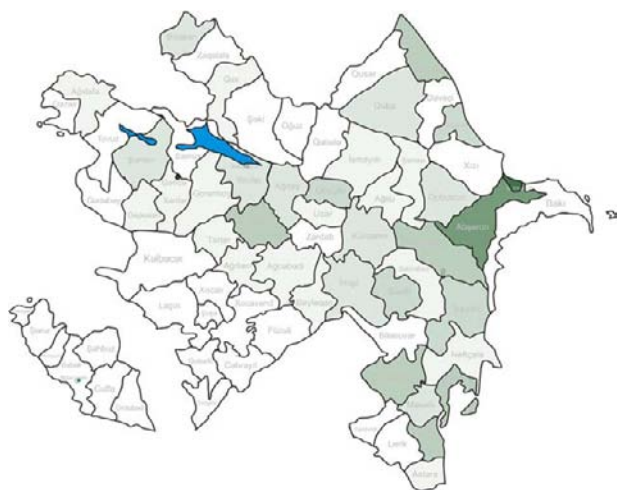
Figure 1   Spatial GIS data: patients under FLD treatment.

Figure 2   Spatial GIS data: patients under SLD treatment.

Figure 3   Spatial GIS data: patients with HIV under SLD treatment.
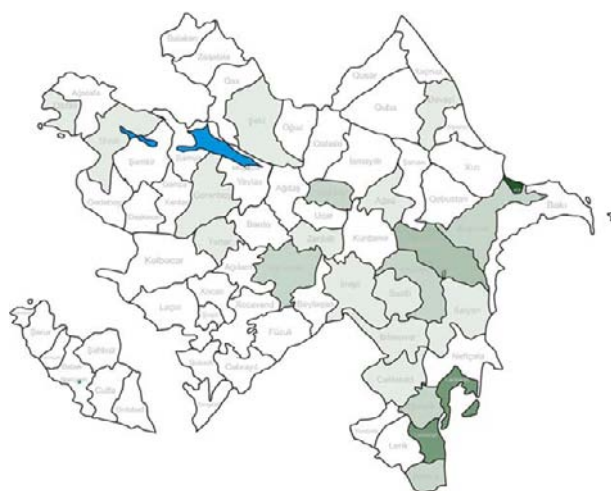
Figure 4   Spatial GIS data: patients with HCV under SLD treatment.

as soon as data are visualised on the map. Visualing TB treatment follow-up became an advance tool during budget and resources reallocation process. The NGO 'Support to Health' within the frame of the project on 'Strengthening TB Control in penitentiary system of Azerbaijan' managed to follow 98% of released patients with the GIS database assistance, while treatment follow up was only 10% in previous years.

OP-237-02   Missing tuberculosis cases: routine symptom-based screening among inmates upon entry to the prison system

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Background: Entry screening can improve the quality of the air in prisons because it leads to increased early diagnosis and treatment then prevents further transmission. However, false information provided by inmates posts challenges for TB screening upon admission.

Design/methods: This retrospective study was to assess TB prevalence among inmates on entry and to explore TB cases missed by this screening method. The study was conducted in a Thai male prison with routine TB program since 2000 and housing 5000 inmates with frequent movement between the prison system and community. In 2011 and 2012, 64 and 56 TB patients were registered respectively. Physical examination on entry for all inmates is mandated in Thailand. A standardized seven-item questionnaire (Cough > 2 weeks, fever, weight loss, night sweat, cough up with blood, history of past treatment and lymph node > 2 cms) was integrated into this process. A clinical score >3 was a criterion for screening positive and eligible for further TB examination. Data of the entry screening forms during the Thai fiscal

year of 2012 (October 2011 and September 2012) were reviewed and entered into SPSS. Names between SPSS and the prison TB register in the fiscal year of 2012 were cross-checked.

Results: A total of 5422 inmates were screened for TB symptoms on entry. Most were Thai (96%) and mean age was 30 years (min–max: 18–86). Screening positive was identified in 204 inmates (4%) and common symptoms among those were weight loss (34%), fever (33%) and cough > 2 weeks (31%). TB disease was diagnosed on entry in six cases (110/100 000) which were a relapse (AFB 3+) case and five transferred-in cases. HIV positive was reported as 17% (1/6). About 63% (10/16) of TB patients who were missed by the entry screening then were later diagnosed as having TB within two weeks to three months after the admission. 60% of missing cases had zero clinical score, while 40% were screening positive. Out of 10 cases, six were new smear positive, two were other with smear positive and two were transferred-in. 40% (4/10) were HIV positive.

Conclusion: TB is prevalent among inmates on admission thus the entry screening remains necessary. However, symptom-based screening should be closely monitored. To increase the integrity of inmate's information, different methods of asking questions should be further considered. In addition, all inmates with screening positive should be followed-up at least three months.

OP-238-02 Unsuccessful and unknown treatment outcomes in tuberculosis patients identified at prison entry screening, Germany, 2002–2008

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Background: Tuberculosis patients in prison are often released while being on treatment as known from a 2006 to 2010 tuberculosis case series in the Berlin prison hospital. While directly observed treatment is ensured within prison hospitals, individual case management, treatment adherence and completion are more challenging outside the prison system. We thus aimed to find out whether tuberculosis patients identified by prison entry screening were more likely to have an unsuccessful or unknown treatment outcome.

Design/methods: We used German tuberculosis notification data from 2002 to 2008 (pooled) to calculate proportions of unsuccessful (treatment default and loss to follow-up) and unknown treatment outcomes stratified by patient groups defined by their mode of case finding (prison entry screening, other screening, contact tracing, passive case finding). Associations of case finding approaches with these treatment outcome categories were assessed using multivariable logistic regression analysis adjusting for demographic

factors (age, sex, and country of birth) and the notification period (2002–2005 and 2006–2008). Deaths were excluded from all analyses.

Results: Among 37 520 surviving tuberculosis patients, overall, 3.5% defaulted treatment, 3.7% were reported as lost to follow-up and for 6.8% treatment outcomes were unknown. In the subgroup of patients identified by prison entry screening ($N = 472$), these outcomes were particularly high: 12.0%, 26.0%, and 8.2%, respectively, adding up to 46.2%. In multivariable analysis, prison entry screening (odds ratio (OR) = 5.9 [95% confidence interval (CI) 4.9–7.2]; and other screening (OR = 1.6; 95%CI 1.4–1.8) were found to be independently positively associated with unsuccessful or unknown treatment outcomes (grouped), whereas odds were lower for contact tracing (OR = 0.7; 95%CI 0.6–0.8) using passive case finding as a reference.

Conclusion: Our results indicate considerable gaps in follow-up and completion of antituberculous treatment among tuberculosis patients identified by prison entry and other screening. Focussed actions and sufficient resources to ensure follow-up of these tuberculosis patient groups are needed to avoid relapses, reduce transmission, and to reach the WHO treatment success rate target of 85% in this specific and other risk groups.

ADVANCES IN CULTURE METHODS

OP-239-02 Re-evaluation of the critical concentration for ethambutol drug susceptibility testing of *Mycobacterium tuberculosis* on BACTEC MGIT 960™

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Background: Upon the transition from the BACTEC 460™ (B460) to the BACTEC MGIT 960™ (M960) method for rapid broth based drug sensitivity testing for *M. tuberculosis*, critical concentrations (CC) were assessed to ensure correlation between results from the B460 and M960. Despite reproducibility issues, a CC of 5.0 μg/mL was established for ethambutol (EMB) on the M960. The aim of this study was to correlate EMB resistance on the B460 with results from the M960 and mutations in the embCAB operon, which are often associated with EMB resistance.

Methods: We selected 32 B460 EMB resistant and 10 B460 EMB sensitive isolates. The minimum inhibitory concentration (MIC) of EMB for these isolates was determined using the M960. The embCAB operon was also sequenced and mutation data correlated to phenotypic sensitivity testing.

Results: All B460 EMB sensitive strains were also sensitive on the M960 (MICs ⩽ 2.0 μg/mL). There were 16 strains resistant at the high B460 CC of 7.5 μg/mL (12: M960 MIC ⩾ 8.0 μg/mL, 3: M960 MIC = 4.0 μg/mL and 1: M960 MIC = 5.0 μg/mL). 14/16 isolates resistant at the B460 CC of 2.5 μg/mL but sensitive at 7.5 μg/mL had M960 MICs of 4.0 and 5.0 μg/mL. There were 18 isolates with M960 MICs = 4 or 5 μg/mL. Many had inconsistent results at the M960 CC of 5.0 μg/mL, but all were resistant at 4.0 μg/mL. 13/18 had embB mutations, which are highly correlated with EMB resistance. All 18 were identified as resistant using the B460 CC of 2.5 μg/mL.

Conclusion: This data shows that an M960 CC of 4.0 μg/mL more accurately identifies strains with a lower level of EMB resistance as identified by the B460. Sequence data confirms that many of the strains that fall into the MIC range of 4.0–5.0 μg/mL on the M960 have mutations in the embCAB operon, specifically in the embB gene, the most common site of mutations correlated with EMB resistance.

OP-240-02   BACTEC MGIT 960™ liquid culture pyrazinamide DST results for MDR-TB isolates compared to status by other phenotypic and genotypic methods

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Background: Pyrazinamide (PZA) is the only anti-tuberculosis compound widely used for both first-line and second-line therapy of TB. However, PZA inclusion in second-line regimens for multidrug-resistant (MDR-TB) cases of TB is rarely based on PZA susceptibility status of the isolates. Two recent studies in South Africa indicated that around half of all MDR-TB isolates include resistance to PZA. Procedures for determining susceptibility to PZA are complicated, and the reliability of assays largely undetermined. However, PZA susceptibility testing in liquid culture is becoming well established, and in this study we compare BACTEC MGIT 960 system with several other assays on a well-characterised series of MDR-TB isolates from South Africa.

Methods: We successfully re-cultured 86 MDR isolates (from a panel of 130 collected in 2001 and stored uninterrupted since then at −80°C) by inoculating 200 μl of each into BACTEC 960 MGIT liquid culture media tubes. For each of these isolates, PZA susceptibility status was known, as determined by BACTEC 460 TB system, Wayne's assay (measuring loss of pyrazinamidase activity as an indication of resistance) and sequencing of the pncA gene for detection of mutations known to be associated with PZA resistance (Mphahlela et al., JCM 2008). Tubes flag-

ging positive were used on day 1 or 2, with 500 μl inoculated into a PZA tube containing 800 μl PZA supplements and 100 μl of PZA drug. Control inoculums contained 500 μl of 1:10 culture dilution.

Results: Of the 86 historical isolates tested by BACTEC 960, all were earlier also tested by BACTEC 460, Wayne's test (80 isolates) and pncA sequencing (80 isolates). BACTEC 960 showed 66% concordance with BACTEC 460 results (25 resistant, 41 susceptible, 11 discrepant), 82.5% with Wayne's enzymatic test (16 resistant, 50 susceptibile, 14 discrepant), and 86.3% with pncA sequencing results (20 resistant, 49 susceptible, 11 discrepant). Sensitivity and specificity of BACTEC 960 relative to pncA mutated isolates as a gold standard indication of PZA resistance were 0.83 and 0.88 respectively.

Conclusion: Our study shows that a high proportion (86%) of MDR-TB isolates truly resistant or susceptible to PZA (pncA gene mutations observed or not observed) was accurately detected by the liquid culture BACTEC 960 assay method. In this series of isolates the probabilities for the false-resistant and false-susceptible results by BACTEC 960 were 12.5% and 16.7% respectively.

OP-241-02   A diagnostic evaluation of the Hardy MODS kit for the diagnosis of tuberculosis and MDR-TB from sputum samples

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Background: MODS is a rapid, inexpensive and reliable liquid culture method that detects *Mycobacterium tuberculosis* alongside rifampicin and isoniazid drug susceptibility. The assay is suited to resource-limited settings, but procurement of consumables from multiple providers can be complex. The Hardy MODS kit provides all materials and standardised reagents in a single box procured with a single order with culture plates that have a sealable silicone lid to minimise biosafety concerns.

Objective: To compare the performance of Hardy MODS Kit (kMODS) to conventional MODS (cMODS) culture in a clinical setting.

Design/methods: 2446 anonymised sputum samples sent to the regional TB reference laboratory from TB suspects were split equally and cultured by cMODS and kMODS. Technicians were blinded to the results of the parallel cultures. Data were analysed using Stata 10. The concordance of results for both TB and

drug susceptibility detection was determined with the use of sensitivity and specificity (with 95% confidence intervals) as well as with kappa values. The z test for comparison of two proportions was used to compare contamination rates and Wilcoxon signed-rank test was used to compare the times to positive results between methods.

Results: kMODS has a high degree of agreement with cMODS for both TB and MDR-TB detection (agreement 97.5%, κ = 0.94 and agreement 99.8%, κ = 0.99 respectively). The relative sensitivity and specificity (including 95% confidence intervals) of kMODS compared to cMODS for TB detection was sensitivity 99.4% (98.5–99.8%) and specificity 98.4% (97.7–98.9%). For MDR-TB detection it was sensitivity 100% (95.0–100.0%) and specificity 99.8% (99.0–100.0%). Median time to culture positivity was significantly shorter for kMODS than cMODS (8.5 days [IQR, 7–11] vs. 10 days [IQR 9–13] respectively; $P < 0.001$). Contamination rates were significantly higher ($P < 0.01$) in kMODS compared to cMODS at 1.1% and 0.1% respectively, but this did not reduce kMODS sensitivity.

Conclusion: MODS kit performed well in comparison to conventional MODS culture. The use of quality-assured bacteriology as provided by the kit is likely to improve early case detection and diagnosis of TB and MDR-TB particularly for laboratories that would benefit from the simplification of culture methods and acquisition of materials.

OP-242-02   MDR/XDR-TB Colour Test simultaneous culture and drug susceptibility results predict tuberculosis outcomes

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Background: Commitment to treating multi-drug resistant (MDR) TB is growing. Many peripheral laboratories lack the facilities to perform drug susceptibility testing (DST), relying on indirect DST performed in reference labs, often with delays of several months. The 'MDR/XDR-TB Colour Test' is a thin layer agar culture method with improved biosafety designed for use in basic laboratories that allows simultaneous TB culture and DST for isoniazid (H), rifampin (R) and ciprofloxacin.

Design/methods: DST results for the Colour Test are assigned by growth in drug-containing agar on the first day of TB growth. On occasion there is delayed growth in a drug-containing well in a plate initially read as susceptible. We followed up 503 episodes of TB in 492 patients diagnosed between April 2009 and February 2011 and used clinical outcomes to assess the clinical significance of different TB growth patterns in the Colour Test. Desirable outcomes were defined as cure or finished treatment. Adverse outcomes were TB recurrence, all-cause mortality, and treatment failure. Hazard ratios (HR) were obtained with Cox regression for H and R separately. We analyzed H-resistance in R-susceptible strains only.

Results: 43 adverse patient outcomes occurred during 521 patient-years of follow-up. Colour Test DST results were available for 79% (399) of the samples. The median time from sample inoculation to results was 20 days (IQR 17–22; maximum 45 days). Among the 351 R-susceptible strains, 16% (57) were H mono-resistant and another 28% (97) had delayed growth in H. Overall 11% (43) were MDR strains and 1.3% (5) were R mono-resistant. Another 26% (103) had late growth in R. Figures 1 and 2 show survival curves for H and R respectively. Initial growth in H had an HR of 6.0 (95%CI 2.2, 17; $P = 0.001$) for adverse outcomes compared to never growth in H. Late growth was similar to never growth (HR 1.0; 95%CI 0.3, 2.1; $P = 1.0$). Early growth in
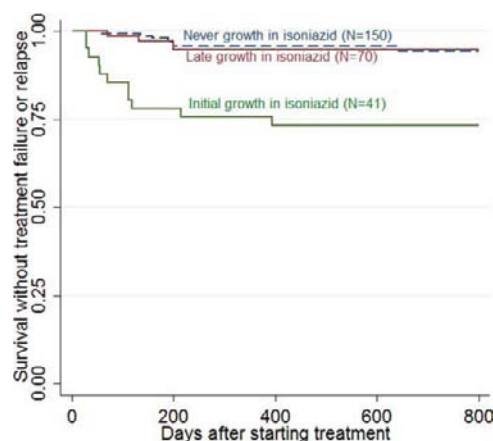
Figure 1 Survival by isoniazid resistance among rifampicin susceptibles ($n = 261$).
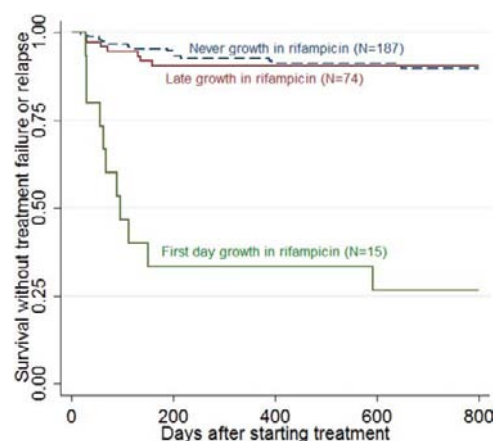
Figure 2 Survival by rifampicin resistance ($n = 276$).

R predicted adverse outcomes with HR = 17 (95%CI 7.4, 40; $P < 0.001$). Late growth was not significantly associated with outcomes (HR 1.5, 95%CI 0.6, 3.9; $P = 0.9$) compared to never growth in R.

Conclusions: The Colour Test provides clinically meaningful drug susceptibility results at the time of first TB growth in an average of 3 weeks and maximum 6 weeks. At this time positive cultures can immediately have a final report sent and the cultures can be discarded or sent for further analysis without further incubation.

OP-243-02   Carbendazim reduces contamination of tuberculosis cultures in the thin layer agar MDR/XDR-tuberculosis Colour Test

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Despite having lower rates of contamination than broth culture, contamination remains a problem in thin layer agar (TLA) TB diagnosis using the MDR/XDR-TB Colour Test technique. We aimed to reduce contamination using the broad-spectrum benzimidazole fungicide, carbendazim.

Methods: Sputum specimens were collected from people with suspected TB disease who lived in the study site of Ventanilla, on the outskirts of northern Lima, Peru. Between January 2012 and April 2013, 1736 sputum specimens were cultured using TLA after sputum samples were decontaminated by mixing with trisodium phosphate in the sputum pot. The TLA plates were divided into four separate, non-communicating quadrants, two of which contained carbendazim 50 mg/l. The other two quadrants contained no carbendazim. The TLA plates were assessed over 6 weeks for signs of TB growth or contamination in any of the four quadrants. Contamination was defined as bacterial, fungal or mixed on the basis of the recognized morphology of each.

Results: The TLA culture quadrants containing carbendazim were overgrown by contamination in 4/3472 (0.12%), less than 38/3472 (1.1%) of the TLA quadrants that did not contain carbendizim ($P < 0.001$). The TLA culture half-plates containing carbendazim were overgrown by contamination in 1/1736 (0.058%), less than 10/1736 (0.58%) of the TLA half-plates that did not contain carbendizim ($P < 0.001$). One of the 1736 TLA plates (0.058%) was completely overgrown by fungus in all four quadrants with and without carbendizim whereas all the

Quadrants $P = 0.0001$		With carbendazim	
		Totally contaminated	Interpretable
Without carbendazim	Totally contaminated	3	35
	Interpretable	1	3472
Half culture plates $P = 0.0001$		With carbendazim	
		Totally contaminated	Interpretable
Without carbendazim	Totally contaminated	1	9
	Interpretable	0	1736

other 1735/1736 (99.9%) of TLA culture plates gave interpretable results in at least one quadrant. Only fungal contamination was found, there was no evidence of bacterial or mixed infection. The proportion of quadrants with growth of *Mycobacterium tuberculosis* and/or of partial fungal contamination that did not inhibit culture interpretation was unaffected by carbendazim.

Conclusions: The morphological differentiation of *M. tuberculosis* from fungal contamination was highly achievable in TLA TB diagnosis. Carbendazim almost completely prevented fungal contamination in TLA plates causing uninterpretable culture results. Carbendazim is a useful addition to TLA plates to prevent contamination of samples during TB diagnosis and thus increase diagnostic yield.

OP-244-02   Use of the nitrate reductase assay in DST proficiency testing

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Background: Among low-cost techniques for drug susceptibility testing (DST) of M tuberculosis, the nitrate reductase assay (NRA) appears promising for a rapid, specific, sensitive and easily implemented DST method. In our Center a TB test-kit and a XDR-test were developed and now they are produced and are approved in RF. The TB test-kit and XDR-test are based on the NRA.

Aim: To determine the sensitivity and specificity of DST with the TB test-kit and XDR-test in frame of annual DST proficiency testing (PT) coordinated by the the WHO Supranational Reference Laboratory (SRL) at the Swedish Institute for Communicable Disease Control, in 2005–2012.

Methods: Yearly PT panels of well charatherised *M. tuberculosis* strains were provided by the SRL. The 2005–2008 DST panels consisted of 20 strains, either susceptible or resistant to 1st line drugs. The 2009–2012 panels contained 20 strains susceptible or resistant to 1st and/or 2nd line drugs. NRA performed using TB test-kit for the susceptibility testing to 1st line drugs and XDR-test for the susceptibility testing to 2nd line drugs. The TB test-kit and XDR-test are ready-for-use LJ media kits with or without drugs and Griess reagent for reading results. Used critical

concentrations of the drugs in the kits were as follows: INH 1.0 μg/ml, RMP 40 μg/ml, SM 10 μg/ml, EMB 2 μg/ml, OFX 3.0 μg/ml, KM, AK and CM 30 μg/ml. DST results obtained with NRA were compared with the SRL network consensus results.

Results: A total of 160 proficiency test strains of *M. tuberculosis* were analyzed within 8 rounds in 2005–2012. Interpretable results were obtained for 159 (99%) strains tested. One strain (INH/EMB-resistant) had invalid results for NRA, and did not show a color change in the control vial after 14 days of incubation. The majority of NRA results (89%) were available at day 10 after inoculation. Obtained DST data showed good to excellent agreement with the SRL consensus results. Accuracy (ratio of the number of accurate results to all results) was estimated for each drug for each round. The mean accuracy of DST for INH was 96.9%, for RMP and SM was 95.6%, for EMB was 98.1%, for KM, AK and OFX was 98.8%, for CM was 96.3%. In 2012, there was complete agreement between the results for all eight drugs.

Conclusion: NRA performed by 'Obolensk' products has been used successfully in DST PT in 2005–2012. Very good agreement were obtained between the NRA and the SRL network consensus results for both 1st and 2nd line drugs.

OP-245-02 Cost-effectiveness analysis of introducing rapid culture in tuberculosis diagnosis in low-income setting with high tuberculosis and HIV prevalence

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Background: Diagnosis of smear-negative pulmonary tuberculosis (TB) based on clinic and chest X-ray fails to detect true TB cases and increases the risk of overtreatment of non-TB cases. In 2007, WHO recommended introducing rapid *Mycobacterium tuberculosis* culture in the diagnosis algorithm of smear-negative pulmonary TB suspects. However, culture requires high level of laboratory infrastructure, equipment and expertise that are difficult to achieve in limited resource setting. We assessed the cost-effectiveness of the introduction of a rapid non-commercial culture method Thin Layer Agar (TLA) together with Löwenstein-Jensen (LJ) culture to improve diagnosis of smear-negative TB at the Homa Bay district hospital (Kenya).

Methods: Data on effectiveness (number of true TB cases treated) were obtained from a prospective cohort study evaluating the effectiveness of a clinical and radiological algorithm with and without *M. tuberculosis* culture in 380 consecutive smear-negative pulmonary TB suspects. The costs of each algorithm diagnosis were calculated using a 'micro-costing' or 'ingredient based' method in which costs were estimated by identifying the resources used for each 'patient'. The value of the resources or 'ingredients' was then estimated from the relevant quantities and corresponding unit price. The cost and efectiveness of the diagnostic algorithm was compared between algorithms with and without culture and the incremental cost-effectiveness ratio (ICER) was estimated.

Results: The clinical-radiological algorithm was less costly (11 690€, with a mean cost per smear-negative TB suspect of 30.8€) than the algorithm with TLA/LJ culture (51 569€, with a mean cost per smear-negative TB suspect of 136€). The cost per true TB treated case without culture was 354.2€ and 859.5€ when the *M. tuberculosis* culture was introduced. The ICER shows that TLA/LJ culture allowed to diagnose 27 more cases for an additional total cost of 39 879€ (1477€ per new detected case).

Conclusion: The introduction of *M. tuberculosis* culture to diagnose smear-negative pulmonary TB can be considered at cost-effective according to WHO standards as the ICER is less than three-fold the GDP per inhabitant (1668€ in Kenya). However, it increased by 3 to 4 times the overall cost. Moreover, it did not reduce the cost due to overtreatment of non-TB cases due to the long delays of culture results compared to the clinical and radiological algorithm. The challenge would be to find a less costly culture method that reduces costs.

OP-246-02 Dynamic microcolony growth monitoring for drug susceptibility testing of ethambutol and pyrazinamide

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Background: A complete overview of the susceptibility to available drugs is crucial for the provision of effective therapy and interruption of transmission of drug resistant pathogens. Susceptibility testing of some antimycobacterial drugs is difficult to perform reproducibly. We have developed a novel culture system for DST, in which the growth of microcolonies from individual CFUs is monitored and microcolonies can be (transiently) exposed to drugs to measure growth rate and susceptibility of individual colonies. We previously demonstrated that this method could be used to distinguish rifampicin (RIF) susceptible and resistant strains of *Mycobacterium tuberculosis*, and detect mixed strains, within 8 days after inoculation and after only 24 hours exposure to RIF.[1] We have

now investigated the performance of this method for testing of ethambutol (EMB) susceptibility.

Design/methods: A panel of 20 tuberculosis strains with known EMB susceptibilities was tested blindly and classified based on a panel of 4 strains with known susceptibilities.

Results and conclusions: After 7 days of growth on non-selective medium, microcolonies were transferred to medium containing EMB and could be classified as susceptible of resistant within 2 additional days. Testing of the EMB panel yielded a 95% accurate classification (19/20 strains). Secondly, the approach is used to set up an assay for pyrazinamide (PZA) susceptibility testing. Inhibition of pyrazinamide susceptible strains could be detected within a similar time frame, and currently optimization of the protocol is being investigated.

Reference
Den Hertog et al., PLOS ONE 5 (6): e11008. doi:10.1371/journal. pone.0011008

OP-394-02   Does clofazimine contribute to the activity of second-line regimens for tuberculosis in mice?

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Background: Because clofazimine is a drug of which the contribution for treatment of tuberculosis in humans is still largely unknown despite the seminal publication of van Deun et al., in 2010, an experimental study was performed to determine its activity in mice.

Design and method: The study was designed to compare the time to culture conversion and the percentage of relapses after treatment cessation in mice infected with *Mycobacterium tuberculosis* and treated with a second-line drug regimen with and without clofazimine. All mice were aerosol infected with an isoniazid-resistant strain, as surrogate of multidrug-resistant *M. tuberculosis*. They were treated 5 days a week for 5, 6, 7, 8, or 9 months with a drug regimen including moxifloxacin 100 mg/kg, ethambutol 100 mg/kg, and pyrazinamide 150 mg/kg; treatment was supplemented by amikacin 100 mg/kg during the first two months. Half of the mice, the test group, received clofazimine 25 mg/kg given by the oral route in addition to this regimen whereas the other half, the control group did not. During treatment decline in lung colony-forming units was assessed monthly using selective 7H11 agar supplemented with 0.4% charcoal to reduce the negative impact of clofazimine carry over. Culture-positive relapse was assessed 6 months after treatment cessation.

Results: At month 2, at the end of the amikacin sup-

plement, the bacillary load in lungs was reduced from 9.74 ± 0.08 log**10** at baseline to 3.61 ± 0.20 and 4.68 ± 0.12 in mice treated with or without clofazimine, respectively ($P < 0.001$). Later, lung cultures became close to negative at month 4 and were negative at month 5 in mice treated with clofazimine, whereas all mice treated without clofazimine remained heavily culture-positive and died or were still culture positive 6 months after treatment cessation. The proportion of relapses was 3/15, 3/15, 5/15, 1/14 and 1/15 among mice treated with clofazimine for 5, 6, 7, 8 and 9 months, respectively ($P > 0.1$). On average, the rate of relapse-free cure among clofazimine-treated mice was 82.4%.

Conclusion: Clofazimine contribution was spectacular in the present experimental conditions.

POSTER DISCUSSION SESSIONS

SERODIAGNOSTICS AND BIOMARKERS

PC-551-02   Point-of-care C-reactive protein testing may facilitate implementation of isoniazid preventive therapy for people living with HIV

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Background: The WHO endorsed a four-part symptom-screen with high negative predictive value (NPV) for active tuberculosis (TB) to facilitate implementation of isoniazid preventive therapy (IPT). However, most people living with HIV (PLHIV) in sub-Saharan Africa are symptom screen-positive, regardless of TB status. We evaluated whether point-of-care (POC) testing for C-reactive protein (CRP), a marker of inflammation, improves selection of PLHIV for IPT.

Methods: We measured POC-CRP levels (normal <10 mg/L) on stored serum samples from HIV-infected adults initiating ART in the Uganda AIDS Rural Treatment Outcomes (UARTO) cohort using the inexpensive and rapid iCHROMATM POC-CRP Reader (BodiTech Med Inc.). We assessed diagnostic accuracy for TB in reference to baseline TB status adjudicated by an expert committee considering all available data up to six months post-enrollment and calculated net reclassification improvement (NRI) to quantify the incremental discriminatory benefit of POC-CRP for selection of patients for IPT compared with the WHO symptom screen.

Results: Of 201 patients, 70% were female with a median age of 34 years (IQR 28–40) and median CD4 count of 137 cells/μL (IQR 83–206); five (2.5%) had active TB. Compared with the WHO symptom-screen, POC-CRP had similar sensitivity (100% vs. 80%; difference −20%, 95%CI −59 to +19, $P = 0.30$) but greater specificity (21% vs. 87%; difference +66%, 95%CI +52 to +79, $P < 0.0001$) for active TB. POC-CRP also had high NPV (99%, 95%CI 97–100). If based on the WHO symptom-screen, no patients with active TB but only 42/196 patients without active TB would have been considered eligible for IPT. If CRP were used instead, one patient with active TB (reclassification of cases = −20%, $P = 0.32$) and 129 patients without active TB (reclassification of non-cases = +66%, $P = <0.001$) would have been reclassified as being eligible for IPT (Figure), an NRI of 46% ($P = 0.03$). In addition, POC-CRP testing would have reduced the proportion of patients without active TB requiring confirmatory TB testing (87% vs. 21%, $P < 0.0001$).
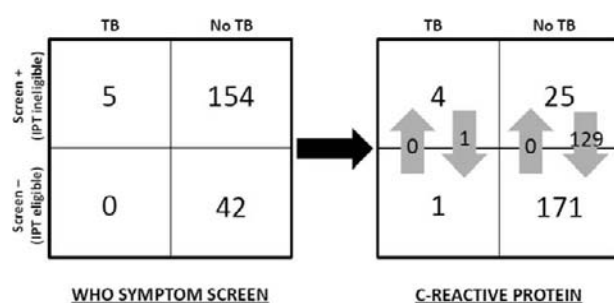
Figure Reclassification of patients eligible for isoniazid preventive therapy.

Conclusions: In a prototypical group of PLHIV initiating ART, POC-CRP testing increased more than four-fold the proportion of HIV-infected adults immediately identified as IPT-eligible and decreased the proportion of patients requiring referral for further TB diagnostic testing. POC-CRP testing could substantially improve implementation of IPT and intensified TB case finding among PLHIV.

PC-552-02   Utility of a serodiagnostic kit for diagnosing *Mycobacterium avium* complex pulmonary disease in Japan

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Background: The diagnosis of *Mycobacterium avium* complex pulmonary disease (MAC-PD) is sometimes difficult because MAC is ubiquitous in the environment. A MAC-specific serodiagnostic kit that measures serum glycopeptidolipid (GPL) core immunoglobulin A antibody by enzyme immunoassay was developed and launched in Japan in 2011. This study evaluated the utility of the kit in routine clinical settings.

Methods: The serodiagnostic kit has been used in routine practice in the NHO Toneyama Hospital since its development. The antibody levels measured by the kit were available for 485 patients with MAC-PD, 133 patients were diagnosed with pulmonary tuberculosis, and 23 with *Mycobacterium kansasii* pulmonary disease from December 2006 to June 2012. As controls, sera were obtained from 265 healthy volunteers, and antibody levels were measured. Of the 454 patients in the MAC-PD group who were evaluated by chest computed tomography, 56 (12.3%) were classified as having fibrocavitary (FC) disease, 359 (79.1%) as having nodular bronchiectatic (NB) disease, and 39 (8.6%) were unclassifiable.

Results: The levels of GPL core antibody in the MAC-PD, pulmonary tuberculosis, *M. kansasii*, and control groups were 7.23 ± 10.83, 0.398 ± 2.06, 0.16 ± 0.47, and 0.08 ± 0.13 U/mL, respectively; the levels were significantly higher in patients with MAC-PD ($P < 0.0001$). When the cutoff was set at 0.7 U/mL, the sensitivity and specificity were 78.6% and 96.9%, respectively. The antibody levels in 50 patients diagnosed on the basis of bronchial wash culture were significantly lower than those in 435 patients diagnosed on the basis of sputum culture ($P < 0.0001$); the positivity rates in the former and latter groups were 54.0% and 81.3%, respectively. Antibody levels were significantly higher in patients with FC disease than in those with NB disease and those who were unclassifiable ($P < 0.0001$). The positivity rates for the detection of FC disease, NB disease, and unclassifiable disease were 80.5%, 80.4%, and 51.4%, respectively.

Conclusion: The serodiagnostic kit demonstrates good sensitivity and specificity in large sample sizes. It could be a useful supplemental tool for diagnosing MAC-PD in clinical practice.

PC-553-02   Acute phase reaction in pulmonary tuberculosis during treatement

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It is well known that acute phase proteins rapidly increase in many infective, traumatic, malignant and autoimmune conditions. Tuberculosis is one of them.

The aim of our study was to estimate prognostic value of C-reactive protein and alpha 1 acid glycoprotein. We investigated 46 patients (39 men and 7 women), mean age 42.89 ± 13.2, with smear positive pulmonary tuberculosis, microbiologically confirmed with culture. The acute phase proteins were measured in sera using nephelometric method. The sera were taken on the day of admission and: 5th to the

7th day, 30th and 60th day during therapy. Statistically analyze was made using Student's t-test. Statistically significant differences were found for C-reactive protein between the first and third measurement ($P <$ 0.04) and the first and fourth measurement ($P <$ 0.018). Significant differences were also found for alpha 1 acid glycoprotein between the first and second measurement ($P < 0.000006$), the first and third ($P < 0.000005$), the first and fourth ($P < 0.0002$), second and fourth ($P < 0.00005$), as well as between the second and third measurement ($P < 0.0004$).
Conclusion: These two acute phase proteins gradually decreased during therapy, which helps in monitoring the course of the disease and the response to chemotherapy, with other words these can be helpful in the prognosis of the disease.

PC-554-02   Usefulness of serodiagnosis for *Mycobacterium avium* complex lung disease in Taiwan

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Background: Non-tuberculous mycobacteria lung disease (NTM-LD) becomes an important clinical concern. Among NTM, *Mycobacterium avium* complex (MAC) is one of the most common species causing lung disease, especially in eastern Asia. However, diagnosis of NTM-LD remains a big challenge in clinical practice because microbiology tests for MAC are neither timely nor efficient. Hence, more rapid and accurate diagnostic test should be developed. Among the candidate test, MAC sero-diagnosis will be probably helpful to differentiate NTM-LD from colonization and had been reported in Japan but not yet well investigated in other countries.
Design/methods: This study prospectively enrolled patients in multi-centers in Taiwan. Patients were recruited as MAC-LD, MAC-colonization and other lung disease groups according to NTM diagnosis guidelines of American Thoracic Society. We collected participant's plasma to examine the MAC glycopeptidolipid (GPL) core immunoglobulin A antibody. We analyzed the diagnostic help from MAC serodiagnosis.
Results: During the study period, MAC-LD and colonization was defined in 53 and 14 patients, respectively. We also enrolled 13 *M. kansasii*-LD, 38 other NTM-LD, 48 patients with pulmonary tuberculosis (TB) and 42 without active infection. In comparing to other groups with different lung disease status, patients with MAC-LD were older. There was 33% having underlying co-morbidity in MAC-LD, similar with those with mycobacterial lung disease. In regard

to serum level of MAC GPL antibody, MAC-LD patients had higher value compared to every other group (Figure). In multivariate logistic regression, age (OR 1.08, 95%CI 1.01–1.15) and MAC GPL antibody level (OR 3.43, 95%CI 1.16–10.17) were the only significant factor for predicting MAC-LD from colonization. ROC curve analysis revealed that serum MAC GPL antibody had the higher power discriminating MAC-LD from MAC colonization (AUC = 0.77) and the optimal cut-off value of MAC GPL antibody was 0.73 U/mL (sensitivity 60%; specificity 93%).
Conclusion: The MAC GPL antibody level can discriminate MAC-LD and colonization with an intermediate sensitivity (60%) but an excellent specificity (93%) using a cut-off value of 0.725 U/mL.

PC-555-02   False positive results for MTB-LAM: the search for contamination

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Background: LAM is a lipopolysaccharide specific to the cell wall in the genus *Mycobacterium* and is released when mycobacteria are affected by the host immune system. The lipopolysaccharide is filtered by the kidneys and can subsequently be detected in the urine of TB infected individuals.
Methods: The LAM-ELISA was evaluated in a general population study, with more than 17 000 individuals of all age groups and both genders. Participants were visited annually for specimen and data collection.
Results: In 2006—the first of five annual surveys—2918 positive LAM screening results were found among 17 369 analysed urine samples (16.8%), which exceeded all reasonable expectations of detectable TB cases. For the Mbeya region 3600 confirmed TB cases were reported in 2006, which translates to 31 culture-confirmed TB cases in a population of 17 369 participants. After protecting the urine collection container from dust, the percentage of LAM-positive urines dropped to 10.3% suggesting soil as an contaminating factor. However, the results were still beyond reasonable expectations, so in addition to dust also other contaminating factors were suspected. Artificial urine contamination with Candida albicans or blood, as well as urinary tract infections with different bacteria led to only insignificant changes in the optical density (OD). In order to explore the significance of stool as a contaminating factor, LAM negative urine samples of 13 individuals

living in Mbeya, Tanzania and of 12 individuals in Munich, Germany were mixed with 80 mg of stool from the respective individual. The solution was centrifuged and the supernatant diluted in a series of 1:1 up to 1:8, causing a significant increase of OD in 23 out of 25 individuals. As non-tuberculous mycobacteria such as *M. gordonae* and others are present worldwide in tap water and soil and have been described in human stool, it is possible that NTMs are the causative agent for contamination. If urine is collected under field conditions, where mid stream urine collection in sterile containers cannot be guaranteed, false positive results of the MTB LAM ELISA due to stool contamination are likely.

Conclusion: We found the performance of the MTB LAM ELISA significantly influenced by different environmental factors. Dust and soil, but also stool can lead to increased OD values and thus false positive results of the MTB LAM-ELISA, whereas contamination with blood, as well as bacterial or fungal organisms had no influence.

PC-556-02   Point-of-care urine lipoarabinomannan for diagnosis and treatment response of pulmonary tuberculosis in sputum smear-negative suspects

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Background: A rapid, point-of-care test to monitor response to tuberculosis (TB) treatment would be valuable. Our objective was to evaluate a rapid urinary lipoarabinomannan (LAM) test for initial diagnosis and assessment of response among TB suspects commencing treatment.

Design/methods: We conducted a prospective study between Oct 2007–Nov 2009 in Durban, South Africa. Eligible participants were adults (≥18 years) with ≥2 TB symptoms for ≥2 weeks, either with ≥2 negative sputum smear microscopy (AFB) results or a non-productive cough, and not taking anti-TB medications. We obtained one baseline nebulized sputum sample for AFB and mycobacterial culture prior to TB treatment initiation. We performed rapid urine LAM (Determine™ LAM TB, Alere Inc.) testing on samples collected at baseline, 2-months, and 6-months, and scored positive results from 1 (low) to 5 (high). We calculated diagnostic accuracy of urine LAM at initial diagnosis using sputum culture-positive *Mycobacterium tuberculosis* as the gold standard. We assessed changes of urine LAM test results during TB therapy among those with and without culture-

confirmed pulmonary TB, using Fisher's exact test, paired *t*-tests, and repeated measure logistic and linear regression models.

Results: Among 90 participants, 44 (49%) were female; mean age was 36.9 years. Eighty-two of 88 (93%) participants tested were HIV-infected; mean CD4 count was 199/mm³. Fifty-seven (63%) participants had culture-confirmed pulmonary TB. Diagnostic sensitivity of urine LAM was 42% (95%CI 29–56%) overall, and 65% (95%CI 41–85%) among those with CD4 <100/mm³. Diagnostic specificity was 85% (95%CI 68–95) overall, and improved to 97% (95%CI 84–100) when using a LAM score ≥2 as positive. The percentage of LAM test positive decreased significantly during the first 2 months of anti-TB therapy for both the entire cohort and HIV-infected participants ($P < 0.0001$). In multivariate analyses adjusted for age and gender, the percentage of LAM test positive decreased significantly among those with culture-confirmed pulmonary TB during 6 months of therapy ($P < 0.0001$), and had no significant change in those without TB (Figure).
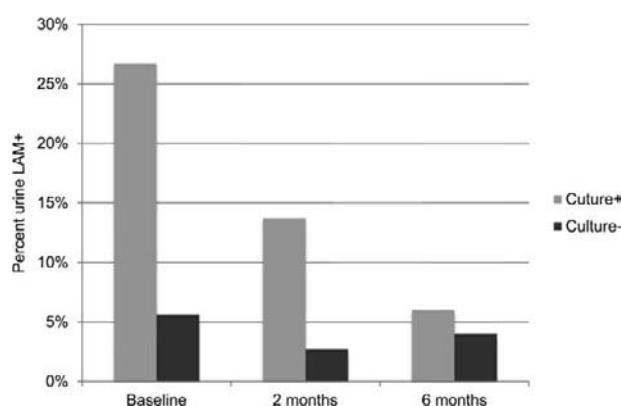
Figure Percent urine LAM positive during 6 months of anti-TB therapy among sputum culture-positive and culture-negative for pulmonary TB.

Conclusion: Among TB suspects, point-of-care urine LAM had moderate sensitivity and high specificity for diagnosing pulmonary TB, and decreased linearly among those with culture-confirmed pulmonary TB receiving therapy. Urinary LAM may be a valuable and inexpensive biomarker for monitoring treatment response of TB.

PC-557-02   Diagnostic accuracy of rapid, point-of-care C-reactive protein testing in HIV-infected pulmonary tuberculosis suspects in a tuberculosis-endemic region

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Background: Rapid, clinic-based tests are needed to diagnose sputum smear-negative tuberculosis (TB) in HIV-infected adults in resource-limited settings. We sought to determine the diagnostic accuracy of point-of-care C-reactive protein (CRP) testing, when combined with symptomatic, radiographic, and clinician assessments, in a TB-endemic region.
Design: We enrolled HIV-infected TB suspects between Aug 2009–Oct 2010 at Edendale Hospital in KwaZulu-Natal, South Africa. Eligible participants were adults ($\geqslant$18 years) with a cough for $\geqslant$2 weeks, either $\geqslant$2 negative sputum smear microscopy (AFB) results or a non-productive cough, and not taking anti-TB medications. Upon enrollment, a study nurse collected $\geqslant$2 nebulized sputum samples for AFB and mycobacterial culture and performed point-of-care (POC) CRP testing (NycoCard CRP test; Axis-Shield; Norway) on whole-blood. Each participant had a chest radiograph, was assessed by a nurse for TB symptoms (cough, fever, nights sweats, weight loss), and was examined by a physician. We calculated diagnostic accuracy of the rapid CRP test using sputum AFB- or culture-positive for *Mycobacterium tuberculosis* as the gold standard.
Results: Among 84 participants, 50 (60%) were female, mean age was 34.3 (S.D. $\pm$ 7.8) years, and median CD4 count was 174 (IQR 77–254)/mm^3. Forty-five (54%) participants were diagnosed with pulmonary TB. Fifty-nine (70%) and 42 (50%) participants had a POC CRP result $\geqslant$10 and $\geqslant$25 mg/L. Diagnostic sensitivity and specificity were 95% (95%CI 74–99) and 51% (95%CI 35–66) for CRP $\geqslant$10 mg/L, and 77% (95%CI 63–89) and 73% (95%CI 58–85) for CRP $\geqslant$25 mg/L. When using criteria of $\geqslant$3 TB symptoms and CRP $\geqslant$10 mg/L, test sensitivity was 92% (95%CI 73–99) and specificity was 53% (95%CI 38–68). When using a testing approach of CRP $\geqslant$25 mg/L and a positive nurse assessment of symptoms, test sensitivity was 72% (95%CI 61–87) and specificity was 78% (95%CI 63–89). A physician with radiography results had a sensitivity of 69% (95%CI 59–86) and specificity of 76% (95%CI 60–87), and when incorporating CRP $\geqslant$50 mg/L, sensitivity improved to 85% (95%CI 69–94) and specificity was 73% (95%CI 58–85).
Conclusion: Among HIV-infected TB-suspects, rapid CRP testing had moderate diagnostic accuracy for detecting active TB, and performed as well as a physician with a chest radiograph. Rapid CRP testing may be an inexpensive and accessible diagnostic test for active TB among HIV-infected adults in TB-endemic regions.

PC-558-02   Urine and blood IP-10 are associated with active tuberculosis disease in adults and children in high tuberculosis endemic countries

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Background: Urine IP-10 has been detected in low tuberculosis (TB) burden countries in adults with pulmonary diseases including active TB. Aim of this study is to evaluate whether urine IP-10 can be detected in adults and children with pulmonary diseases in TB endemic countries and if these values correlate with blood IP-10 and urine parameters.
Design/methods: We enrolled 33 healthy adults donors (HAD), 42 adults with active TB and 133 children with a suspect of active pulmonary TB in Uganda and Tanzania within the EDCTP TB CHILD Project. Active TB was defined by microbiological and clinical means whereas 'no active TB' definition included respiratory disease other than TB. IP-10 was evaluated both in urine and blood by ELISA and the results were correlated with diagnosis, HIV-status, demographic features, urine parameters. Median and interquartile range were calculated. Mann-Withney with Bonferroni correction was used.
Results: Among adults, IP-10 was significantly higher in blood and urine of patients with active TB compared to HAD ($P < 0.0001$; $P < 0.04$ respectively) and with HIV-TB compared to HAD ($P < 0.0001$; $P = 0.0003$ respectively). Among children, IP-10 was significantly higher in blood of active TB and 'no active TB' patients than HAD ($P < 0.0001$ both). Urine IP-10 was almost significantly higher in active TB compared to HAD ($P = 0.05$). In HIV-infected children, IP-10 was significantly higher in blood of patients with HIV-TB compared to HAD and 'no active TB' patients ($P < 0.0001$ both) whereas urine IP-10 was significantly higher in HIV-TB compared to HAD ($P = 0.002$). A good discriminatory capacity to distinguish active TB from 'no active TB' was found in blood ($P = 0.004$), not in the urine. A significant ($P < 0.0001$) but mild correlation between urine/blood IP-10 was found. No correlation of urine IP-10 with urine leukocyte counts, ketone, glucose, nitrate and PH was found.

Conclusion: These preliminary results show that urine and blood IP-10 are associated with active TB disease in adults and children compared to healthy subjects independently of HIV status and TB-burden country (low/high). However IP-10 has a moderate discriminatory capacity to distinguish active TB from 'no active TB'. A moderate but significant correlation of urine IP-10 with blood IP-10 levels was found. The finding that IP-10 can be detected in children's urine with lung diseases can open new strategies to detect markers of inflammation in districts different from blood.

COUNTRY, COMMUNITY AND FLASH IN TUBERCULOSIS: THE ROLE OF CIVIL SOCIETY

PC-559-02   Effects of community volunteers on community tuberculosis care in Oyo State, Nigeria

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Background and challenges to implementation: Many communities in Oyo State, Nigeria are still unaware of existence or availability of tuberculosis (TB) DOTS Centers. Whereas ignorance, illiteracy, erroneous belief and low-knowledge did not enable majority members of both urban and rural communities to be aware that TB can be cured and TB treatment is free. Therefore, positive effects of Community Volunteers on Community TB Care (CTBC) cannot be over-emphasized.

Intervention or response: Under the Global Fund CTBC Round 9, the Civil Society for the Eradication of Tuberculosis in Nigeria—TB Network Oyo State Chapter in collaboration with Oyo State Tuberculosis and Leprosy Control Program (TBLCP) and Health Alive Foundation (HAF) selected 10 Local Government Areas (LGAs) with high prevalent rates of TB in Oyo State. 15 Community Volunteers (male and female) were selected from each of the 10 Local Government Areas (LGAs) on Ward basis. Total of 150 Community Volunteers (CVs) were trained on CTBC and have been creating awareness on TB, identifying People to be suspected of TB, referring them to TB DOTS Centers for screening, drug adherence counseling, contact tracing, tracking defaulters, providing home-based care, attending monthly/quarterly review meetings, participating in community outreach education and public rallies.

Results and lessons learnt: Within First Quarter of 2013 (January–March 2013), the Community Volunteers (CVs) referred 521 people suspected of TB (269 male 252 female) to TB DOTS Centers, 421 people (214 male 207 female) appeared for screening, 102 smear positive to TB were detected, 28% of TB cases detected in 10 LGAs were from the trained Community Volunteers.

Conclusions and key recommendations: CTBC Program need to be scaled up to more LGAs and communities within their jurisdictions. More CVs need to be trained. This will enhance early case detection, appropriate referral system, necessary treatment, care and support as well as proper follow-up. The CTBC will reach the down-trodden people at the grassroot level to enable them the community populace in abject poverty transformed into leading quality and well-being lives at large.

PC-560-02   Former tuberculosis patients improve tuberculosis case detection in rural and mining communities of Eastern Democratic Republic of Congo

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Background: In the context of rural and mining communities of the South-Kivu province in the Democratic Republic of Congo (DRC), the province has case notification rates that are 25% of the national incidence estimates possibly due to poor access to health services. Active case finding (ACF) consists of screening for TB outside the traditional health facilities. This approach has shown to be very effective to increase TB detection in other African settings with low detection rates. Through a TB REACH grant, we involved former TB patients to actively screen people for TB symptoms in their community. State the setting, methods, desired outcomes, procedures and techniques used to collect and analyse information. Include a description of participants, procedures, measures and appropriate statistical analyses.

Results: The intervention was implemented in 19 subdistricts that had no history of participation with ACF interventions. These areas provide care to an estimated population of 1.2 million, comprising rural and mining communities. Starting progressively in April 2012, 240 volunteer former TB patients were recruited to perform verbal screening for TB symptoms in their community and referral of suspects for smear microscopy and GeneXpert testing. Volunteers
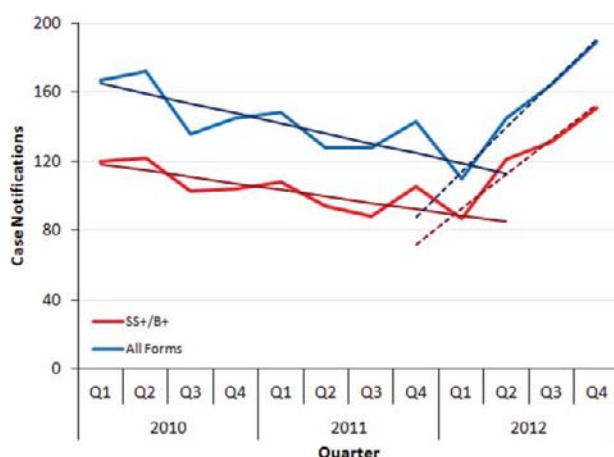
Figure   Trends in case notification pre/post ACF intervention for bacteriologically confirmed (SS+/B+) cases and all forms of TB.

received financial support for the logistical costs linked to their activities (mainly reimbursement of local transport costs). Project staff supervised them regularly. National TB Program (NTP) notification data from these facilities were modeled to measure changes in notification trends pre- and post-ACF intervention. During quarters 3 and 4 of 2012, 18 261 verbal screening events were conducted by former TB patients, resulting in the detection of 1361 (7.5%) suspects with symptoms suggestive of TB. All newly identified TB suspects were referred for smear microscopy testing. The intervention significantly increased the rate of case notification. Regression analysis shows a 3.7% declining trend over two years was replaced by an estimated 20.2% growth quarter on quarter post-implementation ($P < 0.0001$). These activities resulted in a 46.1% increase in new smear-positive TB notifications in NTP data in the last six months of 2012 compared with the same period in 2011.

Conclusion: This study shows that involvement of volunteer former TB patients groups for active case finding is an effective way to improve case detection. This intervention should be considered for scale-up to improve TB case detection, especially in areas of difficult access and poor case detection rates.

PC-561-02   Needs-based communication programmes substantially support tuberculosis control and prevention

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Background: GF R9 Project Axshya is being implemented in 15 districts of Punjab out of 300 in India by the Union as Principal Sub Recipient. Population Service International (PSI) one of the Sub Recipients implements is part of this project in five districts of Punjab (North India) namely, Ludhiana, Gurdaspur, Tarn Taran, Hoshiarpur and Jalandhar. The objective of the project is increased access to quality TB care through Civil Society Participation and Community Engagement.

Objective: To assess the output and outcome of communication and social mobilisation activities from the MIS of the programme being maintained by the sub recipient in terms of direct reach and direct outcomes.

Methodology: The paper analysed events organized in 2011 and 2012 that include 2405 TB Info Mela, training of 359 Ayurvedic Doctors, training of 1246 ASHA (Accredited Social Health Activists) on BCC tool kit and 1130 road shows and street theatre. Nearly 100 000 people were covered directly through these programmes and about one million populations indirectly.

Results: During the period (Apr 2011 to Dec 2012), 48 330 persons covered under direct outreach through 2405 TB Info Melas (community outreach on TB sensitisation). One to one IPC held with 21 133 persons among which, 2848 TB suspects referred for sputum testing and 38% (1079) of them did the sputum test and 154 found positive. 359 trained AYUSH doctors identified 855 TB suspects and 570 (67%) among them got tested and 108 found positive. 14 among them put on DOTS under observation of AYUSH doctors. 239 referrals have been made through trained ASHAs, 201 (84%) tested for TB and 75 cases found positive and put on DOTS. During the period, as a whole, from the selected areas of the project, 1850 suspects have been examined for TB and 337 were confirmed TB. The positivity rate is 18% among the referrals got tested.

Conclusion: Effective communication and social mobilisation is the key to enhance the outreach and detecting cases from the inaccessible areas. In the community engagement interventions, the positivity rate is also quite high. RNTCP should adopt the practice like TB Info Mela and involvement of non-allopathic doctors and rural health care providers for detecting cases and involving them in the programme as well.

PC-562-02   Prevalence of non-communicable diseases in a rural area of Bangladesh

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Background and challenges to implementation: Non-Communicable Diseases (NCDs) prevalence and death rates can be accounted for by emerging NCD epidemics in developing countries. The World Health Report 2001 had indicated that NCDs account for almost 60% of deaths and 46% of the global burden of disease. Seventy-five per cent of the total deaths due to NCDs occur in developing countries. The population of Bangladesh is likely to double in the next 50 years, with a major shift from a young population to a much-older population with consequent implications for healthcare, especially for NCDs. With demographic transitions taking place the disease patterns of the past century are changing. There is increasing evidence to suggest that the epidemiologic transition is well underway in Bangladesh and other less developed countries. The countries like Bangladesh are facing a double burden, with a huge load of infectious diseases and an increasing burden due to NCDs. Rural areas are particularly suffering the most and the situation is compounded by less availability of adequate health service, low literacy among population and most importantly poverty.

Intervention or response: This cross-sectional survey was conducted in a village of Comilla District during the July to August of 2009. List of the households of the village was collected from the government health assistant assigned for the ward. In the village 873 households were listed finally. A sample of 92 households was selected randomly from the list according to computer generated random number. A pre-designed semi-structured questionnaire was developed for using as data collection instrument. Data was collected by face-to-face interview by the investigator. Population characteristics were assessed by generating descriptive statistics. Overall and age specific of prevalence were calculated with its 95% confidence interval. The prevalence of individual NCDs was also calculated.

Results and lessons learnt: Describe the results and impact of the project. Explain the potential application or benefit to other programmes. Describe what worked and what did not work and the evidence that led to this determination.

Conclusions and key recommendations: The implication of current study finding is, staying rural area does not necessarily provide immunity against NCDs, Hence Combat against NCDs should include rural residents too.

PC-563-02   La contribution de l'initiative TB Reach à la détection de cas additionnel de tuberculose au Burkina Fazo : leçons apprises et défis

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Contexte : Le taux de détection de la tuberculose au Burkina Faso demeure bas (32% contre 70% attendu selon le rapport 2012 du PNT). Afin d'améliorer cette situation, le PNT et le PAMAC ont obtenu de Stop TB partnership un financement pour le dépistage de cas additionnels de tuberculose dénommés « TBREACH ».

Objectif de l'intervention : Rechercher la tuberculose au sein des populations à accès géographique, économique et culturel limité au dépistage et aux soins de Tuberculose.

Cibles :
- Les populations pauvres des quartiers non lotis d'Ouagadougou et de Bobo.
- Les clients et les vendeurs des marchés d'Ouagadougou, de Bobo et de Tenkodogo.

Méthode d'intervention : Les animateurs des associations ont été formés à la reconnaissance des signes de la tuberculose et à la collecte de crachat ; de façon périodique, des visites « portes à portes » sont réalisées dans les quartiers non lotis et des visites « boutiques à boutiques » sont réalisées au niveau des marchés ; la recherche de cas suspects de TB se fait sur la base de l'existence d'une toux de plus de 14 jours. Avec le consentement du cas suspect une collecte de crachat est réalisée dans un lieu indiqué (hors de la présence des gens) ; les crachats collectés sont acheminés vers le CDT ; l'animateur procède à un feed-back des résultats de l'examen au cas suspect qu'il soit négatif ou positif.

Points innovants de la stratégie : 1) Offre de services personnalisée ; 2) Service de santé se déplace vers les populations cibles (auparavant le cas suspect référé devait se rendre au CDT) ; 3) collecte et transport de crachat par les associations.

Résultats : En 6 mois
- 28 463 personnes des quartiers non lotis touchées
- 363 cas suspects identifiés
- 363 crachats collectés
- 36 TPM+ dépistés
- 272 visites au marché effectuées

- 7372 clients et vendeurs touchés
- 274 cas suspects identifiés
- 109 crachats collectés
- 7 TPM+ dépistés.

Leçons apprises : Il existe des cas additionnels de TB à rechercher au niveau de certains groupes spécifiques. Il existe des cas de tuberculose dans les communautés à habitation précaire qui ne sont pas déclarés Le dépistage mobile (collecte de crachat auprès du cas suspect) permet d'accroître l'adhésion des cas suspects de tuberculose au dépistage.

Défis : Maintenir la recherche de cas de tuberculose chez ces cibles après l'arrêt de financements.

PC-564-02 Tuberculosis care and control among the urban poor: faith-based NGO meets the challenge in urban slums of Uttar Pradesh, the most populated state of India

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Background and challenges to implementation: Urban slum-dwellers are at high risk of acquiring TB infection and require intensive focus and support as they face inequities in accessing timely diagnosis and full duration of anti TB treatment. Gautam Buddha (GB) Nagar district, an industrial suburb of Uttar Pradesh (UP) State,located in the National Capital Region (NCR) in India, has high population density and registered 52% population growth in the preceding decade, due to immigrants settling in several slum clusters.

Intervention or response: KNEUS a Catholic Health Facility, associated with CBCI CARD, has earlier been active at grass-root level for leprosy eradication, and currently operates 9 Designated Microscopy Centres (DMC) and DOT Centres to provide TB diagnosis and treatment in slum areas of several districts of UP, including 2 such centres serving about 285 000 persons in slum clusters of Bhangel and Sector 10 in GB Nagar district. The services are provided in resource-poor settings, in rented health centres each with a minimal staff comprising of lab technician, DOT provider and visiting doctor. The centres are linked to PPM Schemes and receive support from RNTCP in the form of free drugs, free lab reagents and logistics and annual grant-in aid.

Results: In year 2011,
1 2 of the 13 DMCs (15%) in the G B Nagar district were managed by KNEUS
2 KNEUS DMCs conducted 26.1% of sputum microscopies and yielded 25.8% of the positive cases diagnosed, in the district
3 31.7% of cases registered in the district received DOT at the KNEUS DOT Centres

Contribution of KNEUS dispensaries in case detection and case holding in urban slums of Gautam Buddha District of Uttar Pradesh State in India

Indicator	Reporting Unit	Contribution
No. of TB suspects undergoing sputum examination in 2011	Total in District G B Nagar	10519
	DMC at KNEUS Bhangel	1539
	DMC at KNEUS Sector 10	1205
	Total by KNEUS	2744
	Contribution by KNEUS (percentage of total in district)	26.10%
No. of examined suspects found sputum positive in 2011	Total in District G B Nagar	1578
	DMC at KNEUS Bhangel	215
	DMC at KNEUS Sector 10	192
	Total by KNEUS	407
	Contribution by KNEUS (percentage of total in district)	25.80%
No. of TB cases put on DOT in 2011	Total in District G B Nagar	3674
	DOT centre at KNEUS Bhangel	596
	DOT centre at KNEUS Sector 10	570
	Total by KNEUS	1166
	Contribution by KNEUS (percentage of total in district)	31.70%
Success rate among NSP cases as reported in 2011	District G B Nagar	90%
	DOT centre at KNEUS Bhangel	94%
	DOT centre at KNEUS Sector 10	96%

4 KNEUS DOT Centres reported 94% (Bhangel) and 96% (Sector 10), treatment success rate, compared to 90% for the district.

Lessons learnt: NGO DMC and DOT Centres, strategically located within slum areas, improve access and acceptability of services and thereby enhance case detection and case holding, with better treatment outcomes.

Conclusions:
1 Locally active NGOs have better acceptance by the community and are able to contribute more effectively and efficiently.
2 Awareness generation and outreach support strengthens urban DOTS.
3 Sustained focus, good planning and strategic partnerships are essential to fight TB among the urban poor.

PC-565-02 Barriers to tuberculosis treatment from the perception of community members; findings from knowledge, attitude, and practice survey in Nigeria

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Background: Accessibility to TB diagnostic and treatment services in the community remains indispensable to TB control especially in the context of patient centered approach to case finding and case holding.

Methods: Data used was from the Knowledge, Attitude and Practice (KAP) conducted for National TB and Leprosy Control Program (NTBLCP) in Nigeria, in December 2012. This study involved a cross-sectional approach with a mixed method of both quantitative and qualitative research methodologies. It was conducted in six states; representing each of the six geo-political zones of the country. From the quantitative, among the community members, a total of 3021 (male 1413 [47%] and women 1608 [53%]) were interviewed. Their economic profile shows that (88%) of the respondents had a source of livelihood at the time of the survey, and 2643 (88%) had ever heard of TB. Of these, 139 (5%), has ever been diagnosed of TB.

Results: At the bivariate level, analysis reveal barriers to TB treatment services with significant statistical result among those who have been diagnosed of TB: ignorance about where TB services are located: 48.2% ($P < 0.001$), non-availability of TB services in the local health facility: 71.2% ($P < 0.01$), treatment centres too far: 62.6% ($P < 0.001$), and cost of treatment: 84.2% ($P < 0.01$). At the multivariate level, respondents who are economically empowered are 100 times more likely to encountered any of these barriers than those who have no source of livelihood (OR = 2.0, CI 1.56–2.61, $P < 0.0001$).

Conclusions and key recommendations: Effective TB services must consider mitigating barriers for maximum impact in low resource and developing countries where these barriers most likely impede uptake of TB services even among those who can afford the services.

PC-566-02   Reaching the unreached is critical for tuberculosis control

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Background and challenges to implementation: Despite significant achievement in TB control, Bangladesh still faces high morbidity and mortality related to TB. Success on key TB control indicators varies widely in different geographical locations and is much lower among certain vulnerable populations. Delays in case detection remain a major problem especially in remote rural areas such as tea gardens. The tea garden workers are from marginalized ethnic groups, have traditionally faced added challenges accessing health and social services, and are highly dependent on their employers to access needed TB services.

Intervention or response: To build awareness and improve TB case detection and increase access to DOTS for TB patients in tea garden communities. The USAID TB CARE II project identified community partners to strengthen provision of TB services in 157 tea gardens in Bangladesh, with a total population of 650 000. To facilitate awareness building activities among tea garden community members, the project supported training of volunteers from 157 gardens as Tea Garden Facilitators (TGF) on conducting awareness sessions among the tea garden workers, health workers, and tea garden management. They were also trained on TB screening, collection and transportation of sputum to microscopy centers, link TB patient with DOTS providers, conduct contact and defaulter tracing, patient counseling. They screened suspects and collected sputum samples through house hold visits and weekly sputum collection centers established at the tea garden premises.

Results and lessons learnt: The project supported orientation on basic signs and symptoms of TB for tea garden community women, factory workers, cured TB patients and other community members. Between July and December 2012, Tea Garden Facilitators collected sputum samples from 1461 TB suspects and found 122 smear positive TB, 2 smear negative and 1 EPTB cases among them. A relatively high proportion of female TB suspects and cases were identified (39% and 37% respectively) which is more than the usual findings of the country.

Conclusions and key recommendations: There is a strong need to raise awareness about the risk of TB among tea garden communities. Specialized interventions targeting these communities are required to increase knowledge of TB and to improve access to TB services for this vulnerable population.

PC-567-02   Tuberculosis case detection in the state of Maharashtra in India: has civil society been able to make a difference?

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Background: Project Axshya is a civil society initiative and is being implemented in five districts in the state of Maharashtra by Population Services International (PSI) in partnership with The Union. The objective of the project is to support the TB control programme and provide assistance in improving TB case detection among marginalised and vulnerable population. The project was implemented by PSI in five districts of Maharashtra for the past two years through advocacy, communication, social mobilisation (ACSM) and PPM approaches.

Intervention/methodology: Interpersonal communication (IPC) activities were conducted in select TU/DMCs across the project locations in the five districts of Satara, Sangli (Rural & MC), Kolhapur (Rural and MC).The population that was targeted was marginalised and vulnerable populations in the age of 18–54 years. Communities were mobilised through individual and group sessions including engagement

of community care providers and frontline health workers through robust mechanisms. IPC tool developed after thorough research was used to convey key messages to the communities: 'Cough for two weeks or more could be TB', 'visit nearest DMC for free sputum test', 'TB is curable and treatment provided free of cost'. TB suspects were identified and referred to DMCs for an early diagnosis of TB and the data was collected over a period of time for analysis.

Results: The multifarious efforts that were put in for an effective ACSM and PPM implementation were analysed by the number of cases that were detected in the focussed DMCs and the proportion of new cases detected through the project referrals were ascertained. The data analysed for the period April–December 2012 showed that the following proportion of new cases in the select DMCs of the five districts were contributed through the project efforts: Satara (10.7%); Sangli rural (7.7%); Kolhapur rural (10.3%); Sangli MC (6.5%) and Kolhapur MC (8.7%).

	Total cases in focussed DMCs	TB cases detected through Project Axshya PSI intervention	
		n	Percentage
I. District: Satara			
Apr–Jun '12	158	11	7.0
Jul–Sep '12	146	22	15.1
Oct–Dec '12	163	17	10.4
Subtotal	467	50	10.7
II. District: Sangli rural			
Apr–Jun '12	132	12	9.1
Jul–Sep '12	200	12	6.0
Oct–Dec '12	133	12	9.0
Sub total	465	36	7.7
III. Kolhapur Rural			
Apr– Jun '12	181	17	9.4
Jul–Sep '12	201	18	9.0
Oct–Dec '12	198	25	12.6
Subtotal	580	60	10.3
IV. Sangli MC			
Apr– Jun '12	150	12	8.0
Jul–Sep '12	131	6	4.6
Oct–Dec '12	150	10	6.7
Subtotal	431	28	6.5
V. Kolhapur MC			
Apr– Jun '12	130	12	9.2
Jul–Sep '12	219	15	6.8
Oct–Dec '12	120	10	8.3
Subtotal	469	37	7.9
Total	2412	211	8.7

Conclusions and key recommendations: The ACSM and PPM approaches adopted by PSI and The Union through Project Axshya Initiative has made significant contribution in the case detection in Maharashtra in the implementing geographies. The evidence gathered is recommended for utilisation for adoption similar settings and scale up across other high TB burden districts to improve detection of TB among marginalised and vulnerable populations.

PC-568-02 Reaching the unreached: piggybacking on an existing platform

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Background and challenges to implementation: Bihar, the last state to implement DOTS based TB control program in India (RNTCP), still detects only around 30% of expected cases under the program even in 2012 which is far less than it is expected under RNTCP (70%). In repeated field evaluations under the program involving interviews with TB patients it was found that a sizeable proportion of patients have not even heard about TB until they themselves contracted the disease.

Intervention or response: Indian farmers fertiliser cooperative limited (IFFCO) is a farmers cooperative network. In Bihar under the Kisan Sanchar Limited (IFFCO KSL), cellular phone based voice messages (VM) are used to transmit information regarding weather conditions, crop market prices etc to 250 000 farmers since long time and they have already benefitted from these services and have developed a trust in the messages from IFFCO. It was in this context that the TB program sought the support of IFFCO to take the messages regarding TB symptoms, diagnosis and treatment and services under the program to the farmers using the existing VM platform in Bihar. Under the provision of corporate social responsibility IFFCO agreed to make available the existing VM platform to take the messages on TB once a week to this large network of farmers completely free of cost.

Results and lessons learnt: The message was transmitted starting 10th April 2013; the first week message (50-second message on TB symptoms) was heard by 178 107 farmers. This means more than 70% users accepted the VM and benefitted from this service directly in a week on a one to one basis out of 250 000 total subscribers and around 850 000 population indirectly. There is a mechanism in-built to get their feedback through a toll-free number. By far this is one of the largest IEC activities in TB in the state and largest partnership activty as well.

Conclusions and key recommendations: Farmers trust the messages from IFFCO and therefore the message related to TB will also be accepted with importance by the farmers since they consider the messages through IFFCO as genuine. So once the message regarding TB is delivered through the existing VM platform, it is expected that it will definitely increase awareness especially among the rural farmer community. Program has developed messages related to adherence to treatment, drug resistant TB, etc. as well to the list of messages which will be transmitted every week as VMs.

PC-569-02   The role of NGOs in creating awareness programme on RNTCP in Delhi, India: challenges and expectations

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Background: This study aims to identify external, internal challenges and expectation of NGOs in delivering RNTCP awareness programs. Despite many challenges, NGO's under Axshya project have been engaged in mobilizing effective demand for tuberculosis services. In urban area NGOs have an important role in strengthening community institutions by sensitizing the residential welfare associations, rickshaw puller associations, self help groups, religious congregations and other influential people. Challenges faced by these organizations in organizing awareness programme can be broadly categorized as challenges within community, their own internal challenges, and challenges within partnership.

Design/methods: The study includes case studies of 6 local NGOs working within the jurisdiction of New Delhi Municipal Council and Lok Nayak Chest Clinic. Quantitative data on activities conducted by NGO's against given targets of Axshya programme have been collected for period 2012–13. Qualitative data on perception of NGO partners on relevance, effectiveness, and sustainability of the awareness programme have been collected through in-depth interviews of organizational stakeholders and field workers. Data on their expectations from supporting organizations have also been collected through structured interviews. Both quantitative and qualitative data have been triangulated and compared to identify challenges faced by these organizations in an urban set-up. The results are measured through content analysis of respective challenges faced during 2012–13.

Results: The challenges shared by all NGO's are lack of motivated people for participation, unavailability of influential stakeholders, minimal support of influential people to community volunteers, lack of financial support for community volunteers and poor communication with DMC staffs. The expectation against resolving these issues has been told as conducting large scale awareness activities with involvement of local leaders, inputs from support organisations on motivating influential community members and service providers.

Conclusion: The paper examines the facts on challenges, expectations and suggestions of NGO's for successful implementation of intervention.

PC-570-02   Ukraine's first 'TB Flash Mob' raises new interest in the tuberculosis epidemic

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Background and challenges to implementation: Ukraine's Luhansk region has the fourth highest rate of TB incidence in the country with an average rate of 79.1 TB cases per 100 000 people in 2012. Despite these dire statistics, negative attitudes towards TB treatment and public misconceptions about TB transmission are still prevalent. Looking for new approaches to improve TB awareness, the USAID Strengthening Tuberculosis Control in Ukraine project and Luhansk Medical University leveraged the occasion of World TB to organize a surprise TB awareness campaign.

Intervention or response: An impromptu student dance 'flash-mob' at the city's main shopping mall was the center piece of the campaign, involving about 100 volunteers dancing to a TB preventative slogan 'Tuberculosis doesn't choose! Be healthy!' while another 50 volunteers distributed booklets and balloons with TB facts and campaign messages to shoppers. The event resulted in wide-scale media coverage, including 5 key national TV channels and regional outlets with a combined viewership of about 3 million people. The event was recorded also on video (http://www.youtube.com/watch?v = E-RY-t6jFaU) reaching additional viewers.

Results and lessons learnt: The 'Be Healthy' message and event format easily attracted 1000 spectators who willingly took information materials and shared their opinions about TB infection. The campaign not only attracted interested shoppers, but also resulted in an estimated 280 000 people exposed to TB-related messages through mass media broadcasts. A brief poll conducted among spectators indicated that a flash mob is an effective tool to raise interest and attention to TB messages.

Conclusions and key recommendations: A positive message and campaign format is effective in both educating adults and combating social stigma. Most people that typically avoid association with socially stigmatized public health issues were open to learning about TB transmission and treatment facts, particularly when associated with a fun, spirited, dance event at their favorite shopping mall. Shoppers excitedly commented that the event has changed their

attitude to health care. Dancers and medical students from over a dozen countries mentioned that the flash mob format inspired them to organize similar events to raise TB awareness in their communities.

A TWO-WAY STREET: TESTING AND SCREENING FOR TUBERCULOSIS AND HIV

PC-571-02 Tuberculosis cases detection in people living with AIDS in a large city, Brazil, 2012

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Background: Tuberculosis (TB) is the leading cause of opportunistic disease to affect individuals infected with HIV/AIDS. The HIV/AIDS epidemic is seen as a major source of concern for TB policies (WHO, 2004), requiring mobilisation towards control programs of both diseases.

Objective: To analyze TB diagnostic actions offered to people living with aids (PLWA) in a large city in southeast of Brazil.

Methods: Descriptive study, survey type, conducted by interviews with PLWA followed by five local ambulatories of HIV/AIDS from August 2011 to February 2012. A structured questionnaire was used to collect data regarding offering of tuberculin skin test (TST), chest X-ray and sputum smear (SS). Data were analyzed through descriptive statistical techniques. To analyze TB diagnosis in PLWA, indicators were constructed using the mean value obtained by the sum of all interviewees' responses to each question dividing by the total respondents. The indicators were categorized as satisfactory (average values near to 4 and 5), regular (close to 3) and unsatisfactory (near to 1 and 2).

Results: An estimated number of 1200 PLWA are followed by HIV/AIDS ambulatories in the city. Among these we interviewed 301 individuals, of which 51% informed a satisfactory offering of TST. 40% and 80% informed that chest X-ray and SS exam, respectively, were never offered. We highlights that the study site present a TB-HIV co-infection proportion of 30% in the last years. Regarding the offering and request of exams when TB signs and symptoms are perceived by respondents, the indicators of X-ray and TST request were classified as regular; the sputum smear indicator was evaluated as unsatisfactory, being that this exam was never requested (Figure). 17% of respondents reported feeling the need
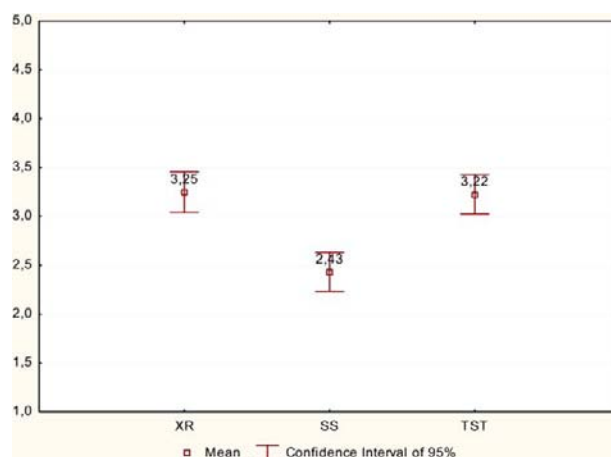
Figure V32 – Offer/request of X-ray from TB symptoms; V33 – Offer/request of sputum smear from TB symptoms; V34 – Offer of tuberculin skin test (annually).

for X-ray and 6.5% of SS when signs and symptoms of TB were identified.

Conclusions: We identified the provision of unsystematic actions to diagnose TB in PLWA. Despite recommendations of the national TB/AIDS control programs, practices related to TB diagnosis are poorly performed by the local health team during cases follow-up. Professionals need to be sensitive for the importance of TB detection in PLWA.

PC-572-02 Prospective assessment of diagnostic delays among HIV-infected clients with presumptive tuberculosis at HIV testing and counselling centers in Zimbabwe

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Background: HIV-infected persons are at much greater risk of dying if their TB diagnosis is delayed. We assessed whether availability of Xpert MTB/RIF reduced diagnostic delays among HIV-infected presumptive TB cases.

Design/methods: Through a TBReach project, we introduced LED fluorescent microscopy at 4 PSI HIV counseling and testing centers (HTCs) in urban/peri-urban areas and Xpert MTB/RIF at 2 of these HTCs. We evaluated prospective cohorts of HIV-infected presumptive pulmonary TB cases with any cough for diagnostic delays through up to 90 days follow-up and assessed whether TB was confirmed and whether TB treatment was initiated. We abstracted data with a standard questionnaire at the HTCs and the NTP referral clinics. We calculated odds ratios (OR) with

95% confidence intervals (CI) for clients' documented TB diagnostic disposition by the following diagnostic categories: smear-positive (SS+), smear-negative (SS−)/Xpert (GX) not done, SS−/GX+, and SS−/GX−. We also compared mean delays (in days) in a diagnostic disposition by diagnostic categories.

Results: To date, between May 2012 and February 2013, 559 presumptive cases were evaluated and had documented diagnostic dispositions as follows: 48/313 (15%) SS−/GX not done, 101/117 (86%) SS+, 13/15 (87%) SS−/GX+, 2/114 (2%) SS−/GX−. Compared to SS−/GX not done, SS+ cases and SS−/GX+ were 6 times more likely to have a disposition [OR = 6.3, 95%CI 3.7–10.7 and OR = 6.5, 95%CI 1.5–28.8], respectively, whereas SS−/GX− were 5 times less likely to have a disposition [OR = 0.2, 95%CI 0.15–0.25]. 140 clients started anti-TB treatment including 24 SS−/GX not done, 101 SS+, 13 SS−/GX+ and 2 SS−/GX−. Mean delays in a documented diagnostic disposition were greatest for clients with SS−/GX not done (38.4 days) compared to SS+ clients with 3.9 days ($P < 0.001$), SS−/GX+ clients with 6.1 days ($P = 0.004$) and SS−/GX− clients with 4.5 days ($P = 0.2$) [See Table].

Diagnostic category	Number with diagnostic disposition	Mean (minimum-maximum) delay, days	Median (minimum-maximum) delay, days	One-way ANOVA *P* value
SS−/GX not done	48	38.4 (0–90)	20.5 (0–90)	Reference
SS+	101	3.9 (0–90)	2.0 (0–90)	<0.001
SS−/GX+	13	6.1 (1–11)	7.0 (1–11)	0.004
SS−/GX−	2	4.5 (0–9)	4.5 (0–9)	0.2

Conclusion: SS+ or SS−/GX+ TB cases were more likely to have a documented disposition and have a shorter delay compared to presumptive TB clients with SS−/GX not done and SS−/GX−. Xpert MTB/RIF may reduce diagnostic delays among GX+ patients as we observed, but this will be a minority of those screened in most settings. Further strategies for tracking and treating all presumptive TB patients should be considered to properly and timely rule-in or rule-out TB among HIV-positive persons including those without access to GX or with negative GX results.

PC-573-02 Scale-up of provider-initiated HIV testing and counseling for tuberculosis patients in 26 provinces in Viet Nam, 2007 to 2012

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Background and challenges to implementation: The World Health Organization recommends provider-initiated HIV testing and counseling (PITC) to all TB patients. In Viet Nam, PITC has been implemented since 2007 in three provinces, expanding to 26 provinces in 2012, with counseling and serological testing offered by TB program staff.

Intervention or response: HIV testing and referral data from quarterly reports of 26 provinces from 2007–2012 were analysed.

Results and lessons learnt: Among 147 658 registered TB patients, 5337 (3.6%) were known to be HIV-infected at the time of TB diagnosis. Of 142 321 with unknown HIV status, 131 712 (92.5%) received HIV counseling and 129 208 (98%) of these consented to testing. A new diagnosis of HIV was made for 3216 (2.5%) patients and the overall HIV prevalence in TB patients was 5.8%. Of the 8533 HIV-infected TB patients, 64% were successfully referred to HIV care facilities increasing from 59% in 2008 to 69% in 2012. A total of 38% had a documented CD4 cell count, 76% received co-trimoxazole preventive therapy, and 38% received antiretroviral therapy (ART) during TB treatment increasing from 27% in 2008 to 53% in 2012.

Conclusions and key recommendations: These findings demonstrate the practicality and acceptance of PITC and support the need to expand PITC to TB care and treatment settings in Viet Nam as a routine service. Despite improvement in HIV care referral and ART rates over time, low rates of ART indicate that important barriers remain and more efforts are needed to provide integrated care to HIV-infected TB patients.

PC-574-02 Increasing detection of tuberculosis, TB-HIV and rifampicin-resistant tuberculosis using Xpert® MTB/RIF: the TBXpert Project

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Background: In June 2012 the UNITAID executive board approved funding of US$25.9 million for the TBXpert Project, a multi-partner initiative to procure and implement 230 GeneXperts and 1.4 million Xpert MTB/RIF cartridges in 21 low- and middle-income countries between 2013–2015. The TBXpert Project represents a game-changing approach to TB diagnostic testing using scale-up of Xpert MTB/RIF as a major driver of diagnostic policy change and a path-finder for market stimulation.

Methods: The WHO Stop TB Department provides overall project management and oversight for the

TBXpert Project. The Stop TB Partnership's Global Drug Facility is responsible for procurement of Xpert MTB/RIF commodities. The TB REACH initiative is providing complementary funding of 10–12 million USD for implementation at selected sites aiming to increase case detection. The African Society for Laboratory Medicine is coordinating the provision of technical assistance in five African countries. Interactive Research and Development is implementing social business models in three Asian countries to increase access for patients seeking care in the private sector. The EXPAND-TB Project is providing complementary central-level laboratory capacity in 15 of the TBXpert countries. Global Laboratory Initiative partners are collaborating with National TB Control Programmes to establish and implement Xpert MTB/RIF at country level and provide needed guidance, technical support and complementary funding.

Results: Expanding access to Xpert MTB/RIF testing in the TBXpert Project is expected to rapidly diagnose 143 000 incident TB cases (range: 96 000–189 000), 22 000 incident HIV-associated TB cases (range: 14 000–30 000), and 32 000 rifampicin-resistant cases (range: 24 000–40 000).

Conclusions: The UNITAID-supported TBXpert Project will improve case detection of TB, TB-HIV and rifampicin-resistant TB among vulnerable populations in low- and middle-income countries, facilitate the rapid initiation of appropriate treatment, and increase access for patients seeking care in the private sector and non-NTP public sector. Intended market effects of the TBXpert Project interventions are the expansion of markets and improved access, as a result of the reduced cartridge price (US$9.98) negotiated with partners within the framework of the TBXpert Project, which represents a game-changer for rolling out molecular diagnostic tools.

PC-575-02   Barriers to provider initiated HIV testing and counseling among tuberculosis patients in Myanmar

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Background: In Myanmar, HIV prevalence among new TB patients is estimated at 10.4% and only one-third (31%) of TB patients have ever tested for HIV. In December 2010, PSI/Myanmar started a provider initiated testing and counseling (PITC) program in the franchise network of 111 Sun Quality Health (SQH) clinics to provide PITC to TB patients. Testing was provided free of charge to patients, and doctors were paid a small ($2) incentive for each HIV test performed. This study examines barriers to PITC among TB care providers and TB patients in Myanmar.

Methods: Using a semi-structured questionnaire, in-depth interviews were conducted with 14 SQH doctors and 16 patients receiving TB treatment at 10 different SQH clinics in Myanmar. Patients and doctors were selected purposively stratified by having tested for HIV (vs. not) and 'high' vs. 'low' performing doctors. Coding and data analysis were carried out using MS word and MS excel. Interview transcripts were analyzed thematically.

Results: The most common factor that was found to hinder doctors' initiation of PITC was their unwillingness to test people they considered to be at low risk of HIV. Most doctors interviewed mentioned this reason for not providing the test. About half reported being too busy to provide counseling and testing, whilst a number stated the lack of availability of ART as a reason for not testing. For TB patients, a majority stated that fear of an HIV positive result as a barrier to testing. Self perception of being at low or no risk for HIV infection was also a key barrier for some patients interviewed.

Conclusions: The findings from this qualitative study suggest that focus should be given to changing providers and patients' perceptions around HIV risk. Guidelines that recommend opt-out HIV testing for all TB patients should be re-emphasized and actively promoted to providers. Patients should be educated to understand the increased risk of having an HIV infection amongst TB patients. Decentralization of ART needs to move forward, and providers should be encouraged and supported to develop networks to ensure access to ART for HIV positive TB patients.

PC-576-02   Evaluation of the implementation of tuberculosis screening among HIV-infected patients in Ho Chi Minh City and Hanoi, Viet Nam, 2008–2011

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Background: To reduce the burden of tuberculosis among people living with HIV (PLHIV) the World Health Organization recommended intensified case finding (ICF) as a key component of the 3 I's initiative. In 2007, the Viet Nam Ministry of Health (MOH) issued national guidelines on TB diagnosis on PLHIV by asking about cough, fever and weight loss. We conducted an evaluation to define the quality and coverage of TB screening in PLHIV attending outpatient HIV care and treatment clinics in Hanoi and Ho Chi Minh City.

Methods: A retrospective cohort study was conducted of records from adult HIV-infected patients in 5 outpatient clinics from 2008–2011. We provided a training in complete data abstraction to 8 study team's members. Patient chart data were abstracted regarding TB screening in HIV clinics and TB diagnosis in TB clinics. A qualitative interview to understand knowledge and practices of TB screening among the healthcare staff in these clinics were conducted. Data in the qualitative study was protected for confidentiality.

Results: Among 489 HIV-infected patients, 461 (94%) were screened for TB every year, while 28 (6%) had never been screened for TB during the study period. Of the 384 (79%) HIV patients screened at the last visit, 326 (87%) were asked about cough and fever, and 177 (47%) about cough, fever, night sweats. There was no association between being screened for the 2 and 3 symptoms and age group, HIV transmission routes or ART status. During interviews of the 12 healthcare staff's knowledge on TB screening, 9 (75%) of them shared that TB screening should include cough, fever, weight loss and night sweats and that screening should be done at all visits.

Conclusions: Most PLHIV were screened for TB at least annually but not consistently with the MOH recommended symptom questions nor at the most recent visit. Since knowledge of screening guidance was high among healthcare staff, other barriers to screening need to be assessed and addressed.

PC-577-02   HIV testing of patients with tuberculosis in Montreal, Canada

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Background: Routine HIV testing of TB patients is recommended by professional and public health organizations in Canada. However, compliance of the physicians with the recommendations is poor. We defined the proportion of TB patients tested for HIV and the burden of HIV-TB co-infections; evaluated TB treatment outcomes and analyzed factors influencing them.

Methods: All TB cases are mandatory reported to the Montreal Department of Public Health and all cases from 2004 to 2009 were retrieved for analysis. The outcome variables were the presence of HIV testing, HIV status and TB treatment outcome. The data was analyzed, fully adjusted for demographic, clinical and TB risk factors characteristics and chi-square test for trends was performed.

Results: 778 TB patients were included in the analysis. Overall, HIV status was known for 45.8% (*n* = 356) of TB cases. The proportion of patients with re-ported HIV status significantly increased from 42.9% in 2004 to 70.1% in 2009 (*P* < 0.001). HIV testing was mainly reported from subjects born in the Caribbean (AOR 2.8, 95%CI 1.4–5.7), Central/South America (AOR 4.9, 95%CI 1.7–14.3) and Sub-Sahara Africa (AOR 3.0, 95%CI 1.5–6.1); with pulmonary disease (AOR 3.0, 95%CI 2.0–4.4); and injection drug users (AOR 4.7, 95%CI 1.3–17.0). HIV-TB co-infection was found in 9.3% of patients with known HIV status, and in 4.2% of all TB patients. However, there is no significant decrease in the proportion of HIV-TB co-infected patients over the study period (*P* = 0.6). HIV-TB cases were more likely males (AOR 2.6, 95%CI 1.04–6.5), originated from Sub-Sahara Africa (AOR 8.0, 95%CI 1.6–41.2) and had concomitant medical conditions (AOR 4.8, 95%CI 1.4–16.2). Overall, 83.4% (*n* = 597) of patients were cured and 6.8% (*n* = 49) died. Factors independently associated with the patient death were: male gender (AOR 2.1, 95%CI 1.1–4.2), aged from 60 and older (AOR 7.6, 95%CI 2.1–27.6) and presence of concomitant medical conditions (AOR 2.1, 95%CI 1.1–4.4). Among those with reported HIV status, HIV positive patients were more likely to die compared to HIV negative (AOR 6.1, 95%CI 1.1–35.0).

Conclusion: Although the reporting of HIV status among TB patients increased over the study period, targeted HIV testing of patients still occurs. Higher risk of death for HIV positive TB patients may be attributed to late diagnosis of HIV status and late ART initiation.

PC-578-02   PITC of tuberculosis suspects and prevalence of HIV among tuberculosis suspects in Kinshasa and Kisangani, Democratic Republic of Congo

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Background and challenges to implementation: Though recommended by the WHO, provider-initiated HIV testing and counseling (PITC) of persons suspected of tuberculosis (TB) is not widely implemented in most resource-poor settings. Moreover, very limited data have been reported on the HIV seroprevalence among TB suspects.

Objective: To describe our experience scaling-up of PITC for patients with symptoms suggestive of TB (suspects) and determined HIV seroprevalence among suspects seeking care in TB clinics in Kinshasa and Kisangani, Democratic Republic of Congo (DRC).

Intervention or response: Between November 2011 and December 2012 we implemented PITC in 65 and 13 TB clinics in Kinshasa and Kisangani in two waves:

32 and 6 clinics in Kinshasa and Kisangani, respectively in November 2011 and the remaining in August in Kinshasa and September 2012 in Kisangani. In each of the clinics, personnel involved in outpatient consultations were trained on TB symptoms screening and a system was set-up to tract suspects identify and monitor their access to effective PITCT. HIV testing was done according to WHO strategy III. **Results and lessons learnt:** Overall, 28 568 TB suspects were registered in Kinshasa of whom, 22 215 (78%) were counseled, 20 169 (91%) were tested, and 2657 (13%) were found to be HIV+. In Kisangani, 4451 suspects were registered, 3481 (78%) of them counseled, 3449 (99%) tested, and 372 (11%) were found to be HIV+. In Kinshasa, while the proportion of suspects tested increased almost linearly from 28% in December 2011 to stabilize around 90% in the last quarter of 2012 (Q42012), the prevalence of HIV followed the inverse trend from 18% in November–December 2011 to 11% in Q42012 but was always above the prevalence among TB confirmed cases which was stable around 11%. In Kisangani, no particular trend was noted over time, but contrary to Kinshasa, the prevalence of HIV among suspects was lower among TB suspects that among confirmed TB cases (11% vs. 17%).

Conclusions and key recommendations: In settings of relatively low HIV prevalence and low HIV testing like the DRC, PITC of TB suspects can be an efficient way to detect large numbers of new HIV cases and improving access to quality TB and HIV care and treatment.

PC-579-02   Improving uptake of HIV testing among tuberculosis patients in Delhi, India

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Background and challenges to implementation: TB-HIV collaborative services act as an entry point for prevention and care of HIV negative patients and as treatment support for the TB-HIV positive patients. Despite the successful implementation of TB-HIV collaborative package in Delhi in 2009, Integrated Counseling and Testing Centre (ICTC) remains poorly utilized as only 58% registered TB patients knew their HIV status in 2011. Delhi State TB Department in collaboration with Delhi State AIDS Control Society rolled out a new strategy in 2012 for improving the uptake of HIV services among TB patients. The strategic framework was devised to improve cross referrals and enable early initiation of antiretroviral therapy and co-trimoxazole prophylaxis in the field. **Intervention or response:** The study was conducted to assess the impact of the revised strategy on the uptake of HIV services among TB patients, reasons for late uptake and non-uptake of TB-HIV services. Cross-sectional study was carried out in two diagnostic and treatment centers of Central Delhi. Data was collected from January 2012 to December 2012. Registered TB patients (new and retreatment) were interviewed on a predesigned questionnaire at the end of five months of treatment. **Results and lessons learnt:** In 2012, out of the total 552 TB patients interviewed, 524 (94.9%) had been tested for HIV by the end of fifth month of their TB treatment. In them, 13 patients (2.4%) were HIV positive. All of them had been initiated on ART and CPT during continuation phase of TB treatment. It was also observed that 91% of study subjects had been tested for HIV within two weeks of TB diagnosis. Among the 28 patients with non-uptake of these services, 15 patients (53%) had left locality and 13 patients (47%) were still alive. The most significant variables associated with non uptake of HIV test were age of more than 45 yrs, rural residence, illiteracy, patients in retreatment regimen and lack of awareness regarding HIV/AIDS ($P < 0.05$). The main reasons reported for non-uptake of HIV tests by the 13 alive TB patients was a) no one referred them to ICTC (18.5%), b) there was a long distance between TB treatment centre and Integrated Counseling and Testing centre (ICTC) (14.8%) and that c) they were unaware about HIV testing centre location (11.1%). The reasons for non uptake that remain are not related to the interventions like deaths and default. Modifiable ones like lack of awareness, illiteracy and patients on retreatment regimen need to be addressed on priority.

Conclusions and key recommendations: Provider initiated testing and counselling services supplemeted with the revised strategic framework has resulted in high uptake of HIV testing among registered TB patients in Delhi. The proposed health system intervention provides a sustainable improvement in the capacity and uptake of services in field conditions.

PC-580-02   Contribution de l'initiative TB Reach pour la détection précoce des cas de tuberculose dans trois villes du Burkina Faso

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Contexte/défis/cibles : Le PNT du Burkina Faso a bénéficié d'un financement de TB Reach pour la détection précoce de cas additionnels de tuberculose. L'initiative a été planifiée de janvier à décembre 2012. L'un des objectifs est d'assurer la recherche systématique de la tuberculose (TPM+) chez les

clients des Centres de conseil volontaire (CDV) et des patients VIH+ suivis dans les hôpitaux des 3 villes les plus touchées par le VIH. La mise en œuvre de l'initiative a été assurée par les Programme TB et communautaire.

Les populations cibles étaient les clients des CDV et les PvVIH suivies dans les hôpitaux de ces 3 villes du Burkina Faso:

- Ouagadougou la capitale avec une population estimée à 1,5 million d'habitants. 12 CDV et 8 structures de PEC des PvVIH ont été inclus.
- Bobo-Dioulasso la ville économique avec une population estimée à 900 000 habitants, 3 CDV et 5 centres de PEC des PvVIH ont été inclus.
- Koudougou avec une population estimée à 600 000 habitants, 1 CDV et 1 centre de PEC des PvVIH ont été inclus.

Intervention : Tout client de CDV ainsi que les PvVIH bénéficiaient systématiquement de l'administration d'un questionnaire basé sur les 5 critères de recherche de la TB de l'OMS. En cas de réponse affirmative à au moins une des questions par le client/PvVIH, celui-ci était considéré comme suspect et bénéficiait d'un examen de recherche de BAAR dans les crachats et/ou Rx pulmonaire. Les rapports d'activités étaient produits mensuellement et transmis au PNT pour compilation, analyse, et rétro-information aux acteurs.

Résultats/leçons apprises : L'initiative a permis de dépister 71 cas additionnels de TPM+ (sur 138 prévus), soit un taux d'atteinte de 51,45%. En outre, 71 cas additionnels de TPM− et TEP ont été diagnostiqués en 1 an. L'initiative a permis de confirmer l'existence de cas additionnels de TB à travers cette stratégie novatrice, de rendre les CDV capables de dépister les cas de TB, mais aussi de renforcer le partenariat entre acteurs communautaires et de santé, tant au niveau central qu'au niveau périphérique. Le démarrage tardif et timide des activités n'a pas permis entre autres l'atteinte de l'indicateur.

Conclusion : L'initiative a permis de démontrer la complémentarité et le tandem existant entre 2 types d'acteurs (communautaires et de santé) à travers la détection de 142 cas de TB additionnels en 1 an. Une prolongation de 6 mois sans coûts additionnels a été accordée afin d'améliorer l'atteinte de cet indicateur.

PC-581-02   HIV testing of patients admitted to a pulmonary medicine ward, with or without tuberculosis diagnosis, Mahosot Hospital, Vientiane, Lao PDR, 2008–2009

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Background: HIV infection is the strongest risk factor for the development active TB. Lao PDR, the country with high prevalence of TB. In 2008, the Lao ministry of health set up the TB-HIV collaboration program at Mahosot hospital. The study aims to assess both the HIV testing rate and HIV prevalence rate among inpatients with or without a diagnosis of TB.

Design/methods: A 2-year retrospective study (Jan 2008–Dec 2009) of inpatients at Pulmonary Medicine Ward, Mahosot Hospital. Review of all medical records of tuberculosis (TB) patients and others (unidentified for TB) whom were clinically suspected of having HIV infection admitted during the study period. Data were collected using a standardized case record form. HIV infection was diagnosed based on dual positive reaction with two different rapid test kits: DETERMINE® HIV-1/2 (Abbott Japan) and UNI-GOLD® Recombigen HIV. An ELISA confirmation test was used only in case of rapid test discordance. Statistical analysis was performed using Stata version 8.2. Chi-square test at two-sides significance used for univariate analysis. A multiple logistic regression model was built to identify independent variables associated with HIV infection. Statistical significance was taken at $P \leq 0.05$.

Results: Among 954 patients recorded, 8 patients were excluded, because HIV infection had been diagnosed prior to admission. 750 patients had a diagnosis of TB, and 196 did not, but were suspected of having HIV infection based on clinical grounds. The overall rate of HIV tests performed was 48.4%; among the TB patients the rate was lower: 34.9%, meaning that quasi 2/3 were not tested for HIV. Comparing with those not tested, the tested patients were more likely to be young, aged 25–44 years (OR, ~2; 95%CI, 1.3–3.2), and to have a clinical suspicion of HIV infection (OR, 52.3; 95%CI, 45.1–6.05e). The overall prevalence rate of HIV infection was 14.4%, with those suspicions of HIV infection 26%, and those diagnostic of TB 5.7%. Multivariate analysis showed that three factors were independently associated with HIV infection: age 25–34 years (OR, 2.5; 95%CI, 1.1–3.8), being divorced (OR, 3.02; 95%CI, 1.4–4.6) and having clinical suspicion of HIV infection (OR, 2.1; 95%CI, 1.3–2.9).

Conclusion: HIV testing rate is still very low at our hospital. Conversely, the prevalence rate was very high: 6 to 26 times the national general prevalence (<1%). This is the first study about the practice of HIV testing in TB and non TB patients admitted in hospital in Lao PDR, since WHO recommended all TB patients being tested for HIV. It seems necessary to identify the barriers to the HIV testing implementation, and to build up the health personnel's capacity.

PC-582-02   Factors related to absence of HIV screening among tuberculosis patients in Lima, Peru

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Background: HIV screening among tuberculosis (TB) patients is a standard of care recommended by WHO as it allows early initiation of antiretrovirals (ARV). In 2006, the Peruvian National TB Program (NTP) implemented the strategy nationwide. As HIV prevalence in general population is low and TB rates are high, HIV is managed in referral centers while TB is managed in peripheral health facilities where voluntary counselling and testing for HIV (VCT) occurs. We sought to determine the proportion of patients screened for HIV and the factors associated to not being screened.

Methods: From March 2010 to December 2011 we enrolled new smear positive pulmonary TB adults in 32 primary care health centers and one district hospital in a peri urban district in Lima. NTP staff would offer VCT to all patients. All tested patients received a post test couselling and those with a positive result were immediately referred to the corresponding hospital where ARV were provided. TB treatment was provided at the peripheral health center. We registered sex, age, marital status, educational level, drug and alcohol use and the health facility were TB diagnosis was made. Patients that declined the VCT were registered as such. The district is artificially divided in a higher and lower area. The former is less urbanised and with more disperse health facilities than the latter.

Results: Among 1295 enrolled TB patients, 987 (76.2%, 95%CI 73.82–78.48) were screened for HIV and among the 308 (23.8%, 95%CI 21.54–26.18) not screened, 118 (38.3%, 95%CI 33.06–43.85) declined the test. Among those tested, 23 (2.3%, 95%CI 1.52–3.42) were HIV positive. Patients with higher education had a lower risk of not being tested than those with incomplete schooling, OR 0.71 (95%CI 0.51–1.01, $P = 0.05$). In the multivariable analysis, patients reporting use of drugs were more likely not to be tested, OR 1.61 (95%CI 1.16–2.22), as were patients attending health facilities located in the highest area of the district, OR 2.86 (95%CI 1.92–4.17). Drug use was the single factor associated to declining a VCT (OR 1.85, 95%CI 1.03–3.33) when controlling for all other variables.

Conclusions: An acceptable proportion of TB patients were screened for HIV in our study population in Lima. Adressing constraints at health facilities and in specific populations could increase VCT to reach universal testing among TB patients.

OUTBREAKS AND IMMUNOLOGY IN CHILDHOOD RESPIRATORY DISEASES

PC-583-02   Changes in intrathoracic lymph nodes in children with different results of immunological tests

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Objective: To identify changes in intrathoracic lymph nodes in children with different result of immunological tests.

Methods: At children department of Saint-Petersburg Institute of Phthisiopulmonology were examined 120 patients aged from 3 to 14 years during 2010–2012 with positive immunological tests (Diaskintest® and QuantiFERON-TB Gold). Diagnostic complex included: Diaskintest® (DST)—immunological skin test, QuantiFERON-TB Gold (QFT-G), and multislice computer tomography angiography (MCT-AG). According to the results of the Diaskintest® and QFT-G patients were divided into 2 groups: I group—negative reaction of immunological tests ($n = 64$), II group—with positive tests ($n = 56$).

Results: The results of measurements of intrathoracic lymph nodes in CT angiography for the short axis in the axial projection presented in the Table.

Table   The size of the lymph nodes (mm) in children with different results of immunological tests

Size of the lymph nodes, mm	I group ($n = 64$)	II group ($n = 56$)
<0.2	46.8% (30)*	17.8% (10)
2–5	29.8% (19)	1.8% (1)
>5	23.4% (15)	80.4% (45)*

Children in the I group have significantly higher (46.8) size of the lymph nodes <0.2 mm and in the II group, >5 mm (80.4% vs. 23.4%, $\chi^2 = 33.93$, $P < 0.001$).

Conclusion: Positive results of immunological tests are accompanied by reaction of lymph nodes in children over 5 mm in contact with tuberculosis requires in-depth examination to exclude tuberculosis of intrathoracic lymph nodes.

PC-584-02   Immunological parameters in children with tuberculosis infection

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Objective: To identify features of immunological parameters in children with different activity of *M. tuberculosis* infection.

Methods: 213 patients from 3 to 14 years old were

examined at children's phthisiopulmonology department during 2011–2013. All patients were examined by Quantiferon-TB Gold (QFT-G) and based on its results they were divided in two groups: I group ($n = 82$)—patients with negative QFT-G results, II group ($n = 131$)—with positive results. Diagnostic complex included: DIASKINTEST® (DST), computer tomography examination (CT), assessment of leucocytes' subsets (CD3$^+$, CD4$^+$, CD8$^+$, CD4$^+$/CD8$^+$, CD16$^+$, CD20$^+$, CD25$^+$, CD95$^+$, HLAII), cytokines (TNF-α, IL-2, IL-4, INF-γ), the phagocytic activity of neutrophils (phagocytic number, phagocytic index, phagocytic completeness). The results were compared between groups.

Results: The results of the DST and QFT-G tests were comparable: negative results of DST were significantly higher in I group (76.8% (I) vs. 3.1% (II) ($P < 0.001$) and positive results—in II group (96.9% (II) vs. 23.2% (I) ($P < 0,001$). Specific abnormalities of intrathoracic lymph nodes by CT were diagnosed significantly more often in II group (83.3%, $P = 0.001$) compared with I group (40.2%). No significant difference in leucocytes' subsets between groups was revealed. Levels of CD3$^+$ (52.2% (I) vs. 56% (II)) and CD8$^+$ (22.6% (I) vs. 24.4% (II)) were decreased in both groups vs. normal ranges while level of CD95$^+$ (18.49 (I) vs. 20.22 (II)) was increased in both groups. Levels of TNF-α (686.71 ± 70.75 (I) vs. 962.37 ± 91.88 (II) $P = 0.05$), IL-2 (173.58 ± 24.23 (I) vs. 280.45 ± 26.61 (II) $P = 0.05$) and IFN-γ (18749.94 ± 1566.68 (I) vs. 20729.58 ± 1396.93 (II) $P = 0.05$) INF-γ were significantly higher in II group compared to I group. The number of stimulated neutrophils (phagocytic number) was significantly higher in II group (42.3% (I) vs. 65% (II) ($P < 0.01$), vice-versa phagocytic completeness was higher in I group (1.05 ± 0.07 (I) vs. 0.94 ± 0.06 (II)).

Conclusions: Positive result of QFT-G indicates activity of TB-infection and is comparable with positive results of DST. It is associated with increase of cytokines' levels (TNF-α, IL-2, INF-γ) and activation of neutrophils. Patients with positive result of QFT-G significantly more often have specific abnormalities of intrathoracic lymph nodes by CT.

PC-585-02 Immune status indicators in children and adolescents with drug-resistant tuberculosis

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Background: Increased rate of pediatric drug-resistant (DR) tuberculosis is a sign of impaired host immune protection, reducing treatment effectiveness. We aimed to study the immune status indicators in pediatric DR pulmonary tuberculosis (PTB).

Methods: 24 children and adolescents with DR PTB and 19 patients with drug-sensitive (DS) PTB were subjected to immunological examination. We determined peripheral blood lymphocyte populations (CD3+, CD4+, CD8+, CD16+, CD20+). ELISA assay was used to assess the induction of interferon-gamma (IFN-gamma) in blood cell cultures treated with the specific *Mycobacterium tuberculosis* antigens, and to assess the serum IFN-gamma, IL-4, and IL-8 cytokine levels.

Results: Pronounced abnormalities in T-cell component of immune system were found in patients isolating DR MTB: decreased CD3+ counts (51.3 ± 0.9% in patients with DR PTB; 56.8 ± 2.1% in DS PTB; $P < 0.05$), decreased CD4+-lymphocyte content (36.3 ± 1.1% in DR PTB; $P < 0.001$). Hence, CD4+/CD8+ ratio decreased down to 1.2 ($P < 0.05$) on average. All patients had heightened CD20+ counts, with no significant differences found between patients isolating DR *M. tuberculosis* or DS *M. tuberculosis*. Level of CD16+ in a group of patients with DR PTB was 17.3 ± 1.1%, and 20.7 ± 1.2% in a group with DS PTB, $P < 0.05$. Serum IFN-gamma levels in patients with DR PTB tended to decrease compared to patients with DS PTB. The level of IFN-gamma induction during incubation in the presence of PPD was assessed as 189.4 ± 47.8 pg/mL in children and adolescents with DR PTB, while patients with DS PTB had higher IFN-gamma production rates: 247.0 ± 64.9 pg/mL on the average. Similar tendency was observed during incubation of blood samples in the presence of recombinant ESAT-6 and CFP-10 antigens. IFN-gamma induction levels in patients with DR PTB and DS PTB were 74.0 ± 17.6 pg/mL and 136.8 ± 31.8 pg/mL, respectfully ($P < 0.05$). An inverse relationship was found between the extent and severity of tubercular process, and IFN-gamma induction levels in whole blood of PTB patients treated with *M. tuberculosis* antigens. IL-8 levels in patients with DR PTB were found to be increased up to 71.0 ± 36.8 pg/mL (12.6 ± 4.5 pg/mL in children and adolescents with DS PTB), and IL-4 cytokine content in patients with DR PTB tended to grow.

Conclusions: We observed the following features of DR tuberculosis in children and adolescents: decreased T-cell lymphocyte content, imbalance in regulatory lymphocyte subpopulations, and reduced specific anti-tuberculosis immunity.

PC-586-02   Contact investigation of tuberculosis-exposed newborns: outbreak in the maternity ward of Madre Theodora Hospital, Campinas, Sao Paulo State, Brazil, 2012

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Background: Tuberculosis (TB) in child presents specificities that must be considered during its diagnosis investigation. The pulmonary clinical presentation is different from adults because it used to be smear negative. In April and August 2012 the Campinas Epidemiological Surveillance Group (CESG) received the notification of two children hospitalized with TB in Campinas municipality. It was investigated common points among children and was certified that both children were born at maternity ward of Madre Theodora Hospital (MTH). Thus, the Hospital Control Infection Commission (HCIC) discovered that one staff, a nurse, was restrained by medical order and hospitalized/diagnosed with pulmonary TB. From November 2011 to June 2012 were listed 1300 newborn babies (NBB) where 50.0% were residents in the municipality of Campinas and other 50.0% were residents in other 19 municipalities nearby mainly in municipalities of Sumare, Paulinia and Hortolandia. The majority of these contacts were evaluated by MTH, but 175 children who did not were attended by institution cited above were evaluated by CESG and Sao Paulo State TB Control Program (TCP-SP). The objective was to evaluate the NBBs, contacts of healthcare worker (HCW), identifying and treating TB cases and latent TB infection (LTBI) of Campinas region.

Method: Were evaluated children from Campinas region born from November 2011 to June 2012 where they were called out and done tuberculin skin test, chest X-ray, anthropometric assessment, and medical consultation.

Results: Were attended 175 children by CESG/TCP-SP where first, 40 children were from Sumare, 15 from Hortolandia and 20 from Paulinia. Second, were attended children born between November–December 2011 because of one child was diagnosed with TB in November 2011. In that moment were attended 51 children from Sumare, 27 from Hortolandia and 22 from Paulinia. No TB case was found and 17 children (9.7%) were diagnosed with LTBI where treatment were initiated and orientation and a letter was sent to the respective pediatricians who followed-up on a monthly basis during all treatment period. Add to this data the results of more 1000 children attended by MTH which identified 19 TB cases and 94 LTBI.

Conclusion: The contact investigation of maternity ward enabled the identification of TB and LTBI cases that are being adequately treated. The late diagnosis of HCWs can increase the disease transmission, mainly in more immunosuppressed as the NBBs. Otherwise, in Brazil, TB is a serious public health problem and HCWs are a vulnerable population and, therefore, to transmit the disease. Adequate measures of periodic exam for these professionals must be implemented.

PC-587-02   Diagnostic value of interferon-gamma release assays in childhood tuberculosis

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Background: Interferon-gamma release assays (IGRAs) are used to detect latent or active tuberculosis infection, measuring immune responses against *Mycobacterium tuberculosis* specific antigens. However, in patient groups where the direct detection of acid-fast bacilli in sputum often fails, such as children or HIV infected individuals, the use of these methods might contribute to a more timely diagnosis of TB.

Methods: Sensitivity and specificity of QuantiFERON-TB-Gold and an in-house TB-ELISPOT were evaluated in a prospective study with a minimum follow-up of 12 months. 157 children aged six month to 13 years with suspected tuberculosis were assigned to predefined diagnostic subgroups, based on microbiological and clinical findings.

Results: Sputum culture confirmed the diagnosis of tuberculosis in 25 (15.9%) of 157 children. The Quantiferon-TB-Gold detected 20 (80.0%), (95% confidence interval (CI) 65.1–97.1), the ELISPOT 19 (78.8%), (95%CI 59.7–94.8) of these cases on the first day of the study. The sensitivity of Quantiferon-TB-Gold was higher in HIV negative compared to HIV positive children, with 90% (95%CI 55.5–99.7) vs. 69% (95%CI 38.6–90.9) respectively. For 23 cases tuberculosis could be reliably excluded and the TST was negative Quantiferon-TB-Gold tested positive in none of the children of this group, the ELISPOT tested positive only once. In the group of 63 children with probable TB, 10 children, who improved without mycobacterial treatment showed a positive Quantiferon-TB-Gold. This would be defined as 'latent TB'. For the Quantiferon-TB-Gold, indeterminate results were more often seen in HIV positive than in HIV negative children, 12.4% vs. 3.9% respectively (RR 3.2, 95%CI 0.9–11.3). Indeterminate results were associated with mortality, as

28.6% of children with indeterminate results at presentation died, but only 8.7% of children with valid IGRA-results (RR 3.4, 95%CI 1.2–9.8; $P < 0.05$), which was mainly explained by the HIV-positive status.

Conclusions: Both IGRAs demonstrated a good sensitivity in paediatric patients assigned to clearly defined clinical groups. Specificity is difficult to calculate, when latent TB can not be excluded. Indeterminate results of immune biomarkers such as IGRAs should be monitored carefully as they are associated with enhanced mortality and a valid result could contribute to a more timely diagnosis and treatment of TB.

PC-588-02 Recurrent wheezing is associated with intestinal protozoa in Warao Amerindian children in Venezuela

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Background: While in developed countries the prevalence of respiratory allergic diseases is rising, inflammatory diseases are relatively uncommon in rural developing areas. High prevalence rates of helminth and protozoan infections are commonly found in children living in rural settings and several studies suggest an inverse association between helminth infections and respiratory allergies. No studies so far have investigated the relationship between helminths and protozoa and respiratory atopic disease in rural children under 2 years of age.

Design/methods: From August to November 2012, 229 Warao Amerindian children aged 0 to 2 years were enrolled in a cross-sectional survey to investigate the association of helminth and protozoan infections with recurrent wheezing and atopic eczema in the Orinoco Delta in Venezuela. For the assessment of recurrent wheezing, the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire adapted for use in infants was used. Atopic eczema and nutritional status were assessed by standardized questionnaires and physical examination. A stool sample was requested from all participants and intestinal helminths and protozoa were detected by means of microscopy and real-time polymerase chain reaction.

Results: Prevalence rates of atopic eczema and recurrent wheezing were high, respectively 19% and 23%. The prevalence of helminth infections was 26% and

Table Factors associated with recurrent wheezing in Warao Amerindian children 0 to 2 years of age

	Recurrent wheezing ($n = 16$)	No recurrent wheezing ($n = 45$)	P value
Age, months, mean (SD)	18 (3)	17 (4)	0.018
Sex, n (%)			0.070
Male	19 (68)	46 (48)	
Female	9 (32)	49 (52)	
Malnourished, n (%)			
Stunted (height-for-age Z score < -2 SD)	18 (64)	45 (47)	0.12
Underweight (weight-for-age Z score < -2 SD)	8 (29)	21 (22)	0.48
Wasted (weight-for-height Z score < -2 SD)	2 (7)	8 (8)	1.0
Parasitic infections, n (%)			
Any parasitic infection	15 (94)	30 (66.7)	0.047
Helminth infection	10 (63)	27 (60.0)	0.86
Protozoa infection	13 (81)	21 (46.7)	0.017
Protozoa pathogenic	13 (81)	20 (44.4)	0.011
Protozoa non-pathogenic	2 (13)	4 (8.9)	0.65

the prevalence of protozoan infections was 59%. Recurrent wheezing was significantly positively associated with age. Pathogenic protozoan infections (i.e., *Giardia lamblia*, *Cryptosporidium parvum* and *Dientamoeba fragilis*) were significantly associated with a high prevalence of recurrent wheezing (Table). No significant association of helminth infections with recurrent wheezing was observed. Children with recurrent wheezing showed a higher prevalence of atopic eczema than children without recurrent wheezing (32% vs. 16%, $P = 0.055$). This indicates that recurrent wheezing in young children may be a marker for susceptibility for the later development of atopic asthma. The prevalence of chronic malnutrition (stunting) was significantly higher in children with atopic eczema compared to those without atopic eczema (65% vs. 45%, $P = 0.019$).

Conclusion: High prevalence rates of atopic eczema and recurrent wheezing in Warao Amerindian children under 2 years of age were related to stunting and intestinal pathogenic protozoan infections respectively.

PC-589-02 Vaccination of children with tuberculosis disease

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Background and challenges to implementation: Assessment by clinical and immunological characteristic after vaccination Pnevmo-23 inchildren with tuberculosis of intrathoracic lymph nodes.

Intervention or response: In department of children's were examined 42 patients age from 3–14 years with various manifestations of tuberculous infection. Diagnostic complex included: Diaskintest® (DST),

QuantiFERON-TB Gold (QFT-G) and multislice computer tomography (MCT). After examination were divided children in tow groups: I group ($n = 24$)—infected by *Mycobacterium tuberculosis* according tuberculin test (TT), but have not LTBI and tuberculosis disease; II group ($n = 18$)—patients with tuberculosis of intrathoracic lymph nodes. All of them were vaccinated against pneumococcal disease vaccine Pnevmo23. The vaccination was carried out after 4 months of treatment. We assessed: leucocytes' subsets (CD3^{+}, CD4^{+}, CD8^{+}, CD4^{+}/CD8^{+}, CD16^{+}, CD20^{+}, CD25^{+}, CD95^{+}, HLAII), the level of cytokine-induced (IL1β,4,6, IFN-γ, TNF-α), specific Ig (A, M, G classes) were detected before the vaccination, on the 14th, and 30–45th days after the vaccination.

Results and lessons learnt: The incidence of post-vaccination reactions as children in group I and in group II did not exceed the level indicated by vaccine instructions. None of children had any marked worsening of the infectious process (tubercular infection). In group II was determined by CD4 + (36.1 ± 1.4%). 30–45 days after the vaccination the initial data (CD4+ 39.3 per ±1.8%). No significant differences in number of major subpopulations of lymphocytes compared to age norm of healthy children, including CD16+ (15.1 ± 3.1% (I) vs. 13.0 ± 1.4% (II)) and CD25+ (14.8 ± 2.1% (I) vs. 13.9 ± 1.01% (II)) cells. In both groups the level of IFN-γ increased in 2 times in comparison with the original, and this trend continued up to 30 days.

Conclusions and key recommendations: The frequency of local and general reactions after introduction of the vaccine Pnevmo23 inthe monitored groups did not exceed the permissible level. In children with tuberculosis not determined aggravation TB infection, which confirms the immunological safety of vaccination of this group of children. No significant differences in immunological and clinical parameters after vaccine process is not detect in children with infected by *M. tuberculosis* and TB patients.

PC-590-02 Tuberculin skin test interferon-γ release assay and chest X-ray results in a prospective study of Warao Amerindian childhood tuberculosis contacts

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Background: A unique aspect of tuberculosis (TB) in children is the rapid progression to disease, typically within the first year following infection, unlike in adults, where latent TB infection (LTBI) can persist for decades without progression. Interferon-γ release assays (IGRAs) have emerged as a more specific alternative to the tuberculin skin test (TST) for the diagnosis of LTBI, especially in Bacille Calmette-Guérin (BCG) vaccinated children. Studies on IGRA performance in children from high TB burden low income settings are important to assess the need for the use of these costly and technically complex assays.

Design/methods: From May 2010 to December 2010, 207 HIV-negative Warao Amerindian childhood TB contacts under 16 years of age were enrolled for TST, IGRA and chest X-ray (CXR) performance at inclusion and at 12 month follow up. Children did not receive chemoprophylaxis.

Results: On inclusion, IGRA showed less positive results than TST (52% vs. 58%, $P = 0.017$). In multivariate analysis including age, sex and malnutrition as independent variables, presence of a BCG scar was not associated with TST positivity (OR 0.93, 95%CI 0.31–2.8). TST positivity rates were higher in children with CXR lesions characteristic of definite inactive TB (OR 10.6, 95%CI 1.3–86.5) while no association of IGRA positivity with CXR was observed.

On inclusion and during follow-up, respectively 13 and five children were diagnosed with active TB. Of the TST-negative children on inclusion, 16% (95%CI 8–28) became TST-positive during follow-up but none of them was diagnosed with active TB. Children with active TB that were put on anti-TB drugs were significantly more likely to convert from IGRA positive to negative compared to children without active TB (OR 11.0, 95%CI 2.3–52.9).

Conclusion: The TST correlated better with CXR findings of LTBI than the IGRA in Warao Amerindian childhood TB contacts while TST results were not significantly influenced by previous BCG vaccination. Replacement of TST by IGRAs is therefore not recommendable in this resource-constrained setting. The only potential role for IGRAs in this area may be the monitoring of response to anti-TB drugs as successful treatment of active TB was accompanied by reversion of IGRA results. Our study highlights the importance of the introduction of repeated TST testing and chemoprophylaxis in this area as a substantial number of children became TST positive or developed active TB during follow-up.

PC-591-02 Children exposed to multidrug-resistant tuberculosis with additional amikacin resistance at a home-based daycare centre: a contact investigation

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Background: Resource limitations in high-burden settings may prevent contact investigation of children exposed to adults with infective TB. Drug-resistant TB (DR-TB) exposure may pose a similar risk for child contacts compared to drug-susceptible (DS) -TB.

Design/methods: A descriptive contact investigation of children exposed to an adult with smear-positive multidrug-resistant (MDR) TB with additional amikacin resistance, at a home-based daycare in Cape Town, South Africa. All children were investigated for TB exposure, infection and disease in a standard manner.

Results: The source case started category I treatment in Jan 2013 (3+ AFB smear-positive sputum; no culture or DST obtained). After poor clinical response, mycobacterial culture obtained in Apr 2013 was positive with resistance to isoniazid, rifampicin, and amikacin. Treatment changed to MDR therapy and contact investigation was done. A daycare was run in the home where he resided throughout the period under review, although he had limited direct interaction with the children.

36 children <15 years were identified as potentially exposed as part of the contact investigation. 19 consented for the study. 17/19 were <5 y, median age 2.9 y (range 0.7–7.8 y); none were HIV-infected. The standardized TB contact score was 4 for all children. At initial evaluation, 18/19 had a TST, of which 6 (33%) were reactive (≥10mm); 0/21 had chest X-rays suggestive of TB. None had symptoms or other indications of TB disease. 17 received the locally recommended 6 month MDR prophylactic regimen of ofloxacin, ethambutol, and high-dose isoniazid. 14/17 (82%) completed at least 6 months of follow-up; none were diagnosed with TB disease. 8 with initially non-reactive TSTs had repeats ≥6 months later; 0/8 were reactive.

Conclusions: TB at daycare centers results in large numbers of children exposed, with high TB contact exposure gradient, similar to that found in household contact investigation of DS-TB in the setting. Delay in sputum culture and DST of the index case prolonged the exposure period in the present study. Eventual active identification and MDR preventive treatment may have averted MDR cases in these children. Child contact tracing remains important for TB control; with DR-TB, the benefit may be even greater. When children present with TB without a known source case, contact investigation at daycares should be considered, especially when DR-TB is involved.

GLOBAL ISSUES IN LUNG HEALTH

PC-592-02 Prevalence of components of metabolic syndrome in pregnant women with obstructive sleep apnoea/hypopnoea syndrome

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Background: Pregnancy is associated with possibility of high prevalence of sleep disordered breathing including Obstructive Sleep Apnoea/Hypopnoea Syndrome (OSAHS) which reaches its peak during third trimester. Gestational weight gain, decrease in pharyngeal luminal size and alteration in pulmonary physiology are likely to predispose to sleep disordered breathing. Such a scenario during pregnancy may lead to higher maternal morbidity and bad foetal outcome.

Objective: To study the prevalence of components of Metabolic Syndrome among third trimester pregnant women with OSAHS.

Materials and methods: Third trimester pregnant women from IMCH were participated in the study. Study period was from August 2010 to July 2011. Total subjects were categorised in to two groups as cases and controls. 100 Berlin questionnaire negative women were taken as controls and 100 Berlin questionnaire positive, OSAHS positive (AHI > 5) women were taken as cases. All subjects underwent a thorough clinical, anthropometric, obstetrical examination and biochemical tests such as complete blood count, blood sugar and lipid profile. The parameters were compared between cases and controls. The level of significance was kept at 5%.

Results: When the results were compared, it was found that OSAHS positive pregnant women were older ($P < 0.0001$), of higher weight ($P = 0.003$), of higher BMI ($P < 0.0001$), of larger neck circumference ($P = 0.005$) and of higher gestational age ($P < 0.0001$). There were higher prevalence of elevated systolic ($P = 0.01$) and diastolic ($P = 0.002$) blood pressure, abnormal fasting ($P < 0.0001$) and post prandial ($P = 0.02$) blood sugar, abnormal cholesterol ($P = 0.006$) and triglyceride levels ($P < 0.001$), and abnormally low HDL levels ($P < 0.001$) in OSAHS positive women. The overall prevalence of Metabolic Syndrome, as per modified NCEP ATP-III criteria, in OSAHS positive third trimester pregnancy in this study was 52% vis-à-vis 8% in OSAHS negative third trimester pregnant women. There was no difference between primi and multi gravidae.

Conclusion: OSAHS in pregnancy is found to be associated with higher prevalence of Metabolic Syndrome. The components of MS are risk factors in pregnancy which can lead to higher maternal morbidity and poor fetal outcome. Control of risk factors along with definite treatment of OSAHS can definitely improve the fetal and maternal health.

PC-593-02   High prevalence of concomitant latent tuberculosis infection in newly diagnosed lung cancer patients in Taiwan

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Background and challenges to implementation: Tuberculosis (TB) and lung cancer patients share common risk factors. Patients with history of TB are associated with increased risk of lung cancer. Lung cancer is also a well-documented risk factor for the development of active TB. However, the prevalence of latent TB infection (LTBI) in lung cancer patients and clinical predictors for LTBI remains to be elucidated.
Intervention or response: From 2011 to 2012, newly diagnosed, pathology-proofed lung cancer patients from four referral medical centers in Taiwan were enrolled for analysis. The presence of LTBI was determined by QuantiFERON-TB Gold In-Tube (QFT-GIT). Demographic profiles, clinical characteristics, and clinical presentations were obtained from enrollment interview. The occurrence of active tuberculosis were also followed.
Results and lessons learnt: During the study period, a total of 210 newly diagnosed lung cancer patients were enrolled in this study with available QFT-GIT results. Among these patients, 63 (30%) were diagnosed with LTBI, 128 (61%) were diagnosed as without LTBI, and 19 (9%) showed indeterminate results. As compared with patient without LTBI, those with LTBI were older (72.6 ± 10.8 vs. 68.0 ± 12.9 years old, $P = 0.011$), more likely to be smoker (74.6% vs. 57.8%, $P = 0.024$), to have previous history of anti-TB treatment (9.5% vs. 2.3%, $P = 0.028$), to have COPD (39.7% vs. 17.2%, $P = 0.001$), and have lung

cancer that occurred in pulmonary TB prevalent location (69.8% vs. 46.9%, $P = 0.003$). In multivariate analysis, the presence of COPD (OR 2.66, 95%CI 1.24–5.73, $P = 0.012$) and lung cancer that occurred in pulmonary TB prevalent location (OR 2.84, 95%CI 1.42–5.71, $P = 0.003$) were independent predictors for the occurrence of concomitant LTBI. During the follow up period, one patient was diagnosed of active pulmonary tuberculosis after the treatment with chemotherapy and radiotherapy. Regarding mortality, lung cancer patients with LTBI demonstrated lower mortality as compared with those of non-LTBI patients in Kaplan-Meier survival analysis, although without statistical significance.
Conclusions and key recommendations: Nearly one-third of lung cancer patients in Taiwan are associated with concomitant LTBI. The comorbidity of COPD and lung cancer that locate in PTB prevalent area are independent predicting factors for the presence of LTBI and screening of LTBI should be considered.

PC-594-02   Analysis of the impact of tuberculosis on the evolution and progression of COPD and respiratory failure in relation to smoking habits

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Background: Tuberculosis, and after healing, often leaves permanent damage and cause structural and funcional bronchopulmonary disturbance. The aim of this prospective clinical study was to investigate the incidence of tuberculosis (TB) sequel among patients treated in intensive respiratory care unit and their influence on development and evolution on COPD and respiratory failure.
Design/methods: The study was enrolled 425 pts average age 66.21 y treated in intensive respiratory care unit in Clinic for Lung Disease Clinical Center Nis, from 1 January to 31 December 2012. We analyzed demografic data, lab., gas analyses, X-ray findings according Snider score, and spirometric parameters of lung function. The X-ray examination recorded TB sequel in 130 pts—30.6% (87 m, 43 f) average age 61.54 y (41–79).
Results: The analysis of severity radiological findings according Snider score showed: massive in 71 pts (54.7%), moderate in 27 pts (29.7%) and minor in 32 pts (24.6%). Among 71 pts with massive radiological findings 59 pts—80% had global respiratory failure, and 12 pts—20% partial. All this pts had statistically shorter interval—average 5 y between sustained TB and the occurrence of COPD, than pts with moderate and minor radiological extensive of TB— 13 y. Among 71 pts with massive TB sequel 54 pts —76% were current smokers, 5 pts—7% were ex-smokers, and 12 pts-17% were nonsmokers, among 27 pts with moderate TB radiological findings 11 pts
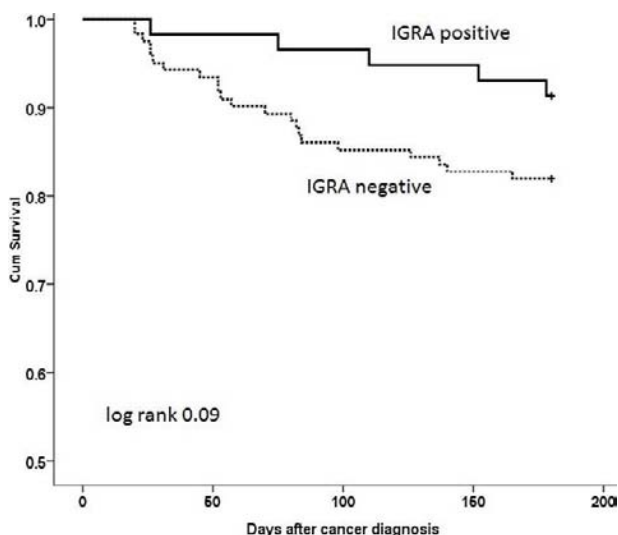
—40.8% were current smokers, 2 pts—7.4% were ex-smokers and 14 pts—51.8% were nonsmokers, and among 32 pts with minor TB sequel 9 pts—28.1% were current smokers, 5 pts—15.6% were ex-smokers and 18 pts—56.3% were nonsmokers.

Conclusion: The results of our study suggests that massive and moderate TB sequel according Snider score, male sex and smoking habit are important predictor for occurrence and statistically significant faster evolution of severe COPD and global respiratory failure in population of TB patients.

PC-595-02   Preliminary results from the laboratory phase of ECRHSIII in Melbourne

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Background: The European Community Respiratory Health Survey (ECRHS) was the largest international study of lung health in young adults.

Aim: To describe changes in chronic respiratory diseases and symptom prevalence in adults as they age.

Design/methods: 876 young adults participated in ECRHS in Melbourne in 1992. Of 722 eligible surviving subjects, 543 (75.2%) completed postal or telephone screening questionnaires in 2012. 451 were invited for clinical testing including a more extensive interviewer administered questionnaire, asking about symptoms, treatment and health service utilization for respiratory disease.

Results: Of the first 100 subjects to attend the laboratory, 57 were female. The mean (SD) age was 56.3 (5.6) years. The most common respiratory symptoms reported were shortness of breath after exertion 46, wheezing 31, nocturnal cough 31, daytime cough 18, chest tightness 18, productive cough 10, nocturnal shortness of breath 10, shortness of breath at rest 7 and morning cough 6. 49 had ever smoked and 7 were current smokers. Ever smoking was associated with wheeze ($P = 0.012$), shortness of breath after exertion ($P = 0.01$), but not daytime cough, sputum or chronic bronchitis. Dr diagnosed asthma was reported by 32; 13 reported an attack within the last 12 months and 16 were taking medication. Chronic bronchitis was reported by 13, but none reported a diagnosis of emphysema or COPD. Short acting beta agonists and combination LABA/steroid inhalers were used by <20% of respondents.

Conclusion: The cohort remains highly symptomatic, although most have not been diagnosed or treated. Longitudinal analysis of the complete data will be conducted to determine whether there have been changes in the prevalence of respiratory symptoms or diseases over 20 years.

PC-596-02   Long-term, low-dose erythromycin monotherapy for *Mycobacterium avium* complex lung disease

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Background: Multidrug regimens are initially withheld in mild and stable cases of pulmonary *Mycobacterium avium* complex (MAC) disease, because the timing of treatment is still being debated. Although most patients are observed without any treatment, some of them receive an erythromycin which has no evidence of cross resistance to clarithromycin in MAC with hope to the anti-inflammatory effect of the macrolides. The aim of this study was to evaluate the effects of erythromycin monotherapy compared with those of untreated controls in patients with pulmonary MAC infection.

Design/methods: This was a multicenter retrospective cohort study consisting of 31 patients who were treated with erythromycin monotherapy and 72 patients who were observed without any medication. Patients who had already received the standard therapy were excluded. The primary outcome was the prognosis until exacerbation requiring multidrug regimens, using the propensity scores to reduce the selection bias of erythromycin administration. A secondary outcome included their response rates to multidrug regimens after exacerbation as surrogate variables for cross resistance with clarithromycin.

Results: Erythromycin monotherapy suppressed exacerbation throughout the 7-year observation period after the diagnosis of pulmonary MAC disease ($P = 0.045$, Breslow test). In multivariate analysis, erythromycin group tended to prevent the exacerbation although no statistical significance (hazard ratio, 0.50; 95%CI 0.20–1.24; $P = 0.13$) was found after being adjusted by the propensity score. The response rate to the multidrug regimens after exacerbation in the erythromycin group [78% (7/9)] did not differ from that in the control group [62% (13/21); $P = 0.34$].

Conclusion: Erythromycin monotherapy for patients with pulmonary MAC disease may suppress the exacerbation without adverse events inducing cross resistance with clarithromycin.

PC-597-02   Association between elevated blood glucose and the presence of nontuberculous mycobacteria

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Background: Diabetes mellitus (DM) is a known risk factor for tuberculosis. However, it is not known whether elevated plasma glucose levels and/or DM are associated with nontuberculous mycobacteria (NTM) infection. This relationship was investigated in the present study.

Design/methods: Data for this cross-sectional study were derived from a prevalence survey conducted in 2010 for the primary outcome measure of the cluster-randomized Zambia South Africa TB and AIDS Reduction (ZAMSTAR) trial in 24 high TB and HIV burden communities in South Africa and Zambia. Of the 90 601 adults who gave consent for the survey, 64 463 had evaluable culture results and of these, 39 167 had plasma glucose results and were included in analysis. Elevated plasma glucose level was defined as ≥ 11.1 mmol/l, in a random sample. In order to detect NTM in sputum samples, positive cultures were subjected to 16s DNA sequencing. Individuals sputum positive for *M. tuberculosis* were excluded from the analysis. The crude relationship was investigated using chi-square test statistics.

Results: Of the 39 167 individuals included in the study, 614 (1.59%) had NTM in their sputum and elevated plasma glucose levels were recorded in 712 (1.82%). After excluding individuals sputum positive for *M. tuberculosis*, the prevalence of sputum NTM was 2.11% among individuals with elevated plasma glucose levels and 1.58% among individuals with non-elevated plasma glucose levels (risk ratio 1.34, 95%CI 0.81–2.22; $P = 0.26$).

Conclusion: In this population, the presence of NTM in the sputum was not associated with an elevated plasma glucose level. Our study was limited by having random blood glucose estimation only and therefore may not pick up all cases of diabetes.

PC-598-02   Lessons learned from a global approach to strengthening monitoring and evaluation efforts in national tuberculosis programs

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Background: As national TB programs (NTPs) are under greater pressure from the government and donors to show results, the monitoring and evaluation (M&E) skills of NTP staff need to be strengthened.

Intervention: The USAID-funded program, TB CARE I, initiated a global, multi-year approach to strengthening NTP M&E systems in 16 countries. In 2011, the project team conducted a needs assessment among 30 NTP and TB CARE I M&E officers to identify strengths and weaknesses of M&E systems and to assess the officers' knowledge and skills. Using the assessment results, the project team conducted a three-day in-person M&E training for 30 NTP and project M&E officers from 16 countries. Participants developed mini-M&E action plans for their country, and then implemented these plans in 2012. To further support these efforts, the project team facilitated four virtual trainings.

Lessons learned: Participants were highly satisfied with the in-person workshop and gave 75% of the sessions a score of 85% or higher based on content utility and clarity. Attendees recommended that the workshop be extended and repeated, and requested more time to share experiences and strategies for resolving common M&E issues in their respective countries. Officers from 81% (13/16) of the participating countries developed M&E action plans and in-country teams successfully implemented 85% (11/13) of these plans. While difficult to measure the effect quantitatively, participants reported that the workshop and implementation of the mini-M&E action plans led to verifiable improvements in their M&E systems' performance. Virtual trainings were partially successful; while more than 75% of the M&E officers visited the learning site during the first session, attendance dropped subsequently to about 33% in the last session. Less than half of those who participated in the virtual trainings actively contributed to the discussions. Implementation challenges included troubleshooting internet connectivity issues, engaging 'silent observers', and evaluating the training utility.

Conclusions: In-person M&E training coupled with mini-M&E action plan development led to improvements in NTP M&E systems. This approach allowed participants to resolve key issues affecting their M&E system, rather than attempting to solve all of their problems at once. The virtual training was less successful, but enhancing participant engagement and improving internet access may increase the effectiveness of virtual training.

PC-599-02 Missed opportunities in the management of respiratory diseases in a primary care unit, Veracruz, Mexico

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Background: In many low- and medium-income countries, the programs aimed to manage respiratory diseases at the primary care level are poorly developed or limited, and the quality of care offered is often of a low standard. In Mexico, pulmonary tuberculosis (PTB), chronic respiratory disorders, particularly asthma and chronic obstructive pulmonary disease (COPD) are frequently under- or misdiagnosed. Inadequate prescription and overuse of antibiotics and underuse or unavailability of inhaled corticosteroids is common.

Objective: To determine the magnitude of missed opportunities for identification and management of adult patients with respiratory diseases (RD) at the primary care level within the framework of WHO 'Practical Approach to Lung Health'.

Methods: During March 2013 we conducted an observational study in a primary care unit in Orizaba, Veracruz, Mexico. A standardized questionnaire was administered to all patients over 15 years of age seeking consultation with the primary care physician before and after consultation. We collected information on sociodemographic, epidemiological, and clinical variables including those associated with respiratory diseases (smoking, biomass cooking fuels, asthma, tuberculosis, COPD, among others). After consultation, we interviewed the patient on medical diagnosis, prescribed tests, and therapeutic management.

Results: We interviewed 653 adults; 113 (17.3%) referred respiratory symptoms of more than 2 weeks duration. After consultation 51 (7.8%) received a diagnosis of respiratory disease. Main syndromes were pharyngitis 20 (39%), pharyngo-tonsillitis 16 (31%), bronchitis 4 (8%), PTB 2 (4%), COPD and emphysema each one 1 (2%). Only 3 (6%) patients were identified by health workers with RD, two of them were diagnosed with pulmonary tuberculosis, the other was in treatment.

Conclusions: Detection of patients with RD is low at the primary care level. It is urgent to reinforce measures that improve the quality of care among health personnel. Strategies should include all the components involved in the integrated processes of management of respiratory diseases. Innovative strategies of promotion and prevention in communities and groups at risk should also be conducted.

PC-600-02 Exposure to indoor air pollution from secondhand tobacco smoke and use of biomass fuels in homes with active tuberculosis disease in Klerksdorp, South Africa

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Background: Exposure to indoor air pollution (IAP) from secondhand tobacco smoke (SHS) and use of biomass fuels is hypothesized to increase the risk of tuberculosis (TB). This pilot study estimated prevalence of these risk factors in households of patients with active TB.

Design/methods: Household members participating in a contact tracing active case-finding study in townships of Matlosana around the town of Klerksdorp, South Africa were recruited. Questionnaires recorded personal tobacco use, exposure to SHS, and use of biomass fuels in the home. Air nicotine monitors were placed in the home for 14 days, and hair samples were collected from each individual as a marker of exposure to tobacco smoke. We measured personal tobacco use, exposure to SHS, and exposure to use of biomass fuels at the household and individual levels.

Results: In total, 96 adults and 24 children (<18 years) in 48 households participated. Twelve (27%) participants with a known status were HIV infected, and no additional cases of TB were detected. A total of 11 (23%) households reported use of kerosene/paraffin or biomass as the primary or secondary fuel used for cooking, and 8 (17%) reported use of these for heating. In 43 homes where an air nicotine monitor was placed, 30 (70%) had detectable levels of nicotine. Among adult respondents, 17 (20%) reported current daily smoking. In homes with an air nicotine monitor, 9 (12%) adults reported anyone smoking in the home at least monthly, however 54 (77%) lived in a home with detectable air nicotine values. Exposure to SHS outside of the home was reported by 23 (35%) of adult non-smokers. Hair samples were available from 42 (48%) adults and 13 (65%) children. Among those with available hair samples, 14 (58%) adults reporting no current smoking or snuff use had detectable hair nicotine and 5 (38%) children had detectable levels of hair nicotine.

Conclusion: Exposure to indoor air pollution from SHS and use of biomass fuels is highly prevalent in homes of patients with active TB in townships of Matlosana, South Africa. Additionally, individuals markedly underreport SHS in the home. Tobacco use,

exposure to SHS, and indoor air pollution from use of biomass fuels may compound TB risk in those with HIV infection. Future research should aim to further characterize exposure in these types of communities and assess their independent contribution to TB disease in the context of HIV infection.

TUBERCULOSIS CONTROL AMONG VULNERABLE POPULATIONS: PRISONERS AND MINERS

PC-601-02   Controlling tuberculosis in Kenya prisons through screening of inmates at admission

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Background and challenges to implementation: The prison population is at high risk for tuberculosis (TB) due to poor living conditions and confinement. Prison and civilian populations actively interact leading to increased TB transmission. Only 64% ($N = 109$) of Kenya prisons have health facilities characterized by inadequate; space for service provision, staffing and laboratory services. Inadequate transportation, security concerns and inadequate knowledge of prisons officer limit access to public facilities outside prisons leading to delay in diagnosis and proper management of diseases in these congregate settings.

Intervention or response: From 2011 International Medical Corps, with PEPFAR funding through CDC, supports TB screening using 'Prisoner's Health Record' [PF10 Form] in Kenya prisons. Officers in charge of prisons received one day orientation on importance of TB screening and control in prisons. Documentation officers were trained on administration of PF10. At admission information on demographic profile, offence, and TB screening that include cough more than 7 days, weight loss, previous and current history of TB treatment were collected from inmates. Inmates who responded with a 'YES' to any of the TB questions were classified as TB suspects and referred for further review by clinicians. TB suspects following review by clinician was sent for laboratory investigations. Those diagnosed with TB were put on treatment and received adherence counseling. Inmates were also trained to report any coughers among them for screening at the clinic. Medical transfer form was filled in for TB patients being transferred to other prisons or released. Data for 60 069 inmates admitted to 20 Kenya prisons was analyzed using SPSS.

Results and lessons learnt: A total of 60 069 individuals comprising 53 297 (89%) males and 6772 (11%) females were screened. 52 705 were freshly admitted

from court and 7364 were transfers from other prisons. 749 out of 3129 suspected TB cases from screening by documentation officers were confirmed as suspects by clinicians. Overall 24% ($n = 749$), of TB suspects were diagnosed with TB. Only 6% ($n = 205$) of those diagnosed with TB were not put on treatment. Coughers yielded 180 more TB cases.

Conclusions: TB screening using PF 10 form increases coverage of TB screening in prisons and provide opportunity for early detection and treatment of TB cases. Control of TB in prisons is a perfect opportunity to control TB in the community as well.

PC-602-02   Active search of tuberculosis cases in a Peruvian prison system: pilot intervention based on inmate leaders acting as community health workers

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Introduction: Inmate population is vulnerable to tuberculosis (TB). We report preliminary results from an ongoing intervention aimed to improve TB case detection in an overcrowded Peruvian prison (8000 inmates in 26 quarters, with 6% TB prevalence by 2011).

Methods: The Prison's TB Control program (TBCP) actively searches for TB suspects (cough >14 days) in prison's quarters and obtains sputum smear for laboratory analysis. Until recently, active search was mainly dependent on part-time support by health delegates (HDs), inmate community health workers (CHWs) in charge of multiple health activities. In August 2012, a group of CHWs dedicated exclusively to TB search (DS group) was enrolled and trained along HDs to work in parallel. This study compares initial differences in TB search outcomes between these groups. We compare performance indicators based on secondary routine health data from August and September 2012; sputum sample quality was considered as routinely assessed by laboratory staff.

Results: The TB active search strategy evaluated 1475 TB suspects (mean age 32.6, SD 10.3) during 38 workdays. The HD group ($n = 26$, each working at different days) evaluated 1095 TB suspects during 32 workdays; the DS group ($n = 5$) evaluated 380 TB suspects during 14 workdays. Obtained sputum samples were 770 for the DS group and 2242 for the HD group; those of good quality were 51.6% for the DS group and 45% for the HD group (P value < 0.05). Detected TB cases detected were 54 (compared to 59 before intervention) and all started treatment. The HD group detected 18 cases (3.3% case detection rate—TB cases/suspects evaluated) and the DS group detected 36 cases (4.7% case detection rate), with

no statistically significant differences between both groups.

Discussion: Initial results are positive for fully dedicated CHW in terms of TB case detection, but there is still need to improve patient selection and sputum collection.

PC-603-02   Prevalence of latent *Mycobacterium tuberculosis* infection among professionals at a criminal establishment

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Background: People working in the penitentiary system present a higher risk for tuberculosis (TB) disease due to the high incidence of this disease between inmates. This phenomenon is due to closed condition of prison environments, providing so long periods of proximity between people, which toughly favors the transmission of *Mycobacterium tuberculosis*. The method applied for identification of infected individuals depends on local specificities and infrastructure. The purpose of this investigation is to describe the prevalence of latent *M. tuberculosis* (LTBI) between professionals of a criminal establishment.

Intervention: This is a cross-sectional study developed in professionals working in a male criminal establishment, gateway to the state prison system of Minas Gerais, Brazil, between July and August 2011. Tuberculin Skin Tests (TST), considering positive the results ≥ 5 mm, and a search for respiratory symptoms (cough during ≥ 2 weeks) were developed in individuals who previously accepted to participate in the study. Bacilloscopy, sputum culture, and sensitivity test for *M. tuberculosis* were executed.

Results: All workers of the aforementioned criminal unit accepted to participate in this investigation, being 67 (66.3%) of male gender and 34 (33.7%) of female one. Out of 60 (59.4%) individuals who were submitted to TST, 35 (58.3%) presented positive result. The number identified of respiratory symptomatic individuals was of 3.0%. No case of TB was found.

Conclusions: The prevalence of LTBI between professionals working in penitentiary system of the state of Minas Gerais is high. It is necessary the early TB detection between the inmates, as well as biosafety measures to prevent the possible transmission of this disease to penitentiary system professionals.

PC-604-02   Tuberculosis case detection, prevention, and treatment in small mines in South Africa: a response to the SADC declaration

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Background: TB disease is a critical occupational hazard among miners in South Africa. In many mines, effective efforts to reduce the risk of TB or link miners with TB services are uncommon or uncoordinated. This is especially true in the country's smaller mines which may not have their own health service. Many mine owners recognize the need to improve access to TB services and can serve as a valuable partner to TB control stakeholders.

Aim: Develop a coordinated response to TB in small mines through increasing early detection of TB cases and intensified TB case finding.

Methods: A Public Private Mix strategy has been applied by the USAID TB Project in South Africa to support 5 small mines (1 coal mine and 4 platinum mines) in Limpopo Province to respond to TB. The project assisted to develop formal linkages between the mine managers, the DOH and local public sector TB service providers, and local community based TB outreach campaigns and treatment services, to improve access to TB prevention, diagnosis, treatment, and follow up services for miners. Interventions included empowering mine employees about TB and the services available through DOH, raising awareness and demand for TB programs; assisting in the delivery of TB services in the mines; and confirming that existing occupational health programs incorporate TB screening. Intensified TB case finding (ICF) and HIV counseling and testing (HCT) was conducted in the mines with the support of DOH through provision of sputum bottles, test kits. The TB Project conducted TB screening and provided information, education and communication materials and assisted with sputum transportation to the nearest public health laboratory services.

Results: 663 miners were reached in the 5 mines that participated in the ICF and HCT campaigns. 161 miners were TB suspects. Sputum was collected for 131 and tested for TB. One mine had a GeneXpert on site for testing and the other 4 mines sent sputum to the nearest public health laboratory. ICF in mines is a key component for early case finding, and needs to be scaled-up.

Conclusion: Actively finding miners with TB and providing them with treatment early is critical, especially in small mines that do not have clinics on site. ICF and HCT outreach campaigns in small mines needs to be scaled-up and linkages to communities surrounding the mines needs to be established during ICF and HCT campaign.

PC-605-02   Prevalence of latent *Mycobacterium tuberculosis* infection and incidence of active tuberculosis in individuals deprived of liberty

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Background: The prison population is considered as having high risk for tuberculosis (TB) development. The STOP TB strategy professes the necessity of give a direction to actions for incarcerated people. The implementation of an active search for respiratory symptoms (RS), and the execution of thoracic radiogram, are both recommended, mainly on the moment of admission to penitentiary system. The early identification and treatment success are the more effective measures for prevention of TB transmission. The method to be utilized should take into account the local context and available resources. This work intends to describe the prevalence of Infection *Mycobacterium tuberculosis* latent (LTBI) and the incidence of active tuberculosis, in individuals deprived of liberty after their admission into prison system.

Intervention: This was a cross-sectional study developed between July and August 2011, in a male criminal establishment, gateway to the state prison system of Minas Gerais, Brazil. Tuberculin skin tests (TST), considering positive the results ⩾5 mm, and a search for respiratory symptoms (cough during ⩾ 2 weeks) were developed in individuals who previously accepted to participate in the study. Bacilloscopy, sputum culture, and sensitivity test for *M. tuberculosis* were executed.

Results: Out of a total of 1222 inmates, 1148 (93.4%) accepted to participate in this investigation. Eight hundred eighty-six inmates (77.2%) were submitted to TST, and 512 (57.8%) of them presented positive result. The number identified of respiratory symptomatic individuals was of 275 (24.0%). The incidence of active pulmonary TB corresponded to a value of 273/100 000 inhabitants. The prevalence of LTBI was of 57.8%. It was not found any case of multi-drug resistant TB (MDR-TB).

Conclusions: Both, the incidence of TB and the prevalence of LTBI, are high in the population being admitted in the penitentiary system of the state of Minas Gerais, with a rate that is 13.7 times larger than expected for this Brazilian region. It is necessary a better screening for early detection of TB in such places, as well as to prevent of this disease transmission.

PC-606-02   Treatment follow-up of tuberculosis patients after discharge from prison using comprehensive approach

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Background and challenges to implementation: Treatment follow up project for ex-prisoner/TB patients is set up and implemented by local NGO, taken into account the social and motivational tools. The Project places special emphasis on strengthening adherence to TB treatment by identifying the factors lead to treatment interruption among ex-prisoners.

Intervention or response: The implementation of post-prison treatment follow up project started in March 2011 by national NGO 'Support to Health' with the support of Main Medical Department of the Ministry of Justice. The treatment adherence rate used to be very low in previous years before the project started. In order to tackle treatment interruption problems, needs were assessed and motivational tools were identified and through effective involvement of NGO accordingly;

Patients discontinued treatment;

Factor: as soon as they feel better or think that treatment does not help due to side-effect problems.

Respond: conducting education and counselling activities in prison prior to release and after among ex-prisoners until treatment is completed.

Factor: Social problems and joblessness due to being sick or for being ex-prisoner.

Respond: Patients were supported with incentives and enablers to be motivated to arrive DOT centres to take medications.

Results and lessons learnt: Post-prisoner/TB patients' treatment adherence varied from original TB patients in civilan sector, however, this problem is being successfully tackled through involvement of national NGO. Thus, by April 2013, 175 drug-sensitive TB

(DS-TB) and 94 drug-resistant TB (DR-TB) patients were discharged from prison and continued treatment in the civilian sector. Out of 269 patients in total only 4 patient discontinued their treatment after release. Continuation of treatment was ensured 98% among released patients, while it was only 10% in previous years.

Conclusions and key recommendations: By involving national NGO, in view with strengthening treatment adherence, patient support project has been fully organised and adherence to treatment has been entirely achieved. Project shows a significant success since all the released TB patients can be followed-up using social and motivational tools.

PC-607-02 Tuberculosis burden in the prisons of Mbeya Region, Tanzania

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Background: There is a consensus that prisons are a reservoir for TB infection and therefore pose a risk for increased transmission. Delayed diagnosis and difficulties in completing treatment lead to prolonged transmission and increased risk to develop multidrug resistant TB. New approaches and innovative and improved diagnostic tools are needed to address the problem and clear this reservoir.

Design/methods: A prisoners held in the prisons of the Mbeya Region from November 2010 to November 2011 were screened for TB by collecting morning and spot sputum samples for fluorescence microscopy. Spot sputa further underwent Xpert MTB/RIF assay. Carrying out the screening exercise twice within one year ensured that all inmates of the Mbeya Region were captured. Furthermore, from March 2011, all entries into the penitentiary system in Mbeya were subjected to TB screening upon admission, using the same diagnostic algorithm. Inmates and new admissions with positive smear and/or Xpert result were referred for treatment initiation. All prisoners were offered HIV testing and staging during screening.

Results: A total of 2539 TB screenings were performed on inmates over one year. The diagnostic yield of microbiological positive cases resulted in a prevalence of 1.95% in this cohort. Furthermore, a total of 5319 admissions were screened within a 21 months period (seven reporting quarters) and a prevalence of microbiological positive cases of 4.53% (between 6.45% and 2.76% per quarter) was detected. Both cohorts showed a steady decline of positive cases over the intervention period. 9.8% and 45.5% of TB positive cases were detected by microscopy alone in the inmate and entry cohort, respectively. The majority of positive cases was identified through the Xpert MTB/RIF® assay.

Conclusion: TB prevalence in new admissions to the penitentiary system was higher than amongst inmates, and more smear positive and thus potentially infectious cases were identified amongst new admissions. A significant decline of TB in the prisons can only be achieved by not only targeting the inhabitants of the facilities, but also new entries, who seem to be an equally important reservoir for TB transmission. The slow decrease of positive cases over time, as well as the improvement of diagnostic yield with new methods, indicates that TB control in the prison population should not only rely on improving the diagnostic tools but also on maintaining active screening efforts.

PC-608-02 Comparison of induced and spontaneous sputum for the diagnosis of pulmonary tuberculosis in Colombian jails

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Background: To compare security of induced sputum (IS), quality of sputum sample, and diagnosis of PTB between IS and spontaneous sputum (SS) in prisoners.

Design/methods: Cohort study. Among 1305 people with respiratory symptoms, 72 cases were diagnosed with PTB. They were followed-up every month for the first six months, or until the end of anti-TB treatment. Three sputum samples were taken (1 IS and 2 SS) on consecutive days at baseline and during each follow-up. The IS was done using hypertonic saline solution (5%). Before the procedure, salbutamol was applied. Each patient was clinically evaluated before, during, and 30 minutes after the IS. Presence of any adverse event was registered. This study was approved by the Ethics Committee of the University. The first SS and the IS samples were stained with auramine, and cultured in Löwenstein-Jensen (LJ), MGIT and thin-layer agar (TLA) for detection of resistance to rifampicin and isoniazid. Variables recorded from sputum samples were: consistency, presence of mucus and blood, volume in milliliters (ml), and time to detection of *M. tuberculosis* in each culture. Concordance between IS and SS was calculated using Kappa coefficient. Time to detection of *M. tuberculosis* was determined in each culture and was compared at baseline and during follow-up.

Results: 353 IS and 364 SS were evaluated in 72 PTB

patients during follow-up. Breathlessness was present in 1.6% (7/351) of procedures during IS, and 1.4% (6/344) after IS. There were no deaths, hospitalizations or other complications. IS samples had 81% of thick consistency compared to 64.7% of SS, 10.3% of IS samples were saliva vs. 23.5% of SS; and 32.1% and 41.3% had <1 ml in IS and SS, respectively. Concordance between IS and SS to diagnose PTB was 0.74 (95%CI 0.61–0.88), 8 cultures were positive from IS samples but negative by SS; and 5 cultures were positive from SS samples but negative by IS. The time medians to detect *M. tuberculosis* in LJ, TLA and MGIT at diagnosis were 25, 13 and 7 days, respectively, and one month after anti-TB treatment was started, the time medians in LJ, TLA, and MGIT were 35, 27 and 15 days, respectively.

Conclusions: IS is a safe procedure to use in jails when SS is not feasible. IS allowed us to detect more positive cultures compared to SS. It is important to use a rapid culture to diagnose PTB in jails. During follow-up, IS allowed to have a good sample to determine if patients were cured by the end of the treatment.

PC-609-02 Communication strategy in the penitentiary system of Azerbaijan

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Background and challenges: Prisoners constitutes most vulnerable MARP in general population for TB. As part of TB control project the Main Medical Department (MMD) of the Ministry of Justice (MoJ) makes efforts to yield disease awareness among detainees and prison personnel in two principal directions: regular Health Education (HE) and personnel capacity building.

Intervention or response: Awareness rise activities have been implementing by MMD since 1995, supporting by Governmental and International Partners, such as GFATM, ICRC, WHO, GLC, etc. Cumulatively designed HE skills and materials on TB and TB-HIV co-infection (posters, flyers, booklets, calendars, etc.) are persistently distributed among detainees in correctional facilities (CF) and prison staff. They are adjusted for two ways of communications building up a trust to the treatment and prison personnel served in penitentiary system (PS). A range of educational movies on TB topic were filmed and are shown in penitentiaries. Copies are available from www.prisonhealth.az. MMD works on peer-to-peer education among prisoners and this activity brings good results already. As part of MMD MoJ communication strategy, HE and counseling sessions aimed to ensureadherence to TB treatment is implemented by NGO 'Support to Health' after release. Working closely with PS Medics the NGO keeps up communication among ex-prisoners and former caregivers.

One of the MMD MoJ TB Training Centre (TC) in prisons work directions is to train non-medical PS staff on health in prisons, including TB, HIV and infection control measures.

Results: MMD MoJ developed one of the best practices of communications used in PS. Being user-friendly, the video HE materials reached a wide response among prisoners and prison staff. Implementation of comprehensive HE policy contributed largely to TB treatment defaulters' number (from 27% to 2% in 5 years) reduction and consequently, increased treatment success rate, ensured good understanding of TB issues among prison staff and detainees, decreased stigma and had significant impact on overall health in prison. Within the last year around 745 sessions were conducted by 'Support to Health' covering about 1300 patients. Already almost 30 participants from high and middle prison administration have participated to trainings, conducted in TC throughout 2012.

Conclusions: Uninterrupted implementation of efficient HE policy in prisons should be permanently updated and followed.

PC-610-02 Feasibility and performance of the GeneXpert® MTB/RIF assay for the diagnosis of pulmonary tuberculosis in a highly endemic penitentiary system

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Objective: Assess the feasibility and performance of the GeneXpert assay for the diagnosis of pulmonary tuberculosis (TB) under routine conditions in a penitentiary health service.

Methods: The study was performed from August 2011 to July 2012 in the Rio de Janeiro (RJ) State prison system (31 000 inmates, 37 prisons, 2010 TB

incidence rate: 2486/100 000). Inmates who were diagnosed as pulmonary TB cases by the pneumologists of the prison system on the basis of AFB smear-positivity (Ziehl-Neelsen staining) of at least one out of two sputum collected one day apart or, if sputum smears were negative, strong clinical and radiological evidence of active TB, were included in the study. Sputum samples were cultured on Ogawa-Kudoh medium and tested using the GeneXpert assay. Bacteriological examinations, including the GeneXpert assay, were performed by the technicians of the prison laboratory system. TB cases were tested for HIV antibodies. The protocol was approved by the ethics committee of the ENSP-FIOCRUZ (RJ).

Results: Out of the 433 TB cases (HIV seroprevalence, 9.2%) included in the analysis, 263 (60.7%) were AFB smear-positive among which 246/263 (93.2%) were culture-positive. Among the 246 smear-positive/culture-positive cases, 243 (98.8%) were Gene Xpert-positive and among the 17 smear-positive/culture-negative subjects, 13 (76.2%) were Gene-Xpert-positive; out of these 13 smear-positive/culture-negative subjects, 9 had a smear result with a low concentration of bacillus (1 +). Interestingly, out of the 170 smear-negative cases including 89 culture-positive cases, 121 (71.2%) were GeneXpert-positive. Out of the 89 smear-negative/culture-positive cases, 84 (94.4%) were GeneXpert-positive as well as 37/81 (45.7%) smear negative/culture-negative cases. The GeneXpert identified 6 rifampicin-resistant cases (1.4%).

Table Results of GeneXpert, AFB smear and culture in 433 cases diagnosed as tuberculosis in a highly endemic penitentiary system

Smear	Cult+ Gene-Xpert+	Cult+ Gene-Xpert−	Cult− Gene-Xpert+	Cult− Gene-Xpert−	Total
Positive	243	3	13	4	263
+++	79	1	3	1	84
++	58	1	1	0	60
+ ou <	84	1	9	2	96
s/inf	22	0	0	1	23
Negative	84	5	37	44	170
Total	327	8	50	48	433

Conclusion: The GeneXpert assay proved applicable in the routine of a penitentiary system health service with the advantages of providing a rapid and accurate diagnosis based on the examination of a single sputum sample, thus simplifying the problem related to successive transfer of inmates to the health service. This test allowed an early diagnosis of many smear-negative cases whose early diagnosis is of particular significance in such an overcrowded and poorly ventilated environment to limit the intra-institutional transmission.

PC-611-02 Tuberculosis control actions in male prison service of Joao Pessoa, Paraiba, Brazil

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Background: Tuberculosis is a global public health problem and has been diversified itself between populations and human groups. This qualitative study aims at identifying and analyzing the tuberculosis control actions towards prisoners according to the determinations of Brazilian Health Plan to prison service concerning the care performed and/or provided in the male prison service of Joao Pessoa, in Paraiba/Brazil.

Design/methods: This is a qualitative research; seven male prisoners with tuberculosis background reported in 2011 took part in the study. The data was collected from December 2011 to February 2012 by means of semi-structured interview. The technique of thematic content analysis was used in order to identify the units of meaning.

Results: The results shows that the tuberculosis control actions in prison service are defective due to the delay in diagnosis, to problems in health care related to accessibility outside prison and to lack of knowledge about the disease. Consequently, the prejudice and stigma attached to tuberculosis only deepen.

Conclusion: Actually would be useful develop a work process in health care inside the prison considering the guidelines of Brazilian Health Care Plan in Prison Service and Brazilian Tuberculosis Control Program. It is recommended the implementation of compensatory policies actions, in the perspective that in addition to free medication it will be secured to the sick inmates' effective health care and preserved their human rights.

PC-612-02 Tuberculosis screening and mapping of miners and ex-miners in Swaziland

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Background and challenges to implementation: Swazilnad is one of the sending countries of miners to South Africa. The SADC Heads of State declaration on TB in the mines requires concerted efforts to curb the burden of TB in the mines. The Health Care improvement project in Swaziland (URC) in collaboration with Swaziland Miners Association (SWAMMIWA) and National Tuberculosis Control programe conducted a mapping exercise of current and ex-miners within the Nkwene community located in the Shiselweni region in March 2013. This activity was a

recommendation from the first TB in Mines Conference held in Manzini, Swaziland, October 2012. Miners, exminers and their families are at risk of tuberculosis but referral and follow-up system to ensure access to continued treatment are weak.

Intervention or response: A pilot study was designed to design a system for mapping miners and ex-miners and to quantify the TB burben of miners in their communities, strengthen referral and follow-up system to ensure access to continued treatment. Registration of mine workers from four chiefdoms in the Shiselweni region was done by five officers. The registrations were led by the ex-miners themselves and 5 mapping officers were also engaged. One led the registrations while the four were on the mapping and health assessment front. All the mapping officers were distributed to the different chiefdoms in the community for registrations on the first day. Health assessments, home assessments and mapping of the miners after registration were done from the second day onward. GIS mapping gadgets were used to map the miners and the miners ID number (COY number) he used in the mines was used to save the coordinates. During health assessments, the forms were completed and TB screening was also done and miners screening positive tested.

Results and lessons learnt: Five miners and ex-miners out of 160 had TB and five ex-miners had a history of previous TB.

Conclusions and key recommendations: There is need to actively seek former mine workers who could have developed TB and silicosis and link them to TB services.

AFB SMEAR MICROSCOPY

PC-613-02   No added value of Ziehl-Neelsen performed on auramine-positive samples for the detection of *M. tuberculosis* and exclusion of NTM

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Background: There is a push to switch from Ziehl-Neelsen (ZN) to auramine microscopy. Despite WHO guidelines that one staining method is sufficient, in some countries national guidelines prescribe that auramine positive samples should be confirmed with ZN. We investigated the added value of performing ZN to confirm auramine positive samples as well as how consistently restaining with ZN was applied in this setting.

Design/methods: Using diagnostic data from 10 276 respiratory samples collected from 5525 patients tested for tuberculosis (TB) at the Municipal Health

Service of Amsterdam between 05/2006–10/2011 we determined the diagnostic accuracy of auramine alone and of confirmation of auramine positive samples by ZN.

Results: Of the 141 TB complex positive samples detected by auramine on which ZN was performed, 32 (22.7%) were negative by ZN. A similar percentage (24.0%, 6 out of 25 samples) of negatives was found for samples containing non-tuberculosis mycobacteria (NTM) species, thus making it impossible to distinguish between TB and NTM based on the ZN result. ZN results were lacking for 64 auramine positive samples. Interestingly, the proportion of missing ZN data was much higher for auramine positive samples containing TB than NTM: TB was cultured from 195 auramine positive samples, of which 54 (27.7%) had no ZN result. Of the 26 NTM positive, auramine positive samples only 1 (3.8%) sample was not examined by ZN.

Conclusion: A positive auramine result followed by a negative ZN result could not be used to exclude TB or indicate the presence of NTM species. Thus, confirming auramine positive samples with ZN in this setting provided no clinically informative information and is a waste of resources. In spite of this it is interesting to note that samples which grew an NTM were more likely to be reexamined by ZN, possibly as a result of a combination of sample characteristics as well as 'suspicious' microscopic appearance.

PC-614-02   Sputum conversion at the end of 8 weeks among Category 1 tuberculosis patients: how reliable are the peripheral laboratory results?

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Background: In resource-poor settings like Nigeria, the diagnosis of TB is mainly by direct smear microscopy (DSM). Because of limitations of DSM, slide rechecking is very necessary especially because of potential differences in the quality of DSM between various laboratories (labs). Anecdotal evidence suggests that the quality of DSM from peripheral labs (PLs) in Nigeria may not be high but this observation has not been systemically investigated. This study sought to fill this gap by assessing the quality of Week 8 DSM performed by PL in Nigeria.

Design/methods: The study was carried out in 5 states selected through multi-stage sampling from south and central parts of Nigeria. The states were Akwa Ibom, Anambra, Enugu, Kogi and Ogun. A cross-sectional review of all week 8 TB smear slides (1595 slides) reported in the first quarter of 2011 by PL was done.

Each slide was independently reviewed by 2 quality controllers (QCs) using light microscope (LM) and also crosschecked with fluorescent microscopy (FM). Analysis was done using SPSS v.17.

Results: For the entire 5 states, sputum conversion rate (SCR) reported by the PL (91.5%) was significantly higher than that by QC (70.9%) by LM (χ^2 = 103.1, $P < 0.05$) and by FM (χ^2 = 148.4, $P < 0.05$). Specifically, Akwa Ibom PLs reported SCR of 94.9% vs. 88.0% obtained by QCs through light microscopy (LM) (χ^2 = 12.95; $P < 0.05$), and 77.6% by FM (χ^2 = 52.7, $P < 0.05$). In Anambra State, PLs reported statistically significant higher SCR of 83.8% than SCR of 75.6% obtained by QC using LM (χ^2 = 6.63; $P < 0.5$), and by FM (χ^2 = 6.63; $P < 0.05$). Kogi State SCR from PLs was 98.1% relative to QC value of 68.4%, through LM (χ^2 = 64.8; $P < 0.05$), and by FM, 60.7% (χ^2 = 84.3; $P < 0.05$).

Conclusion: The SCR reported by PL in each state was significantly higher than those obtained by QC suggesting many false negative reports by PL. This implies that the results of SCR from the peripheral labs may not be totally reliable. Therefore, training and re-training of lab staff should be emphasized. Internal and external quality checks should also continue to be practiced in the national TB programme.

PC-615-02 Bleach sedimentation reduces the number of mycobacteria visible on sputum smear microscopy

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Background: In developing countries pulmonary tuberculosis (TB) diagnosis continues to rely on the century-old Ziehl-Neelsen (ZN) technique of staining sputum smears for microscopy. This procedure has the limitations of biohazard to laboratory personnel and low sensitivity because acid-fast bacilli (AFB) concentration in sputum specimens is too low for microscopy detection in approximately half of culture-positive patients. Bleach is used in several protocols to sterilise sputum for microscopy but this has undefined effects on the diagnostic sensitivity of sputum smear microscopy.

Objectives: To determine the effect of bleach sedimentation protocols on the concentration of visible AFB for sputum smear microscopy.

Methods: Sputum samples from microbiologically confirmed TB patients were used to prepare conventional direct smears and were then divided into four one-ml aliquots that were shaken with an equal volume of 5% bleach. For the bleach-rapid protocol, the mixture was then sedimented for 45 minutes. For the bleach-overnight protocol, after 15 minutes, ten-ml water was added and sedimented overnight. For the bleach-centrifuge protocol, after 15 minutes, 30 ml saline water was added and the mixture was centrifuged. In all cases the sediment was then applied to duplicate plain microscope slides and duplicate albumin-treated slides. One of each slides was stained with the ZN stain and the other with the Auramine-O stain. The number of AFB visible in 100 fields was counted using an iLED microscope with 100× magnification.

Results: All bleach protocols significantly reduced the number of visible AFB independently of the staining conditions ($P \leq 0.001$). Overnight sedimentation reduced AFB counts significantly more than rapid sedimentation. Bleach treatment with centrifugation was less sensitive than any other technique ($P < 0.01$), reducing AFB counts approximately 30-fold. Albumin pre-treatment of microscope slides did not affect AFB counts ($P = 0.7$). Significantly more AFB were visible with auramine staining than with ZN staining ($P < 0.05$).
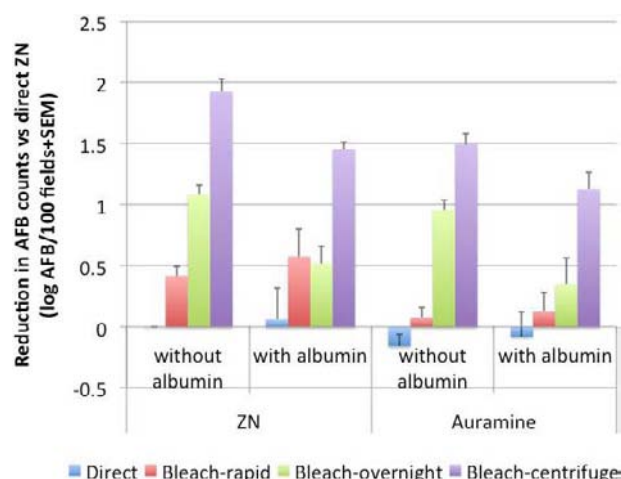
Conclusions: Although bleach improves sputum smear microscopy biosafety, all three bleach techniques that we evaluated reduced the concentration of visible AFB, especially when integrated with centrifugation. The quantitative methodology that we developed precisely defines the concentrating/diluting effect of microscopy protocols and may allow optimisation of sputum treatment with bleach to increase diagnostic sensitivity.

PC-616-02   Baseline data for field evaluation of FDA vital staining for detection of viable *M. tuberculosis* and assessment of culture performance during follow-up

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Background: Identification of acid-fast bacilli (AFB) in the sputum smear during tuberculosis therapy is in some settings considered a predictor of patient infectivity and treatment failure. However, the meaning of positive smears at follow-up examination is not always clear. Smear microscopy cannot distinguish between AFB that is alive or dead. There is a strong interest for a rapid and simple method able to elucidate the real value of a positive AFB smear during treatment follow-up.

Design: The study was conducted at national reference Laboratory in Rwanda to evaluate baseline data and to prepare the launching of an operational study to evaluate the FDA vital staining. We retrospectively evaluated a cohort of 205 adult patients (142 men and 63 women) diagnosed with new case pulmonary tuberculosis.

Result: Of the 205 patients, delayed sputum smear and culture conversion occurred in 91 (44%) and 47 (23%) patient beyond 2 months, respectively. Sputum smears remained positive for AFB beyond 5 months of therapy in 13 patients (6%). Of the 13 patients with positive smears after 5 months, 10 (77%) converted to negative culture results before negative smear results, and 3 (23%) had persistently positive culture results. Thus, in this study population, there were only three true treatment failures beyond 5 months.

Conclusion: Persistent sputum smears positive for AFB at the end of treatment do not necessarily indicate treatment failure but is more likely to be associated with negative culture results due to the presence of nonviable mycobacteria. Based on the baseline data presented here, we proposed to investigate the feasibility of implementing the FDA vital staining in Rwanda where microscopy remains the only one tool widely accessible for TB treatment monitoring.

PC-617-02   Rendement d'une série d'examen de crachats dans le diagnostic de la tuberculose au Rwanda

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Contexte : Le diagnostic bactériologique de la tuberculose (TB) repose dans une large mesure sur l'examen microscopique direct des frottis d'expectoration. Les patients ayant une tuberculose pulmonaire bacillifére c'est-à dire à microscopie positive sont la source la plus importante de la transmission de *Mycobacterium tuberculosis* dans la collectivité. L'Organisation mondiale de la Santé (OMS) et l'Union Internationale Contre la Tuberculose et les Maladies Respiratoires (UITR) suggéraient l'examen microscopique sérié de trois crachats chez les patients suspects de tuberculose pulmonaire avant d'exclure un crachat positif.

Objectif : Etudier le rendement de 3 crachats donné dans 2 jours successifs.

Méthodologie : C'est une étude rétrospective et analytique à partir des données du registre du laboratoire, recoupé avec celui des consultations et hospitalisation du centre hospitalo-universitaire de Kigali. Les suspects donnaient le premier crachat le même jour du diagnostic puis un crachat du lendemain matin et le troisième prélevé juste après à l'hôpital. Ensuite nous avons calculé le rendement supplémentaire et la sensibilité du deuxième crachat par rapport au premier et le premier et le deuxième crachat au troisième.

Résultats : Sur les 415 patients retenus comme suspect de tuberculose pulmonaire, tous ont pu donner au moins un crachat. Le premier crachat a été donné par tous les participants (100%), tandis qu'on a recueillie le deuxieme que chez 364 (87%) et chez 360 (86,6%) le troisieme. Donc une perte de 55 patients (13%) qui ne sont pas venu le lendemain ou non pas pu trouver les 2 autres crachats. Comme bénéfice du deuxieme et troisieme, nous avons trouvé que le second échantillon apporte 4,2% de plus que le premier, tandis que le troisième nous donne 1,4% de plus que le premier et le second. La sensibilité dans notre cohorte etait de 93% pour le premier crachat et il augmente de 4% pour le 2éme crachat et 1% pour le 3éme crachat.

Conclusion : Cette étude a constitué un plaidoyer pour l'instauration de la stratégie de 2 crachats en 2 jours. Il soulève néanmoins une réflexion sur celle de 2 crachats en 1 jour vu le nombre non négligeable de patients qui ne viennent pas le deuxième jour.

PC-618-02   What is the prognosis for tuberculosis treatment when sputum smear test is positive in the second month? Brazil, 2006–2011

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Objective: The non-negative sputum smear results in new cases of pulmonary TB at the end of the second month of treatment have been considered to be a predictor of infectiousness and treatment failure, which could predict the favorable or non-favorable evolution of the case at the end of treatment. This study

aims to understand the prognosis for the TB treatment in Brazil when the sputum microscopy test result was positive in the second month of treatment.

Methods: A retrospective cohort study was conducted using secondary pulmonary TB case data for patients who were 15 years of age or older, obtained from the Information System Notification Disease (SINAN) from 2006 to 2011. A logistics regression model was used to estimate the odds ratio and its respective 95% trust interval in order to evaluate the effect of the sputum smear follow up test result in the second month for poor prognosis cases.

Results: Patients with sputum smear-positive results in the second month of TB treatment responded with poor prognosis in the sixth month, with a risk that was 27 times greater for an unfavorable evolution in relation to negative cases. At the end of treatment, considering the positive cases at the end of the second month, 10.7% of the patients tested positive. In relation to control exams during the period, 32% of the patients did not follow the NTP norms by receiving control sputum.

Conclusion: Despite the study limitations, we confirm that patients with smear-positive test in the second month resulted in a poor prognosis, indicating the need for more precise monitoring in these cases.

PC-619-02   Diagnostic and bacteriological control in patients 15 years of age or older with pulmonary tuberculosis, Brazil, 2001–2011

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Objective: Bacteriological research is very important for both diagnosis and to improve tuberculosis (TB) treatment, one of the Brazilian National Tuberculosis Control Program priorities. This study aims to identify the use of direct sputum smear microscopy for the diagnosis and monitoring of patients who are 15 years of age or older with pulmonary tuberculosis in Brazil from 2001 to 2011.

Methods: A retrospective cohort study was conducted with 570 210 cases of pulmonary TB. The data were grouped into two periods (2001 to 2005 and 2006 to 2011) due to changes in 2006 regarding the notification of tuberculosis cases in SINAN. The second sample included the sputum smear variables for diagnosis and monitoring during the first, third, and fifth months. For the 2006 to 2011 period, the variables for the sputum smear microscopy monitoring tests from the first to the sixth months were analyzed. The statistical software SPSS version 18 was used for these analyses.

Results: Around 86.3% of the patients in Brazil with pulmonary TB had the sputum smear microscopy diagnoses for TB. The first and second sputum samples examined using sputum smear for patients with two samples confirmed 69.4% and 4.5% of the TB cases, respectively. More than thirteen percent of the pulmonary TB cases did not have bacteriological confirmation of the diagnosis, and in the follow up group, one third of the patients were not examined using the sputum microscopy. For all the cases with sputum smear-negative diagnoses, only 21.0% were later examined using a BAAR culture, of which 44.5% were positive.

Conclusion: The limitation in the use of direct sputum microscopy exams in Brazil can be partially attributed to the limited availability of microscopy in Basic Care services, human and material resources logistics, the lack of compatibility between the national and state-level information systems, and the lack of new technologies that facilitate the diagnosis of TB.

DEVELOPING HUMAN CAPACITY TO IMPROVE TUBERCULOSIS CONTROL

PC-620-02   Expanding knowledge, enhancing practice, eliminating tuberculosis: an introduction to the DR TB Training Network for health care workers

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Background/challenges to implementation: Due to improved global surveillance approaches to uncover increased drug-resistant tuberculosis (DR TB), many countries are struggling to address the growing demand for effective DR TB clinical management and programmatic strategies. New opportunities to acquire skills to address the aforementioned challenges are needed.

Intervention/response: The DR TB Training Network, an interactive online learning site, provides practitioners and program managers with tools and opportunities to learn from experts, share information and best practices, and train other healthcare professionals. Participants engage in both online activities (case discussion series) and live interactive opportunities (webinar courses). Offline opportunities, specifically fellowships, exist for participants at programmatic management of drug-resistant tuberculosis (PMDT) Technical Assistance Centers in Lesotho, Peru, or Rwanda. A variety of additional resources—clinical training courses, DR TB tracking tools and registers, and patient education materials—are available for adaptation to local contexts as well.

Results/lessons learnt: Since its launch in November of 2011, the DR TB Training Network has educated over 300 participants from 93 countries. Based on the knowledge and skills acquired either directly through

the DR TB training network or via onsite fellowship opportunities, participants have greatly benefitted professionally. Participants have implemented new DR TB activities and strategies within their national TB programs, expanded their professional networks by collaborating with other professionals in the field, and received professional promotions with international TB organizations.

Conclusions: An applied and blended instruction method allows participants within high burden TB settings, who otherwise would not have an opportunity to learn about DR TB, the opportunity to do so via electronic media. Given the increased demand for technology to engage learners, the DR TB Training Network creates opportunities that can then foster change at both the global and country level, resulting in improved programmatic and clinical management of DR TB. By expanding these opportunities to more participants, the burden of DR TB on the global community can be minimized.

PC-621-02   Tablet computers and capacity building for MDR-TB of health care workers in low-resource settings

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Background and challenges to implementation: In contrast to drug-susceptible tuberculosis (TB), treatment of multidrug-resistant TB (MDR-TB) is more complex and resource-intensive. The programmatic management of drug-resistant TB (PMDT) therefore demands more managerial and technical skills on the part of the health practitioners. As countries worldwide scale up PMDT, the need for capacity-building of practitioners is heightened. The World Medical Association and New Jersey Medical School Global Tuberculosis Institute created a free, online training course to address this need. Funding for the original course content, which is based on the World Health Organization (WHO) recommendations, was made available by the Eli Lilly MDR-TB Partnership. New advances in mobile technology, in particular tablet computer 'apps', were conceived as a way to extend the reach of this training in low-resource settings by making content the training course available on apps. Enabling the app to run offline was prioritized in order to accommodate users without constant access to the internet.

Intervention or response: Apps for Android and Apple platform tablets were created in early 2013 with financial support from WHO and made available for free download through Google Play Store and Apple App Store. Due to the nature of the content and multimedia clips, it was believed that viewing on smartphones would be suboptimal for learning. Each app was field tested to identify programming and usability issues prior to launch.

Results and lessons learnt: Although primarily intended for 10-inch screen tablets, the Android app was also useable on 4 inch smartphones. Sound features and links to documents and websites for further reading proved useful. In addition to customary press releases, the apps were marketed via social media and organizational Facebook and Twitter accounts, as well as press releases, blogs, and listservs (e.g., mHealth working group).

Conclusions and key recommendations: Continued use of these applications will be evaluated using the download statistics of the repository sites. The easily updated nature of apps will facilitate the sharing of latest developments in MDR-TB care. We envisage that the effectiveness of apps to inform health care workers worldwide will increase as the penetration of low-cost Android mobile devices expands in low-resource settings (A demo of the app is proposed linked to the presentation of this abstract at the UNION Conference).

PC-622-02   Implementing the multi-method adherence assessment tool amongst tuberculosis patients in Swaziland

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Background and challenges to implementation: Tuberculosis (TB) remains the leading cause of death among patients infected with HIV/AIDS. TB Retreatment cases continue to be high amongst registered cases at 1149/9180 (13%), posing a greater risk to develop resistance strains to TB drugs. Cases of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) are on the increase, and cases have been confirmed in Swaziland. One of the causes of high retreatment cases is poor adherence. Information on adherence levels will be one of the markers that will indicate program success in ensuring safe and effective use of first line medicines as well as second line thus avoiding amplified resistance and further development of drug resistant TB.

Intervention or response: A stepped wedge approach was used in implementing the MMAT. This entailed conducting a pilot assessment of the tool and adapting it to the TB program. Adherence Officers' capacity was strengthened through training on adherence monitoring and reporting. And lastly printing and distributing of the tool to adherence officers and treatment supporters to submit reports on adherence levels on a monthly basis.

Results and lessons learnt: The tool was piloted in
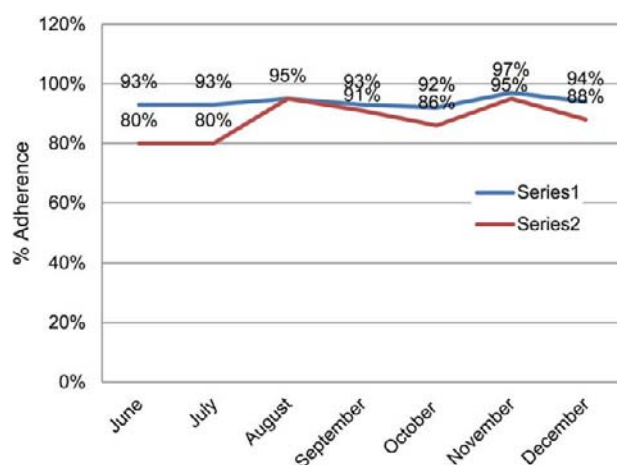
Figure Average adherence scores for TB patients in Swaziland.

14 facilities and average adherence score of 75% was recorded. A total of 110 adherence officers and treatments supporters across the country were trained on administering the tool. The officers reported every month adherence levels of patients they support from June 2012 to date. A total of 816 reports were submitted and the average adherence score was 93%. Since the inception of the project, adherence scores for susceptible TB patients have been consistently above 90% and for multidrug-resistant TB patients adherence levels at baseline were 80% but have since improved to 88% by December 2012. Please see figure for the results.

Conclusions and key recommendations: The participatory process used in Swaziland has yielded a program-driven and owned process. This can be replicated in other countries. A formal assessment should be carried out to determine the impact of the MMAT, to help institutionalize the MMAT in the different health care facilities.

PC-623-02   AFB smear microscopy proficiency of graduating students in the field of medical laboratory science in three Ethiopian universities, 2012

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Background: Microscopy remains the mainstay of rapid tuberculosis (TB) case detection. In most countries, especially those with the highest burden of TB, the direct Ziehl–Neelsen (ZN) smear is still the most common test. However, its sensitivity depends on the diligence of the technician and on use of the appropriate technique. The co-epidemics of Human Immunodeficiency Virus (HIV) infection and TB, especially in Africa, and concerns that the ZN smear has lower sensitivity in those with HIV infection, have stimulated interest in practical methods to improve microscopy. **Objective:** To assess the performance of students graduating in field of Medical Laboratory Science in detecting and quantifying Acid Fast Bacilli using sputum smear microscopy.

Methodology: A cross-sectional study was conducted in Addis Ababa University, Jimma University, and University of Gonder. All graduating medical laboratory science students with a total number of 124 were included. Percentage of Major error (HFP and HFN) and minor error (LFP, LFN and QE) are dependent variable and grade of bacteriology course, sex and age of the student are independent variable of the study.

Results: Of 124 students graduating in medical laboratory science in 2012 evaluated by proficiency test (PT), the mean score was 87.1% and overall PT score ranged from 40–100%. Overall there were 24 (19%) major errors and 117 (81%) minor error. From panel slide reading, the total number of students that report major error are 18 (14.5%), i.e., 14 (11.3%) HFN, 2 (1.6%) HFP and 2 (1.6%) HFN and HFP). In this study, there were a total of 80 (64.5%) students that report minor error (10 (8.1%) LFP, 31 (25.0%) LFN, 14 (11.3%) QE and others report multi-error (19 (15.5%) LFP and QE, 4 (3.2%) LFN and QE and 2 (1.6%) LFP and LFP).There was a significant statistical association between acid fast bacilli microscopy proficiency score and grade (score) of introduction to bacteriology and diagnostic bacteriology courses ($P < 0.05$, $P = 0.04$, CI = 95%).

Conclusion and recommendation: From this study, the proficiency to read sputum smear by graduating batch students who have taken pre-service training (students from University-002) were better than the rest (University-001 and University-003) which hasn't taken pre-service training yet. Students that report major errors were, 6 (12.8%), 1 (5.3%), 11 (19.0%) for university-001, 002 and 003 respectively. Thus, the study has highlights the importance of training in improving the acid fast bacilli microscopy results. In addition, intensive practical session during studentship must be given a great concern.

PC-624-02   What does it take? Assessing human resource requirements for tuberculosis control in India

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Background and challenges to implementation: Global shortages of health human resources (HRH) and the challenges they pose for achieving the MDGs have been well documented. While the human resources requirements of some services, such as HIV and AIDS care and treatment, have been studied, the

staffing requirements of TB supervision and service delivery have received much less consideration.

Intervention or response: This presentation details the findings of two rapid human resources assessments requested by the Indian Central TB Division in 2011 and 2012 and conducted through the USAID-funded India TB Program. Methods used included time-utilization and time-task observations in addition to record reviews and interviews. The assessments covered 19 districts in at total of seven states; samples were small and were intended to provide informative, but not statistically reliable data.

Results and lessons learnt: Findings indicated that treatment supervisors could not effectively address the populations to which they were assigned and would need to be doubled in order to meet needs. Laboratory supervisors, on the other hand, were found to be largely underutilized and TB diagnostics were observed to take only a fraction of lab technicians' time (2–3 hours) in any given day, thus suggesting that laboratory technicians should have integrated responsibilities. Providers spent an average of 5 minutes per patient to provide quality TB screening, 25 minutes per patient for treatment initiation and 12 minutes for TB DOTS per patient per encounter. Time investment of medical doctors was calculated to take less than 30 minutes per day for TB suspects and TB positive patients starting treatment. A more complete assessment of total workload for various cadres and the added burden of MDR-TB services would need to be taken into consideration to assess feasibility.

Conclusions and key recommendations: The findings of these studies informed the new RNTCP National Five-Year Strategic Plan, which proposes an expanded supervisory workforce and better integration of other cadres with the national health system. The Central TB Division's commission of these rapid assessments provides an important model for TB human resources assessment and national evidence-based planning for health human resources contributing to TB control.

PC-625-02 Enhancing capacity of public health professionals in quality assured data capture

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Background: Programme data used for operational research is routinely collected by health service personnel and recorded either in a paper-based format or directly into electronic databases. Data sources will contain some errors and which have to be avoided to ensure quality. Quality assured data capture is often the most neglected part in the curriculum of medical colleges. Initiative has been taken to enhance capacity of medical college professionals working in close collaboration with National Tuberculosis Control Programme on quality-assured data capture using EpiData software with the vision that this becomes a part of regular curriculum in medical colleges and public health teaching institutions. 2 day workshops on 'Efficient, Quality assured Data capture using Epidata' were conducted at 2 Medical Colleges and 5 day course on Advanced Epidata in India.

Intervention: The entire curriculum of the course is based on the usage of EpiData software. Every session consists of a presentation, demonstration and practice by the participants. The course content are in the form of coloured print outs and the structured CD-ROM. The sessions were video-captured to explore if these can be used as teaching/learning resource. Candidates who have performed exceptionally well in previous courses and who are committed to being resource persons are trained in Advanced EpiData.

Results: An aggregate of 59 medical college professionals are trained on EpiData/Advanced EpiData. The overall mean score accorded to the course was 4.62 by the participants. A self-sponsored course on EpiData Analysis was organised by the trainees. Some of the trained participants are being used as facilitators. DVDs and CD ROM prepared are being disseminated to faculties to assist them in conducted such trainings in their colleges. These DVDs will also be used to train wider network through virtual training. The course is highly appreciated and suggested for recommendation to others. Few participants faced difficulty with CHK commands, section on safety of data set and suggested to extend the course.

Conclusion: There is expansion of training on quality-assured data capture using EpiData amongst public health professionals. Possible next steps will be inclusion of course in curriculum of medical colleges, creation of pool of resource persons and application of EpiData software by trained health professionals on their research projects and ensuring quality data in operational research.

PC-626-02 Health E Lungs: web-based learning for frontline social care professionals

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Background: TB and respiratory diseases disproportionately affect socially excluded communities in UK inner city areas. High rates of tobacco and illicit drug use are compounded by poor diet and living conditions and problems accessing and remaining engaged with health services. Respiratory care for these communities is often characterised by under-diagnosis,

sub-optimal clinical management for long term conditions, and unplanned hospital admissions due to exacerbation of conditions that would otherwise respond to planned treatment. Many of the most vulnerable individuals have more contact with social care professionals than health workers. These frontline social care workers are an untapped and valuable resource to promote respiratory health among socially excluded communities but virtually no training and awareness resources are readily accessible for non-clinical professionals.

Intervention: Find&Treat, Southbank University and Brickwall Health are developing a user friendly, interactive, free online learning resource for nonclinical professionals working with socially excluded communities in the UK. This aims to enhance knowledge and understanding around the importance of early detection, engagement and case management. The package will be sponsored over a 5 year period, which will cover ongoing running and support costs.

Results and lessons learnt: Developing respiratory training and awareness resources for workers with minimal health care training, and limited knowledge of anatomy and physiology presents challenges. We have piloted and tested a range of information resources with frontline staff and used these findings to inform the language, style and content of the on-line resources. E learning appears highly acceptable and allows workers to study in their own time, in a location of their choice. Our aim is to formally evaluate the impact of this training on knowledge and awareness and opportunities for improving the respiratory health of service users.

Conclusions: Non-clinical professionals working with socially excluded communities can play an important role in safeguarding and improving the respiratory health of service users. Specifically tailored resources provided through an E learning platform have the potential to reach high numbers of frontline workers who can directly disseminate messages and promote better engagement with respiratory health service.

PC-627-02   Assessing knowledge, attitudes and practices regarding *Mycobacterium tubercolosis* infection risk among health science students in a tuberculosis-endemic setting

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Background and challenges: South African health care workers, including health science students (HSS), are at increased risk of contracting tuberculosis (TB). HSS working in TB-endemic settings require knowledge of TB control measures to reduce their risk of occupationally-acquired disease.

Intervention: HSS at Stellenbosch University participated in a cross-sectional interventional study, consisting of questionnaires administered before and after a structured intervention imparting knowledge and awareness of occupational TB risk and control measures. The 1-hour intervention included personal accounts by medical professionals affected by TB and information on how to reduce occupational risk through infection prevention and control (IPC) measures. TB risk, knowledge, attitudes and practices were surveyed and compared for 327 students.

Results and lessons learnt: HSS overestimated their risk of developing TB, but underestimated the mortality associated with drug-resistant tuberculosis (DR TB). Reported practices at Tygerberg Hospital (TBH), Western Cape showed that 62% ($n = 182$) interacted once a week or more with patients who had defaulted on TB treatment. Only 8% reported that N95 respirators were always available where needed ($n = 177$). Natural and mechanical ventilation were reportedly not used in clinical areas (60%, $n = 179$ and 55%, $n = 164$, respectively). Additional DR TB-IPC measures, such as airborne precaution signs and a 'closed door' policy for isolation rooms were reportedly inadequately utilized. Pre-intervention knowledge of personal protective equipment use was poor but improved by 20% post-intervention (0.575 vs. 0.775 out of 1 [$P = 0.0000$]).

Conclusion: HSS lack knowledge of TB control measures including protective equipment usage and report poor implementation of TB-IPC in their training institution. A structured educational intervention increased students' awareness of occupational TB infection risk and knowledge of TB-IPC measures. More opportunities for training in TB-IPC are urgently needed for HSS in TB-endemic settings. A similar intervention could be included in all health science curricula to protect students and future professionals, and enable them to educate colleagues.

PC-628-02   Barriers of capacity building among medical staff working in tuberculosis control in designated hospitals in Shanghai

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Background: Human resource (HR) development is one of the essential points of Stop TB Strategy developed by WHO in 2006. A shortage of quality, motivated and sustainable work force has been widely recognized as one of the most important challenges for achieving the Stop TB targets and MDGs. In 1998, Shanghai identified TB designated hospitals for strengthening TB diagnosis and treatment, but the weakness in HR capacity building in TB designated hospitals became more certain now. The objective of the study was to explore the barriers occurred in individual, institutional and social levels, to improve HR capacity building in TB designated hospitals.

Design/methods: Qualitative and quantitative research methods were employed. A questionnaire on employee satisfaction (ES) and training status and demands was investigated with all 364 TB medical staff in 30 TB designated hospitals, 17 districts in Shanghai in 2012. Regarding ES, the dimensions included 'work environment' (D1), 'equity on income and welfare' (D2), 'job approval/acknowledge' (D3), and 'work pressure' (D4). Likert-type scale items were adopted and the total score were 100. Seventy-five interviews were conducted with district TB programmes officials, leaders, administrators and TB medical staff in TB designated hospitals in 4 districts to understand the individual, institutional and social factors that impact capacity building.

Results: (1) There were 5 times and accumulative 6 days training per medical staff in the past year. The basic knowledge of 'TB prevention and treatment' and 'infectious disease prevention and treatment' were selected by TB medical staff as the most in need for training. Relatively, 'research article writing' and 'research design and data analysis' were chosen as the most shortage knowledge. (2) The ES score was just 54.29 ± 11.51. Dimension scores from the lowest to highest were respectively D2, D4, D3 and D1. (3) There existed the significant difference of work environment, income and individual career development between the TB medical staff and other similar profession and position in hospitals.

Conclusion: A hierarchical classified training system has been set up for TB medical staff. However, the innovative training interventions that are able to meet individual demands, the incentive policies, such as special subsidies and title promoting need to be developed by hospitals and governments for better HR development on Stop TB targets.

PC-629-02   Impacto de la búsqueda de casos de tuberculosis pulmonar en personas indígenas de México, enero-junio 2012

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Marco de referencia: Diagnosticar y curar los casos de tuberculosis pulmonar en población indígena es primordial, debido a la alta vulerabilidad que este tipo de población representa en México.

Intervención o respuesta: En coordinación con personal de salud de 17 estados de México con población indígena, se realizó la búsqueda intencionada de sintomáticos respiratorios (tos con flema mayor a 15 días) para diagnosticarlos e ingresarlos a tratamiento estrictamente supervisado (DOT) hasta su egreso por curación. Se óbtuvo la información y analizó desde los sistemas oficiales nacionales de tuberculosis.

Resultados y enseñanza: Se realizaron 217 operativos para la búsqueda de sintomáticos respiratorios en aéreas indígenas de 17 estados de México, se detectaron 4438 sintomáticos respiratorios, se diagnosticaron 640 casos, de estos 485 curaron (78%), 88 término de tratamiento (14%). 7 fracasos (1%), defunciones 15 (2%), abandonos 17 (2.7%), traslados 4 (.5%), continúan en tratamiento 9 (1.4%).

Conclusiones y recomendaciones: Trabajando en grupos vulnerables como son los indígenas, con la participación coordinada con el personal de salud y autoridades estatales para realizar las actividades de búsqueda de casos de tuberculosis pulmonar e ingresarlos a tratamiento para llevarlos a la curación, nos permite romper con la cadena de transmisión en este grupo de población altamente vulnerable. Aunque el porcentaje de casos en población indígena respecto a la población no indígena no es elevado, si lo es cuando se mide a través de tasa de incidencia, esta si rebasa hasta el doble la media nacional.

TUBERCULOSIS MOLECULAR EPIDEMIOLOGY

PC-630-02   Profile genotype analysis of *Mycobacterium tuberculosis* in a high-incidence area in Brazil over the last 10 years

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Background: Despite increasing interest in possible differences in virulence and transmissibility between different genotypes of *M. tuberculosis*, very little is known about how genotypes within a population change over decades. Molecular typing of *M. tuberculosis* isolates is a powerful tool for studying the

dynamics of TB transmission and can provide important information about the identity of the strains circulating in a region. Our aim was to analyze the genotypic profile of *M. tuberculosis* in Metropolitan Area of Vitoria–ES, Brazil, and to determine whether there was change in the *M. tuberculosis* genotype profiles during this period.

Design/methods: We conducted a longitudinal study, observational in Metropolitan Area of Vitoria–ES, Brazil, in a series from 2000/2001 and 2011. Clinical and demographic epidemiologic characteristics were collected through to the national surveillance system (SINAN). Laboratory information about the isolates was obtained from laboratory records. We analyzed 640 *M. tuberculosis* isolates from as many pulmonary TB patients using IS6110-RFLP method. Strains with identical or closely related IS6110 RFLP patterns were considered to belong to a cluster indicative of recent transmission. Clustering and Simpson's diversity index was calculated for different years of IS6110 RFLP genotypes.

Results: A total of the 640 isolates was selected for this study (186 from year 2000, 160 from year 2001 and 294 from year 2011). Of these, 229 (35.8%) isolates were grouped into 68 distinct clusters. The majority of the clusters exhibited an IS6110 copy number ranging from 2 to 17 (mean, 10). Our results showed that there was an increase in amount of isolates in clusters in 2000 for 2011. Among those, named number families ES14 and ES19, had the majority of clustered strains. Simpson's diversity index based on RFLP patterns was for 0.98; 0.96 and 0.99 for 2000, 2001 and 2011 years, respectively. By bivariate analysis, sex, age, HIV infection, and TB clinical form showed no statistically significant difference for patients belonging to cluster patterns and those that had unique patterns.

Conclusion: The results of this study demonstrated the importance of molecular typing in understanding the transmission dynamics and that public health measures to interrupt new transmissions need to be emphasized for TB control in Metropolitan Area of Vitória-ES, Brazil.

PC-631-02   *Mycobacterium tuberculosis* Uganda genotype has significantly increased tendency to form granulomas

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Background: *Mycobacterium tuberculosis* has evolved into a number of widely distributed and genetically diverse lineages and sub-lineages exhibiting variable disease phenotypic characteristics demonstrated in epidemiological studies and animal models. Uganda genotype, one of the sub-lineages is the commonest cause of tuberculosis in Kampala but its phenotypic characteristics has not been studied. We studied the clinicopathological characteristics of patients infected with Uganda genotype as compared with those infected with non-Uganda genotypes.

Design/methods: Between 2010 and 2012, 129 patients (mean age 28.3 yrs) with tuberculous lymphadenitis were enrolled and had their lymph node aspirate cultured. We genotyped each isolate by two standard PCR-based techniques, region of difference (RD) analysis and spoligotyping. The patients were classified into those infected with Uganda and those infected with non-Uganda genotypes of *M. tuberculosis*. Clinical pathological parameters in the two groups were compared using crude and multivariable logistic regression model with adjustment to confounding factors.

Results: Of the 129 patients infected with *M. tuberculosis*, 69 (53.5%) were infected with Uganda genotype. Uganda genotype was significantly associated with granuloma formation (95%CI 1.2–7.5, $P = 0.02$) after adjusting for sex, age and HIV but no differences in the clinical and radiological features between the two groups were identified.

Conclusion: Uganda genotype is the predominant cause of tuberculous lymphadenitis in Kampala and is significantly associated with granuloma formation. Cytomorphological features of tuberculous lymphadenitis partially depends on bacterial determinants, This has implications on future vaccine and product design.

PC-632-02   Molecular epidemiological characteristic of *Mycobacterium tuberculosis* strains circulating in Kazakhstan

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Background: Despite the focused attention to the problem of drug-resistant tuberculosis (TB) in Kazakhstan, *Mycobacterium tuberculosis* population structure and genetic mechanisms of drug resistance, as well as the epidemiological significance of different genotypes of the agent to date are still poorly understood. Objective: study of genetic variety of *M. tuberculosis* populations circulating in Kazakhstan and evaluation of epidemiological significance of strains of different genotypes.

Methods: Clinical-laboratory study, microbiological study for tuberculosis of 570 patients with pulmonary TB from four regions of Kazakhstan. Genotyping of *M. tuberculosis* strains by methods of VNTR-typing (R. Frothingham et al. 1998), IS6110-inverse PCR (I. Mokrousov et al. 2006), spoligotyping (J. Kamerbeek et al. 1997), hybridization on oligonucleotide biochip 'TB–biochip (MDR)' for revealing mutations in *rpo*B, *kat*G, *inh*A and *ahp*C genes (V. Mikhailovich et al. 2001) were used.

Results: Population of *M. tuberculosis* in studied regions was heterogeneous by chromosome DR-locus: among 31 spoligotypes the representatives of Beijing (71.6%), T (12.8%), LAM9 (5.2%), Harlem (4%), MANU2 (2.4%), U (1.2%) genetic families were. VNTR-analysis revealed 27 different genotypes of *M. tuberculosis*: 25 isolates with unique structure for this sampling, 306 strains belong to 27 clusters. The most frequent variants are VNTR-genotypes 42435 (41.4%), 22232 (9.4%), and 42432 (5.7%).

Beijing genotype strains are characterized by heterogeneity on ETR A, B, C, D and E (32 types) markers, 56.6% out of them have an allelic profile 42435. Beijing genotype and dominating variant strains, in difference from the other genotypes, have a high transmission and more high rate of primary multidrug resistance (25.9% and 10.1%, accordingly, $P < 0.05$) and resistance to streptomycin (61.1% and 34.2%, accordingly, $P < 0.05$), they are more frequently associated with infiltrate lung TB ($\chi^2 = 15188$, $P < 0.05$) and development of complications ($\chi^2 = 44029$, $P < 0.05$), persistence of high level resistance to rifampicin and izoniazid due to mutation of rpoB531TTG (58.2%) and *kat*G315ACC (92.5%).

Conclusions: Due to the predominance *M. tuberculosis* strains of a single genotype for DR-chromosome locus in the areas, to study the molecular epidemiology of TB other methods of genotyping must be used additionally. The most clinical and epidemiological important genotype in investigated regions is the dominant genotype Beijing with VNTR-42435 allelic profile that characterized by MDR.

PC-633-02   An overview of central nervous system tuberculosis in an endemic nation

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Background: The present study details the clinico-microbiological profile, drug susceptibility and treatment outcome of *Mycobacterium tuberculosis* complex of tuberculous meningitis.

Material and methods: It was a clinical prospective study from 2010–2013. 425 subjects (>12 years); 98 culture confirmed, 248 clinical TBM and 79 non TB cases were included. Clinical presentation, cyto-biochemical, and radiological findings were obtained. Culture was performed by Bact/ALERT 3D automation system, Real-time PCR by Genosen's *M. tuberculosis* kit, Rotor gene 6000 using primer targeting 16s r RNA segment of *Mycobacterium tuberculosis* genome and Amplified *Mycobacterium tuberculosis* direct test (AMTDT). Isolates were confirmed by Accuprobe and subjected to drug susceptibility testing by S.I.R.E kit (Biomerieux, France). H37Rv was used as the control strain.

Results: Clinically suspected TBM cases presented with fever 90.2% (312/346), altered sensorium 66.8% (231/346) and neck rigidity 59.8% (207/346). Comparing with culture, AMTDT was 81.2% sensitive and 47.5% specific followed by real time PCR (76.2 and 27.9%), radiology (71.0% and 84.0%), cytology (56.5% and 79.4%) and biochemistry (43.5% and 88.2%). On comparing with clinical diagnosis, AMTDT was (71.2% and 87.5%) followed by radiology (69.2% and 80.4%), real time PCR (68.6% and 86.6%), cytology (49.0% and 70.5%) and biochemistry (40.8 and 88.4%) respectively. *M. tuberculosis* grew in 98/346 (28.3%) which was resistant to isoniazid 35.7% (35/98); ethambutol 29.6% (29/98) streptomycin 23.4% (23/98) and rifampicin 4.1% (4/98). The mortality was 44.9% (77/167); good recovery with antitubercular drugs observed in 38.3% (64/167) and 16.7% (28/167) recovered with one or the other disability (hearing loss, speech loss, vision loss, paralysis).

Conclusion: Using culture as gold standard, molecular assays showed reasonable sensitivity but poor specificity whereas biochemistry and radiology had better specificity. Clinical suspicion resulted in all assays having good specificity with molecular assays doing well in sensitivity along with radiology The drug resistance in TBM is associated with a high mortality and morbidity complicating this dreaded disease.

PC-634-02   New insights into molecular epidemiology of *Mycobacterium tuberculosis* in the most populous state of Australia

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Background: Mycobacterial interspersed repetitive unit-variable tandem repeat analysis (MIRU-VNTR) has been applied to examine population dynamics and clustering rates of *Mycobacterium tuberculosis*. The aim of this study was to investigate the dynamics of *M. tuberculosis* epidemiology since 2006–2008 and the relative impact of common lineages of *M. tuberculosis*.

Methods: Total 930 culture confirmed tuberculosis cases identified in 2010, 2011 and 2012 in New South Wales (NSW), Australia were analyzed. *M. tuberculosis* isolates were prospectively genotyped by 24 loci MIRU-VNTR method and lineages were assigned using miruvntrplus.org. The associations between *M. tuberculosis* lineages, patient demographics, sites of infection and drug resistance were explored using descriptive statistics.

Results: While the proportion of Beijing lineage isolates (28.2%) has not significantly changed since

previous report (Gallego et al. 2009), the frequency of East African Indian (EAI) and Central Asian lineages (Delhi/CAS) has increased up to 28.7% and 12.7%, respectively. Cases due to Beijing lineage were more likely to be associated with respiratory disease and drug resistance ($P < 0.05$) whereas EAI strains and Delhi/CAS were associated with non-respiratory TB ($P < 0.001$ and $P < 0.05$, respectively). Age of patients was significantly associated with lineage ($P < 0.0001$). In particular, the age of those who affected with Delhi/CAS (mean age 37) was significantly less than of those affected by *M. tuberculosis* Beijing (mean age 42, $P < 0.05$) or *M. tuberculosis* EAI (mean age 44, $P < 0.01$). Further the age of those affected by Harleem lineage (mean age 59, $P < 0.05$) was significantly higher than people affected by any other lineages detected in NSW. Recent evidence from China suggested that *M. tuberculosis* Beijing with 22332 5173533 MIRU-VNTR allele can be highly transmissible and related to multi-drug resistance (Hu et al. 2011). We found 85 cases of *M. tuberculosis* with these MIRU-VNTR alleles in our patient population. And 10 *M. tuberculosis* isolates were monoresistant to any first line tuberculosis drugs and 1 isolate was multi-drug resistant.

Conclusion: EAI strains of *Mycobacterium tuberculosis* recently overtook Beijing family as a prevalent cause of tuberculosis in New South Wales, Australia. Despite this change in molecular epidemiology of *M. tuberculosis*, the rates of recent transmission in NSW remain low.

PC-635-02   High prevalence of human herpes virus type 8 infection in patients with pulmonary tuberculosis

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Background: Tuberculosis patients, similar to those with human immunodeficiency virus (HIV) infection, have abnormalities of cellular immunity. There is a relatively high prevalence of human herpes virus type 8 (HHV-8) infections reported in HIV-infected patients without Kaposi's sarcoma as compared to general population. However, little is known regarding HHV-8 infection in tuberculosis patients.

Design/methods: Blood samples were collected from 101 pulmonary tuberculosis patients before treatment and 101 age- and sex-matched healthy controls, and were analyzed for lymphocyte and monocyte counts and HHV-8 antibody and DNA.

Results: Pulmonary tuberculosis patients had much lower and higher mean lymphocyte and monocyte counts than did healthy controls, respectively ($P < 0.0001$, both). The seropositive rate of HHV-8 antibody was significantly higher in tuberculosis patients (30/101, 29.7%) than in controls (15/101, 14.9%) ($P = 0.0112$). Seropositive rates in male and female tuberculosis patients were not significantly different ($P = 0.7096$). HHV-8 antibody titers in patients also significantly exceeded those in controls ($P = 0.0058$). All subjects were negative for HIV antibody. Three patients negative for HHV-8 antibody had positive results for HHV-8 DNA (544, 899, and 1011 copies/mL) and one patient positive for HHV-8 antibody had HHV-8 DNA (1415 copies/mL). HHV-8 seropositivity was not associated with clinical manifestations of HHV-8 infection, such as Kaposi's sarcoma, primary effusion lymphoma, and Castleman disease.

Conclusion: Seroprevalence of HHV-8 was significantly higher in untreated pulmonary tuberculosis patients than in general population, and was not associated with lymphocyte or monocyte counts, or gender.

PC-636-02   MIRU cluster frequency in 2006–2012 in Denmark

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Background: In 2005 MIRU VNTR replaced RFLP IS 6110 as standard genotyping method of *Mycobacterium tuberculosis* in Denmark (DK). This study examines the results of MIRU subtyping in DK in 2006–2012.

Design/methods: 3140 MIRU VNTR 24 loci genotype results were available from the Danish genotyping database at Statens Serum Institut on 13 December 2012. 1265 genotypes were excluded leaving 1875 MIRU examinations from nearly 100% of incident culture positive TB patients in DK 2006–2012.

Results: Of 1875 included genotypes, 1145 (61.1%) were clustered and 730 (38.9%) unique. They were distributed on 874 MIRU VNTR genotypes. 144/874 (16.5%) genotypes became clustered and 730/874 (83.5%) remained unique.

Danes: The genotypes represented 728 Danes. 561 (77.1%) were clustered, and 167 (22.9%) were unique. Detailed cluster frequency analysis among Danes in age groups showed that a high majority (>80%) of TB cases were clustered until the age of 60.

Greenlanders: 309 Greenlanders had *Mycobacterium tuberculosis* genotyped. 281 (90.9%) were clustered, and 28 (9.1%) were unique.

Immigrants: Genotype was retrieved from 838 immigrants; 304 (36.3%) were clustered and 534 (63.7%) were unique.

MIRU-VNTR/RFLP IS 6110: In 2006, the overall MIRU-VNTR cluster frequency was 40.4% (and RFLP cluster frequency was 41.0%). Cluster frequency applying both genotyping methods was 30.9%.

Clustering/observation time: The average MIRU-VNTR 1-year observation cluster frequency for all was 41.4% (36.7–46.3), 2-years observation cluster frequency was 49.8% (43.4–54.2), and 5-years observation cluster frequency was 60.0% (55.3–62.4).

Conclusion: Interpretation of cluster frequencies over time and comparison to other countries are difficult and should be made for separate population- and age-groups.

PC-637-02 The contribution of *Mycobacterium tuberculosis* properties to tuberculosis manifestation

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Background: Macroorganism and pathogen *Mycobacterium tuberculosis* characteristics are essential for tuberculosis (TB) manifestation. Evaluation of inter-linkages of *M. tuberculosis* properties, their contribution to the clinical picture of TB can be the basis for the successful treatment of this infection.

Design/methods: *M. tuberculosis* isolates from 97 patients with pulmonary TB were characterized by spoligo- and IS6110-RFLP-typing, drug resistance (DR) patterns and conferring mutations, cytotoxicity (CT, ability to cause the death of the THP-1cells) and analyzed according to TB intoxication intensity, hematology data, respiratory symptoms, radiographic characteristics, which were registered before treatment start, after 3 and 6 months.

Results: 52.8% of the *M. tuberculosis* strains belonged to the Beijing family (Bj), 20.4%—LAM, 11.1%—T, 10.2%—N, 1.9%—X. MDR/XDR fraction in Bj strains (71.0%) was greater than in LAM (31.8%) ($\chi^2 = 8.165$, $P = 0.004$). In clusters A0 and B0 of family Bj *M. tuberculosis* MDR/XDR strains were 86.7% and 90.1%, in other—52.2%. In 88.1% MDR/XDR *M. tuberculosis* strains carried rpoB Ser531→Leu, in 97.6%—katG Ser315→Thr. 28.2% strains showed high CT, 29.1%-intermediate, 42.7% —the low one. There were no CT correlation with DR, mutations types and genotype families. Registered intoxication symptoms, significant peripheral blood parameters' shifts, massive bacterioexcretion, two-sided and polysegmental TB specific lesions, cavities formed in the earlier periods were often associated with high CT and MDR together. Although there was no statistically significant TB manifestation differences of different *M. tuberculosis* genotype families TB-MDR patients with TB malignant development were often producing *M. tuberculosis*-Bj with high CT (81.8%) compared with patients with less malignant disease (22.2%).

Conclusion: *M. tuberculosis* CT did not correlate with the DR, mutations and genotype. High CT often associated with greater clinical and radiographic changes. In general *M. tuberculosis* genotype did not affect the picture of the process, but MDR patients with TB malignant development more frequently produced *M. tuberculosis*-Bj with high CT.

PC-638-02 Molecular characterization of novel *Mycobacterium tuberculosis* genes Rv0679c and Rv0180c in Indian clinical isolates

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Background: Sequencing of whole genome of *Mycobacterium tuberculosis*, helped in determining the genes associated with biology and pathogenicity of the pathogen. Recent studies by Manuel A Patarroyo (2010) explored the possibility of two novel genes Rv0679c and Rv0180c as probable genes associated with disease. They demonstrated that these are associated with LAM and lipid molecules on the outer surface by imunoprecipitation technique. They also indicated the probable role of these proteins in the invasion of pathogen to epithelial and macrophage cell lines. As of date there is no report on molecular characterization status of these two genes in any clinical isolate. In light of the above we are interested in determining the molecular characterization of Rv0679c and Rv0180c genes by identifying the polymorphism in Indian clinical isolates of TB patients.

Methods: Thirteen culture-positive clinical isolates obtained from TB patients were assessed in the study. All the isolates were investigated for polymorphisms in the Rv0679c and Rv0180c genes by PCR and DNA sequencing. Genomic DNA isolation was performed using CTAB (Cetyltrimethyl ammonium bromide) method as described by Honore et al. 2001. The PCR analysis was performed by Caceres SM et al. method (2011). Amplification was carried out by using primers Fp (5′-CGCTACCCACTCCCG-3′) and Rp (5′-CTTGTTGTTCGCACCAC-3′) of Rv0679c, and Fp (5′-GCACCCAACCCCAAGCG-3′) and Rp (5′-CCCCGAAGTCCCGTAGC-3′) for Rv0180c genes. The length of Rv0679c gene is 498 bp and the length of Rv0180c gene is 1359 bp. Polymerase Chain reaction was carried out in a thermocycler (Bio-Rad, California, USA) where reaction mixture consists of 1 μL of 5 pmol of each primer, 22 μL of molecular

grade water, 1 μL of genomic DNA and 25 μL of 2× master mix (Bangalore Genei, Bangalore, India which consists of Taq DNA Polymerase, dNTPs and an optimum reaction buffer), in a total volume of 50 μL. Amplification conditions were set for 5 min at 95°C followed by 30 cycles of 94°C for 1 min; 56°C for 1 min; 72°C for 45 sec, followed by a 5 min final extension. Genomic DNA of *M. tuberculosis* H37Rv was used as control. Amplified products were visualized on 2% agarose gel. PCR products of different clinical isolates were commercially sequenced to assess for polymorphism (SciGenom labs, Kerala, India). Single-nucleotide variations (SNVs) were identified using ClustalW2 which is a general purpose multiple sequence alignment program for DNA (http://www. ebi.ac.uk/Tools/clustalw2/index.html). It attempts to calculate the best match for the selected sequences, and lines them up so that the identities, similarities and differences could be seen.

Results: Thirteen clinical *M. tuberculosis* isolates of TB patients were collected from Blue-Peter Research Centre-Lepra, Cherlpally, Hyderabad, India. In our study the expected amplified products were observed in all the clinical isolates with the primers used which is around 350 bp of Rv0679c and 373 bp of Rv0180c respectively. PCR products were sequenced commercially and homology assessment was done comparing with wild type of Rv0679c of *M. tuberculosis.* Our results indicate that the amplified product is highly conserved in all the 13 clinical isolates assessed. Hence we speculate that this gene could be conserved across the isolates. The expected amplified product of Rv0180c gene was positive in all the clinical isolates assessed. The PCR products were sequenced commercially. Homology assessment was done comparing with Rv0180c of wild type. The total gene is around 1369 bp, out of which we assessed for 300 bp region ranging from 212250 to 210892 of the genome. Out of 13 samples assessed, in 6 individuals we found the polymorphism of G to T at 258 position of the gene. In one individual SNP is observed at location 364 with G to T nucleotide change. Interesting observation is that SNP in these individuals is at two different locations such as 258 and 364; however the polymorphism being G to T remains the same. The SNPs observed in Rv0180c are at 258 and 364 location which is equivalent to 211150 and 211256 position of the genome of H37Rv wild type strain.

Conclusion: Our results indicate the frequency of Rv0180c polymorphism is around 53% in clinical isolates assessed compared to Rv0679c which is conserved, within the amplified region of the genes. To consolidate the findings more clinical isolates are under screening.

PC-639-02 Unusual large-scale chromosomal rearrangements in *Mycobacterium tuberculosis* Beijing B0/W148 cluster isolates

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Mycobacterium tuberculosis Beijing family isolates are geographically widespread, often hypervirulent and associated with drug resistance. One fourth of Beijing genotype strains circulating in Russia belongs to the so called B0/W148 clonal group according to restriction fragment length polymorphism analysis. The aim of the present study was to investigate features of these endemic strains on a genomic level. Four *M. tuberculosis* isolates of the Beijing B0/W148 cluster were sequenced using a pyrosequencing approach (454/Roche FLX) with greater than 10-fold of coverage. All individual reads generated using the 454 platform were mapped to H37Rv genome using the 454 GS Reference Mapper (Roche 454 Life Science, USA). The data obtained was compared with published genomes of the *M. tuberculosis* strains, including the one of W-148 from the same B0/W148 group. Phylogenetic tree was built based on overall SNPs extracted from genomic DNA sequences after excluding SNPs for PE-PPE and PGRS protein families by using the MEGA 4 program. Phylogenetic analysis demonstrated a close similarity between the genomes of four Beijing B0/W148 strains under study and published earlier genome of W-148 strain. This gave us an opportunity to analyze structural genomic rearrangements within this group. Whole genome alignment between W-148 and the reference H37Rv *M. tuberculosis* strain revealed two large chromosomal inversions in the W-148 genome. According to our hypothesis the largest inversion reversed the orientation of 3 megabase (Mb) of the chromosome. The second one occurred in the previously inverted region and partly restored the orientation of 2.1 Mb inner segment of the chromosome. These two inversions were flanked by partial or complete copies of mobile genetic element IS6110 and touched large parts of genome. Detailed PCR-analysis of our sequenced strains (*n* = 4) revealed the rearrangements in their genomes identical to those ones found in W-148 strain. This is another example of genomic rearrangements in the *M. tuberculosis* in addition to the published recently cases of large-scale duplications. These events occurred in the similar region of genome, which leads to the assumption that this region is unstable. The described cases suggest that large-scale genomic rearrangements in the currently circulating *M. tuberculosis* isolates may occur more frequently than previously considered, and we hope that further studies will help to determine the exact mechanism of their formation.

FOOD FOR THOUGHT: NUTRITION AND OTHER ISSUES

PC-640-02   Macronutrient intake and body composition of pulmonary tuberculosis patients in Tbilisi, Georgia

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Background: Malnutrition and lean tissue wasting are common in tuberculosis (TB), yet little information is available on habitual dietary intake of macronutrients and links with body composition in TB patients after diagnosis.
Methods: Dietary intake was obtained in a placebo-controlled, randomized, clinical trial of high-dose vitamin D (1 400 000 IU over 16 weeks) in patients with pulmonary TB in Tbilisi, Georgia. Food intake was obtained using a validated tool specific to Georgian culture at baseline (within 7 days of diagnosis of TB disease) and again at 8 weeks and 16 weeks; specific nutrient intake was per NDS-R software. Body composition was determined at baseline and weeks 8 and 16 by body mass index (BMI; kg/m²) and bioelectrical impedance analysis (% body fat and % fat free mass). Descriptive statistics and mixed linear regression methods were used.
Results: 192 subjects (mean age 35 y; 59% male) were studied. Total energy intake at baseline averaged 53 (49–56) kcal/kg/day (95%CI), comprised of 35% fat, 55% carbohydrate and 12% protein. Energy intake significantly increased over time to 59 (56–64) kcal/kg/day (week 16 + 8% over baseline; $P = 0.0096$). Protein intake averaged 1.6 (1.4–1.7) g/kg/day at baseline and significantly increased over time to 1.8 (1.7–1.9) g/kg/day (week 16, +11% over baseline; $P < 0.0001$). Fat intake averaged 2.1 (1.9–2.3) g/kg/day at baseline and significantly increased over time to 2.4 (2.2–2.6) g/kg/day (week 16, +14% over baseline; $P = 0.0047$). Macronutrient intake was similar between vitamin D and placebo groups. BMI significantly increased over 16 weeks and was similar between treatment groups (between visits $P < 0.0001$, treatment effect $P = 0.0513$). There were no significant differences in body composition as determined by % of fat mass or % fat-free mass between treatment groups or over time.
Conclusions: Mean daily dietary intake of energy, fat and protein were adequate at TB diagnosis and increased over time in this patient cohort, independent of administration of high-dose vitamin D. Increased macronutrient intake occurred concomitant with increased BMI over time, without a change in the proportion of body composition accounted for body fat or fat-free mass.

PC-641-02   Increasing trend of isolation of non-tuberculous mycobacteria from respiratory specimens in Serbia

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Background: Nontuberculous mycobacteria (NTM) are increasingly associated with pulmonary disease, which is partially due to the improvements in the laboratory techniques for identification of these bacteria. The molecular identification of NTM was introduced into the Serbian National Reference Laboratory for Tuberculosis (TB) in 2009. This study analyzed the isolation rates of NTM from respiratory specimens and prevalence of NTM pulmonary disease over the four-year period, 2009 through 2012, in Serbia.
Method: Mycobacterial culture results of respiratory specimens obtained over the study period were retrieved from the national TB database and analysed retrospectively. In total, 395 cultures recovered from respiratory specimens were identified as NTM in Serbia over the study period. Species-level identification of the isolates was carried out by the GenoType Mycobacterium CM/AS (HAIN Lifescience) assays. The 395 NTM cultures were isolated from 325 patients. The laboratory record of each patient was reviewed, and the microbiological criteria of the American Thoracic Society NTM disease definition were used to identify cases of NTM pulmonary disease.
Results: The annual rates of NTM among patients with positive mycobacterial cultures recovered from respiratory specimens, one culture per patient was counted, were as follows: 4.4% in 2009; 5.5% in 2010; 11.2% in 2011; and 10.8% in 2012. Species-level identification was achieved in 274 (69.4%) cultures, while the remaining 121 were identified as *Mycobacterium* sp., and considered contaminants. In total, 10 different species of NTM were recognized, with *M. xenopi* being the most common ($n = 98$; 24.8%). Out of 325 patients, 42 met the ATS criteria for NTM pulmonary disease. The case rates per 100 000 population were as follows: 0.08 in 2009; 0.12 in 2010; 0.17 in 2011; and 0.19 in 2012. Most cases were due to *M. xenopi* ($n = 19$; 45.2%), followed by *M. avium* ($n = 7$; 16.7%) and *M. abscessus* ($n = 5$; 11.9%).
Conclusion: The isolation rates of NTM from respiratory specimens as well as the case rates of pulmonary NTM disease are increasing in Serbia. This is obviously related to the improved laboratory detection of NTM. Nevertheless, the results may also reflect an actual increase in the incidence of NTM. As the incidence rate of TB declines in Serbia, namely from 37 in 2003 to 18 in 2011, an increase in the proportion of pulmonary disease caused by NTM may be expected.

PC-642-02   Severe Vitamin D deficiency may increase progression to EPTB amongst immune-competent immigrants to Calgary, Canada

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Background: While Canada has a lower incidence of tuberculosis (TB) compared to other countries, control remains a concern among the foreign-born emigrating from TB-endemic countries, who account for 66% of the nation's TB cases. In Calgary, a midwestern city of one million people on the 51st parallel, extra-pulmonary TB (EPTB)—a more severe form of disease—occurs more often than expected among the foreign-born (90% of TB cases). We hypothesized that changes in vitamin D status following immigration may help explain the high rate of EPTB in Calgary.

Design/methods: A case control design was used. Cases were defined as consenting foreign-born patients presenting to the Calgary TB Clinic with culture-confirmed pulmonary or extra-pulmonary TB between June 2006 and July 2011 ($n = 81$). Controls were defined as consenting foreign-born patients presenting with LTBI within three months of a case and matched to cases by sex ($n = 81$). Patients with immune-suppressive disorders or chronic renal failure were excluded from the study. Vitamin D levels were measured from blood drawn within one week of diagnosis of TB or presentation with LTBI using the RAA method. Moderate Vitamin D deficiency was defined as 25O HVitD <80 pmols/L and severe deficiency was defined as 25O HVitD <25 pmols/L. A proportional odds model was considered, but the Brant test suggested a violation of the proportional odds assumption ($P = 0.01$) and a conditional logistic regression was underpowered, so a standard logistic regression model was used. We considered region of emigration (Africa/Asia), time since immigration (years), and age in the model.

Results: Of the 162 patients participating, 13% had sufficient, 76% had moderate, and 10% had severely deficient Vitamin D levels. Among cases, 55% had EPTB. Those with severe Vitamin D deficiency had 3.14 greater odds of developing EPTB (95% 1.05–9.37) compared to those with moderate or sufficient vitamin D levels, controlling for age and years since immigration. Although we were unable to perform conditional regression with other confounders, matching on sex means the estimated OR would have been higher with some loss to precision.

Conclusion: Our data suggest that severe Vitamin D deficiency amongst persons who have immigrated to Calgary from TB-endemic countries may in part explain the high rates of EPTB found in this population.

PC-643-02   Clinical characterization of symptomatic patients with non-tuberculous mycobacteria in Zambian prisons

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Background: The distribution of non-tuberculous mycobacteria (NTM) in developing countries is largely unknown, particularly in those with a high tuberculosis (TB) and HIV prevalence. Evidence suggesting a low burden in Africa is being refuted by recent studies, particularly from South Africa. We describe the clinical characteristics of a patient population identified with NTM species under a World Health Organization-funded TB screening program in a Zambian prison.

Methods: The Zambian Ministry of Home Affairs in partnership with the Centre for Infectious Disease Research in Zambia implemented a TB and HIV screening program in Lusaka Central Prison. Inmates and staff underwent TB screening using symptoms, digital radiography, sputum smear microscopy and culture, alongside optional HIV testing. Two sputa were examined using fluorescent microscopy. The best quality sputa was cultured on solid (Löwenstein-Jensen) and liquid (BD Bactec MGIT 960) media. All acid-fast bacilli positive cultures that were also cord factor positive by Ziehl-Neelsen staining were identified with the MPT 64 antigen test while those without cording were identified using the GenoType® Mycobacterium CM (Hain Lifesciences). Chest radiographs (CXRs) were read by an experienced radiologist.

Results: From January to April 2011, 1458 inmates and staff were screened, 1411 (97%) were male, mean age was 32.8 years (standard deviation: 9.3). *M. tuberculosis* was isolated from sputum samples in 56 (3.8%) participants and NTM in 80 (5.4%). Amongst those with NTM, 15 were HIV positive and 8 had a prior history of TB. Species identified were: 51 *M. fortuitum*, 5 *M. intracellulare*, 2 *M. abscessus*, 1 *M. gordonae* and 1 *M. scrofulaceum*; 20 were *Mycobacterium* species; however the diagnostic kit was unable to make a full identification. 62/80 (77.5%) had ≥1 symptoms compatible with TB, 24/80 (30%) had abnormal CXRs, and 6/80 (7.5%) were clinically diagnosed with pulmonary TB.

Conclusions: The high percentage of participants with symptoms and abnormal CXRs indicate the potential clinical significance of NTM in this population. Without NTM screening a significant proportion of symptomatic patients could be misdiagnosed

with pulmonary tuberculosis and receive inappropriate treatment. Accurate diagnosis of NTM infection could improve clinical outcomes. Simpler diagnostic tests for NTM and further assessment of NTM epidemiology are required.

PC-644-02   Micronutrient status of pulmonary tuberculosis patients in Tbilisi, Georgia

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Background: Several micronutrients are important in immunity and may influence tuberculosis (TB) outcomes. Data on micronutrient status in TB disease are limited and studies on micronutrient supplementation are inconclusive.
Methods: We obtained serial blood samples in subjects enrolled in a placebo-controlled, randomized, clinical trial of high-dose vitamin D in pulmonary TB in Tbilisi, Georgia. Serum concentrations of selected minerals and trace elements were determined by inductively coupled argon plasma spectrometry at baseline and week 16 of study. Dietary intake was obtained using a validated instrument specific to the Georgian culture (Clinical Nutrition, 2013) at baseline and at 16 weeks. No subject consumed specific micronutrient supplements other than the experimental vitamin D. Descriptive statistics and paired and unpaired t tests were used where appropriate.
Results: A total of 189 subjects with TB disease and 19 non-infected household control subjects were studied (TB subjects, mean age 35 y; 59% male; controls, mean age 40 y; 36% male). Serum iron levels were 24 ± 20 (SD) umol/L at baseline and increased to 25 ± 15 umol/L (+4%; $P = 0.0059$) at 16 weeks. In contrast serum copper levels fell from 27 ± 5 to 21 ± 5 umol/L at week 16 (-22%; $P = <0.0001$) and serum magnesium from 0.85 ± 0.13 to 0.82 ± 0.12 mmol/L (-4%; $P = 0.0353$). Levels of manganese, zinc, potassium and sodium did not change. Baseline serum copper levels were significantly increased in TB subjects vs. controls ($P < 0.0001$), but other micronutrients were similar. Mean daily dietary intake from food sources for all micronutrients were similar between TB patients and controls. In TB patients, dietary intake of all micronutrients except magnesium significantly increased from baseline to 16 weeks. All measured micronutrients met at least 100% of US dietary reference intakes.
Conclusions: Micronutrient intake appears adequate in this TB patient cohort. Minor changes in serum levels of specific micronutrients occurred over time with the exception of copper. Copper levels were increased in TB vs. control subjects, but fell over time despite increased dietary intake, suggesting increased copper utilization in TB disease.

PC-645-02   Macronutrient deficiencies among HIV-positive women with tuberculosis in Dar Es Salaam, Tanzania

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Aim: Patients with tuberculosis frequently present with malnutrition but the specific macronutrient deficits in these patients has not previously been quantified. We assessed dietary energy and protein deficits among HIV-infected women in Tanzania with newly diagnosed tuberculosis and changes in diet during treatment.
Methods: We enrolled HIV-positive women with newly diagnosed tuberculosis and assessed anthropometric characteristics, dietary intake, and food insecurity. Energy and protein intake were determined using Tanzania Food Composition Tables, and compared to dietary recommendations for persons with HIV and tuberculosis to estimate deficits. Patients were re-evaluated after 4–6 months of tuberculosis treatment.
Results: Among 43 women at baseline median CD4 count was 209 (range 8–721), and 19 (44%) had a CD4 < 200; 20 (47%) were on antiretroviral therapy (ART). BMI was <18.5 in 25 (58%), and the median food insecurity score was 6. Median kcal/day was 1693 (range 1290–2633) compared to the 2658 estimated need; median deficit was 875 kcal (range -65–1278). Median gm protein/day was 42 (range 27–67) compared to the 77-estimated need; median protein deficit was 35 gm (range 10–50). Median weight gain among 29 patients after 4–6 months was 6 kg.
Conclusions: HIV-positive women with tuberculosis have substantial 24-hour deficits in both energy and protein intakes, report significant food insecurity, and frequently fail to gain weight on tuberculosis treatment. Enhanced dietary education together with macronutrient supplementation of 1000 kcal with 40 g protein may be required to improve health outcomes in these women.

PC-646-02   Non-tuberculous mycobacteria co-infection in an immigrant population on tuberculosis treatment in Ciudad Juárez, Mexico

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Background: There has been frequent recovery of non-tuberculous mycobacteria (NTM) in control cultures of patients undergoing treatment for active

tuberculosis (TB) disease at Clinica Medica Internacional in Ciudad Juárez, Mexico. There are identified risk factors for the development of NTM pulmonary disease, such as direct exposure to natural reservoirs, including soil, water and animals. Also a correlation has been observed between the phase of treatment of the patient and NTM growth on control cultures.

Objective: To demonstrate the co-infection of NTM and *Mycobacterium tuberculosis* complex and demonstrate the direct relationship between phase of treatment and NTM growth in cultures of patients undergoing treatment for active TB disease.

Methods: A retrospective study was performed on the medical records of 76 active TB cases diagnosed and treated by direct observed therapy (DOT) at Clinica Medica Internacional from 2009 to 2012. All cases were confirmed by culture, regardless the sputum smear results and monitored monthly during the whole treatment with sputum smears and cultures.

Results: Of 76 active TB cases studied, 40.7% (31 patients) grew at least one NTM in any of their cultures. 67% of all culture positive cases for NTM were on maintenance phase (INH and RIF), while 33% were on intensive phase (INH, RIF, EMB and PZA).

Conclusions: It is very important to highlight the prevalence of active TB disease and NTM co-infection, which according to this statistics, 4 out of 10 TB patients grew an NTM in their cultures. As seen on the results, almost 7 out of 10 patients were on a two-drug regimen (maintenance phase), factor which may suggest a positive correlation between the phase of TB treatment and NTM growth. Also, the clinical condition of the patients did not change after NTM isolation. Due to the high prevalence of NTM growth, the clinician should note the importance of identifying NTM's on cultures of patients under medical treatment for active TB disease.

PC-647-02 Family consent to participate in validating performance of verbal autopsy for measuring deaths due to tuberculosis in Kenya

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Background: While tuberculosis remains a key public health challenge globally, mortality resulting from it remains largely unknown in sub-Saharan Africa (SSA). Although autopsy provides the only means of determining the exact cause of death, consenting by family members has remained low in SSA mainly because of poor acceptance as a result of cultural, religious beliefs, lack of adequate post mortem facilities and human resource. Informed consent is usually required from a deceased's legal next of kin before any form of autopsy (invasive, noninvasive or verbal) is performed for whatever purpose. The reasons for autopsy refusal are scantly published in African settings. This study documented the willingness of families to consent to autopsy and possible reasons for failure to participate.

Intervention: A cross section survey was done in a Health and Demographic Surveillance System (HDSS) site in Siaya County, Kenya. The target population was family members of the deceased aged one year and above who died of respiratory related illness. Community mobilization was undertaken prior to recruitment exercise. Once a death occurred, the study coordinator was notified immediately by a village reporter. A community interviewer visited the family for screening and consent. Once consent was granted, the body was transportation to hospital for post mortem within 8 hours.

Results: Out of 1072 deaths that were reported to the HDSS during the study period (31 July 2012 to 28 February 2013), 144 (13.4%) met the inclusion criteria and were notified to the study team. Out of the cases notified, 54% (n = 78) were recruited after consenting. Of those who were not enrolled, 6% declined, 6% needed to bury immediately, 16% were due to logistical challenges while 11% had the bodies already embalmed at home. Only 3% had no one available to consent while 3% did not have required documents.

Conclusion and recommendation: There is high acceptance by families to consent for autopsy. Domestic embalmment of bodies while awaiting burial is a common practice. Logistical issues pose a key challenge to recruitment process. There is need to sensitize communities on the importance of professional embalmment of bodies. Investing in adequate logistics is key in such studies. Studies in a non-HDSS setting for purposes of comparing the findings are recommended.

PC-648-02 Epidémiologie de la tuberculose extra pulmonaire en Algérie

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Contexte : Plus de la moitié des cas de tuberculose en Algérie sont des cas extra pulmonaire. Une augmentation inexpliquée du nombre des cas de TEP est constatée annuellement contre une baisse régulière des cas de tuberculose pulmonaire.

Objectif : Analyse de l'épidémiologie de la tuberculose extra pulmonaire avec les données du programme national de lutte contre la tuberculose.

Methodes : Analyse des données recueillis annuellement des cas de tuberculose de 1975 à 1981 de huit départements parmi les 48 et exhaustive depuis 1982. Les caractéristiques démographiques des cas de tuberculose pulmonaire et extra pulmonaire ont été comparées à partir des données du système d'information

électronique installé depuis 2011. Les cas de tuberculose extra pulmonaire englobaient l'atteinte ganglionnaire, pleurale, osseuse, génito-urinaire, méningée, péritonéale, et les autres localisations.

Resultats : Parmi tous les cas 55.7% étaient des tuberculose extra pulmonaire y compris ganglionnaire (52,2%), pleurale (22,2%), péritonéale (6,5%), ostéo-articulaire (3,9%), génito-urinaire (2,3%), méningée (1,1%) et les autres localisations (13,1%). En comparaison avec la tuberculose pulmonaire, la tuberculose extra pulmonaire prédomine surtout chez les patients de sexe féminin sauf pour la localisation pleurale. Les enfants sont plus susceptibles à développer une tuberculose ganglionnaire ou méningée alors que la probabilité d'une tuberculose vertébrale et péricardique augmente avec l'âge.

La surveillance épidémiologique permet de constater:

- Une augmentation annuelle régulière du nombre de cas de tuberculose extra pulmonaire, comparativement à une baisse annuelle du nombre de cas de tuberculose pulmonaire,
- Une inversion des proportions de la tuberculose pulmonaire et extra pulmonaire à partir de 2001. Le taux de TEP passe de 17% des cas de tuberculose en 1977 à 55,7% en 2011.

Conclusions: L'épidémiologie de la tuberculose extra pulmonaire diffère de celle de la tuberculose pulmonaire, et sa proportion ne cesse d'accroître depuis les années 90. Des études complémentaires sont nécessaires pour identifier les causes de l'augmentation proportionnelle des ces cas.

PC-649-02 *Mycobacterium fragae* sp. nov., isolated in Brazil

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Background: *M. fragae* is a recently described mycobacteria species, isolated from three sputum samples of a patient of the Ceará state in Brazil. The *M. fragae* is most closely related to the species *M. celatum* and *M. kyorinense*.

Design/methods: In order to characterize the isolates we carried out phenotypic, genotypic tests and clinical review. We sequenced the nearly complete 16S rRNA gene, and obtained partial sequences of the hsp65 and *rpo*B genes and performed a phylogenetic analysis, conducted using the concatenated sequences.

Results: The sequencing and phylogenetic concatenated tree clearly distinct *M. fragae* isolates from all other closed species. *M. fragae* is a slow growing mycobacteria with smooth and unpigmentated colonies. The patient from which *M. fragae* was isolated

has a history of pulmonary disease, having undergone 3 treatments. During the third the patient was put on a treatment course specific for NTM, with amikacin, clarithromycin, and ethambutol. The baciloscopy and culture results have been negative along the course of treatment.

Conclusion: *M. fragae* is a pathogenic species, new cases should be investigated to assess its real occurrence in Brazil and other countries.

MANAGING TUBERCULOSIS: FROM EPIDEMIOLOGY TO TREATMENT

PC-650-02 Supporting the MDR-TB survey in Nigeria: national tuberculosis reference laboratory experience

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Background: The Nigerian National Tuberculosis and Leprosy Control Program (NTBLCP) and the United States Government (USG) collaborated and conducted the initial MDR-TB survey in Nigeria with the aim of establishing actual MDR-TB burden in Nigeria. The National TB Reference Laboratory in Zaria (NTBLTC) was responsible for conducting TB culture and Line Probe Assay (LPA) from samples collected from ten states in the northern part of Nigeria.

Method: Smear positive samples of new and retreatment patients identified in selected TB diagnostic centers were forwarded to the NTBLTC for first screening with LPA. All positive specimens from LPA and a proportion of negatives were then processed and cultured using solid media (Löwenstein-Jensen). All positive cultures were aliquoted in transport media and shipped to the TB CDC Atlanta Supranational Reference Laboratory. All samples received from the selected health facilities were assessed based on the acceptance criteria in the survey protocol before being subjected to LPA and culture.

Results: A total of 1761 samples were received from the 30 participating sites representing 96% of the expected samples (1824). Out of the total samples received, 54 (3.1%) were rejected based on the rejection criteria. 28 (93.3%) sites submitted their complete targeted samples size while 2 (7.6%) failed completion. Six (20.0%) sites have some of their samples rejected. Major challenges were nonadherence to SOP for documentation, quality of samples, inadequate sample volume, improper specimen container leading to leakage/drying of samples and delay by courier services. At the reference laboratory,

challenges encountered include human resources, erratic power supply and weak logistic management system for reagents and other consumables.

Conclusion and recommendation: Our conclusion was that adherence to SOP by peripheral participating laboratories in specimen collection, storage and transport and effective logistic management systems are important prerequisite for MDR-TB survey.

PC-651-02   How to reduce the initial defaulter rate among pulmonary tuberculosis patients diagnosed under DOTS programme?

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Background: An initial defaulter is defined as a diagnosed sputum smear positive patient who has been recorded in the lab. register but who has not been placed on either a DOTS treatment regimen or non-DOTS regimen, and has not been referred for treatment outside the district. Initial default is an obstacle to effective TB control. It should be brought down to minimum.

Design/methods: This study included sputum smear positive patients diagnosed during the period Jan 1, 2005 to Dec 2012, i.e., 8 years in Jhandewalan district, New Delhi, India covering a population of 550 000 Lacs. As the patient has to visit the treatment centre frequently and monitoring is done by sputum examination at regular intervals, before starting the treatment the health worker visited the patient's house to confirm the address, motivate him and to nominate the Contact person. Out of total 5270 smear positive patients diagnosed, 351 patients could not be put on treatment.

Results: There were 351 (6.7%) initial defaulters. Out of those 197 (56%) could not be traced due to wrong address, 60 patients (17.1%) were taking private treatment, 52 patients (14.8%) died before starting the treatment, 22 patients (6.3%) left the district without any information and 20 patients (5.7%) refused treatment.

Conclusion: Main causes of initial default are:
1 Wrong/incomplete address recorded in the lab. register.
2 Patient opting for private treatment.
3 Patient seriously ill at the time of sputum examination.

By adopting the following measures, the initial default rate can be brought down to the minimum:
1 The lab. tech. to record the correct address with land marks. the phone no. (mobile and land line) of the patient and the contact person should be recorded.
2 The supervisory staff to interview and motivate all the diagnosed smear positive cases.

3 The IEC activities should be strengthened so that the patient reports for sputum examination in the early stage of disease.

PC-652-02   Vitamin D insufficiency common among HIV-infected breastfeeding mothers in Pune, India, but not associated with risk of postpartum tuberculosis

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Background: Some studies have associated VDI with the risk of tuberculosis (TB) but the relationship between VDI and TB in HIV-infected postpartum women in a TB endemic region has not been well established. We hypothesized that VDI is associated with postpartum TB among HIV-infected women.

Design/methods: We performed a nested case control study among mother-infant pairs enrolled in the Six Weeks Extended Nevirapine (SWEN) India trial, to assess the association between maternal vitamin D levels and postpartum TB. Cases were 33 mothers with postpartum TB and controls were 66 mothers with no TB matched on CD4 cell count and viral load category. Maternal 25 (OH) D levels were measured on stored sera (Diasorin radioimmunoassay) collected peri-delivery; VDI defined <32 ng/ml, moderate deficiency <20 ng/ml; severe deficiency <10 ng/ml. Conditional logistic regression analysis was performed to assess the association between vitamin D levels and maternal TB, adjusting for age and occupation.

Results: Overall, the median age was 23 years (interquartile range (IQR), 21–26); median CD4 count and HIV viral load were 338 cells/ml (IQR 220–486), and 12 013 copies/ml (IQR 1258–102 370) respectively. Median vitamin D levels among cases and controls were 16 ng/ml (IQR 10–19) and 16 ng/ml (IQR 10–19) respectively (Figure). Among cases and controls, VDI was 97% vs. 100%; moderate deficiency 85% vs. 85% and severe deficiency 27% vs. 26%, respectively. Neither moderate (aOR 0.955, 95%CI 0.283–3.22, P = 0.942,) nor severe (aOR 1.17, 95%CI 0.392–3.51, P = 0.775,) vitamin D deficiency was associated with postpartum TB.

Conclusion: VDI and deficiency was highly prevalent among HIV-infected breastfeeding mothers in India but was not associated with postpartum TB. While Vitamin D supplementation may be of benefit to pregnant women it is unclear if there would be any benefit to reduce risk of TB in this population.

PC-653-02   Control of sputum culture after 2 months of treatment for culture positive pulmonary tuberculosis

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Background: Standard is 6 months of treatment with 2HRZE/4HR, when resistance is not present. Relapse of TB after 6 months of treatment is higher, if sputum cultures after 2 months of treatment are still culture positive for *Mycobacterium tuberculosis*, than it is, if cultures are negative at this time. It is recommended to prolong continuation treatment with 3 months, if culture after 2 months treatment is positive for MT and the patient has pulmonary cavities. In Denmark up to 13% of pulmonary TB cases may have relapse.
Aim: To see if sputum cultures for *M. tuberculosis* were performed after 2 months of treatment in patients with culture positive pulmonary TB in Denmark in 2004 and 2010.
Methods: All cases of culture positive pulmonary TB in DK in 2004 and 2010 were identified. All cultures performed in these patients in the third month after initiation of treatment were identified.
Results: Twenty-seven per cent (50/188) of patients in 2004 and 39% (79/205) in 2010 were examined and had negative culture in third month of treatment or earlier. Cultures were positive for *M. tuberculosis* in 7/188 and 11/205 in the two years and 70% and 56% respectively had no examination of sputum in the third month after initiation of treatment.
Discussion: If treatment control is not performed by sputum culture for *M. tuberculosis* after 2 months, an important indicator of treatment effect and compliance is lost, and it is more difficult to decide whether treatment duration should be prolonged. Treatment control with culture of sputum for *M. tuberculosis* after 2 months of treatment, should be performed in patients with culture positive pulmonary TB whenever possible.
Conclusion: Control during treatment of TB is not performed as recommended in DK. Control should be improved in order to regulate treatment duration and optimize treatment results.

PC-654-02   Role of non-governmental organisations in management of drug resistant tuberculosis

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Background: Before Programmatic Management of Drug Resistant TB (PMDT) was universally available in Mumbai, India, non-governmental organisations (NGOs) were the only source of affordable treatment for drug resistant TB (DR TB) patients.
Objective: To describe the role of NGOs in management of DR TB before PMDT was universally available in Mumbai, India.
Methods: Providers' perspective was documented through interviews with administrators ($n = 11$), clinicians ($n = 5$), staff/volunteers ($n = 4$), chest physicians who referred patients to the NGOs ($n = 6$) from 12 NGOs. Eighteen randomly selected patients from six NGOs were interviewed to document their experiences. Lists of drugs provided and patient records for past three years for three NGOs were analysed.
Results: While all NGOs facilitated access to drugs, only some supported investigations (3/12), or provided nutritional support (3/12), counselling (2/12) and active follow-up of registered patients (3/12). 15/18 patients had been diagnosed and 7/18 had taken MDR-TB treatment before reaching NGO. 4/18 patients had extra-pulmonary TB. Group-5 drugs accounted for 15% of total drugs prescribed. High costs of drugs resulted in patients missing or diluting the doses when required to buy medicines. 6/17 patients were unwilling to take treatment from public sector because of inconvenience of DOT and dissatisfactory past experiences.
Conclusion: NGOs can play a complementary role in management of DR TB by reaching services to groups currently not covered by the RNTCP, are reluctant to access public sector, or have XDR TB; and by providing social support services that are crucial for treatment adherence but currently not part of the RNTCP. To contribute to the TB control initiative in India NGOs must ensure quality of care.

PC-655-02   Determinants of consultation, diagnostic and treatment delays among new smear-positive pulmonary tuberculosis patients in Morocco: a cross-sectional study

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Background: Delays in diagnosis of pulmonary tuberculosis and initiation of effective treatment increase morbidity and mortality due to this disease as well as the risk of transmission in the community. The aim of this study was to determine consultation delay (patient delay), diagnosis delay and treatment delay (health system delays). Factors relating to these delays were analyzed.
Design/methods: We conducted a cross-sectional survey in 12 selected provinces and prefectures within 11 out of 16 administrative regions in Morocco. 250 eligible and consenting newly diagnosed smear-positive pulmonary tuberculosis patients were interviewed at the time of their registration within Diagnosis of

Tuberculosis and Respiratory Diseases Reference Centers (CDTMR) or Integrated Health Centers (CSI) from March to May 2012 using a pretested and structured questionnaire.

Results: The median total delay was 46 days (interquartile interval 29–84 days), with 72% patients delaying for more than 30 days. Patient delay (median 20 days; IQI 8–47) is higher than health system delay (median 15 days; IQI 7–35). The means were 66.8; 36.0 and 30.3 days respectively. Being illiterate, thinking symptoms will disappear by themselves, having financial constraints or feeling fear or stigma were associated with patient delay (aOR 7.15, 95%CI 1.96–26.06; aOR 5.02, 95%CI 2.57–9.82; aOR 4.01, 95%CI 1.59–10.16; OR 4.48, 95%CI 1.10–19.51 respectively). Consulting first in the private sector or having three or more medical consultations before the diagnosis was associated to health system delay (aOR 1.75 and 3.94, 95%CI 1.01–3.01 and 1.81–8.56 respectively).

Conclusion: Patient and health system delays contributed to total delay. A mechanism is needed to increase health-care providers' suspicion of tuberculosis so that proper investigations can be done during first consultation. Education campaigns that behind general information on TB, focus on tuberculosis transmission prevention through early and efficient diagnosis and treatment of patients must be implemented.

PC-656-02 Exploring tuberculosis treatment outcome distribution by gender in Afghanistan, 2009–2011

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Background: Afghanistan is among the world's 22 countries with the highest burden of tuberculosis (TB). Annual TB incidence in Afghanistan is 189 per 100 000 populations and prevalence is 351 per 100 000 populations. Afghanistan's national TB data shows a gender imbalance, with 66% of all reported TB cases among women. Treatment outcomes among notified smear positive (SS+) TB cases by gender were not known. In collaboration with the National TB Program, the USAID-funded TB CARE I project in Afghanistan and its implementer, Management Sciences of Health, conducted a study to explore treatment outcome by gender in Afghanistan to inform future TB programming.

Design/methods: The project team collected TB data that had been recorded by health facilities in seven provinces from 2009 to 2011. The team also reviewed clinic registers from the same period and tallied male and female TB patients' treatment outcomes. The sample size included 4086 (female 2681, male 1408) patients (CI 99%, precision 2.9%, prevalence of outcome 50%, all SS+ cases 39 000).

Results: The cure rate among females was 89.4%, compared to 85.2% among males (CI 99.9%, $P > 0.00001$). Treatment outcomes among female were distributed as follows: 2397 (89.4%) were cured; 35 (1.3%) completed treatment; 2432 (90.7%) were successfully treated; 95 (3.5%) failed treatment; 73 (2.7%) died; 28 (1%) defaulted from treatment; and 41 (1.5%) transferred out. Treatment outcomes among male were distributed as follows: 1200 (85.2%) were cured; 28 (2%) completed treatment; 1228 (87.2%) were successfully treated; 34 (2.4%) failed treatment; 72 (5%) died; 42 (3%) defaulted from treatment; and 29 (2.1%) transferred out of treatment.

Table Treatment outcome distribution by gender, 2009–2011, Afghanistan

	Total cases evaluated n	Successfully treated n (%)	Cured n (%)	Completed treatment n (%)	Failed treatment n (%)	Died n (%)	Defaulted from treatment n (%)	Transferred out of treatment n (%)
Female	2681	2432 (90.7)	2397 (89.4)	35 (1.3)	95 (3.5)	73 (2.7)	28 (1)	41 (1.5)
Male	1408	1228 (87.2)	1200 (85.2)	28 (2)	34 (2.4)	72 (5)	42 (2.1)	29 (2.1)

Conclusion: Treatment cure and success rates are significantly higher among female SS+ TB patients compared to male patients. Male TB patients are more likely to die and females to failure from TB. Thus, we strongly recommend improvement of default among men and failure among women, also, identifying underlying causes of deaths and failure among men and women respectively in Afghanistan.

PC-658-02 Complex treatment approach for patients with destructive pulmonary tuberculosis by application of endobronchial valve

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Background: At the present, the infiltrative pulmonary tuberculosis acquires new clinical characteristics, it becomes increasingly more aggravated. Specific infiltration is more widespread, there is early appearance of cavities and positive bacteriology. There is a growing number of cases caused by drug-resistant *Mycobacterium tuberculosis*. The number of treatment success for cases is declining.

Purpose: To study the effects of endobronchial valve application on the current of the disease in patients with ineffective treatment of destructive infiltrative pulmonary tuberculosis.

Design/methods: A total of 102 patients were selected

with destructive infiltrative pulmonary tuberculosis with failure in treatment. Randomly selected patients were divided into 2 groups: group 1 (main)—49 patients in treatment that underwent installation of endobronchial valve, group 2 (comparison)—53 patients receiving officially recommended standard TB chemotherapy (Executive Order #109 from 21.03. 2003). Patients were selected for the study after establishing failure of pure therapeutic treatment. Outcomes were analyzed at the end stage of hospitalization and at the follow-up after 3 years.

Results: The main group has achieved closure of cavity in 33 (67.3%) cases, in comparison group—in 11 (20.7%) ($P < 0.0001$, χ^2). Cavities remain in 2 (4.1%) patients of the main group and in 17 patients (32.1%) of the comparison group ($P = 0.0002$, TTF), other patients of both groups underwent surgery for cavity closure. Increased period of cavities closure and reduced number of treatment success were noticed in the comparison group, $P = 0.0001$ (log-rank test). Long-term treatment results were followed up in 59 (57.8%) patients. Of these, the main group—32 (65.3%) patients and the comparison group—27 (50.9%) patients. Clinical cure was observed in 33 (55.9%) patients: 26 (81.2%) patients of the main group and in 7 (25.9%) of the comparison group (RR 3.41, 95%CI 2.68–4.15, $P < 0.0001$, χ^2). Relapses in Dispensary Group III were observed in 5 (8.5%) patients: in the main group—in 2 (6.2%) patients, in the comparison group—in 3 (11.1%) ($P = 0.4$, TTF). Exacerbations were observed in 21 (35.6%) patients. In the main group of 4 (12.5%) patients had exacerbation, in the comparison group—17 patients (63.0%) (RR 3.87, 95%CI 3.02–4.72, $P = 0.0001$, χ^2).

Conclusion: The application of the endobronchial valve for patients with ineffective treatment of destructive infiltrative pulmonary tuberculosis can significantly increase patient chances for clinical cure by therapeutic measures (RR 2.72, 95%CI 2.3–3.14). Long-term results of this treatment technique demonstrated that the odds of clinical cure increased by 3.4 times and the number of exacerbations decreased by 3.9 times.

MEDICAL MANAGEMENT OF TUBERCULOSIS

PC-659-02   Waiting too long for spontaneous resolution of cough: health care seeking behaviors among advanced pulmonary tuberculosis patients in urban and rural Thailand

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Background: High death rates in TB patients, along with a high proportion of smear positive cases among all TB cases have been noted in Thailand. During the National TB Prevalence Survey in 2012, 31% (44/142) of bacteriologically confirmed TB cases were categorized as having advanced disease (having a lesion in both lungs). Despite the availability of universal access to care for Thai citizens, these individuals remain undiagnosed is important to understand why. This study explores the lived experience of advanced TB patients on health care seeking behaviors.

Design/methods: A qualitative study was nested into the 2012 Survey with the ethical approval of the Thailand Ministry of Public Health. Informed consent and confidentiality procedures were followed. In-depth interviews and observation at respondents' homes were carried out with six advanced TB patients and a mother of the patient who had died. The respondents were consecutively recruited from two settings with the highest TB prevalence in urban and rural clusters. To complement the findings from the patients, two group interviews ($n = 4$ and 6 in two sites) with local health care staff were conducted. The data were analyzed by content analysis.

Results: All respondents had a cough for 3–6 months and waited as they thought that their symptoms would resolve spontaneously. All urban patients started seeking care from pharmacies when their symptoms did not improve; pharmacies being closer to their homes and no waiting time. They did not seek care at hospitals as they perceived their symptoms to be minor. In contrast, rural patients made visits to hospitals or private clinics, but they were treated by the doctors as having a general respiratory disease. Rural patients reported that their respect for doctors prevented them from asking questions. Participants in the group interviews explained that TB case finding strategies relied on self-presentation of symptomatic individuals and primary health care providers depended on the hospital to inform them of a TB case before they can take actions.

Conclusion: Perceptions about spontaneous resolution of cough play a key role in care seeking behavior, despite the universal access to care. Improving referral role of pharmacies and primary health units and strengthening hospital procedures for effective case finding and diagnosis should be considered. Awareness campaigns to emphasize that cough >2 weeks need medical examination are needed.

PC-660-02   Tuberculosis suspect identification and referral service in private lower clinics and drug outlets: assessing a pilot program in Ethiopia

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Background: Tuberculosis is one of the major public health problems in Ethiopia and low case detection rate and delay in diagnosis and treatment of cases is the major challenge of the national TB program. In Ethiopia, the private sector is already a major actor in the health care delivery system and as such is currently playing a significant role in terms of prevention and control of TB nationwide. With the objective of improving TB case detection and case management outcomes in Ethiopia, PHSP started a pilot TB suspect identification and referral service by recruiting 45 lower clinics and 30 drug outlets in two high TB burden regions in 2012. After implementation of the pilot for nine months this assessment was done to determine effectiveness of the pilot program.

Methodology: A quantitative cross-sectional assessment with supplementation of qualitative part was conducted in October 2012 in 68 of the pilot facilities using a prepared data collection tool.

Result: During the nine month pilot period, a total of 424 cases of TB suspected were identified and referred in 68 of the pilot facilities (41 lower clinics and 27 drug outlets). Feedback on the outcome of the diagnosis of the suspected cases was obtained for 89 (24%) of the referred cases. Of the 89 suspects for whom referral feedback was obtained, 73 (82%) were diagnosed to have some form of TB by the referral receiving facility whereas only 15 (18%) suspected cases were confirmed not to have TB. Of the 424 suspected cases identified and referred, 361 (85%) were referred by lower clinics and only 63 (15%) were referred by drug outlets.

Conclusion: Lower clinics and drug outlets are effective in early identification and referral of TB suspects. If this pilot program is scaled up to all similar facilities in the country, it could have a significant impact on TB prevention and control as early case detection and referral for treatment helps to prevent transmission within communities.

PC-661-02 Standard operating procedures improve tuberculosis case detection in Arusha, Tanzania

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Background and challenges to implementation: From 1990 to 2000, Tanzania had an average tuberculosis (TB) incidence rate of 10%. The following decade (2000 to 2010) this incidence rate dropped to just 1.6%. In 2009, the country achieved the World Health Organization's target of 70% TB case detection, and this has sustained. Despite these achievements, many TB cases remain undetected in Tanzania. In response, the Program for Appropriate Technology in Health (PATH) and Management Sciences for Health (MSH) began working with Tanzania's National TB/Leprosy Programme to implement the USAID-funded TB Indefinite Quality Contract (IQC) in 2010. Together, these partners developed standard operating procedures (SOPs) for TB case detection and implemented these at 24 health facilities in the Arusha region, from January to September 2012.

Intervention or response: TB IQC trained 32 regional and district health management teams and 120 health care providers from 24 health facilities to implement the new SOPs for case detection. The project team also trained 24 regional and district TB supervisors to conduct supportive supervision at the 24 facilities. Participants in these trainings developed action plans for SOP implementation. During the implementation period, TB IQC conducted supportive supervision visits with the regional and district management TB teams to monitor the action plan implementation and collect data on the impact of SOPs. In addition to site visits, TB IQC also facilitated health facility TB-HIV meetings and trained 300 health care providers who were not involved in TB control to use the SOPs for TB case detection. The project team helped seven district medical officers compose and send letters of appreciation to encourage and incentivize health facilities and staff toward high-performance in TB case detection.

Results and lessons learnt: After eight months of the SOPs implementation, data from the 24 health facilities showed that the number of TB cases notified had increased by 71.6% for all forms of TB (459 in January 2012 to 788 in September 2012) and 27.5% for smear positive TB cases (225 in January 2012 to 287 in September 2012) (see Table).

Table New notified TB cases in 24 health facilities before and after SOP implementation (January–September, 2012)

New notified TB cases	January 2012 (baseline)	September 2012 (after 8 months of SOP implementation)	Percent improvement
All forms of TB	459	788	71.6%
Sputum smear positive TB	225	287	27.5%

Conclusions and key recommendations: This SOP implementation approach has significantly improved TB case detection among the targeted 24 health facilities in Arusha. This implementation approach should be expanded in Tanzania and applied in similar settings to further improve TB case detection.

PC-662-02   Does strategic planning in laboratory support help public health providers and NTP to improve tuberculosis control in Brazil?

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Introduction: Brazil has a powerful Health Care System, structured with a National Tuberculosis Program Control, General Laboratory Coordination, a laboratory network composed by twenty-seven Central Laboratories of Public Health, and a National Reference Laboratory (NRL). Rates of TB incidence and mortality are decreasing. Despite the framework it is necessary to improve the management, to offer more tests to meet the World Health Organization (WHO) recommendations: detection of 75% of pulmonary TB cases by smear microscopy and to cure 85% of patients. The recorded cases of TB disease fell from 71.790 in 2010 to 69.245 in 2011 (3.4%). Brazil reached five years ahead of schedule, the 6th goal of the 'Millennium Development Goal'. WHO estimated that in 2015, deaths ratio should lower in 50% from the year of 1990 to 2015. In 2010, in retreatment cases, cultures were performed in only 26% and in HIV positive serology, patients, 22%. Managers can contribute to improve dissemination and disease control, through practices of strategic planning, aiming situational analysis and plans for necessary activities to reach country needs.

Objective: Contribute to increase supply of diagnostic and control tests, through acquisition of knowledge in planning and strategic management.

Method: Qualitative study developed in two phases. The first one sought to ascertain knowledge gaps in planning techniques, identified through semi-structured questionnaires. The second phase consisted of workshops held in five stages. The two initials were held with staff of NRL, to discuss legal instruments, and analysis of strengths and weaknesses, to meet the organization's national network expectations. The last three included TB chiefs of Central Laboratories and of NRL. Techniques and management tools have been used to exemplify that it is possible to obtain better control of TB, through strategic planning.

Results: The chiefs expressed the need to acquire skills for management and leadership. Problems have been listed. From a strategic matrix, participants choose issues for collective work, based on criteria: seriousness, urgency and governance. Techniques as Fishbone Diagram, 6 Sigma, 5W2H and PDCA cycle were applied. They could identify factors that impact disease control, as structure, process and outcomes.

Conclusion: Analysis of scenarios and SWOT tool could highlight actions needed to empower teams and neutralize adversity. Participants felt more able, and assumed that the training may be a way to improve tuberculosis control in Brazil.

PC-663-02   Treatment outcome of multidrug-resistant tuberculosis patients in modified DOTS-PLUS: a 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 to Feb 2010 with follow-up till 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 sero-negative 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 ± 2.1 months (1–11) and 4.6 ± 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.

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.

PC-664-02   Active tuberculosis case finding: challenges from diagnosis to treatment in Phnom Penh, Cambodia

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Background: A cornerstone of the Stop TB strategy is the scaling up of Active Case Finding (ACF) activities. The impact of ACF depends on effective linkage to treatment and care after TB diagnosis. The aim of this study was to describe the uptake of TB treatment, default after TB initiation, underlying reasons and the required actions.

Design/methods: Within a community-based ACF program targeting the urban poor in the Cambodian capital, door-to-door visits were conducted by community volunteers with TB symptom screening of all household members. Diagnosis mainly relied on microscopy and GeneXpert®. All positive results were sent immediately through SMS to the community TB workers, who visited the patients for referral to the health center. Treatment delay was defined as failure to start TB treatment after the first attempted patient contact after TB diagnosis. Treatment default was defined as any unplanned discontinuation of TB treatment from the patient's side. For these two patient groups, additional home visits were conducted.

Results: Between February 2012 and February 2013, 733 TB cases were diagnosed. Of these, 628 (86%) patients initiated TB treatment after the first patient contact. Amongst the 105 (14%) that experienced a treatment delay, the main reasons were health system/treatment delivery related. Interventions to remediate the problem included counseling ($n = 70$), provision of social support ($n = 55$) and facilitation of alternative treatment modalities ($n = 42$). 84% (88 of 105) were subsequently initiated on TB treatment. Amongst the 716 starting TB treatment, 51 defaulted from treatment, mainly due to health service-related factors. Main reasons for the patient's decision to discontinue included the fact of having experienced drug toxicity ($n = 16$), time constraints ($n = 25$), difficult health service access ($n = 7$). Home visits for counseling, organization of alternative treatment models and support were the most common actions taken. Overall, 65% (33 of 51) subsequently restarted treatment.

Conclusion: More than one in four patients experiences difficulties with access to care and/or treatment continuation, predominantly health service-related. Without appropriate strategies and resources to re-engage these individuals to care and treatment, the overall impact of ACF on TB control could be compromised.

PC-665-02   Increasing case detection through community sputum collection points in southern Malawi

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Background and challenges to implementation: Mulanje, Phalombe, Mangochi Machinga, Neno, and Ntcheu districts (population of 3 373 823) are in the Southern Region of Malawi, Central Africa. Government provides health services including free pulmonary tuberculosis (TB) control. Case detection has been low due to passive approach where patients suspecting to have the infection report to health facilities on their own time, often very late. Until 2006 health facilities providing TB screening were not easy to access resulting in high deaths among TB patients.

Intervention: Project HOPE has been working with the Malawi government to improve case finding through improvement of quality of sputum microscopy, establishment of peripheral sputum microscopy sites, training microscopists, organizing community volunteers to conduct community TB health education, motivation of TB suspects and establishment of community sputum collection points (a community place where sputum is deposited for transportation to microscopy site, CSCP) under the supervision of health surveillance assistants.

Results and lessons learnt: Increasing community awareness, community involvement and empowering community volunteers on TB control activities has increased acceptance of TB control service. 214 CSCPs collect sputum for 64 peripheral microscopy sites established. Of the 14 630 TB SS+ suspects tested, CSPCs accounted for 16.7%; of the 1399 found positive, 11.7% were detected from CSPCs. Differences are found among districts, with some, such as Mulanje yielding 11% positive; while Neno and Ntcheu yielded 2%.
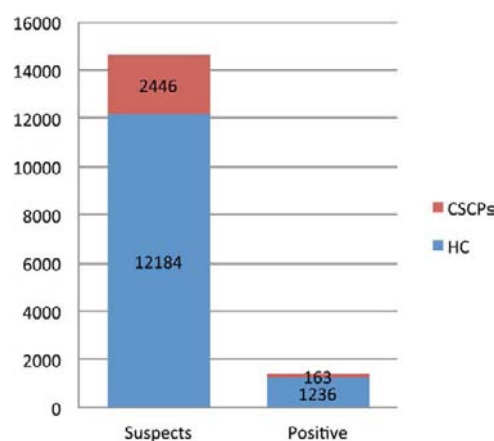
Figure Sputum smear positive TB cases identified by CSCP and health facilities, Mulanje, Phalombe and Neno, October 2011–September 2012.

Conclusions and key recommendations: Community approach, empowerment and involvement in mobilizing and supporting identification of TB suspects and support to TB patients are a very effective approach to improve TB control. CSPCs are making a small but significant contribution to suspect finding. Providing peripheral sputum microscopy service close to the people in the community supported by community sputum collection sites are two better ways of improving TB control activities. District differences indicate a need for bringing the other districts up to speed.

PC-666-02   A published chest X-ray score shows no correlation with baseline bacterial load, but correlates with two month culture conversion in tuberculosis patients

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Background: New markers for disease severity, prognosis and treatment response could help in categorizing patients in need of differential treatment. Ralph et al. have published a simple chest X-ray score, which they found to correlate well with baseline sputum smear grade and month-2 smear status (Thorax, 2010). The power of the latter to predict treatment outcome is increasingly seen as insufficient, so we evaluated the score against culture-based indicators which provide reasonable readings at month 2.
Method: Patients with smear positive TB were consecutively enrolled in two Tanzanian sites, and received Tanzanian standard anti-TB treatment. Sputum culture monitoring was performed at least weekly up to week 8 in liquid culture. Posterio-anterior X-ray was assessed at baseline, and graded according to the published score: percentage of the parenchymal involvement of total visible lung is rated by the investigator, and a factor of 40 is added if any cavitation is present. X-rays were read jointly by two observers in this analysis. Baseline bacterial load was measured as the mean of two measurements of MGIT time to positivity from pre-treatment samples. Culture conversion was defined as at least two negative MGIT cultures not followed by a positive culture.
Results: Data from 28 patients were available for this study. Only 15.6% of patients converted to negative culture during the study. Median chest X-ray score was 51 points, cavitation was present in 21 patients. Neither percentage consolidation, nor cavitation or combined score were associated with baseline bacterial load measured by MGIT TTP. Using Poisson regression, a higher score was associated with lower likelihood for culture conversion at a risk ratio of 0.964 for conversion per point score increase ($P = 0.01$).
Conclusion: The published score showed a surprising lack of correlation to baseline bacterial load, measured by a culture method, in our sample. However, the score significantly correlates to the outcome measure of culture conversion within 2 months. These differences to the publication of the score may be due to the evaluation of viable bacilli by culture in our sample, while the published cohort was tested by smear alone. In our study, culture conversion rates were far below that expected.

PC-667-02   Delay in diagnosis and treatment among tuberculosis patients attending a referral hospital in Taiping, Malaysia

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Background: In Malaysia, there is a rising number of TB cases with associated significant mortality and morbidity. This problem has been compounded by complacency, neglect towards the disease and also contributed by a large population of migrants, both legal and illegal. Furthermore, the control of TB has been challenged by delayed presentation and diagnosis, comorbidities and high treatment default rates especially amongst immigrants. In 2010, the incidence of TB in Malaysia was 66.9 per 100 000 population. The number of new TB cases in the country increased from 15 000 in 2005 to 22,710 in 2012 with an incidence rate of 78.7 per 100 000 population. Amongst the newly diagnosed pulmonary tuberculosis patients, 72% were smear positive. Hence early diagnosis and prompt institution of treatment is important in management of tuberculosis. The objective of this study is to assess factors associated with delay in diagnosis and treatment among TB patients in Taiping, Malaysia.
Design/methods: A total of 93 patients were diagnosed and subsequently treated as tuberculosis in the Respiratory Unit, Hospital Taiping in 2012. Factors associated with the delay in diagnosis and treatment were reviewed. Multivariate logistic regression was used to analyze factors associated with delay among TB patients.
Results: The average time from onset of symptoms to the first medical visit (patient delay) was 74.2 days with median delay of 30 days (range 3–1095 days). The average time from the first medical visit to TB diagnosis (medical practitioner delay) was 27.6 days with median delay of 12 days (range 0–240 days). The average duration from TB diagnosis to commencement of anti TB (treatment delay) was 1.5 days with median delay of 0 days (range 0–47 days).
Conclusion: There is a significant delay in patients

seeking medical care and in diagnosis of tuberculosis. There is no delay in commencing antituberculosis therapy once diagnosis is made. Effective public health education is needed to encourage early medical consultation. Medical practitioner delay is also a factor in late diagnosis.

MDR-TB: FROM RESEARCH TO PRACTICE

PC-668-02   Community and home-based treatment for MDR-TB through an NGO/NTP partnership yields excellent treatment outcomes in Cambodia, 2006–2012

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Background and challenges to implementation: Inpatient treatment for multi-drug resistant (MDR-TB) is burdensome to patients and health systems. As the global MDR-TB epidemic grows and case-detection improves, alternate treatment models are required to successfully manage the anticipated volume of patients.

Intervention or response: The Cambodian Health Committee (CHC), a local non-governmental organization, initiated the Cambodian MDR-TB treatment program in 2006 and scaled this up in cooperation with the National TB Program (NTP). After confirmed or suspected MDR is diagnosed, patients electing to receive home-based MDR-TB treatment are matched with community-based treatment adherence supporters and followed as outpatients by a team of nurses, physicians, and community health workers. Patients who are hospitalized for more than one month of treatment receive similar management after discharge. A standardized treatment regimen is provided. Adherence, side effects, and monthly sputum examinations are monitored throughout treatment by the outpatient team.

Results and lessons learnt: Between 2006–2012, 282 MDR-TB patients started treatment. 67 (24%) initiated community-based treatment and 215 (75) were hospitalized for at least the first month of treatment. 20% were HIV-co-infected. Of patients starting treatment 2006–2010, 98 (68%) were cured, 5 (3%) completed, 12 (8%) defaulted, 2 (1%) failed and 28 (19%) died. There was no statistically significant difference in treatment outcomes for community vs. hospital-based treatment ($P = 0.58$). Baseline BMI < 16 and HIV infection were strongly associated with decreased likelihood of cure or completion (aOR 0.23, $P < 0.001$ and aOR 0.26, $P = 0.012$ respectively). An additional 73 patients were treated for non-MDR drug-resistant TB, with similar outcomes. The program was successfully transferred to oversight by the National TB Program in 2011.

Conclusions and key recommendations: The Cambodian MDR-TB program has achieved comparable cure/completion rates between the inpatient and community-based initiation of treatment arms of the program. The program represents a model collaboration between an NGO and the National TB Program in developing innovation, achieving scale-up and securing sustainability of an MDR program.

PC-669-02   The role of surgery in the treatment of pulmonary tuberculosis at National Lung Hospital, Viet Nam from 2002 to 2012

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Background: Tuberculosis (TB) is still a major cause of morbidity and mortality worldwide and in Viet Nam. The drug resistant—forms and the complications of pulmonary tuberculosis are becoming more and more frequent. Surgical treatment is once again needed to manage these problems. The purpose of this study was to analyze the indications and results of operation which we performed for pulmonary tuberculosis.

Design/methods: A retrospective review was performed of 198 TB patients undergoing surgical treatment for complications of pulmonary tuberculosis and drug-resistant strains of *Mycobacterium tuberculosis* between July 2002 and June 2012 in National Lung Hospital, HaNoi, Viet Nam.

Results: There were 66 women and 172 men with an average age of 44 years (range from 22 to 79 years). Indications for operation were as follows: tuberculoma in 79 patients (39.9%), persistent or drug-resistant disease in 5 patients (2.5%), hemoptysis in 40 patients (20.2%), aspergilloma in 25 patients (12.7%), cavitary sequelae and destroyed lung in 49 patients (24.7%). The techniques utilized included: pneumonectomy in 8 patients (4%); lobectomy in 144 patients (72.7%); bilobectomy in 25 patients (12.7%); segmental or wedge resection in 15 patients (7.6%); thoracoplasty in 4 patients (2%); plombage in 2 patients (1%).There were no operative deaths. Total major and minor postoperative complications occurred in 38 patients (19.2%). Of the patients operated for persistent or drug-resistant disease, 100% have remained culture negative.

Conclusion: Surgery remains an important role in the management of TB patients with others sequelae or complications. Surgical intervention can be performed

with acceptable operative morbidity and mortality and the long-term prognosis after successful operation is very good.

namics of clinical and laboratory results. Surgical interventions are one of priority directions in treatment MDR-TB and XDR-TB of lungs.

PC-670-02   Surgical treatment of patients with pulmonary MDR-TB in a DOTS-PLUS program

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Aim: To study efficiency of operative interventions at patients with MDR a pulmonary TB in the conditions of program DOTS-PLUS.

Methods: Since the year of 2000, there has been implemented DOTS-PLUS program for treatment of pulmonary MDR-TB patients in Tomsk Oblast. By the year of 2010, this program has included 1496 from civilian population, among them, 167 (11.2%) have received some surgical interventions. Before the surgeries, 16 (9.5%) patients have been diagnosed with cavernous form of pulmonary TB, 44 (26.4%) patients with fibro-cavernous TB, 99 (59.3%) patients with tuberculomas, and 8 (4.8%) patients with other forms of pulmonary tuberculosis. Extrapleural thoracoplasty (5–6 ribs) has been used in 12.6% (21) cases, resection surgery—in 144 (86.2%) patients, including 16 (11.1%) patients with both lungs involvement.

Results: All the patients were performed surgical interventions in achieving a favorable background. Anti-TB drugs patients began to take from 2–3 days after the operation, with the obligatory addition of injection drug (Sm, K, Cap), even if it has already been repealed and the patient was in the continuation phase of chemotherapy. In the case of resection of the lung, the period of chemotherapy ranged from 9 to 12 months, and in the case of operations thoracoplasty from 16 to 24 months. Analysis of the results of surgical treatment of 144 (100%) of patients with MDR-TB, which have resection of the lung. The direct result of the resection surgery: cured—143 (99.3%) of the patient, failure—1 (0.7%). After 5 years of follow up in outcome noted: clinically cured—in 130 (90.2%) persons, died—4 (2.8%; patients die from tuberculosis), treatment failure—5 (3.5%) patients, dropped out—5 (3.5%).

Conclusions: A set of drugs and duration of postsurgical chemotherapy (not shorter than nine months) have been decided according to several factors, such as: the results of DST for *Mycobacterium* isolates from patients sputum before surgeries and from resection material, initially diagnosed form of a TB process, extension and complexity of surgical interventions, characteristics of residual process, and dy-

PC-671-02   Treatment outcomes in patients with MDR-TB and XDR-TB in China: retrospective multi-center investigation

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Background: The increasing incidence of multidrug resistant tuberculosis (MDR-TB) and extensively drug-resistant (XDR-TB) is a major concern for TB control programs worldwide. To investigate the characteristics, treatment outcomes and risk factors associated with poor treatment outcomes among patients with MDR- and XDR-TB.

Methods: We retrospectively analyzed TB patients with culture-proven MDR-TB and HIV-negative from July 2006 to June 2010 in five large-scale Tuberculosis specialized hospitals in China.

Results: Among 1662 TB cases with culture-positive for *M. tuberculosis* complex, 965 cases (58.1%) were drug resistant (DR), 586 cases (35.3%) were classified as having MDR-TB, accounting for 60.7% of DR-TB. 169 cases (10.2%) were XDR-TB, accounting for 17.5% of DR-TB, 28.8% of MDR-TB. The patients were divided into XDR-TB group ($n = 169$) and other MDR-TB group (MDR-TB excluding XDR-TB or non-XDR MDR-TB; $n = 417$). The percentage of female from XDR group was 39.1%, significantly higher in comparison with that from other MDR group ($P = 0.034$). In 586 MDR-TB cases, retreated patients accounted for 78.67% (461/586), there being no significant difference between the two groups. There were a much higher proportion of patients with comorbidity, decreased albumin, and cavitary disease among the patients with XDR group compared to patients in other MDR group. The ranges of disease in two groups were both extensive. The course of disease in XDR group was 7.2 ± 8.75 years, significantly higher than that in other MDR group. The resistance proportions of all drugs except isoniazid and rifampicin were significantly higher in patients with XDR-TB than in other MDR-TB patients. In total, 240 patients (40.95%) had treatment success, and 346 (59.05%) had poor treatment outcomes. The treatment success rate in other MDR-TB group was 52.2%, significantly higher than that in XDR-TB group (13%, $P < 0.001$), whereas poor treatment outcomes were more common in patients with XDR-TB than in patients with other MDR-TB (87 vs. 47.8%; $P < 0.001$). In multivariate logistic regression

analysis, treatment success was associated with age less than 45 years, duration of earlier treatment less than one year, a BMI greater than 18.5 kg/m², new case, and 3~4 lung fields in the range of disease. Meanwhile, XDR, diabetes, tumor, decreased albumin and with cavitation were independent predictors of poor treatment outcomes.

Conclusions: The prevalence of MDR- and XDR-TB is high in some areas in China with poor treatment outcome. The presence of extensive drug resistance, low BMI, hypoalbuminemia, comorbidity and previous anti-TB treatment were independent poor prognostic factors in patients with MDR-TB.

PC-672-02   MDR-TB pathway in programmatic management of drug resistant tuberculosis

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Background and challenges to implementation: Monitoring in tuberculosis program is of paramount importance for ongoing planning, implementation and outreach of services. Programmatic management of drug resistant TB (PMDT) requires an intense strategy for enhancing accessibility and optimum utilization of program services. Since the time of implementation of PMDT services in Delhi (2009) till the year 2011, a substantial number of drug resistant tuberculosis (DRTB) patients (21%) could not be initiated on treatment due to accessibility and utilization issues. In addition, there was a median delay of 3 months from DRTB diagnosis to treatment initiation.

Intervention or response: In 2012, Delhi State TB department initiated steps to strengthen DRTB patient tracking mechanism with intensified monitoring tool for diagnosis (starting from acknowledgement of culture and drug sensitivity sample receipt slip from the patient) and treatment initiation. An innovative color coded monitoring pathway was developed for PMDT which had responsibilities assigned to key program staff to ensure timely action on gaps in diagnosis and treatment initiation.

Results and lessons learnt: In the year 2012, out of 11 846 patients suspected for MDR-TB enrolled under PMDT, drug resistant TB was diagnosed in 1793 patients. Of them, 1670 (93%) patients got enrolled under PMDT in Delhi; post implementation of the MDR-TB pathway at each peripheral health center. The red colored monitoring alerts incorporated in the MDR-TB pathway enabled early detection of gaps in diagnosis and treatment of MDR-TB services in the field. With the use of this monitoring tool, there was a significant reduction in the time gap between MDR-TB diagnosis and start of treatment from an average 2–3 months to 2–3 weeks with an aim to reduce the time gap even further to less than 2 weeks.

Conclusions and key recommendations: The color coded monitoring pathway for PMDT enables early detection and timely follow up of drug resistant TB patients under field conditions. This process indicator is simple, useful and effective for improving management of drug resistant TB in high burden settings like India.

PC-673-02   Sputum culture conversion within 90 days predictive of favorable treatment outcome in patients on XDR-TB treatment in South Africa

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Background: We set out to examine sputum culture conversion and treatment outcomes for patients with XDR-TB in an area of high HIV prevalence.

Methods: A retrospective cohort study of patients initiating treatment for XDR-TB in Eastern Cape (EC: 10/06–6/08) and KwaZulu-Natal Provinces (KZN: 10/06–1/08). Patients who had 2 consecutive negative sputum cultures taken at least 30 days apart after treatment initiation were considered to have achieved culture conversion. We compared culture conversion within 90 days of treatment start and first-time culture conversion at any time on XDR TB treatment.

We assigned patients treatment outcomes 24 months after treatment initiation using standard definitions. Patients who were cured or completed treatment were considered to have favorable outcomes, while those who died, defaulted, or failed treatment were considered to have unfavorable outcomes.

Results: Overall, 376 adult patients initiated XDR TB treatment (232 patients from EC and 144 patients from KZN), 348 of whom (92.6%) had complete follow-up information for this analysis. In total, 216 patients (62.1%) were HIV positive, of whom 138 (63.9%) were on anti-retroviral medications (ARVs) at XDR TB treatment start. Treatment outcomes after 24 months of treatment were as follows: 33 patients (12.6%) cured, 13 patients (3.6%) completed treatment, 28 patients (7.7%) default, 213 patients (58.4%) died, and 61 patients (16.7%) failed treatment. Of the 43 patients (12.4%) had at least two consecutive negative sputum cultures within 90 days, 27 patients (62.8%) had a favorable treatment outcome while 16 patients (37.2%) had an unfavorable outcome. Rate of early culture conversion was similar in HIV-positive patients as in HIV-negative patients ($P = 0.55$). Patients who had sputum culture conversion within 90 days of XDR-TB treatment initiation were more likely to have a favorable treatment outcome ($P < 0.01$, Figure). Of the 86 patients (24.7%), 43 patients (50.0%) had a favorable outcome while 50% had an unfavorable outcome. There was also no
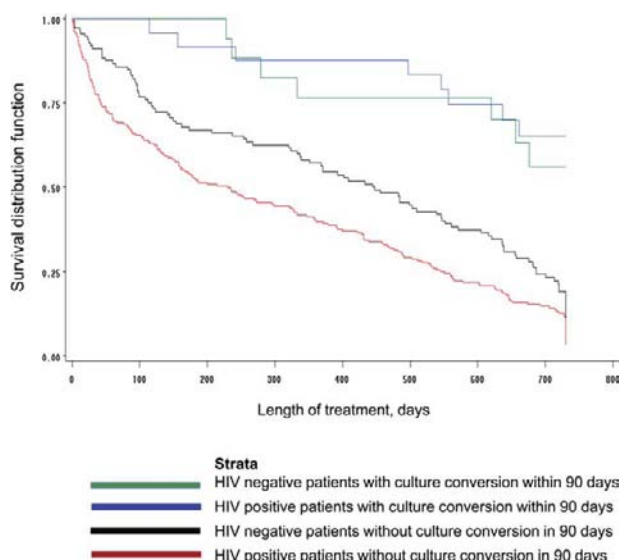
Figure Two-year survival in patients treated for XDR TB in South Africa.

difference in culture conversion at any time between HIV-positive and HIV-negative patients ($P = 0.41$).

Conclusions: Sputum culture conversion within 90 days of XDR treatment start was strongly predictive of favorable outcome, regardless of HIV status. Further analysis will focus on predictors of early and late sputum conversion, as well as overall treatment outcome.

PC-674-02 Outcomes of drug-susceptible and MDR-TB patients started on ambulatory and in-patient treatment in Karakalpakstan, Uzbekistan

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Backgound: Diagnosis and treatment of tuberculosis (TB) began in Karakalpakstan, Uzbekistan, in 2003. Analysis in 2011 showed 4.6% cross-infection with more resistant strains among inpatient (IPD) multidrug resistant (MDR) TB patients, and alarmingly high MDR-TB rates among medical staff. Reducing the risk of nosocomial spread of TB is thus a critical component of TB control in Karakalpakstan.

Design/methods: Outcomes of drugs sensitive (DS) patients treated between April 2010 and July 2012 ($N = 862$), and interim outcomes (default and death by 6 months, culture conversion by 4 months) of MDR patients started between March 2011 and October 2012 ($N = 913$) were compared for patients started in IPD and as ambulatory. DS patients were considered 'transfer to DR treatment' (resistance on diagnostic sample) if failure was declared within 80 days of treatment start, and 'true' failures otherwise. χ^2 and regression analyses were carried out on outcomes for DS and MDR ambulatory and IPD starts. For MDR patients, further analyses were done after controlling for a number of variables including sex, age, previous treatment, cavitary disease, baseline bmi. Statistical analysis was carried out using Stata v.9.

Results: Excluding patients transferred to DR TB treatment (recently revised WHO definitions), success for DS was 76.5% (ambulatory) and 79.3% (IPD). Ambulatory starts had significantly higher default (13.8% vs. 8.3%, OR 1.8, $P = 0.03$) rates. Differences in death (1.8% vs. 1.3%) and failure (7.7% vs. 6.9%) rates between the two were small. Significantly more inpatients transferred to DR treatment (14.6% vs. 7.5%, $P = 0.02$). Death rates in MDR patients did not differ significantly between ambulatory and IPD starts (4.7% vs. 5.2% repectively). Significantly more ambulatory patients defaulted (12.3% vs. 6.8.1%, $P < 0.01$). Of those who were culture positive at diagnosis, significantly more ambulatory patients culture converted by 4 months (87.5% vs. 80.3%, OR 1.7, $P = 0.01$).

Conclusions: Starting TB patients on ambulatory treatment is not associated with worse outcomes for both DS and MDR patients. Success rates and interim outcomes were similar in patients started on ambulatory and IPD treatment. There is need for better understanding of default reasons, and addressing these in patients discharged from hospital. Ambulatory treatment is strategically important in reducing risk of nosocomial spread of DR TB, and to ease the resource burden of prolonged hospitalization.

MANAGING TUBERCULOSIS PUBLIC-PRIVATE RELATIONSHIPS

PC-675-02 Assessment of private health providers' participation in National Tuberculosis Control Programme in South India

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Background: Private practitioners (PPs) are the first choice for seeking tuberculosis (TB) care in India. Since 2001 the Revised National TB Control Programme (RNTCP) engages with PPs through Public Private Mix Schemes (PPMS) to ensure universal access for all TB patients. We studied the nature and the extent of PPs' participation in RNTCP.

Design/methods: We conducted this study in Tumkur district, Karnataka State. It has a total population of 2 681 449 and a private health sector with 287 PPs potentially consulted by TB suspects. We assessed

the formal engagement of these PPs with the existing 10 PPMS, by reviewing RNTCP reports at district TB centre. We examined the registers at RNTCP's sputum microscopy centers (RSMC) in the district, to assess referrals of TB suspects made by PPs during 2011. We analised the proportion of PPs making any referral, the proportion of referrals by PPs out of the total number of suspects seen at RSMC and the positivity rate in suspects referred by PPs.

Results: None of the 287 PPs had formally signed-up for any PPMS. 63% of PPs made at least one referral to a RSMC in 2011. Only 16 PPs referred more than 12 suspects per year. These referrals constituted a very tiny proportion (3.4%) of the total number of suspects examined at RSMC. Sputum positivity rate of PP's referrals was 24%. The Table provides disaggregated analysis by sub-district, and illustrates quite a substantial variability.

Sub-district	Population	PPs making any referral %	Referrals received at RMSC made by PPs %	Smear positive %
Koratagere	383 905	35	1.4	13
Kunigal	510 735	67	2.9	15
Pavagada	391 139	50	1.3	50
Sira	468 699	61	5.7	28
Tiptur	468 085	16	0.5	14
Tumkur	458 886	79	9.2	23
Total	2 681 449	63	3.4	24

Conclusion: Our study demonstrates the complete absence of formal engagement of PPs with RNTCP, 15 years after the start of the PPMS. However, PPs do make referrals to RNTCP, although they represent a tiny fraction of the total number of suspects seen at the RSMCs. The high sputum smear positivity rate seems to indicate that PPs tend to refer TB cases rather than suspects. Efforts are needed to promote the engagement of PPs in RNTCP and to assure correct selection of suspects to be referred.

PC-676-02 Tuberculosis case detection via private pharmacies in Lao PDR

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Background and challenges to implementation: The 2012 tuberculosis (TB) prevalence survey in the Lao People's Democratic Republic found a national prevalence double the previous estimate. Efforts are underway increase active case finding. Since 2011, Population Services International (PSI) has implemented a scheme to engage private pharmacies nationwide in the identification of TB suspects. Engagement of these outlets is important because data show that Lao people often first consult pharmacists when they have a cough.

Intervention or response: PSI trained 600 pharmacists to screen clients for TB symptoms and to refer symptomatic clients to public sector facilities or private clinic providers participating in PSI's social franchise, who are trained and supervised to ensure provision of high quality TB services. Referral cards were used to track pharmacy referrals. From July 2011, quarterly drawings for prizes such as a camera or phone were used to incentivize pharmacists. All pharmacists who provided a referral that resulted in a TB case detection were entered. Due to poor results, the scheme was revised to offer smaller but more immediate, guaranteed incentives. Since October 2012, pharmacists are awarded US$12 phone credit for each successful referral that results in detection of a sputum smear positive TB case and US$1.20 of credit for referrals that meet the screening criteria but do not have sputum smear positive TB. Credit is transferred monthly.

Results and lessons learnt: Routine monitoring data shows that improvement of the scheme has increased TB screening and case detection. Over 600 referral cards have been distributed in 6 months, and 21% were collected at a health facility. The average number of referrals successfully tracked each month increased 41%, from 17 to 24, after the scheme change. Of the successful referrals, TB case detection increased 133%, from 12% to 28%. The majority of TB cases in Laos are screened in the public sector, but collecting referral cards from large public hospitals proved more challenging than collecting from private providers with close relationships to PSI.

Conclusions and key recommendations: These data indicate that appropriate incentives can be used with private pharmacies to increase TB case detection. Such schemes could be an effective way for engaging these providers since costs beyond the incentive are minimal. The National TB program must be actively engaged to accurately track public sector referrals.

PC-677-02 Feasibility and impact of referral of tuberculosis suspects by drug sellers in an urban township, Myanmar

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Background: Prevalence survey 2009–2010 showed that 22% of TB cases with chronic cough visited traditional medicine and drug sellers. Increase of case detection is one of important objectives for NTP.

Objective: To develop and observe feasibility of a model system to increase case finding of TB through

referral of TB suspects by drug sellers in Hlaing Township, Myanmar.

Methods: Out of 129 registered drug shops in the township (population of 118 547 in 2012), 99 drug shops participated in the training in May and June 2012. Pamphlets, posters and referral slips were provided for drug sellers. However, no monetary incentive was given to them. Referral of TB suspects having TB symptoms by drug sellers to township TB centre started in July 2012. Drug sellers kept master list of referred TB suspects at their shops. Two supervisors were assigned to visit all participating drug sellers once a month to collect data. When AFB sputum smear result was negative, transportation fare for chest X-ray examination was provided. Outpatient medical records and all TB recording and reporting forms were reviewed. Also, quarterly evaluation meeting for drug sellers was held with township medical officer (TMO) and NTP officer.

Results: From July to December 2012, 56 out of 99 drug shops referred at least one TB suspect. Total 224 TB suspects were referred and 145 (64.7%) attended to the township health centre. The 'arrival rates' were 64.4% (125/194) for adults (15 years of age and above), and 66.6% (20/30) for children. Smear positivity rates was 14.8% (18/122) for adults. Referred cases by drug sellers accounted for 11.9% (18/151) of smear positive pulmonary TB (PTB) and 9.6% (33/342) of all forms of TB registered in the township in July–December 2012. As a result, the number of TB suspect, smear positive PTB and all forms of TB cases increased 2 times, 1.3 times and 1.2 times respectively from that in July–December 2011 (Figure).
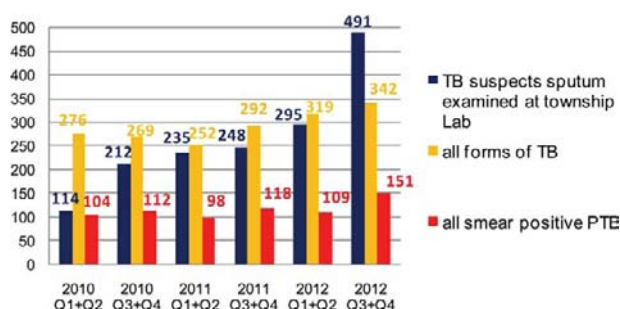
Figure The number of TB suspects examined and notified patients in Hlaing Township, Yangon, Myanmar, 2010–2012.

Discussion: Commitment of TMO influenced positive participation of registered drug sellers into referral system. Monitoring and evaluation (M&E) activities played an important role to identify and solve problems and maintain willingness of drug sellers for referral work.

Conclusion: This model referral system of drug sellers could be developed within existing health system in condition with additional M&E activities in urban area of Myanmar.

PC-678-02 Why do tuberculosis patients take treatment from private health facilities in India? Reasons and challenges

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Background: In India, tuberculosis (TB) treatment in public health facilities is provided free of cost by the Revised National Tuberculosis Control Programme (RNTCP). As per a community-based cross-sectional survey conducted by International Union Against Tuberculosis and Lung Disease (The Union), in 30 districts across the country, of the 609 TB patients identified and interviewed, it was estimated that 278 (46%) were availing treatment outside RNTCP services usually from the private health facilities (despite 85% of them having a monthly household income of less than Indian Rupees 4000 or US$80).

Methods: We conducted a secondary analysis of the survey data and assessed the association between the preferred source of medical care, knowledge of RNTCP and its services and receiving TB treatment from private sector. We also assessed the reported compliance rate with TB treatment and the key reasons for non-compliance.

Results: Of 609 TB patients, those who generally seek health care from private health facilities ($n = 243$) were more likely to be availing treatment from non-RNTCP sources [odds ratio 9.7 (95%CI 6.6–14.2)]. Similarly, those who did not know about RNTCP ($n = 183$) were more likely to avail TB treatment from private sector (OR 3.8, 95%CI 2.6–5.5). Three major reasons for not seeking care from RNTCP sources were long distances from their residence, unfriendly behaviour of the staff and long waiting hours. About 82% of the patients ($n = 331$) on RNTCP services informed that they were taking/took their medications regularly in comparison to only 68% among those who were taking their treatment from non-RNTCP sources ($n = 278$). The predominant reason why patients on non-RNTCP sources could not take the medications regularly was because of the cost incurred in purchasing the medications.

Conclusion: This analysis shows that people who generally prefer medical care from the private sector and those who were not aware of TB treatment provided by RNTCP were more likely to be treated in the private sector. Those who were taking treatment from private sector were more likely to be irregular in taking their medication due to cost incurred in purchasing the medication which will adversely affect the TB Control. There is an urgent need to expand the reach and accessibility of RNTCP services and make it more patient-friendly in order to achieve universal access to TB care.

PC-679-02   Role of graduate medical practitioners: experience of networking with graduate practitioner in BRAC supported areas

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Background and challenges to implementation: In Bangladesh, about 85% people seek health care from private sectors, of which 26% from graduate medical practitioner (GP) and half of them seek care for chest-related problems. GPs have enormous role in TB diagnosis especially smear negative and extra-pulmonary, which is crucial for National TB control programme (NTP). Patients treated by GPs are not reported under NTP due to non-compulsory reporting system. Moreover, information gap and improper linkage also resulting in under reporting of identified cases. BRAC is the largest partner of NTP in controlling TB. Since 1984, its innovative approaches made TB control effort successful. Addressing those gaps and emerging need for proper diagnosis of complicated TB, BRAC began to work with GPs under NTP. The aim of this document is to explore the result of intervention after networking with GPs.

Intervention or response: BRAC started expedition with GP in April 2012 in 12 districts and went for massive scale up in 30 districts in January 2013. It initiated a unique strategy to establish strong linkage and bonding with GPs through quarterly orientation to enhance proper referral and diagnosis of TB case. At the beginning, mapping of all GPs were done by fields staff. GPs were listed on popularity basis and orient by NTP. Program organizers are designated for GP networking in respective area and meet each GP once a week. Separate recording and reporting mechanism has been developed and maintained to explore the contribution.

Results and lessons learnt: During April 2012 to March 2013, a total of 3957 GPs have been oriented through 542 orientation program and they referred 21 281 TB suspects to BRAC. In the reporting period, a total of 110 138 all forms of TB cases were identified. Among them, 72 264 (66%) were smear positive, 17 742 (16%) smear negative and 15 931 (14%) extra-pulmonary. In April 2011–March 2012, total diagnosed cases were 96 187, of which 68 584 (71%) were smear positive, 10 796 (11%) smear negative and 13 478 (14%) extra-pulmonary. The overall case detection is 15% high and smear negative and extra-pulmonary case detection has been increased 39% from previous year.

Conclusions and key recommendations: The increased TB case notification provides evidence of immense role of large growing private health care sector for TB care in Bangladesh. The effort of networking with GPs needs to establish and continue remaining parts of the country to increase case detection.

PC-680-02   Utilización en México de la herramienta 'El camino de la tos a la curación' para fortalecer las acciones de abogacia, comunicacion y movilizacion social en tuberculosis

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Objetivo: Fortalecer las actividades de Abogacía, Comunicación y Movilización Social, a través del análisis situacional de la tuberculosis en 25 regiones del país, con utilización de la herramienta metodológica 'El camino de la tos a la curación'.

Material y métodos: Se realizó análisis situacional de la tuberculosis en 32 estados que conforman el país y se estableció intervenir en los estados con mayor incidencia, mortalidad o curación por debajo de 85%. Se seleccionaron 25 estados en dos etapas (2011–2012), para participar en el Taller de análisis de brechas y planificación de soluciones, con duración de 5 días, en el cual se utilizó la herramienta 'De la tos a la curación', que permite analizar brechas que se tienen desde la aparición de signos y síntomas, hasta llegar a la curación, identificando si las barreras están relacionadas con el sistema de salud (prestación de servicios), la persona o la comunidad. También se capacitó en la utilización de herramientas de ACMS para reducir las brechas y se elaboró Plan de Trabajo.

Resultados: El acompañamiento a los estados participantes, a través de visitas en campo y por vía electrónica, favoreció la implementación de acciones tendientes a reducir las brechas identificadas y el alcance de los objetivos establecidos en el Programa Nacional de Tuberculosis. Los principales resultados están relacionados con el incremento en 40% en el estudio de sintomáticos respiratorios en las unidades participantes, incremento en el número de casos diagnosticados de tuberculosis pulmonar, así como aumento del 30% en la calidad de la muestra y ganancia de 7% en la curación, de acuerdo a la curación basal. La oferta de pruebas de detección de VIH y DM se incrementó entre las personas con TBP. Se involucró a diferentes actores de la sociedad civil, médicos de práctica privada y principalmente se involucró activamente a la comunidad y a las personas afectadas por tuberculosis, a través de talleres de voces e imágenes. Como ganancia complementaria se fortaleció la capacidad de gestión de los gerentes estatales para la mejora estructural y de recurso humano para las actividades de prevención y control de la tuberculosis a través de alianzas estratégicas.

Conclusiones: La aplicaición de la herramienta «El Camino de la Tos a la Curación», permite realizar actividades de ACMS, con el involucramiento de las personas afectadas por TB, en la planeación de actividades orientadas a la disminución de brechas para mejorar el control de la TB.

PC-681-02   Lessons learned in engaging private pulmonologists through public-private mix in Indonesia

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Background: Based on assessments of antituberculosis drugs sales to the private sector in Indonesia, nearly 50% of tuberculosis (TB) patients are managed outside of the national TB control program (NTP) and not notified. As an approach to systematic engagement of the private sector, the Indonesian Society of Respirology (PDPI) in collaboration with the NTP developed a project to engage private pulmonologists in national TB control activities, following the International Standards of Tuberculosis Care (ISTC) and NTP guidelines.
Methods: Pulmonologists were surveyed for their TB patient load and interest in participating. Through 2012, 86 pulmonologists were recruited from 7 districts. Participants received a 2-day ISTC-based training course before enrolling patients. PDPI provided staff members for data collection. Biannual meetings were held to review the cohort assessment by district and hospital.
Result: From Oct 2010–Dec 2012, 5851 patients were managed by pulmonologists and notified to the NTP. Only 36% were treated with free NTP FDC drugs. About 76% had diagnostic sputum smear microscopy, of which 30% were positive. 41% of the smear positive cases had smears checked at the end of treatment intensive phase. Reasons cited for failure to perform smear microscopy included lack of trust in uncertified labs, the cost of smears, and lab working hours. In the first 5 quarters the default rate was 17% and treatment success was 58%. Failure and death totaled less than 2%, the remainders were transferred out or still being treated at the time of review.
Discussion: Significant numbers of TB patients are managed by private pulmonologists and not notified to the NTP; involving these specialists in PPM approaches may be a high yield activity. Labs must be recruited and their service improved. Of concern is the heavy reliance on prescribed, non-program drugs which may be of poor quality. Improved linkages with local public primary care clinics is crucial to reduce defaulters.

PC-682-02   Pathways to tuberculosis care: a comparison of persons started on tuberculosis treatment at the index clinic vs. other public sector facilities in South Africa

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Background: Persons with TB symptoms seek care from a variety of service providers, but the determinants of different pathways are unknown. We compared the characteristics of TB patients diagnosed with TB at the index clinic vs. other public sector facilities.
Design/methods: A representative sample of persons presenting to 40 primary health clinics in four South African provinces being investigated for tuberculosis with sputum microbiology by clinic personnel were followed up for 6 months to determine health seeking behaviour, and TB treatment status.
Results: Amongst 4103 participants with 6 months follow-up, 440 (10.7%) reported starting TB treatment. Of these 66/440 (15%) were initiated by another provider, of which 61% were at a hospital. Persons starting TB treatment elsewhere vs. the index clinic were less likely to report being HIV positive; were more likely to have had greater number of visits and admissions to health care providers, and experienced treatment delay.

	Facility where TB treatment started		
	Clinic of enrolment (n = 374) n (%) or median [range]	Another clinic/provider (n = 66) n (%) or median [range]	P value
At enrolment			
Male gender	211 (55)	41 (62)	0.3
Age, years	35 [18–80]	36 [19–83]	0.8
Previous TB	68 (18)	15 (23)	0.4
Self-reported HIV positive status	198/276 (72)	27/46 (59)	0.07
Body mass index <18.5	74 (20)	12 (18)	0.4
Sputum submitted at another facility prior to enrolment	72 (19)	14 (21)	0.7
At follow-up			
Returned to fetch sputum results from enrolment clinic	374 (99)	56 (85)	<0.001
2 or more visits to any health provider for investigation of TB symptoms before TB diagnosis	150 (40)	35 (53)	0.05
1 or more hospital admission from enrolment to starting TB treatment	19 (5)	31 (47)	<0.001
Days from enrolment to TB treatment start	8 [0–463]	35 [0–412]	<0.001

Conclusion: Improved TB diagnosis at the index clinic has potential to reduce time to treatment and reduce health service use.

INCREASING CASE FINDING PROCESS, PPM, PARTNERSHIPS, LABORATORY DIAGNOSIS

PC-683-02   Urban volunteers can play a vital role in identifying hidden tuberculosis cases in a slum population, Nepal

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Background and challenges to implementation: Urbanization is rapidly increasing in Nepal with many people from villages coming to the city. With the increasing urban population, there are growing numbers of urban slum areas. The health and wellbeing of people in those areas is significantly worse due to poor living conditions, poor access to health services and inappropriate health seeking behavior.

Intervention or response: This cross-sectional study was done at slum areas of Kathmandu urban covering approximately 100000 populations. A team of health care providers and urban tuberculosis volunteers made door to door visit in 500 households. Person who had symptoms suggestive of pulmonary tuberculosis and TB patient's family members were referred to nearby microscopy centre which was run by non-governmental organization (NGO). Three sputum samples including one early morning and 2 spots specimens were collected in two consecutive days. For chest X-ray and other investigation suspects were advices to visit hospitals and medical college where it is appropriate for them.

Results and lessons learnt: Comparing the result of study sites, the number of case notification is increased by 3.4 times (66/222). Out of 222 all forms of tuberculosis (TB), 79 (35.59%) were pulmonary positive, 32 (14.42%) were pulmonary negative, 79 (35.59%) were extra-pulmonary, 11 (4.96%) were retreatment cases followed by 18 (8.11%) other cases. Two third of diagnosed cases were male and their mean age was 38. The prevalence of active pulmonary tuberculosis in slum and semi slum area is 1.5 times higher than general setting. Among total diagnosed cases 86% completed their treatment successfully followed by 2% death, 4% defaulted, and 8% transfer out. Total 343 suspects were referred to microscopy centre. Among them 19 are diagnosed as a pulmonary positive TB. The volunteer's activity contributes 24.05% case finding in study sites. The door to door visits also improve the health seeking behavior of the inhabitants living in the slum areas of the country.

Conclusions and key recommendations: Regular volunteers meeting and interaction helps to motivate urban TB volunteers to take part in TB related intervention. Regular mobilization of volunteers can contribute to increase national case finding rate from the hard to reach area and it can be sustain by including similar activity in the regular programme of National Tuberculosis Control (NTP) Programme.

PC-684-02   International Standards of Tuberculosis Care implementation by pulmonologists in private practice in Jakarta

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Background: Most pulmonologists in Jakarta practice in private hospitals and treat tuberculosis (TB) patients. With the introduction of ISTC and DOTS, pulmonologists are expected to implement the standards in their practice regardless of limitations in their private practice settings. To improve case notification and monitoring of treatment outcomes, the Indonesian Society of Respirology (PDPI) implemented a project in which selected private pulmonologists agreed to manage patients in accordance with the ISTC and National TB Program guidelines.

Method: To validate information from TB case reporting through the PDPI project, we reviewed medical records from the practices of 22 pulmonologists from 16 private hospitals in East, South, and Central Jakarta. Abstractors with TB clinical background collected data from 258 TB patients, diagnosed between October–December 2010, with expected treatment completion by June 2011. We developed a questionnaire and scoring system related to diagnosis, therapy, monitoring, and outcomes of TB treatment to assess ISTC implementation.

Result: We evaluated 12 of 21 standards: 5 diagnostic, 5 treatment, 1 co-morbidity, and 1 public health standards. Four pulmonologists (19%) adhered to all standards, 8 (38%) adhered to 11 of 12 standards, 1 met only 8 of 12 standards, while the rest met varied numbers of standards. Standards 1, 8, 10, and 13 are the most implemented (100%), while standard 11 is implemented the least, by 11 (52%) pulmonologists. Of 258 TB cases, 64% completed treatment, 1% failed, 1% died, 28% defaulted from treatment, and 5% transferred out to another facility.

Discussion: Most of the pulmonologists performed

appropriate ISTC implementation in their private practice. The high number of patients who defaulted from treatment may indicate the lack of patient education given by pulmonologists or the need of a better linkage system among private providers and the health office to ensure continued TB treatment of patients.

PC-685-02   Improving tuberculosis case detection in difficult-to-reach villages of Chhattisgarh and Madhya Pradesh, India, through a door-to-door tuberculosis campaign

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Background and challenges to implementation: Poor health awareness, limited access to health facilities and chronic insurgency problems are key challenges of states like Chhattisgarh and Madhya Pradesh, India. These equally affect the TB program and result in low TB case detection. CARE India in partnership with World Vision India has been implementing GFATM supported TB project in selected low performing districts of two states to strengthen linkages between rural community and health systems. To improve TB case detection in difficult-to-reach villages a pilot initiative of door-to-door TB campaign has been undertaken by CARE India with technical assistance of World Vision India.

Intervention or response: Objectives of door-to-door campaign:

1 To generate TB awareness through household visit.
2 To identify chest symptomatic for TB evaluation.
3 To know current health-seeking practices on TB.

Coverage of door-to-door campaign:
Undertaken in 312 villages of 84 Designated Microscopy Centres (DMCs) of 3 districts (Dantewada, Dhamtari, Kanker) of Chhattishgarh and 4 districts (Dhar, Mandsore, Khargone and Badwani) of Madhya Pradesh.

Period: October 2012–March 2013.

Processes of door-to-door campaign:
1 Selection of villages (low case detection and difficult to reach) in consultation with local TB health staff.
2 Training of local community volunteers who implemented the campaign.
3 Household visit for TB education and identification of chest symptomatic (cough for >14 days).
4 Distribution of IEC materials.

Results and lessons learnt: 93 829 people in 15 365 households reached through the campaign. 374 chest symptomatic identified. 24% ($N = 90$) informed local community health workers and 16% ($N = 60$) visited health facilities. Rest ($N = 224$) neither visited any health facilities/nor inform any health workers.

52% chest symptomatic ($N = 194$; 125 male, 69 female) referred to DMCs for TB evaluation. 92% ($N = 178$; 112 male, 66 female) tested for TB. 26% ($N = 47$; 32 male, 15 female) detected with TB. Positivity rate: 13%. 98% put on DOT within 7 days of diagnosis.

Lessons learnt: TB awareness still low in remote villages with poor health seeking of chest symptomatic including their low turning up for sputum examination.

Conclusions and key recommendations: Door-to-door campaign by existing community volunteers and health workers of the remote villages can be a useful strategy to improve TB awareness and detection in difficult-to-reach pockets of low performing districts of the country.

PC-686-02   Can we identify additional tuberculosis cases through intensified tuberculosis case detection at district hospitals? Experience from Ghana

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Background: In 2011, Ghana's tuberculosis (TB) case detection rate was less than 30%. A national assessment showed that one cause of this low case detection was weak hospital-based TB screening. In response, the USAID project, TB CARE I, worked with the National TB Program (NTP) to develop and disseminate standard operating procedures (SOPs) for TB case detection. The SOPs guide health workers to screen all patients for TB, regardless of their presenting symptoms. TB CARE I piloted the impact of SOPs implementation at six hospitals in two districts in Eastern Ghana, from January to December of 2012. The project's goal was to increase TB case detection at the six hospitals by 10% from the 2011 baseline of 338 detected cases.

Intervention: TB CARE I trained 123 hospital staff to use the new SOPs and TB suspect registers. The NTP then conducted monthly monitoring and supervision visits to provide the hospital staff with additional training, coaching, and mentoring on SOP implementation. In January 2013, TB CARE I reviewed the hospitals' 2012 TB performance outcomes to determine the impact of the SOP intervention on TB case detection.

Results: Between January and December of 2012, 388 920 patients and clients accessed outpatient department services at the six hospitals. The hospital staff screened all of these individuals and identified TB symptoms among 2914 of them. After examining the sputum samples from these patients, the staff
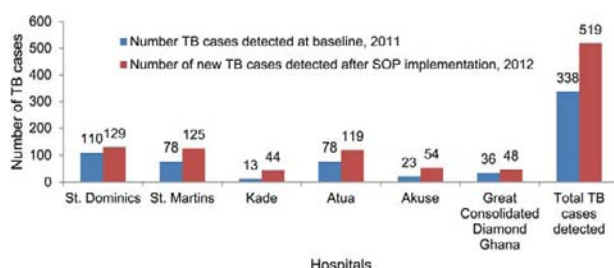
Figure Implementing SOPs for TB case detection improves outcomes in six Ghanaian hospitals.

diagnosed 519 of them (17.8%) with TB; 316 of these patients (10.8%) were diagnosed with sputum smear positive TB. The data show that the 2012 SOP intervention contributed to a 54% increase in TB case detection at the six hospitals (see Figure). Hospital staff enrolled 262 patients in TB treatment in the same hospitals where they had been tested and referred 257 patients (49.5%) to other health facilities for treatment. Only 11 of the newly detected TB cases were among children under the age of 14.

Conclusion: Through the simple and cost-effective SOP intervention, the six hospitals identified 519 TB cases in 2012, 181 more cases than they had identified in 2011. The fact that only 2% of these TB cases were among children reflects a need to improve pediatric TB screening. Furthermore, the fact that 50% of the newly detected TB patients were referred to other facilities for treatment indicates a need to develop a functioning referral and feedback system. If implemented country wide, this intervention has the potential to significantly increase Ghana's TB case notification rate.

PC-687-02   Reaching the underserved: active tuberculosis case finding among urban slum populations in south-east Nigeria

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Background and challenges to implementation: There is documented evidence that active case finding led to increased number of TB cases notified in urban slums in many parts of the world. Nigeria ranks 10th among the 22 high TB burden countries in the world, with many urban slums spread across the country. However, such initiatives are yet to be explored within her urban slum populations which are inadequately reached with TB services but remain at high risk of developing tuberculosis (TB). To address this gap, active case finding was adopted among the inhabitants of three urban slums in two states in south-east Nigeria.

Intervention or response: Under the TB REACH project, German Leprosy and TB Relief Association,

Nigeria initiated active case finding among inhabitants of the urban slums. Screening for TB was performed by general health workers and trained community volunteers in each of the intervention areas through home visits as well as clinic visits for people living with HIV (PLHIV). Sputum samples were collected from identified TB suspects and delivered to designated laboratories, while trained general health workers and laboratory technicians provided TB services in newly established and existing DOTS sites. The project used front loading of sputum samples (two sputum samples collected one hour apart) for diagnosis. Smear negative suspects, including eligible children were provided with free X-ray services. The project was implemented between January and December 2012. Surveillance data were collected and analysed to determine the magnitude of TB cases among the inhabitants.

Results and lessons learnt: Among 167435 individuals screened for TB, 3367 (2.0%) were identified TB suspects while 1079 (0.6%) were diagnosed TB. The diagnosed TB cases show 7.9% increase from the baseline. Childhood TB cases (0–14 years) were 67 (6.0%) which shows significant increase relative to the average of 1.4% notified in southern Nigeria over twelve years (2000–2011). Seventy one per cent (771) of the diagnosed cases were sputum smear-positive. Only 3.0% were extra-pulmonary TB, with spondylitis being the most common form. The inhabitants are now able to access TB services within the slums.

Conclusions and key recommendations: Active TB case finding improved TB cases notified in the urban slums especially among children. There is need to scale-up this strategy to other urban slums in Nigeria to improve overall TB case-finding in the country.

PC-688-02   Evaluation of a tuberculosis and HIV screening program in Lusaka, Zambia

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Background and challenges to implementation: With up to 64% of TB patients co-infected with HIV, integration of TB and HIV services is a priority of the Zambian Ministry of Health (MOH). The vertical TB and HIV systems existing pre-2006 provided limited collaborative activities. Since 2005 the Centre for Infectious Diseases Research in Zambia (CIDRZ) has provided technical assistance to the MOH in the scale-up of TB and HIV services in Lusaka, Southern, Western and Eastern provinces. We reviewed trends in management of co-infected patients from Lusaka District using annual reports from the National TB Program (NTP).

Intervention or response: The MOH CIDRZ TB program aims to strengthen existing TB and HIV services, improve treatment outcomes, reduce mortality among co-infected patients and improve community awareness. Our activities include: a) training health care workers (HCW) in provider-initiated HIV testing and counseling (PITC), TB screening and diagnosis, clinical management of co-infected patients, infection control (IC); b) renovating clinic space to make private rooms for PITC; c) supportive supervision through clinic visits; d) funding data review meetings for monitoring and evaluation; d) supporting peer educators to assist with PITC; e) patient education; f) training treatment supporters in TB-patient support tasks; and g) community sensitization. The program evaluation received ethical approval from the University of Zambia and the University of Alabama at Birmingham.

Results and lessons learnt: We initiated activities in Lusaka District in 2006 with scale-up to 23 sites by 2012. The program has trained 1362 HCW and 29 TB peers in HIV counseling and testing. We have renovated 11 clinics and held 252 meetings with 5300 TB patients, and 200 drama performances. Trends in TB-HIV indicators for Lusaka urban are shown in the Table.

Year-Number of notified TB patients	TB patients with documented HIV status	TB patients HIV Positive	HIV positive TB patients at TB clinics started on cotrimoxazole preventive therapy (CPT)	TB patients started on antiretroviral therapy (ART)
2006 – 16,696	2203 (13%)	1528 (69%)	682 (45%)	676 (44%)
2007 – 15,910	7786 (49%)	5764 (74%)	2863 (50%)	2517 (44%)
2008 – 15,536	9097 (59%)	6409 (70%)	3271 (51%)	2790 (44%)
2009 – 16,568	12,143 (73%)	8685 (72%)	4865 (56%)	3413 (39%)
2010 – 17,247	14,547 (84%)	10,255 (70%)	6932 (68%)	4614 (45%)
2011 – 18,018	14,573 (81%)	10,330 (71%)	8176 (79%)	5004 (48%)

Conclusions and key recommendations: State the implications of the effective public health practice and key recommendations. Highlight opportunities for future programme practice, as well as implications for other programmes or settings.

PC-689-02   Improving tuberculosis case detection in Myanmar through intensified case finding in urban slum areas

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Background: Myanmar is one of 22 high TB burden countries. PSI/Myanmar has provided TB diagnosis and treatment through a PPM (public-private mix) DOTS program since 2004; in 2012, 894 franchised Sun Quality Health (SQH) clinics treated 24230 TB patients. A National TB Prevalence survey in 2010 showed significantly higher prevalence than previously estimated, especially in urban areas. Smear positive TB prevalence in Myanmar's largest city, Yangon, was estimated at more than 240 per 100 000.

Intervention: From 2011, PSI Myanmar implemented a program for intensified case detection in poor, high population density townships of Yangon and Mandalay, with support from TB REACH. The program combined two modalities: interpersonal communications (IPC) and pharmacy franchising;

1 60 trained IPC agents (IPCs) held small community meetings at which TB was discussed, suspects identified, and sputum collected. Suspects were supported through the diagnostic process to treatment at SQH clinics.
2 Staff in 526 pharmacies were trained to identify TB symptoms and provided with IEC and referral materials. They were offered a small incentive payment ($1) for each appropriate, successful referral to SQH clinics.

Results and lessons learnt: Historical trends in NTP TB case notifications in project townships were modelled over the 16 quarters leading to the project period. Using extrapolated trends as a counterfactual, PSI's intervention resulted in an average increase of 9% in New Sm +ve, and all forms, case notification (Table). PSI's MIS system shows 1859 SQH TB patients identified through IPC and Pharma activities during the project period. 80% (1440/1859) of these notified patients are considered 'additional' cases. 88% of registered TB patients were identified through IPC, 12% through pharmacies. IPCs were also more aggressive in identifying symptoms—only 7% of suspects referred for diagnosis through IPCs were notified as cases, compared with 25% from pharmacies. More than 60% of pharmacies did not refer any suspects.

Total TB case notifications, project townships, NTP data			
New smear +ve			
	*Predicted	Actual	Increase	Percent
Mandalay	1,074	1,063	-11	-1.0%
Yangon	4,805	5,374	569	11.8%
Total	5,879	6,437	558	9.5%
All forms			
	Predicted	Actual	Increase	Percent
Mandalay	3,492	4,140	648	18.6%
Yangon	13,261	14,053	792	6.0%
Total	16,753	18,193	1,440	8.6%
Directly reported TB REACH results			
	NS+ve	All Forms	
Mandalay	105	567	
Yangon	589	1,292	
Total	694	1,859	
% Additionality	93%	0%	

Mandalay 1 year data (Q4 2011 to Q3 2012), Yangon 6 months data (Q3 and Q4 2012).
Percentage of TB REACH reported cases that are additional to Project Area notifications. In other words, 80% (557/694) of sm +ve cases reported by TB REACH would not have received treatment without the project.
* predicted value based on previous 12 quarter data.

Conclusions: PSI's IPC model is effective in identifying additional TB cases in high density urban settings in Myanmar. Although IPC is approximately 4 times more expensive than Pharma, it appears that this represents good value; detailed cost-effectiveness comparisons are under way. Work is ongoing to improve the productivity of the pharma channel, through improved selection and IEC tools, and emphasising the importance of referring lower risk suspects.

PC-690-02   Identifying the impact of standard operation procedures for tuberculosis case detection on case notification and treatment outcomes in Afghanistan, 2009–2012

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Background: In 2004, Afghanistan's National TB Program (NTP) worked with the USAID-funded Rural Expansion of Afghanistan Community Health (REACH) project and its implementer, Management Sciences for Health (MSH), to develop standard operation procedures (SOPs) for tuberculosis (TB) case detection and treatment. Unfortunately, the SOPs were not disseminated and health facility staff was not trained on. In response, USAID's TB Control Assistance Program (CAP) and TB CARE I projects, both led by MSH, began helping the NTP to implement the SOPs in 2009. In 2013, the TB CARE I team conducted an assessment to determine the impact of the SOPs implementation on TB screening, case notification, and treatment.

Intervention: As part of the implementation process, TB CAP and TB CARE I projects helped the NTP to update, printing, and disseminating 2000 copies of SOP to health facilities. TB CARE I also helped the NTP train 3072 health facility staff to use the SOPs and established 36 Direct Observed Treatment Short Course (DOTS) centers of excellence. The project team conducted on-the-job trainings and regular monitoring and supervisory visits at these centers. From January to March 2013, TB CARE I collected, reviewed, and analyzed TB data that had been recorded between 2009 and 2012 at 34 (intervention 13, control 21) provinces.

Results: Between 2009 and 2012, TB screening increased by 96% (from 48 630 to 96 750) at the 13 provinces. Furthermore, smear positive (SS+) TB case detection increased by 8.7% (95%CI 6139–6676, $P < 0.014$, OR = 0.06)) and all forms of TB case detection increased by 27% (95%CI 12 454–15 825, $P > 0.00001$, OR 1.3). TB treatment success rates increased by 7% (95%CI 83–90, $P < 0.04$, OR 1.05). The control group showed significantly smaller im-

Table Comparison of key TB indicators in the intervention and control group health facilities, 2009–2012

Indicator	Intervention group health facilities (13 provinces)				Control group health facilities (21 provinces)			
	2009	2011	2012	% change (2009–2012)	2009	2011	2012	% change (2009–2012)
TB suspected cases identified	49,630	99,272	96,750	95% increase	45,812	93,730	84,622	85% increase
TB sputum smear positive cases notified	6,139	7,051	6,676	8.7% (CI-95%, P<0.014) increase	6,358	6,750	6,547	3% increase
TB cases notified, all forms	12,454	14,792	15,825	27.1% increase (P<0.00001)	13,904	13,372	13,545	2.6% decline
Treatment success rate	83%	89%	90%	7% increase	89%	92%	92%	3% increase

provements in TB screening, case detection, and treatment success rates during the implementation period. For example, among the control group health facilities (21 provinces), TB screening increased by 85% (from 45 812 to 84 622), SS+ TB cases increased by 4% (from 6358 to 6547), all forms of TB case detection declined by 2.6% (from 13 904 to 13 545) and the TB treatment success rate increased by 2% (from 89% to 91%). The attached table shows how the intervention and control group outcomes compare.

Conclusions: SOP implementation improved TB screening, case notification and treatment success rate in the project-supported health facilities. SOP implementation should be scale-up in Afghanistan and applied in similar settings worldwide.

PC-691-02   What are the perspectives of private practitioners on mandatory tuberculosis case notification in India?

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Background and challenges to implementation: After a government order making tuberculosis notifiable in India, National TB Programme (NTP) is establishing effective mechanism for TB notification, a step to improve TB surveillance. Almost half the TB patients in India seek care from Private Practitioners (PP) initially. Hence understanding knowledge and practice of PP regarding TB notification will help make TB notification successful on grounds.

Intervention or response: Cross-sectional survey was carried out in seven districts of Gujarat province in India. 174 PPs attending continuing medical education during Jan–March 2013 were selected out of 1491 listed allopathic practitioners in the districts. Structured questionnaire was used to understand the knowledge and practice on TB notification.

Results and lessons learnt: 89% of PP knew that TB is notifiable disease. 42% of PP knew the concept of TB notification correctly. Time spent and responsibility of maintaining records and reports were disadvantages perceived by 35% of PPs. 35% PP concerned that notification will affect privacy and confidentiality of patients. 33% and 43% of PP preferred electronic and telephonic mode for TB notification respectively. 46% PP endorsed concept of provision of free anti TB drugs in private being considered by government of India.

Conclusions and key recommendations: In study population, most of the PP knew that TB is a notifiable disease. However majority of them are not aware of the concept of TB notification. NTP should undertake activities to inform details of TB notification to PP.

Concern of confidentiality and privacy of patient may be addressed by devising flexible patient centered system of notification coupled with information of the same to PP and general community so that this may not be considered as disadvantage.

NTP need to develop user friendly mechanisms for notification such as mobile phone/internet based or call centre based systems and sensitize the private providers on this.

NTP may primarily concentrate on advocacy and encouragement as way ahead for ensuring TB notification. Though few PP opted for financial incentive for TB notification, majority of PP opined that non financial incentives such as feedback on the status of the notified patient, imparting quality training to PP and recognition of their contribution etc as factors which could encourage TB notification from PP.

PC-692-02   Mobilising local community to improve tuberculosis case detection in difficult areas of selected Indian states: experiences of World Vision India

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Background and challenges to implementation: Gross geographic variation like abundance of forests, flood-prone low-lands, mountains and islands and political unrest like insurgencies were key reasons of poor access to TB services and subsequently low TB case detection in many places of states like West Bengal, Bihar, Jharkhand, Chhattisgarh, Orissa, Madhya Pradesh and Andhra Pradesh of India. To overcome the challenges World Vision India (WVI) and its 6 Civil Society partners has been implementing Project Axshya (Axshya means 'TB free') in selected problematic areas of these 7 states with the assistance of Global Fund TB grant since April 2010. The project has completed the first phase of implementation in March 2013 and gearing up for the second phase. **Intervention or response:** Through this project WVI

and partners aimed to engage and empower local grass-root level CBOs and community care givers in TB control and care and link them with Revised National TB Control Program (RNTCP) of India through advocacy, capacity building and mobilization activities. From April 2010 to September 2012 WVI and partners generated TB awareness in 18 201 villages, trained 8363 rural unqualified healthcare providers, 840 CBOs (mostly women SHGs) and 42 industries and conducted 300 TB awareness and screening camps mostly in difficult-to-reach areas. Moreover, during same period, WVI and partners helped 11 655 RNTCP and health staff to develop their health communication skill, retrieved 607 initial defaulter (91% of the target) cases back to DOT. 110 MDR-TB Support Groups (in Andhra Pradesh) and 74 district level TB Forums were created in the project.

Results and lessons learnt: Community care givers, volunteers and CBOs referred 70 880 chest-symptomatic to RNTCP for TB evaluation from April 2010 to September 2012; 4615 sputum smear positive pulmonary TB cases (positivity rate 6.5%) detected and 4223 TB cases (91%) put on DOTS under RNTCP. Irrespective of low positivity rate in referrals WVI and partners demonstrated that advocacy and mobilization of CBOs and community care givers can result in detection of TB cases in difficult to reach areas. The TB Forums and MDR-TB support groups could not produce desired results due to insufficient community linkages and lack of human resources.

Conclusions and key recommendations: The experiences and learning of phase 1 have been strategically utilized to develop the strategies and activities of phase 2 of the project for more effective and sustainable community engagement in future.

PC-693-02   High rates of routine tuberculosis symptom screening are achievable and sustainable at a busy primary care clinic

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Background: Several studies have demonstrated that passive case finding for tuberculosis (TB) at clinic facilities results in a substantial number of missed opportunities to diagnose TB. The World Health Organization endorses routine TB symptom screening at all clinic visits for HIV-infected but not HIV-uninfected individuals. It is unclear whether routine, intensified case finding for all clinic clients,

independent of HIV status, is feasible and sustainable in primary care clinics in high TB burden settings.

Methods: We implemented provider-initiated routine TB symptom screening for all clients at Witkoppen Health and Welfare Centre, a high-volume primary care clinic in Johannesburg, South Africa. Data from 26 520 visits during a 6-month period (30 Jan–27 July 2012), representing 12 427 adults, were collected via routine electronic clinic data systems and retrospective file review. We assess the proportion of clients screened over time and use log-binomial regression to explore the association of gender, age, nationality and HIV status with TB screening.

Results: High coverage rates of TB symptom screening were achieved initially (84.6%) and were sustained during the entire 6-month period (90.9% by week 26, median 90.5%, range 83.1–95.7%). The reason for clinic visit among those not screened for TB was available for 61.3% of all clinic clients and included general care (25.8%), HIV care (25.0%) and ante/post-natal services (23.4%). TB screening coverage rates did not differ by gender (RR 1.00, 95%CI 0.99–1.01), and were slightly higher among older (age $\geqslant$40) (RR 1.05, 95%CI 1.04–1.05) and HIV-positive (RR 1.19, 95%CI 1.17–1.20) clients. Immigrant patients were somewhat less likely to be screened for TB symptoms (RR 0.93, 95%CI 0.93–0.94).

Discussion: A high coverage rate (about 90%) of provider-initiated routine TB symptom screening can be achieved, even at a busy primary care clinic in a high TB-HIV burden area. Intensified clinic-based TB case finding was sustainable without additional human resources and coverage of TB symptom screening did not differ greatly by patient characteristic, indicating the feasibility of widespread routine TB symptom screening among all clinic patients. If replicable in other clinics, policy makers may consider roll-out of this novel strategy to further strengthen current TB control efforts.

PC-694-02 Tuberculosis care villages (Nagari Peduli TB): improvements in tuberculosis control though partnership in West Sumatra Province, Indonesia

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Background and challenges to implementation: One of the tuberculosis control operational policy at the national level is to increase cooperation and partnerships with relevant sectors. In West Sumatra Province, partnership through an effort to include a variety of sectors, including government, private sector and civil society groups. The high burden of tuberculosis problems and limitations of the public sector, leading to the potential for involving other sectors have increasingly expanded.

Intervention or response: Changes in the national political to decentralization system that occurred, to revive the spirit of the people of West Sumatra to re-run the NAGARI system of government. With the enactment of regional autonomy in 2001, the term re-use NAGARI (can be one or more villages) and their privileges. A NAGARI led by a WALI NAGARI, that person is considered the master of all aspects of life in the MINANGKABAU culture and formed KERAPATAN ADAT NAGAI (KAN), a body whose members tungku tigo sajarangan, which consists of religious leaders, intellectuals leaders and cultural leader. West Sumatra Provincial Health Office with The Indonesian Association Agains Tuberculosis make innovation approach cultural structure for TB programs.

Activities undertaken are: 1) revitalization and socialization, 2) implementation of the initial survey, 3) health promotion of tuberculosis, 4) training knowledge, attitude, behaviour of tuberculosis, 5) meetings, discussions, seminars, information through print and electronic media, 6) service approach through NAGARI SIAGA (see Figure).

Results and lessons learnt: This activity was conducted in two districts/cities beginning in 2008, which is in Padang City (Sub District Kuranji: Kalumbuk Village and Korong Gadang Villages) and in Agam District (Sub District Tanjung Mutiara: Nagari Tiku Utara dan Tiku Selatan).

Years 2008–2010, in Padang City increased 1.09 times, 63 cases in 2008 and 131 cases in 2010 (108 by volunteers) and in Agam District increased 0.58 times (57 cases in 2008 and 90 cases in 2010 (46 by volunteers). The results of this activity in addition to a very significant increase in CDR (more than 50% in year 2010 compared to 2008), and also increased community participation against tuberculosis and its controlled.

Conclusions and key recommendations: Raising activities of community participation in tuberculosis control program in Indonesia needs to get more serious attention in the future.

TUBERCULOSIS INFECTION CONTROL

PC-695-02   A continuous quality improvement approach to implementing tuberculosis infection control differently in Botswana

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Background: Botswana has a high TB incidence (455 cases/100 000 population in 2011) and nosocomial transmission of TB in clinical settings is of great concern. Despite availability of comprehensive infection control guidelines and didactic trainings for health workers since 2009, translating knowledge to practice has remained a challenge.

Intervention: In February 2012, Botswana piloted a training package developed by CDC in 10 health facilities. The package included didactic lectures, slides, video, hands-on site assessments tools and coaching to develop facility-specific infection control plans. Follow-up supervisory, support and mentorship visits were built into the program including feedback on progress to facility staff using a simple dash board matrix. Status of implementation on key infection control interventions were identified at baseline and at 6-month follow-up on the color-coded dashboard: RED was 'not being done'; GREEN 'being done and documented', BLUE 'being done but not documented' or YELLOW 'not applicable'.

Results: An average of 65% of the 37 key infection control interventions were flagged RED for all facilities at baseline; after 6 months an average of 19% were designated RED. Notably, 9 of 10 facilities were actively triaging patients and fast tracking coughers for early TB diagnosis and treatment initiation. Facilities were also actively monitoring daily interventions

Figure TBIC implementation progress using dash-board matrix of two sample facilities.

such as opening of windows to ensure adequate ventilation in waiting areas/exam rooms in outpatient clinics. Nine of 10 facilities actively screened healthcare workers for TB and provided N-95 respirators to protect them from acquiring TB.

Conclusions: The pilot program demonstrated positive change in infection control practice in facilities at 6 months after initial training using the CDC package. A simple dashboard was useful in tracking implementation and providing timely feedback to staff for continuous quality improvement. Botswana is considering rolling out this model to national scale.

PC-696-02   Pulmonary tuberculosis and associated factors: a systematic review and meta-analysis

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Background: Although *Mycobacterium tuberculosis* complex is a necessary cause for pulmonary tuberculosis (PTB), the existence of several other factors associated with PTB is undeniable. Associated factors and their respectively level of importance change over time. Therefore, synthesis of recent studies information can provide important evidence concerning PTB new/classic associated factors and consequently contribute for an improved TB control.

Objectives: To identify associated factors for PTB in studies published recently and to quantify significant combined measures for PTB risk factors previously identified.

Design/methods: A systematic review of published articles between 2002 and 2012 was done, following the Meta-analysis of Observational Studies in Epidemiology Group Guidelines. PUBMED and WEB OF KNOWLEDGE databases were searched to identify relevant papers. PTB corresponded to patients with sputum smear-positive or culture positive or abnormal X-ray. Meta-analysis was done to estimate pooled odds ratio (OR), for all associated factors analyzed in 3 or more studies. A random model was applied for all factors except alcoholism (*P*-value for Q statistics = 0.3).

Results: From the 421 articles initially identified, 185 were selected by title, 37 by abstract and 18 were considered for meta-analysis after quality assessment. Among these articles 11 associated factors were included in 3 or more studies and considered for meta-analysis: sex, HIV infection, alcoholism, diabetes, low body mass index (BMI), unemployment, smoking, previous TB contact, being illiterate, incarceration history and being unmarried.

As shown in the Table, only employment and education did not show significant associations with

Risk Factor	Odds Ratio CL95% *significant Odds Ratio	Homogeneity test		Publication bias tests
		Q statistics (p-value)	I² (%)	Beggs or Egger's (CL 90%)
HIV Status (HIV+)	5.9 (3.7-9.3)*	17.5 (<0.001)	83.3	Yes (Egger's test)
Incarceration (previous incarceration)	5.8 (2.5-13.5)*	9.7 (0.02)	69.1	No
Alcoho (alcoholic)	3.8 (3.1-4.5)*	3.7 (0.30)	18.0	No
Contact with TB patient	3.2 (2.0-5.3)*	57.0 (<0.001)	84.2	No
BMI (<18.5/underweight)	3.2 (1.0-10.1)*	25.3 (<0.001)	92.1	No
Smoking (smoker)	2.5 (1.4-4.3)*	50.7 (<0.001)	88.2	No
Employment (unemployed)	2.1 (0.8-5.9)	77.0 (<0.001)	94.8	No
Sex (male)	2.0 (1.0-3.9)*	73.7 (<0.001)	92.9	No
Diabetes (diabetic)	1.8 (1.2-2.8)*	21.4 (<0.001)	81.3	No
Marital Status (single/separated/widowed)	1.7 (1.2-2.3)*	12.1 (0.02)	67.1	No
0 years of schooling/illiterate	1.3 (0.8-2.2)	10.2 (0.02)	70.4	No

PTB. HIV and incarceration history were the strongest significant PTB associated factors. Alcoholism was the most consistent associated factor found. There was evidence of publication bias related with HIV results. Heterogeneity of studies, assessed through I^2, was in general high, in part due to the small number of studies considered for each associated factor.

Conclusion: The 9 significant associated factors identified can be grouped as socio-demographic factors (sex, marital status), behavioral factors (incarceration, alcohol, smoking and contact with TB patient) and disease-related (HIV+, diabetes, low BMI). Because of the small number of studies included in the analysis and their general heterogeneity results must be interpreted cautiously.

PC-697-02   Demonstration model for scale-up of tuberculosis infection control in Ndola, Zambia

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Background and challenges to implementation: In 2011, the Zambia TB CARE I project received funding to support a demonstration of TB infection control (IC) measures in one high TB burdened district called Ndola district, in the Copperbelt province. The goal of the project is to provide safe work practices to reduce TB transmission among people living with HIV and health care workers.

Intervention or response: Infection control interventions were introduced to 15 health facilities between January 2012 and March 2013 including baseline facility assessment, training and development of facility specific TB IC plans, provision of a pocket guide with standards and procedures for work practices,

the FAST strategy, health care worker screening, IEC materials and implementation of minor renovations enhancing ventilation of high risk patient areas. A facility data capture form was developed and data captured using an electronic data management system for key indicators. Quarterly reports were given to the Ministry of Health at national and district level and implementing partners.

Results and lessons learnt: IC safe work practices are being implemented in all fifteen facilities with a 61% improvement observed by December 2012 from a baseline of 27%. District Medical Office upheld the importance of IC and took ownership of implementation processes, with innovative ideas of providing incentives to six community volunteers to support sputum transportation efforts to diagnosing facilities. Facility level IC plans were incorporated in annual facility action plans and budgets for annual district support and funding. The number of patients identified with symptoms of TB rose from 381 in the first implementation quarter to 831 in the fourth implementation quarter, while the average turnaround time to diagnosis and treatment came down from a range of 1–21 days in 9 facilities with an average of 6 days to an average of 4 days.

Conclusions and key recommendations: The project provides a focused and stepwise implementation of TB IC measures in a high burdened TB and HIV environment, emphasizing administrative controls and supporting environmental changes within the framework of the existing national and district health system. Implementation was in line with the national infection control guidelines and infection prevention and control policy that the district can continue to implement in an affordable approach.

PC-698-02   Tuberculosis exposure of patients admitted to the medical ward of a referral hospital in sub-Saharan Africa

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Background: Nosocomial transmission of pulmonary tuberculosis (PTB) is a major problem in resource-limited settings. Cohorting of patients with known or suspected TB has been recommended but its impact on TB exposure remains to be determined.

Methods: To determine the extent to which cohorting of suspected PTB patients results in non-PTB patients being exposed, consecutive admissions to the female medical ward were followed. An index of

exposure based on the number of days and number of patients exposed to with TB, to whom exposed, and proximity of the those patients to a TB case was generated. Duration of exposure was determined retrospectively as the number patient-days that any given individual was in the same cubicle with a source/index case. To quantify exposure, the number of days on the ward was adjusted based on both the number of PTB patients present during those days and the bed proximity between exposed patients and PTB patients. Contact was further categorized as high, medium, low and no contact for the relationship between a susceptible patient and each of the index cases.

Results: 95 patients were followed for a total of 252 patient-days. Of 23 patients initially admitted to the TB ward, TB was diagnosed in 15 (65%) and excluded in 8 (35%). Of 72 patients admitted to the non-TB ward (of whom 5 were moved to the TB ward due to a suspicion for TB during the hospitalization), TB was diagnosed in 4 (6%) during or subsequent to hospitalization. Among the 9 patients without TB who were cohorted on the TB ward, all were HIV-infected and accounted for 27 observation-days of exposure. On the non-TB ward, patients were exposed to TB on 90% of their observation-days. Overall, HIV-infected patients were exposed on 90% of their observation-days. Using an index to estimate the intensity of exposure among patients without TB, we found that exposure was much higher for patients cohorted on the TB ward when compared with patients in the general ward (68.9 vs. 5.5; $P < 0.001$).
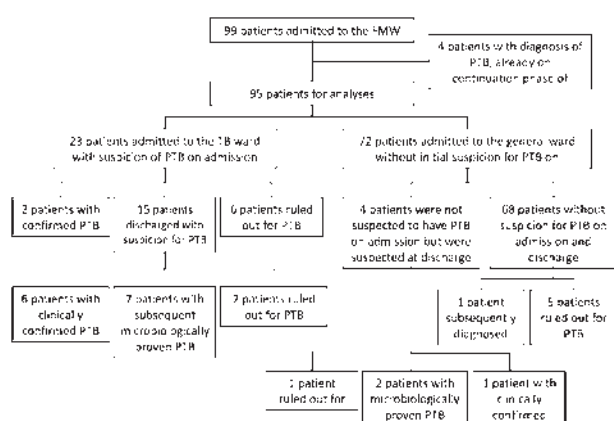
Figure Distribution of patients according to their suspicion for tuberculosis on admission, allocation on the ward and ultimate diagnosis of pulmonary tuberculosis.

Conclusion: These results confirm that substantial TB exposure, particularly among HIV-infected patients associated with use of cohorting measures. Follow-up studies of high risk subjects cohorted on TB wards is warranted to determine if such exposure results in infection or active disease, and if targeted prophylaxis or treatment interventions are justified.

PC-699-02   Impact of tuberculosis infection control measures on time spent at health facility by clients and suspect tuberculosis cases in Afghanistan: cross-sectional assessment

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Background: USAID-supported TB CARE I project assisted national TB control program (NTP) to implement tuberculosis (TB) infection control (IC) measures at health facility level since 2010 in Afghanistan. The aim of this assessment was to determine time a TB suspected case spent from his/her arrival to departure and from sputum collection to diagnosis and treatment initiation at health facilities (HFs).

Intervention: TB CARE I assisted NTP to develop standard operation procedure (SOP) for TBIC, oriented/trained 800 health care staff, developed and disseminated 19 000 pieces of IEC materials, established TBIC committees at 60 HFs and integrated TBIC into infection prevention plan of HFs. We selected convenient sample of 94 (intervention = 42, control = 52) interviews of suspected TB cases from intervention and control facilities in 19 HFs in eight provinces. We utilized questionnaire, documented patients arrival time, detection as suspect, sputum collection, and diagnosis and treatment initiation.

Results: The study discovered that in intervention HFs; mean suspect identification time from his/her arrival was 23 min and their departure was 80.7. Also, mean sputum collection of three samples took 52 h and time to diagnosis and treatment initiation was 54 h. Contrary in control HFs mean suspect identification time was 58.2 min and their departure was 178 min, mean sputum collection time was 73 h and diagnosis and treatment was 79 h.

Table Comparison of time interval in TBIC intervention and control facilities, 2013

Variable	Intervention area (with TBIC measure application)	Control area (without TBIC measure application)
Sample size	42	52
Detect as TB suspect, min	32.1	58.2
Time departed, min	80.7	178.1
Time collected sputum samples at least three from detected suspect case, h	52	73
Time from diagnosis to starting patient on treatment, h	54	79.3

Conclusion: According to study, time interval of TB suspect identification from arrival to departure and from sputum collection to diagnosis and initiating

treatment has significantly low in TB IC intervention health facilities, thus we recommend enhancing TB IC measures to additional health facilities and other similar settings.

PC-700-02   Application of water-soluble nanofilters for collection of airborne *Mycobacterium tuberculosis* in hospital wards

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Aim: Development of techniques for collection and detection of *M. tuberculosis* in airborne particles within wards of TB clinics.

Methods: Water-soluble nanofilters manufactured by electrospinning of polyvinylpyrrolidone (PVP) solutions were employed to collect aerosol in a TB clinic. A filter with an area of 12 cm2 attached to a head-piece of a household vacuum cleaner allowed collection of aerosol at a flow rate of 0.6 m³/min. Collection of aerosol in a hospital ward was performed during 15 minutes. Dissolution of the filter in 0.1–0.2 mL of water liberated all the collected aerosol particles. It was demonstrated that the presence of 3–6% of PVP in the solution did not interfere substantially with the conventional techniques of DNA extraction from the collected probes. DNA was extracted by Boom's technique using home-made siliconized magnetic beads. Quantitative assay of *M. tuberculosis* DNA was based on the real-time PCR using the multi-copy insertion sequence, IS*6110*, and the single-copy fragment of the regX3 gene as primers and fluorogenic hybridization probes. Effect of the filter material on the assay efficiency was estimated by collection of vaccine strain, BCG, nebulized in a closed chamber, 0.8 m³ in volume.

Results: Control experiments in the chamber revealed that when collection was started immediately after nebulization only 10% of the nebulized BCG cells was found on the filter and identified by the specific DNA. When collection was performed simultaneously with the nebulization the fraction of collected material increased to 43%. Probes were collected in each of the 21 hospital wards and tested for the *M. tuberculosis* DNA. Only in 5 of them occupied by patients excreting MBT (according to microscopic tests) *M. tuberculosis* DNA was detected on the nanofilters in the PCR assay. In 4 of these wards ~100 copies of the multi-copy primer, IS*6110*, was discovered. In one ward occupied with a patient having a massive excretion of TB (+++ level in the microscopic assay) we found as many as 5×10^2 fragments of IS*6110* gene and ~10 copies of the regX3 gene on the filter.

Conclusions: Water-soluble filters enable a simple, rapid and highly efficient technique for collection of aerosols into a small volume of liquid probe. The presence of DNA in the probe could be detected by the real-time PCR assay. Combination of these two techniques allows to control contamination of air with TB and other bacteria and prevent hospital-acquired nosocomial infection.

PC-701-02   Factors influencing early tuberculosis case detection in the south-eastern tuberculosis control region of Kenya

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Background and challenges to implementation: Early TB case detection remains an essential aspect of TB control. In 2011, Kenya's case detection for all forms of TB was 81 000 and an incidence rate of 288/ 100 000 population. Of these, 39% were smear positive pulmonary TB cases up from 34% in 2010. Several approaches to increase access to early detection of TB cases have been implemented including facility based screening as well as community-based TB contact tracing and screening involving Community Health Workers (CHWs). From 2011 to 2012, TB Care II partners conducted studies in Kenya, Bangladesh and Zambia to investigate factors influencing quality of TB services. This abstract provides results from Kenya.

Intervention or response: This was a cross-sectional study. Systematic sampling of 23 out of 444 health facilities was done. Face-to-face interviews were conducted with 39 TB healthcare providers and 73 CHWs affiliated with the health facilities. Healthcare providers offering TB services were also observed during client consultation to assess adherence with TB infection management guidelines. Descriptive statistics were calculated.

Results: The average TB knowledge score among the healthcare providers was 61% with the best performed questions relating to transmission of TB at 87%. Their performance on some of the other questions is shown in the Table. Healthcare provider

Table   Provider TB knowledge scores

Area of assessment	Percent who answered correctly*
Population groups at high risk of TB infection	84
Modes of TB transmission	87
Spread of TB infection	87
Symptoms of pulmonary TB	71
Pulmonary TB confirmatory tests	45
First line anti-TB drugs	82
Treatment of TB in pregnancy	50
Confirmation of TB infection	32
Screening for TB active infections	66

* Multiple responses.

observations: only 54% of patients were advised on close contacts TB screening while 46% and 69% were advised on the importance of hand washing plus adequate room ventilation as TB infection prevention measures respectively. Of the 73 CHWs interviewed, 99% correctly identified TB as an airborne disease and similarly persistent cough as a symptom of TB disease. However, only 11% of the CHWs diagnose TB in the community by checking for TB signs and symptoms and referring appropriately.

Conclusions and key recommendations: Correct knowledge of TB transmission and signs and symptoms of active infection is the first step in early TB case detection. When followed with appropriate follow-up care, it reduces chances of TB transmission. Therefore, the TB healthcare provider should undergo training to improve their knowledge on adequate management of a TB patient and how to emphasize TB infection prevention and control practices to every patient consistently. At community level, CHWs should be empowered to diagnose TB and refer appropriately through training and adequate supervision.

PC-702-02 Tuberculosis infection control in over-crowded prisons: mission possible?

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Background and challenges to implementation: Around 80% of Indonesia prison is over-crowded. TB is the 4th of all morbidity in the prisons and DCs and the 2nd leading causes of death among inmates. All prisons and detention centers have clinics with 164 of them implementing DOTS. Case finding in 2011: 7972 TB suspects were identified in Indonesia prisons; 757 (9.5%) were smear positive from total 898 TB cases. However, in 2010, Directorate General of Correction (DGC) had no policy to separate TB suspects/patients in a specific cell, no identified administrative and management measures of TB-IC in the prisons. TB CARE1/USAID provided technical assistance (TA) for TB control in the prison system on policy and strategy at the national level. For implementation support, TB CARE1/USAID supported TB-related activities including TB-IC to 25 prisons in 5 provinces.

Intervention or response: Continuous advocacy and TA were delivered by TB CARE1/USAID to 25 prisons in from 2010. All of them have TB screening strategies (for new inmates and annual mass screening). In 2011, TB-IC self-assessment tool was developed and finalized by team consisted of NTP, DGC, Directorate General of Medical Service, and Indonesian Society of Infection Control, and TB CARE1/

USAID. This tool covers assessment of managerial, administrative, and environment, and personal protective equipment measures. On site assessment using the tool from the central level involving NTP, DGC, TB CARE1/USAID were conducted in 25 prisons. PHO, DHO, Provincial office of MoLHR and Head of prison were involved during the assessment. National TB Program and DGC, with TA from TB CARE1/USAID, developed and finalized TB-IC guideline for prison setting in 2012.

Results and lessons learnt: Up to April 2013, eighteen prisons assigned specific cells for TB patients, 1 prison assigned specific cell for converted patients, the rest put the converted patients back in regular cells. All 25 prisons developed safe system to collect sputum (including the sputum collecting booth), triage, provided open-space waiting area, provided mask for coughing inmates, and 12 prisons do not place TB active patients in the same ward with HIV patients.

Conclusions and key recommendation: TB infection control in the overcrowded prisons though facing many challenges, is possible with the strong commitment from the prison authorities and health unit with continuous advocacy and TA from NTP and partners.

PC-703-02 Now that we are a TB DOTS facility . . . Is it safe to breathe in our hospital?

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Background: The occurrence of TB in the healthcare setting is a serious problem. The Philippine General Hospital (PGH), being a tertiary public health facility with a 1500 bed capacity and a 2000 daily census, invariably sees and admits large numbers of TB patients referred from various smaller hospitals. Over the last ten years, PGH considerably evolved on how patients with TB as well as housestaff who develop TB, were managed. This study looked at the epidemiologic profile of hospital employees who have been diagnosed to have active TB during the periods 2001 to 2012.

Design/methods: This is a cross-sectional retrospective chart review. Charts of employees who were enrolled into the TB DOTS program from 2001 to 2012 were reviewed. Whenever available, employees with TB were interviewed using a structured questionnaire. Clinical profiles were described: community and nosocomial TB exposures, duration of employment, clinical manifestations, diagnostic work up and outcomes. Trends were reported to the Hospital Infection Control Unit for proper action.

Results: 140 PGH employees were diagnosed to have active TB during the 12 years. The frequency of TB cases per year is seen in the Table. Of these, 35 (25%) were physicians, 24 were nurses (17%) and 21 were

	TB patients
2001	6
2002	20
2003	18
2004	25
2005	10
2006	3
2007	9
2008	13
2009	5
2010	10
2011	6
2012	13

utility workers UW (15%). Two cases were confirmed MDR-TB, one of whom died during treatment. Eleven were retreatment cases. Only 36 persons were interviewed. Nosocomial exposures were: direct care of TB patients, intubation, handling of respiratory secretions such as suctioning and closed tube thoracostomy insertion.

Overall, the most common symptoms were weight loss, fever, and cough. EPTB involved mainly pleura and lymph nodes. Diagnostic tests included routine chest X-ray and sputum AFB smears, mostly without culture. Majority claimed to be compliant and completed treatment. Symptom resolution in all patients and sputum conversion in all smear + cases were noted.

Conclusion: When a hospital decides to become a TB DOTS facility, efforts should also include improvements in infection control, more isolation room and availability of protective equipment. These infection control measures which were introduced one at a time may explain the decrease in number of new TB cases.

PC-704-02   Delays in diagnosis and initiation of treatment for pulmonary tuberculosis after implementation of tuberculosis infection control in Uganda

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Background: We aimed to assess the TB treatment delay and determinants associated with delay in two Ugandan districts where tuberculosis infection control guidelines (TBIC) were implemented.
Design/methods: A facility based cross-sectional study was conducted in Mukono and Wakiso districts. Adult pulmonary TB patients within three months of initiation on treatment were included in the study. Data was collected on duration of TB symptoms and on health seeking behaviour. We defined patient delay as the interval between the onset of cough and the first visit to any health care provider. Health system delay was defined as the time interval between patient's first visit to any health care provider and the start of TB treatment. Total delay was defined as the sum of both delays. Data was analyzed using Stata 10. Medians and odds ratios for the three delays were determined. Level of significance was at 95% confidence interval.
Results: The median patient delay was 4 (IQR 2–8) weeks. The median reported health system delay was 10 (4–21) weeks. The median total delay was 15 (8–30) weeks. Factors associated with long patient delay were male sex ($P < 0.001$) and patient not knowing that TB is curable ($P = 0.02$). First visiting a non-public health facility ($P < 0.001$) and patients not knowing that TB is curable ($P = 0.02$) were independent predictors of health service delay. Longer total delay was associated with first visiting a non-public health facility ($P < 0.001$). Present specific findings to date.
Conclusion: This study reveals that there is still a significant TB treatment delay problem in Uganda. Most of the delay was caused by health system delay. There is need for TB advocacy in the community, training of health workers in TBIC and strengthening public-private partnership in TB control. Further research is needed to understand why the delays.

PC-705-02   Airborne infection control in India: a baseline assessment of 35 health care facilities in India

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Background: The transmission of tuberculosis (TB) in health care facilities (HCF) represents a major public health concern. In 2010, national airborne infection control (NAIC) guidelines for tuberculosis control in health care facilities were adopted in India. However, previous policies and practice were not assessed at baseline, nor was the feasibility and effectiveness of these recommended measures.
Objectives: To conduct systematic baseline assessments of AIC administrative, environmental and personal protective policies and practices within HCF in India and assess the level of NAIC implementation after one year.
Methods: AIC measures prior to NAIC implementation were assessed by a multi-agency, multidisciplinary panel of experts who performed site visits to a convenience sample of 35 HCF throughout 3 states in India. Standardized risk assessment included documentation of AIC practices, human resource capacity, administrative and environmental controls. At the conclusion of each assessment, facility-specific recommendations were provided to HCF's to improve policies and practice based on the NAIC guidelines. After one year, each facility was reassessed to determine the interval change in the adoption of NAIC recommendations.

Results: A total of 35 HCF were assessed, including 187 distinct clinical departments across 9 medical colleges/tertiary facilities, 11 district hospitals, 8 primary facilities, 10 antiretroviral therapy centres, and 4 specialized in drug-resistant TB departments. Upon initial assessment, overall infection control systems were found to be poorly developed, with airborne infection control (AIC) components largely absent. Administrative controls were not commonly practiced, and about half of departments needed minor renovation to achieve minimum environmental standards or decompression or segregation. One year after NAIC implementation there were significant improvements across all indicators for administrative and managerial AIC policies and practices (Table).

Table   Uptake of the administrative and managerial control measures: one-year follow-up results from AIC reporting system

Indicator of Administrative AIC Measures	Baseline (n/N)	One year (n/N*)	Percent Change
HCF with IC Committee in place	11/35	27/34	48%
IC committee meeting regularly	8/11	21/27	5%
Written IC plan available	5/35	19/34	42%
Written IC plan includes AIC	0/5	19/19	100%
IC focal point in place	7/35	30/34	68%
Health care worker surveillance (passive/active)	1/35	17/34	47%
Cough hygiene information	6/33	21/34	44%
Screening and fast-tracking#	0/33	20/32	63%
Separation of suspects#	0/33	18/32	56%

* 1/35 HCF did not report, # 2 Labs excluded

Discussion: Across a broad range of health facilities in 3 states, AIC practices at baseline were poorly implemented. A package of capacity building and systems development for HCF based on national guidelines substantially improved implementation of AIC policies and practice.

PC-706-02   The State Sanitary and Epidemiological Service in Ukraine: from focusing on punitive functions to facilitating infection control measures

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Background and challenges to implementation: Historically, two different agencies were responsible for overseeing a safe medical environment in Ukraine: the Sanitary and Epidemiological Service (SES) and the State Service on Socially Dangerous Diseases. The SES was confined to surveillance and punitive actions, rather than implementation of evidence-based tuberculosis infection control (TB IC) measures. Since 2012, the USAID Strengthening Tuberculosis Control in Ukraine Project has been working to address this challenge and improve IC practices by joining the efforts of both agencies.

Intervention: The USAID Strengthening Tuberculosis Control in Ukraine Project encouraged the Sanitary and Epidemiological Service to consider new practices that included technical assistance for TB control and building the capacity of TB facilities to manage SES activities. Over 1000 sanitary inspectors and epidemiologists participated in IC seminars, trainings, and meetings, which contributed to a joint action plan in enhancing the safety of the medical environment. The Project facilitated joint mentoring visits to TB facilities, during which the Project specialists and local sanitary inspectors promoted the WHO-recommended practices of patients' triage, spatial and safety planning of the medical premises to prevent infection, natural and mechanical ventilation, and use of personal protective equipment. To update sanitary inspectors' knowledge on the evidence-based IC approaches, the Project supported participation of the heads of regional state sanitary departments and ventilation engineers in trainings held at the Vladimir, Russia Training Center, the only center in Eastern Europe specializing in TB IC.

Results and lessons learnt: The SES took full ownership of its new role in TB IC and started to provide direct technical assistance to TB facilities. In particular, chief inspectors from the Odesa and Luhansk oblasts implemented managerial decisions to separate smear-positive patients, and assessed needs in improving personal protective equipment. New regulations on SES reform now incorporate the concepts of providing hands-on assistance (rather than on strictly pointing out shortcomings), thus ensuring sustainability of the practices initiated with project support.

Conclusions: Building genuine political commitment and partnership for TB control is critical in improving conventional IC practices and enhancing sustainable IC measures.

PC-707-02   Tuberculosis infection control practices in 19 facilities earmarked for decentralised MDR-TB care in South Africa

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Background: South Africa is facing a growing number of MDR/XDR-TB cases, with more than 5000 MDR-TB patients initiated on treatment every year. To improve treatment outcomes and accommodate the increasing number of MDR/XDR-TB cases, the National Department of Health has endorsed the Multi-Drug Resistant Tuberculosis: A Policy Framework on Decentralisation and Deinstitutionalisation for South Africa. The USAID TB Program funded Philanjalo to support 8 provinces in preparing for decentralisation.

Intervention: We conducted a rapid situational analysis of 19 hospitals and clinics spread through 8 provinces to determine facility readiness for the decentralisation of care. Part of the analysis centred on facility Infection Control practice. Our assessments were

carried out by a multidisciplinary team alongside facility and district health teams and all facilities were aware of the visits prior to engagement. Data were collected using standardised tools from the national policy guidelines.

Findings: Data were analysed using three themes: facility awareness, facility practice and the use of personal protective equipment. The analysis focused on interventions within the control of the facility management. Of the 19 facilities assessed, only 7 had a functioning Infection Control committee, while only 5 had an appointed TB focal person. For facility practice, in the main, ultraviolet germicidal (UV lights) had been installed, but were maintained or cleaned at only 4 of those facilities. Natural ventilation, through opening all available windows, was practiced in 11 facilities and fans or extractors at just 6. In all, just nine facilities provided adequate ventilation for TB patients and suspects. N95 respirators were observed being used by staff members in 11 of the facilities whilst surgical masks were provided to TB patients and suspects in 10.
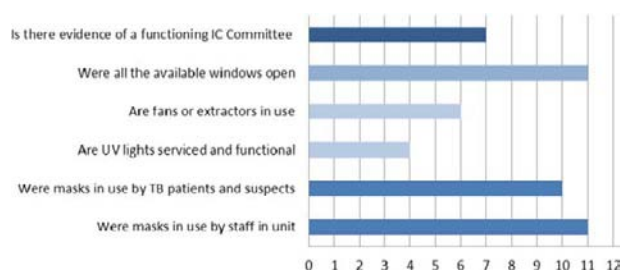
Figure   Infection control practice across 19 facilities.

Conclusion: With potentially infectious MDR-TB patients receiving care in decentralised facilities, district and facility managers need to strengthen TB infection control practice as there is a risk of nosocomial transmission of MDR-TB. This can be achieved through simple, low cost interventions and should be resolved prior to any scale up of decentralisation.

TUBERCULOSIS CONTROL PUBLIC POLICY

PC-768-02   Cost-effectiveness of two new shortened 4-month regimens for treatment of active tuberculosis in Brazil, Bangladesh, South Africa, and Tanzania

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Background: Existing TB drug regimens are long and complex, limiting our ability to adequately treat patients. Shortened regimens have the potential to improve patient outcomes and reduce patient and treatment delivery costs, improving the efficiency of National TB programmes. The REMoxTB trial finished recruitment in nine countries across Africa, Southeast Asia, India, and China. If proven effective, decision makers will demand information on cost and cost-effectiveness of a possible scale-up of the two 4-month, moxifloxacin-containing first-line treatment regimens being tested. We assessed patient and healthcare-related costs and cost-effectiveness of two new 4-month regimens for first-line treatment of TB compared to the current regimen (6-month).

Design/methods: We developed an individual-based simulation model to examine the short term costs and effects of the implementation of two shortened moxifloxacin-containing TB regimens, assuming equivalent efficacy with the 6 month regimen. The implementation of these new regimens is evaluated in four epidemiological contexts and healthcare systems of high TB burden countries: Brazil, Bangladesh, South Africa, and Tanzania. The economic evaluation takes both patient and healthcare system perspective and includes primary data collection in all settings. The comparative performance of the shortened regimens is measured as the incremental cost per disability-adjusted life year (DALY) averted, total health service and patient costs, as well as, cost per person cured or completing treatment. Monte Carlo simulations are used to sample individuals and parameters from their probability distributions repeatedly to generate uncertainty ranges around our estimates of incremental cost per DALY averted. The sensitivity of our results to model parameter value assumptions was assessed in one- and two-way sensitivity analyses. Following a complete analysis, a simplified web-based model will be produced to allow for analysis of additional country situations.

Results: Patient costs were reduced, but the cost-effectiveness (from a healthcare perspective) of REMoxTB in these two settings depended mainly on increased drug costs and decreased delivery costs. The comparative effectiveness of the shortened regimen is also affected by the assumptions on default rates and health outcomes for those individuals defaulting.

Conclusion: Cost effectiveness will be an important consideration in adoption decisions around new TB regiments.

PC-769-02   Medical and social characteristics of patients with pulmonary tuberculosis living in an ecologically unfavorable region

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Background: Tuberculosis is one of the most important unresolved social and medical-biological

problems of today. This disease causes damage not only to the health of the population, but also a serious social and economic cost to society due to disability and premature death, most of the working population.

Aim: To study a complex clinical-social and medical-psychological characteristics of patients with pulmonary tuberculosis living in ecologically unfavorable region.

Materials and methods: Based on the survey 205 patients with pulmonary tuberculosis living in ecologically unfavorable region, identified the major medical and social characteristics of these patients.

Results: Distribution on age and sex showed that majority of patients were male—122 (59.5%) and only 83 (40.5%) female. Most of patients were at working age: among male between 30–49 years 46.7% (Figure). Living conditions in 49 (55.1%) cases were satisfactorily and in 40 (44.9%) cases not satisfactorily, prevailed villagers at 150 (73.1%) cases. Among the working-age population proportion of unemployed patients was 114 (55.6%) patients, although patients with secondary education accounted for 185 (90.2%). Among the cases retired and disabled patients were 34 (16.6%) and 20 (9.8%) respectively. Twenty-nine (32.6%) patients were at risk, previously had contact with TB patients. Bad habits had noted at most patients: smoking in 35 (39.3%) cases, alcoholism in 18 (20.2%) cases, using of chewing tobacco—nasvay 17.8%. Patients with criminal record were 13 (14.6%). 59% of the patients had comorbidities and among them dominated gastrointestinal diseases. Among the clinical forms of tuberculosis dominated infiltrative TB in 95 (46.3%) and fibro-cavernous TB in 78 (38%) cases. 54.6% of patients before the disease did not have a proper idea about tuberculosis, in 31 (15.1%) patients due to the disease had changed the attitude of others.
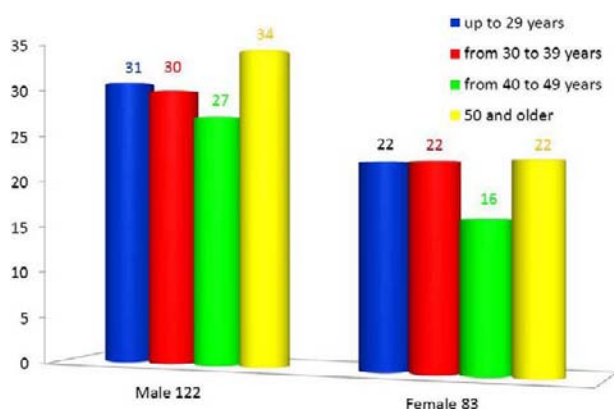
Figure Distribution of patients with pulmonary tuberculosis on age and sex.

Conclusion: The studies allowed for composing a medical-social portrait of the nowadays patient with

pulmonary tuberculosis living in ecologically unfavorable region—this is a man aged between 30 and 49 years (46.7%), a villager, not informed about TB, socially maladjusted, with secondary education, in third of cases who had contact with TB patients, overindulge with alcohol and smoking, with concomitant gastrointestinal diseases, tuberculosis process often had infiltrative and fibro-cavernous character.

PC-770-02   Effectiveness of local tuberculosis control programs in São Paulo, Brazil, 2010: an exploratory analysis

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Background: São Paulo State (SP) is responsible for 20% of the total burden of TB in Brazil. SP is divided into 645 cities and each one has their own local TB control program (TCP). Each local TCP has to deal with the diversity of their settings, leading to different performances. The aim of study was to assess effectiveness of TCP for TB treatment in São Paulo.

Methods: An exploratory study of three non-hierarqical clusters on TB operational indicators. Data were collected in January 2013 from the state TB surveillance system. Treatment outcome rates, proportion of cases reported by their city of residence, proportion of cases on DOT and proportion of contacts traced were calculated using as denominator the available data for each variable. Proportions of missing data on each indicator were also included at the cluster analysis. 466 cities of SP reported new TB cases in 2010, and 410 cities with valid data were included in this study. Multiple correspondence analysis was used to verify association of clusters with population size, TB-HIV co-infection, TB and AIDS incidence, and coverage of primary health care services (community health workers coverage and porpotion of family health units). These variables were categorized into three groups based on the 30th and the 70th percentiles of raw data. The Figure shows the factorial plan.

Results: Cluster 1 (poor performance) was formed by 26 (6.3%) cities and presented higher rates on unfavorable treatment outcomes. Low inhabitants number, countryside region, and low incidence of TB were associated with this cluster. Cluster 2 (good performance) was formed by 260 (63.4%) cities characterized by higher cure rate and higher proportion of cases on DOT. Bigger population size, high coverage of PHC services and high incidence of TB, but low TBHIV co-infection rate were associated with this cluster. The cluster 3 (poor data completeness) showed poor DOT, poor contact tracing and higher proportion of
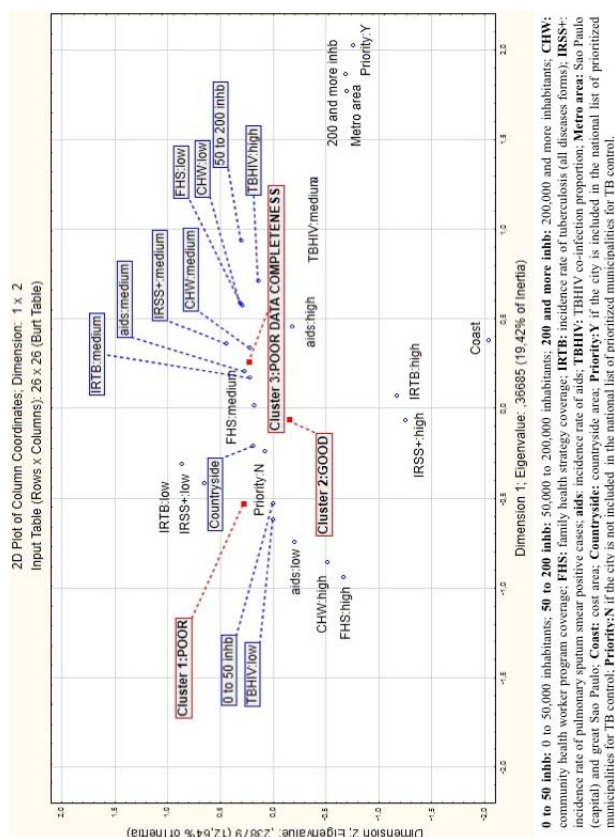
Figure Clusters centroids and factorial plan of variables and local TCP programs in São Paulo State, 2010.

missing data; 124 (30.2%) cities were included in it. Low to medium coverage of PHC services, medium incidence of TB and AIDS (but high TB-HIV co-infection) were associated with this cluster.

Conclusions: TCP in cities with more severe epidemiological status of TB and high coverage of PHC seem to be more effective on the disease control. Missing data may distort the effectiveness of cluster 3, since they have favorable treatment outcomes, but poor DOT coverage and contact tracing.

PC-771-02 Operational research capacity within Tuberculosis National Reference Laboratories of sub-Saharan African countries

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Background and challenges to implementation: Many African countries still struggle with diagnosis of MXDR-TB, laboratory networks are weak and poorly developed, and struggle with uptake of new tests. There has been insufficient operational research (OR) within the National Tuberculosis Reference Laboratories (NTRLs) to strengthen country-specific evidence base for tuberculosis (TB) diagnosis.

Intervention or response: The SAMRC SRL assessed the status of OR within the NRLs of 4 countries, and then had a capacity building and skills transfer activity to enable the countries to conduct research in their TB diagnostic laboratories. Briefing meetings with representatives from the NRLs and the National TB Programme (NTP) were held prior to the assessment activity to discuss TB control strategy in each country. A management requirement gap analysis and baseline assessment was conducted within each NRL using The International Union Against Tuberculosis and Lung Disease guide on OR at country level. In-country workshops were held to address key gaps in skill and knowledge, research questions related to diagnosis of TB-HIV were formulated and protocols were developed.

Results and lessons learnt: All the NRLs lacked experience on OR, showed interest to acquire capacity to perform OR, and identified partnerships with country-specific research focused institutions as key stakeholders. It is recognised that NRLs and other institutions need to balance research activities with other priority initiatives such as to monitor and support the laboratory network. Research agendas were developed, however financial and other incentives that are only available for research activities might lead to misplaced priorities and neglect of the daily support that laboratory networks provide for TB control. Our approach to include NTP managers in the project and other appropriate officials were crucial to identify priorities and gaps and to set realistic OR objectives. In-country workshops resulted in country-specific OR agendas and capacity building.

Conclusions and key recommendations: Sustainability of OR activities once the SRL project is completed and success of planned research will depend on high level political commitment from the NTP, support to laboratory staff and allocation of sufficient resources.

PC-772-02 Bacteriological diagnosis of tuberculosis in São Paulo, Brazil: assessment of data from reporting forms in 2010

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Background: Microscopy examination and culture are still today the essential elements for bacteriological diagnosis of TB. While Brazil is adopting GeneXpert as a new technology to diagnose the disease, more focus has been raised to investigate how the classical methods are used in the current practice. São Paulo state (SP) is responsible for more than 20% of total burden of TB in the country, being an important spot for case detection.

Aim: To analyze bacteriological diagnosis data in SP.
Methods: Data on 16 003 new cases reported in the electronic state surveillance system, in treatment at the year of 2010, were analyzed using descriptive statistics. Proportions of sputum smear (SS), sputum culture (SC); microscopy examination (M), culture (C) and histology exam (H) of others biological materials were calculated.
Results: 83.4% ($n = 13349$) presented pulmonary form and 16.5% ($n = 2640$) were classified as extrapulmonary. No information on form classification was observed in 0.08% ($n = 14$) of records. Among pulmonary cases, 68.3% ($n = 9125$) had a SS positive (SS+) result. Less than a half without SS+ had C performed (48.0%/2028 out of 4244), reaching a proportion of 28.0% (1184 out of 4224) cases with C positive (C+) for *Mycobacterium tuberculosis*. A total of 22.8% ($n = 3040$) pulmonary patients had no bacteriological diagnosis of TB, either for no request of exams or lack of register. Among extrapulmonary cases ($n = 2640$), data on exams of other biological materials show that only 8.6% ($n = 228$) had positive M (M+), and among without M+, only 17.2% ($n = 413$ out of 2412) did C, with a proportion of positivity in 7.6% (183 out of 2412) of cases. For the 2229 extrapulmonary cases left, H diagnosed 36.1% ($n = 804$) of cases. This led to more than a half (54.0%/$n = 1425$ out of 2640) without bacteriological diagnosis. High proportions of missing information and no request of exams was also identified, accounting for almost a half of observations exams (M, C, H) for the extrapulmonary cases (Figure).
Conclusions/recommendations: The reasons for a low bacteriological diagnosis in São Paulo state remains

Figure Proportions of cases according to result of exams recorded at electronic TB surveillance system, São Paulo, Brazil, 2010.

unclear. The results on extrapulmonary cases may reflect the difficulty of diagnosis in this disease form. One may point the lack of completeness in the recording and reporting system for exams results. More studies are needed to comprehend the diagnostic process and potential barriers for exams performing in our settings.

PC-773-02 Refinement of WHO policy guidance on Xpert® MTB/RIF

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Background: WHO first recommended the Xpert MTB/RIF assay in December 2010, with subsequent policy guidance and an accompanying practical Rapid implementation document issued in May 2011. Xpert MTB/RIF is recommended to be used as the initial diagnostic test in individuals suspected of having MDR-TB or HIV-associated TB (strong recommendation), and can be considered as a follow-on test to microscopy in settings where MDR-TB or HIV is of lesser concern, especially in further testing of smear-negative specimens (conditional recommendation acknowledging major resource implications). Due to the evidence available at the time, the recommendations are limited to sputum specimens only. The recommendations apply to children, but based on generalization of data.
Methods: Systematic reviews were commissioned by WHO in early 2013 to collect and analyze the most up-to-date body of evidence on 1) the diagnostic accuracy of Xpert MTB/RIF for the detection of pulmonary TB as an initial diagnostic test, as a follow-on to microscopy and in people living with HIV, and associated rifampicin resistance; 2) the diagnostic accuracy for the detection of extrapulmonary TB, stratified by biological material, and associated rifampicin resistance; 3) the diagnostic accuracy for detection of TB and associated rifampicin resistance in children; and 4) the affordability, cost-effectiveness and resource implications of diagnostic and screening algorithms for scaling-up use of Xpert MTB/RIF. A WHO Expert Group meeting will be convened in May 2013 to synthesize and evaluate the evidence using the GRADE method, and formulate draft recommendations.
Results: Draft recommendations developed by the Expert Group will be reviewed by the WHO Strategic and Technical Advisory Group for TB (STAG-TB) for potential endorsement in June 2013. Pending STAG-TB endorsement, refined WHO policy guidance and an associated manual describing practical and operational considerations will be issued in Fall 2013.
Conclusions: The periodic review of WHO policies on TB diagnostics using the most up-to-date body of
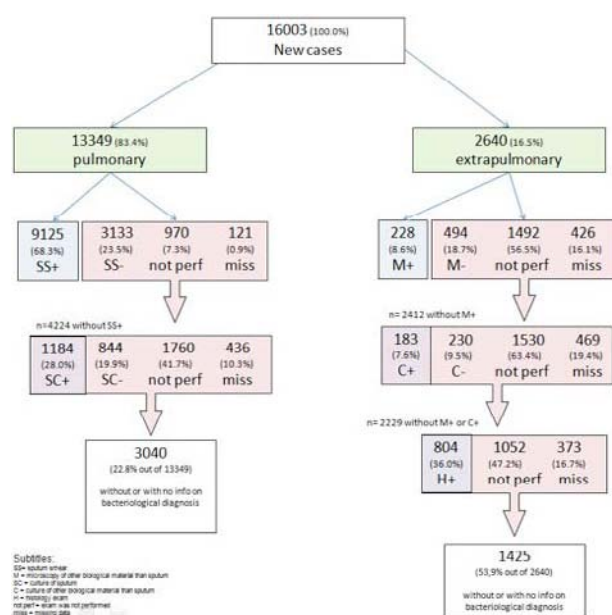
evidence allows for continuous refinement of policy guidance and optimal implementation of diagnostics in countries.

PC-774-02 Outcome favorable to adhesion in the prevention of *Mycobacterium tuberculosis* latent infection within a secondary reference clinic

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Background: The prevention of latent *Mycobacterium tuberculosis* infection (LTBI) using isoniazide decreases by 60% to 90% the risk for this disease. Such variation is due to duration and respective adhesion to treatment.

Intervention: This is a descriptive study analyzing information from medical records of individuals who developed LTBI prevention during the period between 2002 and 2011. The prevention was indicated when the tuberculin skin test (TST) was ⩾5 mm in cases of: individuals bearing HIV/AIDS; use of TNFα inhibitors; use of corticosteroids; fibrotic radiologic alterations suggestive of tuberculosis (TB) sequel; transplanted patients using immunosuppressive therapy and contacts of bacilliferous patients and, finally, TST ⩾ 10 mm, corresponding to silicosis, head and neck neoplasia, renal failure in dialysis treatment, Diabetes mellitus, low body weight, smoking habit, isolated calcification (without fibrosis) at radiograph, and contacts younger than 10 years, vaccinated with Bacillus Calmette Guérin (BCG) less than two years ago. Prevention was also indicated to individuals with tuberculinic conversion. All participant individuals were investigated for active TB before the indication of isoniazide for six months.

Results: In 148 individuals receiving isoniazide: 74/148 (50.0%) were contacts of bacilliferous patients; 6/148 (4.1%) were using corticosteroid; 6/148 (4.1%) had TB sequel without any previous treatment; 16/148 (10.8%) presented tuberculinic conversion; 11/148 (7.4%) were using anti-TNFα; 20/148 (13.5%) had renal failure in dialysis treatment; 2/148 (1.4%) presented isolated calcification at radiograph; and, 12/148 (8.1%) were patients in pre-transplantation phase, or already transplanted, using immunosuppressive agents. So far, one patient developed active TB and only one individual died for other causes. A proportion of 84.5% of patients adhered to 'treatment'. In 6/148 (4.1%) of patients, adverse reactions occurred and the medication was suspended.

Conclusions: The cases outcome in our study was considered favorable, as compared to high abandon rates observed in other Brazilian studies (21.9% and 37.1%). One of the factors correlated to good adhe-

sion to treatment, in this study, was the concern of involved professionals to assure complete understanding by patients, about the importance of medication for TB prevention.

PC-775-02 Pricing and availability of anti-tuberculosis drugs in Viet Nam

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Aims: Viet Nam is a high burden tuberculosis (TB) country; it also carries a high burden of multi-drug resistance. We undertook a survey of pricing and availability of anti-TB drugs to inform policy and regulation of TB drugs.

Methods: Check-lists were used to collect information on availability and sale prices of 27 anti-TB drugs in non-national TB control program (non-NTP) public and private pharmacies/outlets in 6 provinces. The outcome measure of the analysis is the product's availability and range of pricing by province.

Results: A total of 98 outlets were surveyed: 51 in the public sector (general hospitals and commune health posts) and 47 in the private sector (pharmacies and clinics). Access to medicines varied by province. Fluoroquinolones, ethambutol, streptomycin, pyrazinamide, rifampicin, and amikacin were widely available in both public and private outlets. Rifampicin 300 mg tablets were more easily found in the private sector than in the public sector. On the contrary, Paraaminosalicylic acid (PAS) 4 g granules and Capreomycin were not found in any outlets, and PAS 100 g tablets were only found in one outlet. Apart from free anti-TB drugs provided by the NTP, some survey medicines also are available for sale in most of the public outlets. In the private sector, 23/31 surveyed products were available vs. 13/31 in public outlets. The price of anti-TB drugs varied by name and brand. On average, in the private sector pricing for the lowest and highest cost generics were double and triple than pricing of the NTP acquisition cost for first line treatment, respectively. Noteworthy is that the cost

Table Proportion of private outlets with TB medications available

	BD	%	DN	%	HA	%	HC	%	HN	%	QN	%
Quinolones only	7	100	4	50	4	50	1	14	3	38	5	56
Quinolones plus rifampicin 300 mg	0	0	0	0	2	25	0	0	0	0	1	11
Quinolones plus other TB medications	0	0	4	50	2	25	6	86	5	63	3	33
Total private outlets	7	100	8	100	8	100	7	100	8	100	9	100

for a standard treatment for multi-drug resistant TB ranges from US$2600 to US$4000 while it was about US$2000 through the GDF procurement mechanism. **Conclusions:** Anti-TB drugs (first and second-line) are both available in private pharmacies, private clinics, and in some general hospitals. Recommendations were made to ensure that anti-TB drugs are sold with doctor's prescription only. Public-private mix approaches should be expanded and strengthened to ensure adherence to NTP treatment guidelines to prevent the further spread of drug resistance.

PC-776-02   Characterizing tuberculosis genotype clusters along the United States-Mexico border

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Background: In 2010, 60% of reported tuberculosis (TB) cases in the United States (US) were among foreign-born persons, with 21% among Mexico-born persons. Previous studies noted an association between US-Mexico border proximity and higher TB case rates. We examined the effects of county of origin and geographic proximity to the US-Mexico border at time of TB diagnosis on TB transmission, estimated using TB genotype clustering. **Design/methods:** We included cases and corresponding genotyping results reported in the U.S. during 2005–2010. The most likely cluster for each genotype was derived using purely spatial analysis and a discrete Poisson probability model (SaTScan). Cases were categorized as index cases, subsequent cases, or non-clustered cases, and by country of origin as Mexico-born, US-born, or foreign-born other than Mexico (FBO). Transmission index, defined as the number of subsequently clustered cases divided by the total number of index and non-clustered cases, was used to measure cluster growth. Median intervals between cluster members' case dates measured cluster growth rate. Differences between groups were compared using Kruskal-Wallis tests, and trends were analyzed using Cochran-Armitage tests. **Results:** Among 16 588 culture-positive genotyped TB cases, 831 index cases were identified. US-born index cases had the highest transmission index (0.19), followed by Mexico-born (0.13) and FBO (0.10) cases. Clusters with US-born index cases had the shortest median time between clustered cases (97 days; IQR 27–264), followed by FBO (109 days; IQR 31–300) and Mexico-born (138 days; IQR 34–384; $P < 0.05$). Clusters with US-born index cases were more heterogeneous closer to the border; the proportion of subsequent US-born cases declined from non-border states (87.6%) to non-border areas of border states (78.9%) to border areas (43.8%; $P < 0.05$). The decreased proportion of subsequent US-born cases was

accompanied by increased proportion of subsequent Mexico-born cases (3.5% in non-border states, 14.1% in non-border areas of border states, and 56.3% in border areas; $P < 0.05$). **Conclusion:** Clusters following US-born index cases grew larger and faster than clusters with Mexico-born or FBO index cases. In addition, clusters with US-born index cases commonly had Mexico-born cases subsequently, particularly in border areas. Prioritizing TB clusters with US-born index cases for investigation may help prevent subsequent cases among both US-born and Mexico-born persons.

PC-777-02   Anti-tuberculosis drug resistance in São Paulo State prisoners, 2012

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Introduction: Drug resistance to first-line TB schedule is a huge health issue. Awareness of the resistance profile allows that an adequate intervention be introduced in this population. **Objective:** To analyze the resistance found in the population with TB that was submitted to culture plus susceptibility testing (ST) in the Adolfo Lutz Institute (IAL) at the State of São Paulo. **Methods:** A database platform for culture and ST results consolidation was provided by Adolf Lutz Institute (IAL) to the Tuberculosis Division of the Epidemiology Surveillance Center Tuberculosis of São Paulo State, during the 01/01 to 31/12/2012 period, on a weekly basis. TB patients submitted to culture and susceptibility testing (ST) carried out by IAL were included in the study group and analyzed as to TB resistance. Among other categories such as HIV+, drop-outs, re-treatments and health workers were found. However, the main focus was directed to prisoners. **Results:** Of the 3964 patients submitted to ST, analysis revealed 538 individuals (13.5%) presenting some resistance. Also from the total, 896 were prisoners, with 73 (8.14%) showing some resistance distributed as follows: Eight (11%) were R+INH resistants; seven (9%) were poli-resistants (6 with streptomycin (S) + isoniazid (INH) resistance and one with S, INH, PZA simultaneous resistance). A variety of mono-resistances was detected in 58 prisoners (80%), and, most importantly, 31 (53.5%) of which were INH resistants. Of the remaining 3068 study patients, 460 (15%) presented various resistances, while INH mono-resistance was observed in 362 (11.8%) of the cases. **Conclusion:** This analysis, even when carried out on a limited secondary database, demonstrates the importance of having culture + ST being done, in order to know the resistance level in populations with higher risk of developing resistant tuberculosis. This

preliminary data indicates that the prison system should extend a more careful look on resistance search. A constant and careful surveillance may contribute to provide an earlier and effective intervention in resistant tuberculosis treatment thereby reducing resistance transmission.

PC-778-02   Optimizing allocation of rapid diagnostics: the case of Xpert® MTB/RIF in Uganda

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Background: The Xpert MTB/RIF (Xpert) device is being widely adopted by national health programs. In resource-constrained settings, data is needed to guide the allocation of Xpert devices within the health care system to optimize health outcomes.

Design/methods: We investigated the impact of various rollout strategies for Xpert in Uganda using a decision analytic model populated by operational data from the Uganda National TB control program, the National AIDS Control Program, and the Uganda National TB Reference Laboratory. We included health care sites processing at least two smear microscopy specimens daily. We simulated four strategies for device rollout, namely placement of devices in sites based on 1) health center level (sites ranked from highest to lowest, i.e., national referral to health center III), 2) smear volume (sites ranked from highest to lowest volume), 3) antiretroviral therapy (ART) volume (sites ranked from highest to lowest ART volume), and 4) external equality assessment (EQA) performance (sites ranked from worst to best performance). Outcomes included TB case detection rate and number of sites requiring access to the Xpert device.

Results: We included 139 sites that satisfied the criterion of daily smear load mentioned above. These sites contributed 98 000 TB suspects tested by smear in Uganda in 2011. In the absence of Xpert, case detection of TB was 71.8%. Placement of Xpert in sites by EQA performance resulted in superior case detection rates at all levels of rollout (Figure). The difference among strategies was greatest when Xpert was available for 70 000 TB suspects (13.2% additional cases diagnosed using EQA strategy, compared to 11% in the remaining three strategies). At this level the EQA strategy required placement of Xpert at 96 sites compared to 95 sites in the health center level strategy, 90 sites in the smear volume strategy and 112 sites in the ART volume strategy. Results
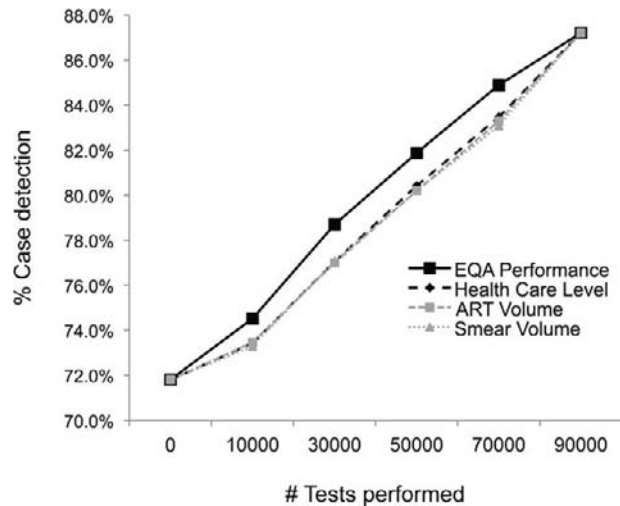
Figure TB case detection rate with increasing rollout of Xpert MTB/RIF, by placement strategy.

remained robust over variation in clinical algorithm (using Xpert in smear-negative suspects vs. replacing all smear microscopy), rates of loss to follow up during diagnosis period, and EQA accuracy.

Conclusion: In Uganda, placement of devices in sites with poor EQA performance yielded the highest case detection rate among all strategies with marginal difference in capital investment. These results represent a novel use of program level data to inform critical decisions surrounding the rollout of new technology.

PC-779-02   The validity of chest radiography for tuberculosis screening of undocumented migrants from the Horn of Africa

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Background: The number of undocumented migrant (UM) who are diagnosed with tuberculosis (TB) in Israel is steadily increasing. The 1999–2010 annual average TB-incidence among Israeli-born and UM was 0.86 and 27 per 100 000 population, respectively. Since 2006, >60 000 UM from the Horn of Africa (HoA) crossed the Egyptian-Israeli border illegally and were detained upon arrival. They were screened for TB while in prison by responding to health questionnaire and by chest X-ray (CXR).

This cross-sectional study aims to evaluate the validity of the interview and CXR in detecting TB among UM from HoA.

Design/methods: We analyzed a random sample of 1087 (20.4%) of all 5335 UM from HoA who were detained in 2009.

Results: TB screening in prison: Of 1087 UM, 62 (5.7%) had CXR demonstrating radiological findings suspected of TB. Of those, 11 were diagnosed with TB (10 had pulmonary-TB and one extra-pulmonary TB). TB point-prevalence among UM was 1000 cases per 100 000 UM. As no additional cases were diagnosed during the imprisonment of this cohort, CXRs' sensitivity, specificity and positive predictive value were 100%, 96.1%, 17.7%, respectively.

TB-patients were more likely to be males, who immigrated from HoA. They responded negatively to most of the items asked in the questionnaire. The detection of 11 TB-patients required 3,750€ to detect a single TB-patient, while the cost for treating one TB-patient in Israel is ~6000€.

TB cases in the community after release: During the years 2008–2010, 88 UM from HoA were diagnosed with TB in the community after being discharged from detention where they were screened for TB. As the community of UM from HoA was estimated ~30 000 UM in 2010, the average annual incidence was 132 cases for 100 000 UM. We traced 56 (63.6%) of the CXR which were performed during incarceration of these 88 UM who were diagnosed in the community. Of those, 41 (73.2%) were unremarkable, 8 (14.2%) demonstrated radiological findings suspected of TB and 7 (12.5%) had non-TB related abnormalities.

Conclusion: CXR-based screening is a valid and cost-saving tool for screening UM from HoA for TB, while the interview has significant limitations. UM should be aware that TB-treatment is free and uncoupled with the legality of their stay, and should be encouraged to seek for to medical care in case they develop TB symptoms.

TUBERCULOSIS SURVEILLANCE, INCLUDING BOVINE TUBERCULOSIS

PC-708-02 Falling through the cracks: challenges of severe childhood tuberculosis reporting in Cape Town, South Africa

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Background: Although the tuberculosis (TB) burden is decreasing globally and locally, the extent of childhood TB remains unclear. WHO released estimated numbers of childhood TB for the first time in 2012. Though data on childhood TB in Cape Town is reflected in routine electronic reports (ETR.net), it is not a focus in routine reporting. The completeness of reporting is also unknown.

Methods: An analysis of routine data from ETR.net was undertaken for the City of Cape Town for 2005–2011, exploring trends in total reported TB cases and in children <5 years. Data in children <5 years was reported and compared total TB cases to smear positive cases. Data of children <5 years diagnosed with severe TB was collected at 2 tertiary and 5 secondary hospitals and compared with data recorded in ETR.net for 2010–11 to assess the completeness of reporting.

Results: ETR.net data shows a declining trend for reported total TB incidence per 100 000 population from 2005–2011 (Table). The trend in reported cases in the <5 year category per 100 000 population however showed an increase to 2010. When evaluated as a percentage of infectious cases, the percentage of cases in children <5 years has also increased. 251 children <5 years were identified at hospitals with severe TB (TB meningitis 60%, miliary TB 11%, disseminated TB 27% and smear-positive TB 2% in children). Of these, only 19 were registered on ETR. net (7.6%).

Table TB trends in Cape Town, 2005–2011

	2005	2008	2010	2011
Total TB cases reported	27 124	30 756	31 496	29 830
TB incidence rate/ 100 000 population	864	819	806	758
TB cases <5 years	2 278	2 952	3 034	2 818
TB incidence rate <5 years of age/100 000 population	760	878	861	781
% TB cases <5 years of age/ total reported TB cases	8.4%	9.6%	9.6%	9.4%
Total smear positive TB cases	14 827	13 803	12 699	12 136
% TB cases <5 years of age/ total smear positive cases	15.4%	21.4%	23.9%	23.2%

Conclusion: Despite a declining overall trend in TB incidence, the trend in children < 5 years has been on the increase to 2010. In addition to this, childhood TB is under-reported with only a small fraction (7.6%) of severe childhood TB cases reported in ETR.net. Both suggest that the TB Control Programme needs to place an additional focus on childhood TB. Establishing appropriate routine indicators to track childhood TB would assist in this. Under-reporting of childhood TB cases in Cape Town could be addressed through establishing routine TB reporting at secondary and tertiary levels of care. Further research is being undertaken to identify whether children diagnosed with severe TB in hospitals access primary health care for routine care and whether there are missed opportunities for early TB screening at this level.

PC-709-02   Trend in the implementation of HIV services among tuberculosis patients in Tanzania: retrospective analysis of program data

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Background: Tuberculosis and HIV are diseases of public health concern in Tanzania. Tanzania ranks number 15 among the 22 TB high burden countries and has HIV prevalence of 5.7% in the general population. HIV is the driver of the TB burden and is attributed to the five-fold increase of notified TB cases in the last four decades. National TB and Leprosy Programme (NTLP) has reported TB-HIV co-infection among smear positive TB cases of 31% in the year 2011. Tanzania started implementation of collaborative TB-HIV activities from the year 2007. The aim was to track the progress so far made by Tanzania in the reducing the burden of HIV among TB patients.

Objective: To describe the trend of implementation of HIV services among TB patients in Tanzania.

Design/methods: We retrospectively analyzed the NTLP yearly reports of the routinely collected data from 2007 to 2011. We calculate the proportion of cases per year in each of the HIV services offered and performed trend analyisis using Stata.

Results: Between 2007 and 2011 there were 315 014 of notified TB cases. Of the notified cases, 247 430 (79%) were tested for HIV and of those tested 97 897 (40%) were co-infected with HIV and 73 871 (75%) were later on registered to an HIV clinic. Only 32 534 (33%) and 85 476 (87%) of the TB-HIV co-infected patients were started on Anti-Retroviral Therapy (ART) and Cotrimoxazole Preventive Therapy (CPT) respectively. The progress of implementation of HIV services over the study period showed; HIV testing among TB patients increased from 50% in 2007 to 87% in 2011. In the same period, TB-HIV co-infection dropped from 47% to 38%. TB-HIV co-infected
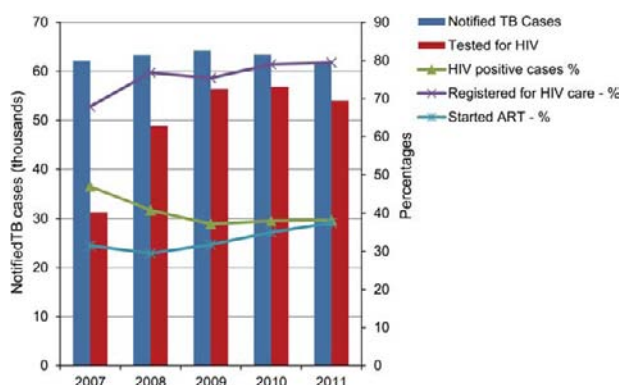
Figure   HIV services in TB patients from 2007 to 2011.

patients registered to HIV care and treatment clinics increased from 68% to 79%, CPT coverage increased from 72% to 95% and ART uptake increased from 32% to 38%. Analysis of trends for HIV testing, registration to HIV clinics, starting ART and CPT showed a significant change of proportions, P values < 0.001, during the study period.

Conclusion: Tanzania has made significant achievements in provision of HIV services to TB patients over the last five years. There is a steady positive increase of proportion of cases tested for HIV, registering co-infected patients to HIV care and treatment clinics and starting them on CPT and ART to patients TB-HIV co-infected patients. However, uptake of ART is comparatively low with minimal increase. Further research is needed to identify the challenges of ART uptake and solutions to increase ART uptake for TB-HIV co-infected patients.

PC-710-02   National Tuberculosis Prevalence Survey in lower south-east Thailand, 2012

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Background and challenges to implementation: Tuberculosis (TB) remains a significant public health problem in Thailand. The pilot of national tuberculosis prevalence survey in 2006, of 64 670 eligible inhabitants, about 1.44% (519/35 965) had symptom and chest X-ray abnormality suggestive TB and 0.11% (100/519) had bacteriologically confirmed TB (smear and/or culture positive). This survey was limited by low participation rate of 55.6% (35 965/ 64 670). A new prevalence survey is necessary to determine magnitude of TB problem and assess the impact of TB control program on the epidemiology of TB.

Intervention or response: From February to June 2012, a cross-sectional survey with multistage cluster sampling, stratified by urban and rural areas, was done in Ubonratchathani and Nakhonphanom provinces. Inhabitants aged ≥15 years, who have lived in 9 communities of those two provinces for at least 14 days, were invited to undergo TB symptom screening and chest X-ray examination. Participants with symptom and/or chest X-ray abnormalities consistent with TB were asked to submit two sputum specimens for smear examination, culture and identification.

Results and lessons learnt: Of 1 353 507 of total population in the 9 communities, 8630 (0.6%) were approached on pre-survey day, 8425 were eligible for enrollment. Of 7312 (86.8%) accepted enrollment inhabitants, 7188 (98.3%) were screened by both questionnaire and chest radiograph. Of 246 (3.4%) were positive symptoms only, 286 (4%) were abnormal chest radiographs only, 69 (0.96%) were positive

symptoms and abnormal chest radiographs. Sputum tests were done for 760 participants, of whom 16 (2.0%) were smear-positive, 35 (4.1%) were culture-confirmed for *Mycobacterium tuberculosis* complex, and 11 (1.3%) were non-tuberculosis mycobacteria (NTM). The estimated prevalence of suspected TB and laboratory confirmed TB was 478/ 100 000 population. Prevalence was 1.7 times as high in men as in women, increased with age (median age = 63) and was higher in urban than in rural areas (617/461 per 100 000).

Conclusions and key recommendations: Prevalence surveys is important role in evaluating TB control activities. The results of this prevalence survey showed a prevalence rate of TB in lower southeast was 2.2 times (405/182) higher than the previously WHO estimated for Thailand in 2010. This indicates that current TB control programs in this area need to be re-evaluated and improved.

PC-711-02   Comparison of mycobacteria recovery rates from slaughter cattle in Cameroon

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Background: The epidemiology of Mycobacterium in cattle in sub-Saharan Africa (SSA) is still poorly understood. Traditional recovery of Mycobacterium from animals has relied on culturing on solid media. However, in recent years access to liquid culture technology (BACTEC 960 MGIT) has become available mainly in human diagnostic laboratories in SSA, significantly reducing time to detection. This paper reports the first comparison of the MGIT (Bactec 960) system and solid culture for cattle tuberculosis in Africa.

Design/methods: A total of 1129 adult cattle slaughtered between April and June 2012 were examined for evidence of tuberculosis at routine meat inspection. Sixty-nine TB lesion samples and 94 non-visible lesion lymph node samples were collected from 136 animals (42 with lesions and 94 without) and transported to the TBRL in Bamenda, Cameroon for processing. A direct smear was made and stained with phenolyted Auramine O stain for fluorescent microscopy detection of AFB before the samples were processed and inoculated on the automated MGIT BACTEC 960 system and Löwenstein-Jensen slants supplemented with glycerol and pyruvate for up to 84 days. Positive growths were screen with TB MPT 64 Ag kit (SD Bioline) for differentiation of NTM from MTC and identified using a line probe assay (Genotype MTBC and Genotype CM/AS) and by genus and RD deletion typing.

Results: Based on the presence of visible lesion a TB prevalence of 3.7% (42/1129) was recorded. We had a recovery rate of 82.6% (57/69) from the lesion sample with the majority of the isolates typed as *M. bovis* (93%, 53/57). There was a greater recovery of NTM by the MGIT system than the solid system from the non-lesion samples with a lone *M. tuberculosis* species isolated only on the MGIT system. Overall 21.3% of the non-lesion samples yielded a positive culture with NTMs being the most recovered (16/18) from the liquid culture. The time to detection of the M. bovis isolates was faster in the MGIT system (SD 10.63 ± 4.15 days) compared to the solid system (SD 22.7 ± 9.44 days). There was a perfect agreement between the MPT 64 test kit and the Hain Line probe assay in differentiating the tuberculous mycobacteria from the non-tuberculous mycobacteria.

Conclusion: The MGIT system can play a key role for the early recovery of mycobacteria from cattle tissues, reducing average recovery by ~12 days. It has the additional advantage that it also greatly enhances recovery of NTMs.

PC-712-02   Feasibility of rapid implementation of case based web application for improving tuberculosis surveillance in India

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Background: From the beginning, India's Revised National Tuberculosis Control Program (RNTCP) used Epi-info based software for reporting. Initially DOS based software was being used for reporting TB unit-wise aggregated information by districts for upward submission to provincial and national level. In 2008, windows based software was launched. However, digitization of information continued to be in aggregated form and report submission being quarterly basis. There was delay of more than 3 months in information usages which did not help much in decision support for individual case management and lead to loss of detailed case wise information.

Intervention: We planned an intervention in April 2012 to develop and test feasibility for rapid implementation case based web application. Software requirement was stated with system architecture based on existing paper based recording and reporting system to design an online software named Nikshay meaning TB Control in Sanskrit. Testing of software was done rapidly by checking with real information on pilot basis. Login IDs and passwords were created for 2 national level, 35 provincial level, 680 distract level and 2800 Tuberculosis Unit level users. 33 448 Health facilities were mapped throughout the

country. User manuals were developed and master trainers trained at national level and software was launched in May 2012. Rapid training cascade was completed in training of provincial level (50), district level (668) and block level (~8000) data entry operators using training videos in English and Hindi, user manual and demonstrations. All health officers and TB officers were sensitized by July 2013.

Results & lessons learnt: Existing infrastructure like computer and internet at district and block level in general health system was used for data entry at block level. Trained data entry operators started entering TB patient wise detailed information in the online software and progress was monitored by districts, provincial and national level. Real-time data entry of TB patients was achieved within 6 months of implementation of 0.12 million cases per month with rapid step-wise increase after interventions of using training videos in English and Hindi, daily SMS to program officers, advocacy with administrators and auto-generation of periodic reports.
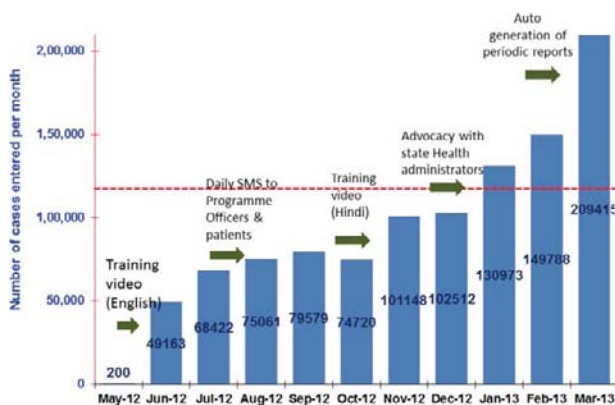
Figure Progress in data entry in case based web applicaton (Nikshay) under Revised National Tuberculosis Control Programme in India.

Conclusion: It is feasible to rapidly develop and implement case based web software system in TB program if the Information Technology is used optimally.

PC-713-02 Rwanda National Tuberculosis Prevalence Survey

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Background: Rwanda conducted its first national TB prevalence survey to estimate the prevalence of bacteriologically confirmed pulmonary TB in Rwanda, describe health seeking behavior and investigate validity of different diagnostic algorithms and risk factors associated with the occurrence of TB.

Methods: The survey was designed following the international guidelines for conduct of TB prevalence surveys. Each eligible subject underwent screening by interviews and chest radiography. Those screening clinically and/or radiologically positive provided two sputum samples, which were examined both in the field by microscopy and at the National Referral Laboratory by microscopy and culture. Participants eligible for sputum examination were also offered HIV testing.

Results: Data were collected in 73 clusters all over the country. A total of 43 126 people were screened for TB, participation rate was very high at 95%. A total of 4709 participants were eligible for sputum examination with 4638 participants submitting samples. Less than 50 TB cases where detected, much lower than expected with 30% of cases being MOTT. HIV testing was readily accepted and 74% of observed HIV positive participants already knew their status.

Conclusion: The national burden of TB is lower than previously estimated. The survey will draw important lessons for the national TB program as input for the new strategic plan.

PC-714-02 Composite Indicator: new tool for monitoring Revised National Tuberculosis Control Programme performance

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Background: The RNTCP uses international benchmarks of 70% case detection rate (CDR) and 85% treatment success rate (TSR) among new smear-positive tuberculosis cases for assessing program performance. Using CDR and TSR emphasizes outcomes; focusing on quantitative benchmarks figuratively with variable disregard to developing systems to monitor appropriate programme practice to achieve a minimum standard of TB care services. Case detection is widely recognized as a highly problematic indicator, mainly because of the uncertainty around TB incidence.

Intervention: Consequently, and in an attempt to improve the quality of TB diagnosis and treatment services (i.e., universal access), the RNTCP developed a novel composite indicator tool following a logical framework pathway. The structure was designed to move beyond narrow-focused outcome indicators, such as case detection, and to encourage a more broad-based analysis of programme implementation. Constituent indicators of the composite score were derived from routinely monitored information,

spanning input, process, output and outcome indicators across various programmatic thematic categories of RNTCP. Specific indicators focused on human resource, financial management, epidemiology, quality of services, drug procurement and distribution, and programme logistic were included.These thematic categories were assigned weights relevant to programme implementation based on a panel of expert's opinion and experience. A standard grading scale was developed, taking into account both current performance and trends of prior reporting periods, to develop a composite score. An automated score at the district, state, and national level can be generated via the RNTCP reporting system, Epi-Centre, using routinely collected aggregated quarterly reports.

Results and lessons learnt: Early results have demonstrated the difference in the quality of the meetings held at national and state level. The reviews are more focussed on processes than the outputs (as in the past) and thus are guiding the programme towards robust servies in place at all levels.

Conclusions and key recommendations: The composite indicators seem to be an effective programme management and monitoring tool to gauge performance. The holistic design brings an incisive insight into programme management through the identification of specific programmatic constraints leading to targeted interventions for improved performance more objectively.

PC-715-02   A baseline survey of the prevalence of pulmonary tuberculosis in a tribal population in central India

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Background: Tuberculosis is a major public health problem in India. However, the information on tuberculosis situation from tribal population in the country is scanty. The present study provides the base line prevalence of pulmonary tuberculosis (PTB) in the tribal population of Jabalpur district in the central Indian state of Madhya Pradesh after DOTS implementation.

Design/methods: A community based cross-sectional tuberculosis disease prevalence survey was undertaken among adults aged 15 years and above in the tribal population of Kundam taluq in Jabalpur district, Madhya Pradesh—a predominantly tribal taluq with ≈70% tribal population—in Jabalpur district, Madhya Pradesh. A random sample of villages predominated by tribal populations was selected from the taluq. All eligible individuals were questioned for chest symptoms suggestive of TB disease. Two sputum samples were collected from all eligible individuals and were examined by Ziehl-Neelsen smear microscopy and solid media culture methods.

Results: Of the 4079 individuals eligible for screening, 3903 (95.7%) were screened for symptoms. The overall proportion of symptomatic individuals was 11.8%. Overall prevalence (culture and/or smear positive) of PTB was 589.3 (95%CI 349.3–829.3) per 100 000 population. The prevalence increased with age and was significantly higher among males (922.4/100 000; 95%CI 486.4–1358.4) as compared to females (291.3/100 000; 95%CI 58.3–524.3; $P <$ 0.001).

Conclusion: The findings suggest that PTB is a major public health problem amongst the tribal population of Jabalpurdistrict in the central Indian state of Madhya Pradesh. There is a need to maintain and further strengthen TB control measures on a sustained and long term basis in the area.

PC-716-02   The epidemiology of *Mycobacterium* species in the northwest Region of Cameroon

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Background: The epidemiology of bovine tuberculosis is still poorly understood in sub-Saharan Africa where the prevalence of different species in livestock populations is largely unknown and the performance of diagnostic tests for surveillance is unclear. This paper describes the prevalence of Mycobacterium species recovered from slaughtered cattle in NW Cameroon in 2012, their spatial distribution and association of lesions and types with bovigam positivity and a cross-sectional study of herds in the same region. This forms part of a larger study across several regions of Cameroon.

Design/methods: 1129 cattle slaughtered at Bamenda abattoir in NW Cameroon were examined for lesions between Feb and April 2012. Up to 3 lesioned LNs per animal were collected plus a random sample of non-lesioned LNs and submitted for culture by MGIT, LJ-pyruvate and LJ-glycerol. A population based cross-sectional study was also carried out in the same region for comparison with the abattoir results and to understand the force of infection, the spatial distribution and performance of the bovigam and TB-Ab ELISAs. The spatial distribution of positive herds, age stratified prevalences and provisional risk factor analysis for positivity will be presented.

Results: 45 animals (~4%) had visible lesions at slaughter in at least 1 lymph node. In addition plasma samples were collected and tested using the bovigam (Prionics) and the TB-Ab ELISA (IDEXX). The results of comparisons between bovigam status, antibody status and culture results will be presented. Provisional analysis suggests some clustering of infected cattle in certain sud-Divisions with the majority of isolates being *M. bovis* though 1 *M. tuberculosis* and

a number of NTMs have also been isolated including *M. phlei*, *M. gordonae* and *M. fortuitum*. 50 herds and 15 cattle per herd have been screened for evidence of TB in a population based sample of herds from the NW region of Cameroon. Age stratified prevalence and spatial distribution will be presented.

Conclusion: Analyses of these data are ongoing and this work forms part of a larger study across several regions of Cameroon including a parallel human study of TB across the same region of the NW of Cameroon. Provisional analysis suggests bidirectional transmission of tuberculosis from cattle to people and visa versa in this region.

PC-717-02   Establishing surveillance of tuberculosis from routine laboratory data in South Africa

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Background: South Africa has the third highest burden of TB in the world, but until recently did not have a surveillance system that produces the information it needs to manage this epidemic. The National Health Laboratory Service (NHLS) provides diagnostic services to over 80% of the population through a network of laboratories and collates test results into an almost real time Corporate Data Warehouse (CDW). We undertook a major project to enable the utility of CDW for public health surveillance for TB.

Design/methods: We extracted individual TB test data from the CDW for 2004 to 2012. The data was recoded to harmonise the variables collected via three Laboratory Information Management systems into single variables, and merged into a single SQL database. The second step involved a 'cleaning' process for demographic data, including the removal of common salutations, harmonization of abbreviations and removal of all non alpha-numeric characters. We used a series of record-linking processes to link multiple specimen records to an individual patient in two phases; firstly an 'exact' linking process for direct matches and secondly a linking process based on probabilistic matching. The linked data with unique case IDs assigned for the same individuals was then linked to results data (using specimen numbers). The full dataset was reshaped and results aggregated so that all records identified to belong to an individual were converted to one record, retaining the first positive result.

Results: For the first time, we have produced a detailed analysis of TB in South Africa between 2004

and 2012, describing the burden of the disease, prevalence trends, and distribution by demographic characteristics. This analysis will be updated quarterly and made available to the National Department of Health and other stakeholders. A subset of aggregated data will be made available to the public via the web.

Conclusion: While databases established for other objectives can be used for public health surveillance, they require extensive work to ensure that the data collected is cleaned and appropriately analysed for public health surveillance. The CDW has tremendous potential for providing extremely useful information to the TB programme in South Africa but requires significant resources to develop this further to serve surveillance purposes on an ongoing basis. In future, TB data can be linked to HIV data to produce an even greater surveillance resource for the country.

PC-718-02   Inventory study involving three data sources: revised tuberculosis incidence in Pakistan

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Background: The National Tuberculosis (TB) Control Program (NTP) Pakistan has officially achieved a TB case detection rate of 64% in 2011 with an estimated incidence rate of 230 per 100 000, but is likely to be missing an unknown number of patients, particularly in the private sector. The main objective of the study was to estimate TB incidence and TB notification in Pakistan in 2012.

Design/methods: The inventory study involving log linear modeling and using three data sources was conducted to find out missing cases in Pakistan particularly in non NTP private and public sector. All providers in public and private sector in 12 randomly selected districts of Pakistan were included. A surveillance system was established among all eligible non-NTP providers in selected districts from January to March 2012.

Results: Record linkage and capture-recapture analysis was conducted. A total of 8346 TB cases were identified after record linkage, with 6061 registered with the NTP. The estimated number of unobserved TB cases was 10 030 (95%CI 7800–12 910), implying the proportion of notified cases was 32% (95%CI 17–49). The calculated annual incidence was 878 000 cases (95%CI 573 000–1 675 000) corresponding to a rate of 497 (95%CI 324–948) per 100 000 annually in the population.

Conclusion: The study estimated a low proportion of cases notified to NTP, with incidence rates higher than official estimates. There is a need to strengthen TB surveillance to reduce under-reporting. The involvement of all health care providers with NTP is likely to improve future completeness of routine TB surveillance notification.

PC-719-02   Assessing the trend of the tuberculosis epidemic in South Africa, 2004–2012. Are we winning the battle?

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Background: World Health Organization (WHO) best estimates put the current annual burden of TB in South Africa at about 400 000 cases, the third highest in the world. Yet, recent surveillance trend data for TB in South Africa has not been analysed on a nationwide basis. In the context of one of the worst co-epidemics with HIV, and the massive scale up of the antiretroviral treatment (ART) programme, it is of importance to understand the trends in the prevalence of TB over the last few years and how both the HIV prevalence and the ART programme have affected the TB epidemic in South Africa.
Design/methods: Specimen-based laboratory testing data on TB in South Africa, from 2004–2012, was de-duplicated and reduced to single-row-per-patient format. The data was aggregated to province and district levels and analysed. We undertook a descriptive analysis of demographical data to characterize the tuberculosis epidemic in South Africa and a time-series analysis for trends. Geospatial analysis was done using ArcGIS software.
Results: For the first time, we have produced a detailed analysis of TB epidemiology in South Africa between 2004 and 2012, describing the burden of susceptible and multi-drug resistant TB (MDR-TB), trends in its prevalence, and the distribution by demographical characteristics and geography. Our data shows that the epidemic appears to have peaked in 2009 and is now declining. The peak correlates in time with the scale up of the ART programme in South Africa. MDR-TB has continued to increase at a steady pace over the years. Detailed results will be presented at the conference.
Conclusion: After several years of increasing prevalence of TB in South Africa, we are beginning to see a decline since 2009, despite the nationwide roll-out of the highly sensitive Xpert MTB/RIF testing in SA. While the HIV co-epidemic no doubt drove the increasing prevalence of TB, the scale up of the ARV treatment programme is the most likely explanation for the decline. During this period, the TB control programme also introduced intensified case finding activities for TB, which would also have increased case identification and control. Our findings show important public health benefits of the investments in patient treatment and disease control programmes in South Africa.

PC-720-02   Prevalence of smear positive pulmonary tuberculosis among health facility patients and their escorts in Bahir Dar, Ethiopia

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Background: Tuberculosis (TB) is one of the leading causes of illness and death in Ethiopia causing up to 18/100 000 deaths annually. In response, the Ministry of Health is implementing routine TB screening of all health service seekers, irrespective of their chief complaints, to actively identify and treat patients, particularly, with infectious forms of TB. However the effectiveness of this approach has yet to be evaluated. From December 2012 to February 2013, the USAID-funded project, Help Ethiopia Address Low TB (HEAL), led by Management Sciences for Health (MSH), conducted a study to evaluate the efficacy of this screening strategy.
Design/methods: In this health facility-based, cross-sectional study, trained nurses conducted exit interview to patients and their escorts over the age of 13 years for TB symptoms using a structured questionnaires. TB suspects recruited gave a sputum for acid-fast bacilli (AFB) microscopy as per the national guideline. Patients who were diagnosed with smear positive pulmonary TB were sent to DOTs clinics for treatment while others were referred to corresponding OPDs for further workup. TB suspects recruitment and patient diagnoses information was entered in to Epi-info version 3.5.1 and then SPSS version 20 for analysis.
Results: Out of 27 931 health facility visitors 1103 (3.9%) were found out to be suspects and out of which only 11 became smear positive pulmonary TB cases. More males than females were identified as suspects (AOR 1.5, 95%CI 1.27–1.76) and more rural than urban residents (COR 1.53, 95%CI 1.32–1.77). There was a lower proportion of TB suspects among individuals who came to the health facilities seeking heath care (AOR 0.75, 95%CI 0.64–0.89), as compared to their escorts. The prevalence of newly diagnosed smear positive pulmonary TB among all visitors was 40/100 000 and the prevalence among those seeking health services was 79/100 000. Among the 11 newly diagnosed smear positive pulmonary TB cases, 2 (18.2%) had no complaints but captured by enquiring of TB signs and symptoms (see table for the detail).
Conclusion: Although more suspects were identified among escorts, but there is no single case of TB. Therefore we recommend that routine screening focus only health service seekers not escorts.

PC-721-02 Heterogeneous tuberculosis case notification rate in Ethiopia. What are the implications for tuberculosis control?

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Background: Ethiopia's TB burden is one of the highest in the world. A 2011 national prevalence survey showed that prevalence of smear positive TB was 108/100 000 population. This estimate had shown a greater reduction in prevalence from previous estimates. However, the survey is short of sufficient data to estimate the prevalence at regional and subregional level. Unavailability of accurate prevalence data is likely to result in inefficiencies and ineffectiveness of TB control program. Prevalence survey are expensive endeavours and may not be feasible to be used at larger scale. The purpose of this analysis is to show the variation in SM +ve case notification rate across district using existing routine health information system and show significance of estimation of burden of disease.

Design/methods: Districts served by the HEAL TB project routinely collect data on smear positive case notification. As part regular monitoring and evaluation effort, the HEAL TB project team compiled one year TB data and population estimates from 87 districts in the Amhara region. The team entered this information into a database prepared for this purpose and CNR for smear postive cases was calculated. The data was exported to ArchGIS and finally the mapping was done using the software. Districts were put into 8 groups based on their case notification rates (see Figure).

Results: TB case notification rates were heterogeneous among districts in five zones of the Amhara region. Some districts like West Armacheho (321/

Figure Smear positive TB case notification rates in districts of the Amhara region in Ethiopia.

100000) and Gindweha (621/100000) had higher case notification rates than other districts. High case notification rates were found in urban districts (see Figure).

Conclusion: Routinely collected data shows that TB case notification rates are heterogeneous across Ethiopia's districts. These differences could be explained by variable efforts in case detection, different degrees of disease prevalence, or other population dynamics. Understanding the burden of TB at the district level is necessary for effective TB prevention and control. Case notification rate (CNR) and other facility-based data should be used to determine relatively more accurate estimates of TB prevalence at the district level. Evidence generated at district level should be used to inform the design and implementation of a cost effective intervention package for TB control at all levels of the health system.

PC-722-02 Incidence of childhood tuberculosis in Manhiça, Mozambique

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Background: Mozambique is one of the 22 high burden tuberculosis (TB) countries and one of the few ones whose TB figures have not improved in recent years. It has one of the lowest case detection rates in Africa and there is a lack of epidemiological information in the country. Children contribute to 15–20% of the overall disease burden, and yet the prevention, diagnosis and treatment of TB among children have been relatively neglected for many years. The objective of the study was to determine the minimum incidence rate (IR) of TB among children under 3 years in Manhiça District, a rural area in Southern Mozambique.

Design/methods: Participants were recruited through passive case detection at the district hospital and peripheral health centers. Improved case detection was obtained through tracing of contacts of adult smear positive pulmonary TB cases. Suspect cases were studied through chest X-ray, aHIV and tuberculin skin testing as well as gastric aspirate and induced sputum sampling. All samples were processed for smear testing using LED microscopy, liquid and solid culture, and mycobacterial molecular identification by Geno-Type® Mycobacterium CM. Patients were followed up for a 7 month period and for study purposes, cases were classified as confirmed, probable, possible or alternate diagnosis.

Results: Out of the 92 000 inhabitants belonging to the study area, 10 120 (11%) were under 3 years of age
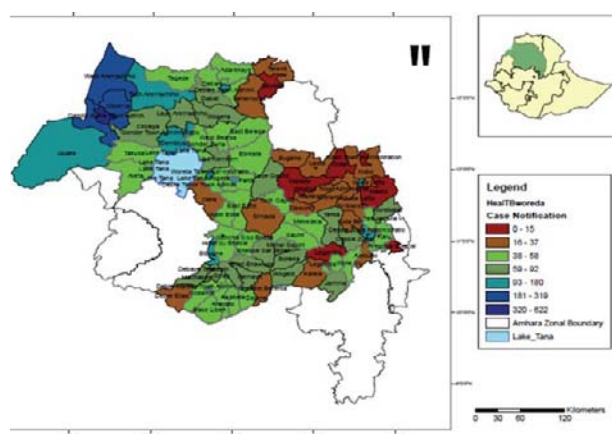
and 806 were recruited as TB suspects. Thirteen had TB culture confirmation (IR 124/100 000). The total incidence rate for both culture positive and culture negative probable cases was 574/100 000 and the prevalence of HIV amongst TB incident cases was 19.2% (14/73). A total of 105 patients initiated TB treatment and the overall mortality was 4.3% (35/806).

Conclusion: To our knowledge, this study provides the first available estimates for pediatric TB incidence in the country and highlights the high burden of disease in this age group.

PREVALENCE OF TUBERCULOSIS AND DIABETES MELLITUS AROUND THE WORLD

PC-723-02   Prevalence of drug-resistant pulmonary tuberculosis with concomitant diseases

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Aim: To study the frequency of drug-resistant pulmonary tuberculosis in patients with concomitant diseases.

Materials and methods: In 2012 we examined 411 patients with pulmonary tuberculosis who were treated at Republican Medical Centre of Phthisiology and Pulmonology at department of therapy 1. Resistance of *Mycobacterium tuberculosis* to rifampicin and isoniazid was determined by methods such as express test MTBDR plus from Hain and test Xpert MTB/RIFF.

Results and discussion: From 411 patients with pulmonary tuberculosis cases without comorbidities were 191 (46.5%), with various comorbidities and their combinations - 220 (53.5%) patients. Among all the patients multi-drug resistance (MDR) forms found at 139 (33.8%) patients. Among patients with comorbidities MDR strains found at 78 (35.5%) patients.

Among comorbidities dominated anemia of mixed origin at 69 (16.8%) patients, diabetes mellitus type I and II at 66 (16.1%), hypertension - 23 (5.6%), nonspecific diseases of the lungs and bronchi - 23 (5.6%), HIV infection - 19 (4.6%), diseases of the gastrointestinal tract - in 15 (3.6%) and heart disease at 14 (3.4%) patients.

MDR strains of MBT at patients with comorbidities met as follows: in patients with anemia mixed origin - 40.6%, diabetes type I and II - 36.4%, with essential hypertension - 21.7%, with nonspecific lung and bronchus - 43,5%, HIV - 21,1%, in patients with diseases of the gastrointestinal tract - 66.7% and with heart disease - 21.4%. Thus, among all studied patients in more than half of the cases were met concomitant illness (53.5%) and the prevalence of MDR-TB among patients with concomitant diseases is quite high - 35.3%, which requires the need for further study of the above category of patients. Efficiency of treatment in this group of patients will depend on the correct therapy of comorbidity and determination of drug resistance.

PC-724-02   Impact of co-morbidities on multidrug-resistant tuberculosis outcomes: a cohort study

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Background: The impact of co-morbidities on multidrug-resistant tuberculosis (MDR-TB) treatment outcomes still remains unclear. The aim of this study was assessment of chemotherapy response among patients with and those without co-morbidities in a setting of individualized MDR-TB care and adequate management of all diseases.

Design/methods: Cohort study was provided among 1238 drug-resistant tuberculosis patients integrated in DOTS+ programme in 2009–2010 years in Georgia. Every patient was routinely investigated for HIV, diabetes mellitus (DM) and viral hepatitis. Also documentary approved diagnosis of other diseases was taken in account. To compare the treatment outcomes of patients with and those without co-morbidity dispersive analysis using Mann-Whitney/Wilcoxon Two-Sample Test (Kruskal-Wallis test for two groups) was provided.

Results: Among 1238 MDR-TB patients only 328 (26.5%) had one or more co-morbidity. 171 patient had chronic hepatitis 'B' or 'C' (20 and 136 cases respectively) - 13.8%, 45 patient (3.6%) - HIV/AIDS, psychiatric diseases - 35 (2.8%), cardiovascular diseases - 27 (2.2%), asthma and COPD - 23 (1.9%) and gastric ulcer - 13 (1.1%). Definitions 'successful treatment' received 44.5% patient with co-morbidities vs. 52.6% without comorbidities. 'Default' - 29. 6% vs. 25. 6%; 'Failure' - 4.9% vs. 4.7%, 'Death' - 11.6% vs. 6.8% ($P < 0.05$). Mortality rate was highest during HIV co-infection (RR-2. 84; 95%CI 1.41–5.74).

Conclusion: Our findings suggest that co-morbidities have serious impact on treatment outcomes in this cohort and were associated with lower successful treatment outcomes and about twice higher death rate. Still, further well-designed, randomized, prospective studies are necessary for the better understanding of the role of comorbidities on MDR-TB treatment process and outcome.

PC-725-02   Alerting tuberculosis prevalence among diabetes mellitus patients, Siem Reap and Prey Veng Provinces, Cambodia

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Background: People with diabetes are at higher risk of developing tuberculosis (TB) than those without diabetes. Tuberculosis affects 8.7 million people and kills 1.4 million worldwide every year.[1] The prevalence of DM (2.3–5.6%)[2] and TB prevalence (0.817%)[3] are among general population in Cambodia. The TB-Diabetes co-morbidity is globally increasing.[4] Yet, there is limited information on the prevalence of this co-morbidity in Cambodia. To assess the prevalence of TB among DM patients registered in diabetes clinics in Siem Reap and Prey Veng provinces, Cambodia.

Design/methods: The cross-sectional survey is conducted in Prey Veng and Siem Reap provinces on 5 Nov to 28 Dec 2012 and 14 Jan to 5 Feb 2013, respectively. 600 DM patients are selected from 2 diabetes clinics. TB screening among DM patients are performed based on the regular appointment, by using the semi-structure questionnaires, sputum smear exam and X-ray followed the national tuberculosis guidelines. Data is analyzed by MS Excel and Epi-Info version 7, statistical analysis is tested with 95% confidence interval (CI) to describe statistics and main categorical variables.

Results: 503 DM patients are screened and statistically analyzed for TB. The mean of age of all respondents in Siem Reap and Prey Veng was 56 (SD 9.84) and 53 (SD 9.16) respectively. The mean age among male and female DM-patients in Siem Reap was 57 (SD 9.46) and 55 (SD 9.96) respectively. The mean age and sex male and female among DM-patients in Prey Veng was 54 (SD 10.32) and 53 (SD 9.27). TB prevalence among DM patients in Siem Reap and Prey Veng was 4.4% (95%CI 2–8.2) and **0.7%** (95%CI 0.1–2.4) respectively.

Conclusion: Mean ages of patients in both provinces are similar (56 and 53 years). The prevalence of TB among DM patients (4.4%) in Siem Reap is high and 6 folds higher than TB prevalence in general population (0.82%). Systematic TB screening among DM patients (regardless of TB symptoms) is crucial to find early TB cases in this research. The correlation with other chronic diseases such as hypertension, HIV/AIDS needs to be conducted for further researches.

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PC-726-02   Prevalence of diabetes Type 2 and pulmonary tuberculosis in Filipinos and treatment outcomes: a surveillance study in eastern Saudi Arabia

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Objective: To study prevalence of diabetes type-2 and pulmonary tuberculosis among Filipino patients and treatment outcomes. Tuberculosis centre of Dammam medical complex (MOH) is a referral centre for the Eastern Saudi Arabia where patients from all government and private hospitals having open pulmonary tuberculosis are admitted for isolation till they are rendered noninfectious. All patients are treated for 6 months under DOTS strategy with 4 drugs (2HRZE) for 2 months as initial intensive phase and 2 drugs (HR) for 4 months as continuation phase.

Methods and materials: We retrospectively reviewed clinical records of 1388 patients admitted with open pulmonary tuberculosis between Jan 2003 and June 2010.

Results: Among 1388 patients, 39% ($n = 542$) were Saudis and 61% ($n = 846$) were non-Saudis. Among these 12.39% ($n = 172$) were Filipinos, 153 males and 19 females respectively. Out of 1388 patients, 114 (7.17%) were found to have diabetes type 2. Among these diabetics, majority $n = 91$ (79.82%) were Filipinos. Sputum conversion was late in diabetic patients resulting in relatively longer hospital stay compared to fellow patients having only tuberculosis.

Conclusion: Our study has shown that one possible risk factor for tuberculosis is diabetes. Majority of TB patients having diabetes type 2, $n = 91$ (79.82%) were Filipinos. Their sputum conversion was relatively late and their hospital stay was longer than their fellow patients having only tuberculosis. Our findings are in agreement with the current literature on the correlation of diabetes and tuberculosis.

PC-727-02   Early therapeutic drug monitoring for isoniazid and rifampin among diabetics with newly diagnosed tuberculosis in Virginia, USA

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Background: Slow responders to tuberculosis (TB) treatment in Virginia have therapeutic drug monitoring (TDM) performed for isoniazid and rifampin. Early TDM at 2 weeks after TB treatment in diabetics was instituted given the high risk of slow response in this subset of the state TB population.

Design/methods: Charts were reviewed for all patients

in whom TDM was performed for the period of early TDM, 12/01/2011 to 12/31/2012. Diabetes was categorized by self-report and patients screened for use of insulin. All patients with diabetes had early TDM for isoniazid and rifampin at the time of estimated peak serum concentration (C2hr) and a single dose adjustment performed if below the expected range. For diabetics with pulmonary TB, the time to sputum culture conversion was assessed as a marker for prevention of slow response.

Results: During the period of early TDM, 21 diabetics had C2hr concentrations performed and 16 (76%) had a value below the expected range for isoniazid, rifampin or both. The median time to early TDM after treatment initiation in diabetics was 23.4 ± 16 days and differed significantly from non-diabetic slow responders, 88 ± 54 days ($P = 0.003$). Fifteen had follow-up concentrations after dose adjustment and 12 (80%) increased to within the expected range (including all for rifampin). Of 16 diabetic patients with pulmonary TB that had early TDM, 14 (88%) converted their sputum culture to negative in <2 months. Including the diabetics that failed to culture convert in <2 months, the mean number of slow responders was 1.2 per month (12.5% diabetic), decreased from pre-intervention rates of 1.6 per month (40% diabetic).

Conclusion: Early TDM for diabetics was operationally feasible, may speed response to TB therapy and can be considered for TB programs with high diabetes prevalence.

PC-728-02   Screening all tuberculosis patients for diabetes mellitus in a tribal tuberculosis unit in Vizianagaram, South India: how effective is it?

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Background: World Health Organization–The Union Framework for Collaborative Activities recommends bidirectional screening of tuberculosis (TB) and diabetes mellitus (DM). The India Tuberculosis–Diabetes Study Group (ITDG) has assessed feasibility and results of screening TB patients for DM with pooled data from more than 60 peripheral health institutions in eight tuberculosis units (TU) acros sIndia. A policy decision has been made by the National TB control programme to implement this countrywide. This study seeks to describe the prevalence of DM among TB patients and number needed to screen (NNS) to diagnose one new case of DM in one such tribal TU (population 0.25 million) in Vizianagaram, South India.

Methods: All TB patients diagnosed and initiated on treatment at 10 peripheral health institutions of the TU during January to September 2012 were screened for DM. Those with unknown DM status were offered random blood glucose (RBG) test and fasting blood glucose (FBG) test if RBG was >110 mg/dl. Blood glucose was assessed using a glucometer supplied by national programme on a capillary blood sample. Those with FBG > 126 mg/dl were diagnosed to be diabetic and those between 110 and 126 were considered as pre-diabetic as per national guidelines.

Results: Of 381 TB patients, 374 (98%) were assessed for DM and 19 (5.1%) were found to have DM. Of a total of 19 DM cases diagnosed, 7 (1.9%) had a previously known diagnosis of DM and 12 (3.2%) were newly detected. About 32 cases of pre-diabetes were detected. Of the TB-DM cases, 15 were referred to diabetic care. Age more than 40 years was a factor significantly associated with DM. The prevalence of DM was higher among those aged 40 years and above, but did not vary by sex, smoking status, HIV status and type of TB (new or previously treated). To detect a new case of DM (i.e., excluding those persons with previously-diagnosed DM), the NNS was 30; among those aged >40, the NNS was 19 and among smokers it was 21 (Figure).
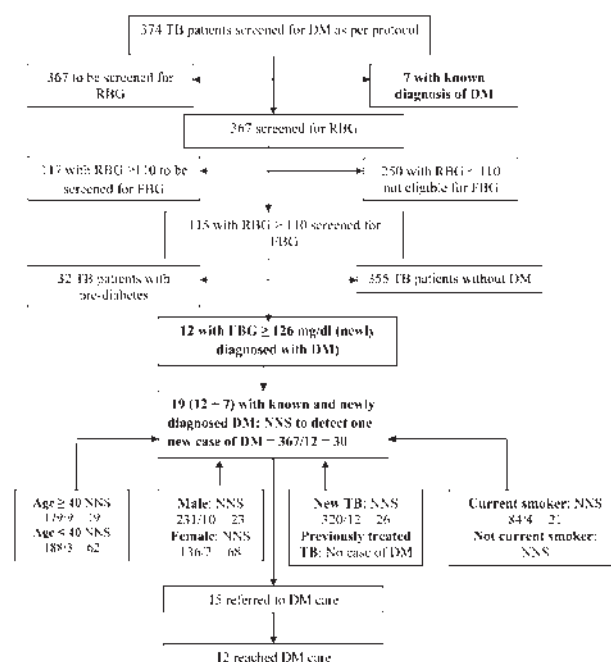
Figure Prevalence of DM among TB patients in Vizianagaram, South India, January–September 2012. TB = tuberculosis; DM = diabetes mellitus; RBG = random blood sugar; FBG = fasting blood sugar; NNS = number needed to screen; pre-diabetes = FBG level 110 to 126 mg/dl.

Conclusion: In the tribal TU of Vizianagaram, South India, DM prevalence among TB patients was low compared to 9% assessed by ITDG indicating a heterogeneous DM prevalence across India. However, the screening process was found to be effective and implementable. Further research is required to understand if linking patients to pre-diabetic and diabetic care can actually lead to better TB treatment outcomes.

PC-729-02   Feasibility of screening tuberculosis patients for diabetes mellitus in Kolar, India

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Background: Previous published studies in India show a very high prevalence of diabetes mellitus (DM) among tuberculosis patients. We aimed to assess feasibility and results of screening patients with tuberculosis for DM within the routine healthcare setting in 17 peripheral health institutions (PHIs) of Bangarpet tuberculosis unit (TU) (Population: 0.5 million), Kolar district, South India. This was part of a country-wide pilot conducted in 8 tertiary care centres and more than 60 PHIs.
Design/methods: During January–September 2012, all the TB patients registered for treatment were assessed for DM. Those with unknown DM status were offered random blood glucose (RBG) test and fasting blood glucose (FBG) test if RBG was >110 mg/dl. Blood glucose was assessed using a glucometer supplied by National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular disease and Stroke (NPCDCS) on a capillary blood sample. Those with FBG > 126 mg/dl were diagnosed to be diabetic and those between 110 and 126 were considered as pre-diabetes as per national guidelines.
Results: Of 362 TB patients, 358 (99%) were assessed for DM and 62 (17.1%) were found to be diabetic—53 (14.6%) with a previously known DM and 9 (2.9%) newly diagnosed. In addition, 11 cases of pre-diabetes were diagnosed. All newly diagnosed DM patients were referred and enrolled into DM care. To detect a new case of DM, the number needed to screen (NNS) among TB patients was 34. Among the New Smear Positive TB patients, the NNS was 19 compared to 25 among previously treated TB cases. More than 75% of the TB patients had their RBG done within 3 days of starting TB treatment and more than 75% of eligible patients had their FBG done within 6 days of RBG.

Conclusion: It is important and feasible to screen patients with TB for DM in the routine setting which could possibly lead to earlier identification of DM in some patients and opportunities for better management of co-morbidity. A policy decision has since been made by the National TB Control Programme of India to implement this intervention countrywide.

PC-730-02   Implementación de un modelo para el abordaje del binomio tuberculosis/diabetes en México

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Antecedentes: En México, la diabetes (DM) es la principal enfermedad asociada a la tuberculosis (TB) presentándose en 18,8% (rango, 10 a 28,6%). Entre 2003 y 2012 los casos TB/DM se incrementaron en 174%, (rango, 0,6 a 9,2 por 100 000 habitantes). Lo anterior llevó a evaluar la implementación de un modelo para la detección temprana del binomio TB/DM así como su tratamiento oportuno e integral.
Objetivo: Evaluar la factibilidad e impacto de la implementación de un modelo para el abordaje bidireccional de las personas afectadas por TB/DM en México en el primer nivel de atención e identificar las necesidades y oportunidades para su cumplimiento.
Metodología: Se seleccionaron 5 sitios piloto para implementar el modelo de abordaje a partir de las notificaciones de casos de TB/DM en los años previos. Se diseñó el Modelo y los instrumentos estandarizados de recolección de información. Se establecieron acuerdos con las autoridades estatales y locales, se capacitó al personal involucrado en los programas de TB y DM sobre tamizaje de TB en pacientes con DM y de DM en pacientes con TB y sobre referencia a tratamiento integral.
Resultados: Entre septiembre 2012 a marzo 2013, se realizaron 866 tamizajes de TB en DM detectándose 38 pacientes (4,3%, rango 2 a 6,7%) con TB/DM que no conocían su diagnóstico. Se realizaron 683 tamizajes de DM en TB, diagnosticándose 47 pacientes (6,8%, rango 2,5 a 12,5%) con TB/DM que desconocían su diagnóstico. Los problemas identificados fueron: falta de voluntad política a nivel estatal y local, necesidad de realizar modificaciones a las Normas Oficiales de TB y DM que incluyan los tamizajes bidireccionales; e insuficiencia de recursos asignados a la detección. El desempeño de cada centro fue variable y dependió principalmente de la motivación, tiempo dedicado, y eficiencia del personal asignado a los programas de TB y DM así como de la participación activa de los pacientes. Los resultados de curación de la TB de manera preliminar son cercanos al

90%, sin embargo habrá que esperar a completar la cohorte a finales de septiembre de 2013.

Conclusiones: La atención integral TB/DM es compleja y requiere de la colaboración y coordinación entre el primer y segundo nivel de atención, así como cambios en la normatividad involucrando la voluntad política a nivel estatal y local. El tamizaje activo incrementa la detección de casos con TB/DM. Es necesario sensibilizar al personal de salud y a los pacientes sobre la atención integral a la TB/DM.

PC-731-02   Outcome of tuberculosis treatment in patients with diabetes mellitus under the RNTCP in Malappuram District, Kerala, India

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Background: India has the dual burden of tuberculosis (TB) and diabetes mellitus (DM), greatest in Kerala State. We aimed to assess, under routine programme conditions, the TB treatment outcomes among DM patients (disaggregated by glycemic control) and compared to that among non-DM patients.

Design/methods: This retrospective cohort review of records included all TB patients aged ≥14 years registered in Revised National Tuberculosis Control Program (RNTCP), Malappuram district, Kerala State from April 2010 to September 2011. DM was diagnosed as per national guidelines and TB treatment outcomes were categorized as favourable (cured and treatment completed) and unfavourable (death, default, failure, switched to second line drug treatment, transferred). Relative Risk (RR) and 95% confidence intervals (CI) were calculated to assess the risk of unfavourable outcomes.

Results: Of 3116 TB patients, 2794 (90%) were screened for DM and 667 (24%) had DM. The proportion with unfavourable outcome among DM was 16.9% ($n = 113$) (RR 1.25; 95%CI 1.02–1.53) and those with unknown DM status (RR 1.67; 95%CI 1.33–2.10) as compared to 13.5% ($n = 288$) among non-DM patients. Among DM patients, those with poor glycemic control or unknown control status had higher risk of unfavourable outcome (RR 2.11; 95%CI 1.11–4.03) as compared to those with good glycemic control.

Conclusion: TB patients with DM and unknown DM status had poorer outcomes as compared to those without DM. Outcomes were worse among DM with poor glycemic control justifying the national policy of routinely screening all TB patients for DM.

PC-732-02   Challenges and opportunities in planning bi-directional screening for tuberculosis and diabetes mellitus Type 2 in Mexico

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Background: The World Health Organization (WHO) has identified DM as a global epidemic. The disease burden is highest in low- and middle-income countries (LMIC), where 80% of all DM deaths occur. At the same time, despite a declining global burden, TB continues to be a major cause of death worldwide, with 90% of cases occurring in LMIC. Mexico is no exception; with an increasing DM epidemic affecting 14% of the population, almost 20% of TB cases have DM. Therefore, screening for TB in people with DM and screening for DM in people with TB is recommended.

Objective: To describe challenges and opportunities encountered in the initial phases of planning bi-directional screening for TB and DM in Mexico within the 'Collaborative Framework for Care and Control of TB and DM' as proposed by WHO and IUATLD.

Methods: A large stakeholder consultation for the development of an evaluation framework to assess the performance of two non-invasive screening technologies to be used within the context of TB-DM bi-directional screening in primary care centers and hospitals. The group includes representatives of the Ministry of Health (heads of the national and state programs of TB and DM), experts from the research and academic field; Mexican regulatory agency (COFEPRIS) and international NGO Program for Appropriate Technology for Health (PATH), who conceptualized the initiative. Funding is currently provided by the United States Agency for International Development (USAID).

Results: The process has been successfully completed. We have identified the following as important elements contributing to this process.

1 Political will of national, state, and local health authorities.
2 Participation and collaboration of both programs at the national, state and local level.

3 Respect to local needs and social and cultural context.

4 Community engagement.

5 Reinforcement of existing infrastructure at primary health centers and hospitals.

6 Modification of present official norms of DM and TB.

7 Participation of regulatory agencies.

8 Advocacy for sufficient resource allocation.

9 Establishing the role of the different partners in relation to study design, implementation and the independent/unbiased publication of results.

Conclusion: The process of initiating collaboration between TB and DM programs is complex and presents challenges and opportunities that require involvement of different public and private agencies, the research community, patients, families and society in general.

PC-733-02   Feasibility and yield of screening of patients with tuberculosis for diabetes mellitus under the tuberculosis program in Anklav Tuberculosis Unit, Gujarat, India

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Background: There has been an international call for investment in collaborative care directed towards tuberculosis (TB) and diabetes mellitus (DM). A countrywide pilot project of screening TB patients for DM was implemented at selected sites in India in 2012. The results of this screening have been reported in terms of aggregate data, and this has encouraged the belief that DM screening and care should be integrated into the national TB control programme. As part of the network of pilot sites, we report implementation findings and lessons learnt in Gujarat, India. The specific objectives of this study were to determine (i) prevalence of diabetes and impaired fasting glucose (IFG) in a cohort of TB patients, (ii) time intervals for making the diagnosis of diabetes and IFG, (iii) demographic and disease related factors associated with diabetes and IFG, and (iv) number needed to screen (NNS) for diagnosing patients with newly diagnosed diabetes and IFG.

Methods: It was a descriptive study of all TB patients (adults and children) registered between January and September 2012. TB patients were asked if they already had DM. Those with unknown DM status were offered random blood glucose (RBG) test and fasting

blood glucose (FBG) test if RBG was $\geqslant$110 mg/dl. Blood glucose was assessed using a glucometer supplied by national programme on a capillary blood sample. Those with FBG $\geqslant$ 126 mg/dl were diagnosed to be diabetic and those between 110 and 125 were considered IFG.

Results: Of 556 TB patients, 553 (99%) were assessed and 36 (6.5%) were diagnosed with DM (14 with DM already known and 22 newly diagnosed) and 39 (7%) with IFG. Median (IQR) time interval from start of TB treatment to DM diagnosis was 5 days (IQR = 1–17). Baseline characteristic associated with increased DM was age $\geqslant$35 years. NNS for all TB patients was 25 for one new DM case and 14 for one new IFG case, with lower NNS in males, age >35 years, smear-positive pulmonary TB, re-treatment patients and those currently smoking.

Conclusion: This pilot project shows that it is feasible and valuable to screen patients with TB for DM in the routine setting, resulting in earlier identification of DM in some patients and opportunities for better management of comorbidity.

PC-734-02   Alarming pre-diabetes and diabetes mellitus prevalence among tuberculosis patients, Siem Reap and Prey Veng Provinces, Cambodia

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Background: Pre-Diabetes Mellitus (pre-DM) and Diabetes mellitus (DM) are an important risk factor for developing TB. TB and DM are leading causes of high co-morbidity in Cambodia. In the general population, prevalence of DM and TB are 5.6%[1] and 0.82%[2] respectively. Diabetes-TB co-morbidity is globally increasing.[3] Yet, there is limited information on the prevalence of this co-morbidity in Cambodia. The main objective is to assess the prevalence of pre-DM and DM among registered TB patients in Siem Reap and Prey Veng from Jan to Jun 2012, Cambodia.

Design/methods: A cross-sectional survey was conducted on 1–9 Nov 2012 and 9–24 Jan 2013. The totals of 940 TB patients randomly were selected from 11 operational districts. We use case definition of pre-DM, DM, and TB based on ministry of health diabetic and TB guideline 2012. Semi-structured questionnaires were used. Glucose meter machine detected the level of glycaemia. Waist circumference and body mass index measured for body weight. Sputum exam and X-ray screened DM among TB patients. Data is analyzed by MS Excel and Epi-Info version 7, statistical analysis is tested with 95%CI to describe statistics and main categorical variables.

Results: 940 TB patients were screened and analyzed for pre-DM and DM. Mean age of all respondents in Siem Reap ($n = 465$) and Prey Veng ($n = 475$) were 48 year-old (SD 15) and 38 (SD 22) respectively. Mean ages for male and female respondents in Siem Reap was 48 year-old (SD 16) and 49 year-old (SD 14). Mean age of male and female respondents in Prey Veng was 36 (SD 22) and 38 (SD 23) respectively. Pre-DM and DM prevalence among tuberculosis patients in Siem Reap was 25% (95%CI 21.5–29.5) and 7% (95%CI 4.8–9.7) respectively. Pre-DM and DM prevalence among TB patients in Prey Veng was 22% (95%CI 18.30–25.9) and 5% (95%CI 3–7) respectively. Prevalence of pre-DM added DM among TB patients in both provinces was 32% (95%CI 28.05–36.55) and 26.50% (22.53–30.47) respectively.

Conclusion: Prevalence of pre-DM and DM in the survey sites (32% and 26.5%) among TB patient is higher than DM among general population (5.6%).[4] DM is more common in the middle age (mean age: 38–48 year-old) than the oldest age (over 65 year-old). Thus, all adult TB patients should be screened for diabetes rather than waiting till elderly.

1 and IVSTEPS survey, 2010, Cambodia.
2 2nd NTP survey Cambodia, 2011.
3 WHO,2011, collaborative framework for TB and diabetes.
4 and IVSTEPS survey, 2010, Cambodia.

PROGRAMMATIC ISSUES IN TUBERCULOSIS CONTROL PROGRAMMES

PC-735-02 Primary health care: tuberculosis treatment evaluation in different regions of Brazil

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Background: Brazil remains among 22 countries with the highest burden of the global incidence of tuberculosis (TB). The cure rate (70.3% in 2010) in smear positive cases is still below the goal established by the World Health Organization.

Objective: To evaluate Primary Health Care (PHC) facilities in TB treatment in different regions of Brazil.

Design/methods: Descriptive study, undertaken in five municipalities of three Brazilian regions. Data were collected through interviews with 1037 health care professionals that were working in PHC in Southeast —Uberaba (UB) 216 and São José Rio Preto (SJRP) 239, South—Foz do Iguaçu (FI) 225 and Northeast—Natal (NA) 240 and Cabedelo (CA) 117. A validated questionnaire was used and indicators were created to evaluate health services in TB treatment: health care professional, staff training, material resources, DOT and TB actions in the community. Those performances were classified according to a standardized indicator to all municipalities as above the mean, on the mean and below the mean.

Results: Health care professionals availability in NA and SJRP presented satisfactory evaluation, but their training and DOT accomplish were considered below the mean. UB presented satisfactory evaluation on all indicators. CA was on the mean, except to material resource and TB actions in the community, as well as SJRP and FI that were below the mean to this last indicator. FI present problems related to their human resources and to DOT conduction, but it was satisfactory evaluated to material resources (see Figure).
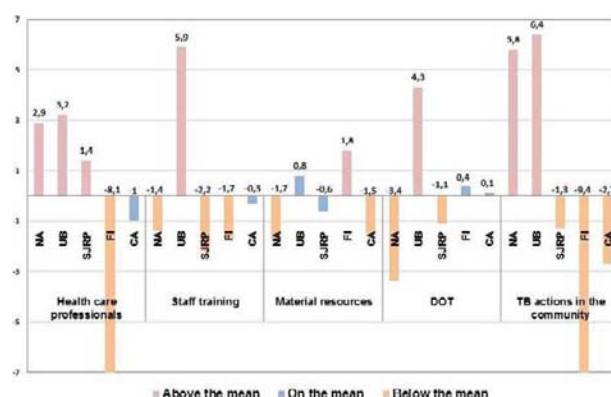
Figure Performance of municipalities of three Brazilian regions according to the indicators health care professionals, staff training, material resources, DOT and TB actions in the community, Brazil, 2011.

Conclusion: The method used allowed the comparison between municipalities and the identification of weaknesses regardless the regional peculiarities and the different local labor processes. It was observed that an investment in PHC structure related to the professionals hiring and training is essential to the accomplishment of DOT and other activities in community to follow-up the TB cases.

PC-736-02   Engagement of non-allopathic/ AYUSH health care providers in tuberculosis care and control: results of two years of implementation

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Background: Non-allopathic health care providers are often the first point of contact for any health problem. This network of providers have been recognised as a cadre for engagement in TB care and control under the aegis of the National Strategic Plan (NSP). Population Services International (PSI) under Project Axshya has been engaged with this cadre of providers with proven results before inclusion in the NSP. The non-allopathic providers were sensitised on TB diagnosis and treatment to improve referrals and engage them as community DOT providers.

Intervention/methodology: The non-allopath providers of thirty districts across six high burden states of Bihar, Punjab, Haryana, Karnataka, Maharashtra and Rajasthan were sensitised through modular trainings to develop and enhance their capacities in TB diagnosis and treatment. The trainings are provided by technical personnel from PSI with support from the key state and district RNTCP staff. Referral cards were also provided for referral of TB suspects to the nearest Designated Microscopy Center (DMC) for sputum test for diagnosis of TB at the nearest health facility which is provided for free. They were also sensitised on recent policy changes of mandatory TB case notification and ban on serological tests for TB in India.

Results: The number of providers trained in the year 1 and year 2 were 1177 and 1136 respectively. A total of 2491 and 5250 TB suspects were referred in the two successive years showing an increasing trend in number of referrals from AYUSH. Of those referred 1408 and 3513 reached the DMC on their own and on being tested 408 and 826 were found to be positive for TB with positivity rates of 29% and 23.5% in two consecutive years of implementation. There has also been an increase in the number of AYUSH becoming DOT providers from 249 in Year 1 to 357 in Year 2.

Conclusions and key recommendations: This model of partnership with non-allopathic health care providers in TB care and control has surely yielded good dividends and returns on investment. However further engagement through training and capacity building of the providers on TB including follow-up for continuous monitoring and supportive supervision would be vital to the sustainability of the model. It is recommended for facilitation of sputum collection and transport from the provider network which would yield even better results.

PC-737-02   Client tuberculosis diagnostic pathway in a municipality in south-eastern Brazil

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Background: Local experiences can be useful to comprehend how different health services provide care for tuberculosis (TB) diagnostic and the pathway done by clients suggest evidences to comprehend this panorama.

Aim: To describe how health care services contributed to the TB diagnosis by looking at the TB client pathway.

Design/methods: Descriptive study, survey type, was conducted in the municipality of Ribeirão Preto, Sao Paulo, Brazil in 2009. Inclusion criteria were adopted: to be TB client, older than 17 years old, resident in Ribeirão Preto outside the prison system, and do not have cognitive disabilities. For data collection, first a questionnaire containing questions on socio-demographic information, as well as on the health service sought for first contact care and the diagnostic hypothesis informed by the medical doctor at the time of this visit. Subsequently, more data were collected from secondary sources in two information systems to get the health services visited by TB clients from their first search for care until the diagnosis. For analysis of the results, the health services were classified into three categories: Primary Health Care (PHC), Emergency Services (ES) and Specialized Services (SS). The data were analysed using descriptive statistics.

Results: One hundred patients were interviewed. ES were the point of entry into care for the majority of clients (69%), followed by PHC (16%), and SS (15%). The service that most requested sputum smear was the SS (57.0%). For X-ray exam, the ES was the one with the highest proportion (41.5%) of requests. The median time between the first visit off all clients to a health service until TB diagnosis was 34 days ([IQR] 9–100 days). Patients who search PHC showed a median time of 33.5 days ([IQR] 23–59 days), ES a median time of 33.0 ([IQR] 8–105 days) and SS the greater median time 64.0 ([IQR] 2–195 days). By observing which health service was responsible for the TB diagnosis in the endpoint of the pathway, SS was responsible for the majority of TB detection (90.0% out of 100). PHC and ES only diagnosed 2.0% and 8.0% of the cases, respectively.

Conclusion: The performance of health service categories for TB diagnosis showed a critical scenario. In PHC and ES, TB clients needed to visit more services categories, making their pathway to diagnosis longer. In SS, they presented a shorter pathway but a delay two times higher than the other categories.

PC-738-02 Interpersonal communication as an approach in tuberculosis care and control in India: lessons learnt from 2 years of implementation in six high-burden states

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Background: India is home to more than two million incident cases of TB every year and civil societies have partnered together in the fight for TB care and control in India. Population Services International/India, is implementing Project Axshya in six high TB prevalence states of India in partnership with the Union. The objective of the project is to improve the self-risk perception to TB related symptoms and improve awareness of marginalised and vulnerable population to TB diagnosis and treatment services thereby improving access with IPC being adopted as an approach across six states with high TB prevalence.

Intervention: Population Services International/India while implementing the program in six states has adopted IPC as an approach to reach out to the target population in the age group of 18–54 years. A qualitative Communication Needs Assessment study was conducted in the six states and evidence gathered from the study gave insights for development of interpersonal communication tool with focussed messages for use during IPC sessions. The tool was used for conducting individual and group sessions and information on TB was provided to the target population on the following key messages: cough for two weeks or more could be TB; visit the nearest diagnostic center for free sputum test; TB treatment is free. TB suspects identified during the IPC activities were referred for TB diagnosis and treatment to the nearest health facility where services were free. The activities were followed up for results over the project implementation period.

Results: During the last two years of the project implementation, around 305 503 individuals were contacted and 15 293 TB suspects/chest symptomatics were identified and referred to the government health facilities to access the free TB diagnosis and treatment services. 4686 persons reached the health facilities on their own after the IPC sessions and were tested for TB diagnosis; 975 persons were detected with active TB and were initiated on DOTS.

Conclusions and key recommendations: Interpersonal communication tool developed after gathering evidence through research has been an effective method of communication and has helped in the detection of active TB cases. It is also recommended to use the IPC approach for further communication and detect more TB cases in India. It is also suggested to understand the reasons for the persons referred who do not reach the health facilities through further research.

PC-739-02 Qualitative study of pathways of patients with diagnostic delay of tuberculosis in Arkhangelsk

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Background: Diagnostic delay increases the time each patients stay infectious and thus the infectious pool in the community. Health systems delay is associated with a patient's visit to the same level of the health system without getting a correct diagnosis. Patients delay is associated with patients and personnel knowledge, attitudes and beliefs; poverty; sex differences; alcohol and other substances abuse; immigration background; low educational level; low awareness of TB; incomprehensive beliefs; self-treatment; and stigma. There is lack of information how these types of delay relate to each other in the social context. It is necessary to have such information in the Russian North with its specific setting to elaborate preventive programs.

Aim: To describe patients' and districts doctors' perceptions of diagnostic delay among TB patients in the Arkhangelsk region and to explain the mechanisms of how delays relate to each other.

Design/methods: Thirty-two informants with TB diagnostic delay experience, aged 23 to 78, were asked during in-depth interview. Eleven doctors, aged from 35 to 53 were randomly selected for focus group discussions. Qualitative approach was used for the study with grounded theory for data analysis.

Results: A model of the sickness trajectory was created to demonstrate the process of TB health seeking including the two types of delays. Two routes described views of the participants (patients and doctors) regarding factors influencing the delayed TB diagnosis trajectory. Two vicious circles of delay towards way to a correct TB diagnosis were identified: the route delay caused by the patients and the route delay caused by the health system. Each route includes three subcategories describing the steps of making decisions (by patient or doctor, respectively to the route). More than 16% of the TB patients followed the diagnostic delay routes.

Conclusion: Two core categories emerged from data: 'Limited willingness to go to health system' and 'Limited resources of health system'. Men reported more frequent patients' delays than women, who more often experienced health system's delay. It was described by different categories, but the core categories are suitable for all groups.

PC-740-02   Impact assessment of a communication campaign to increase knowledge for early detection and treatment seeking of tuberculosis among the general population In India

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Background: India has the highest burden of tuberculosis (TB) in the world with over two million incident cases contributing more than one-fifth of global burden. Lack of knowledge about early diagnosis and treatment seeking is one of the main reasons for huge TB burden. In order to address this knowledge gap, Project Axshya implemented a mass media campaign in India (named as Bulgam Bhai) in 2012. This paper examines the effect of the campaign to improve self-risk perception and enhance the knowledge among general population for TB symptoms for early diagnosis and treatment. It also shows the associations of knowledge indicators with the campaign among the target population.

Design/methods: Two rounds of cross-sectional surveys were conducted, adopting multi-stage cluster sampling approach; baseline in January 2011 ($n = 2731$) and endline in January 2013 ($n = 2551$) using semi-structured questionnaire among adult male and females (18–54 years) in 30 districts across 6 states of India. The main outcomes measures were—knowledge that a 'cough for 2 weeks or more' could be a symptom of TB; 'TB is curable' and 'TB drugs are free'. UNIANOVA technique was used to test for levels of significance between the two rounds and by campaign exposure.

Results: The endline survey reported nearly 42 percent of the respondents were exposed to different communication activities. It also showed that the knowledge about 'cough for 2 weeks or more could be TB' has increased significantly from baseline (84%, CI 83–86; 75%, CI 74–77; $P < 0.05$). Similarly two other knowledge indicators have also shown significant increase from baseline: 'TB is curable' (80%, CI 79–82; 78%, CI 76–80); 'TB drugs are free' (69%, CI 67–71; 60%, CI 57–62). The findings from UNIANOVA indicated significant increase ($P < 0.05$) in awareness about TB among those who exposed in the campaign (96%) than non-exposed group (91%) and also from the baseline (87%). Similarly, the knowledge of 'cough for 2 weeks or more could be TB' was found significantly ($P < 0.05$) higher from baseline 78% and endline non-exposed group 82% to those exposed in the endline (88%).

Conclusion: The results demonstrated significant increase in knowledge indicators over time. It also revealed a positive association between exposure to program activities and increase in knowledge. A well-designed program supported by a media campaign providing evidence based community oriented messages can help in accessing TB related services and thereby to improve self-risk perception for early diagnosis and treatment.

PC-741-02   Factors driving tuberculosis suspects to delay care seeking for tuberculosis diagnostic services: findings from a qualitative study in Yangon, Myanmar

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Background: Myanmar is one of the 22 high TB burden countries. Since 2004, PSI/Myanmar has provided TB diagnosis and treatment services through the Sun Quality Health franchise, a public-private mix approach that engages private providers to offer high quality TB care. Early diagnosis and treatment of TB are important to effectively control the TB epidemic. This study aims to understand factors that prevent individuals with symptoms suggestive of TB from seeking diagnostic services. Findings will inform efforts to improve early access to TB treatment in SQH clinics.

Design/methods: A total of 21 In–Depth Interviews (IDI) were conducted with male and female TB suspects and patients aged 18–60 living in Yangon region. Purposive sampling was used to select participants. Suspected TB cases were individuals with TB symptoms who did not take a TB sputum test at all, or who did not complete 3 sputum examinations. TB patients included those who recently (within 12 weeks) began TB treatment. Coding and data analysis were carried out manually using MS word and Ms Excel spreadsheet. Interview transcripts were analyzed thematically.

Results: People with symptoms suggestive of TB reported a number of barriers to seeking diagnostic services. These include a presumption that their symptoms were not TB, perceived financial constraints, and fear of being stigmatized by the community. High knowledge about TB symptoms and treatment options, family and community support, fear of spreading disease to young children in the family, and perceived severity of symptoms are factors that encouraged individuals with TB symptoms to seek diagnostic services.

Conclusion: The early seeking of TB diagnostic services in Myanmar is influenced by individual barriers and by concern about potential social implications of TB infection. The promotion of early testing and treatment should draw upon the factors that encourage treatment seeking, as identified in this study. Efforts should be made to increase awareness of TB symptoms, the availability of free TB services, and the importance of early testing and treatment.

PC-742-02 Accuracy of classification of relapse tuberculosis cases in the Eden District, Western Cape Province, South Africa

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Background: A 2007 case-finding report from the Eden District of the Western Cape, South Africa found that 24% of all tuberculosis (TB) cases in the district were relapse cases. This study aimed to assess the association between the high reported cases of relapse and misclassification of TB re-treatment cases in the Electronic TB register (ETR.net).

Design/methods: An observational study was undertaken to asses the correctness of the 'TB category' variable amongst retreatment TB cases registered in 2007–2009 using data from ETR.net. All retreatment cases were categorised as 'relapse' or 'not relapse' (retreatment after default, failure or other). A random sample of each group was selected for inclusion in the study and clinical records from their prior TB episode were sought for the 2004–2009 period and evaluated. Clinical folder reviews were undertaken and the current TB episode was reclassified based on the prior treatment outcome. Data was analysed to assess the comparability of the groups and the extent of misclassification.

Results: Of the 5240 retreatment TB patients in 2007–2009 (Figure), 4379 (83%) were registered as relapses and 861 (16%) as non-relapses. Amongst the 250 relapse cases sampled, only 150 (60%) prior clinical records were found. Amongst the 400 non-relapses sampled, 303 (73%) prior clinical records were found. Amongst the relapse group, 114 folders (76%) were correctly classified and amongst the

Figure Flow diagram of all retreatment cases included in the analysis.

non-relapse group 205 (68%) were correctly classified. Cases were incorrectly classified as other retreatment cases.

Conclusion: This study indicates the relatively poor reliability of the 'TB category' variable from routine ETR.net data. This can in part be attributed to using the patient's verbal history to complete this information. If this variable is of importance to TB control, then a different mechanism for identifying the previous treatment episode should be considered (using unique patient identifiers in ETR.net for example to track multiple treatment episodes). The high percentage of folders from the previous treatment episode that were not found may partly reflect the high mobility of the population (cases may previously have been treated in the Eastern Cape Province for example). Due to bias introduced by the large percentage of folders not found and in whom the prior TB episode could not be evaluated, it is not possible to assess the true rate of TB relapse.

PC-743-02 Clinical and socio-demographic aspects of tuberculosis patients and treatment adherence in a Brazilian city, 2012

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Background: Tuberculosis (TB) is a severe disease, but treatable and curable in most cases. According to World Health Organization (WHO), treatment adherence is a multidimensional phenomena, among its dimensions one may highlight the aspects related to the TB patient.

Aim: To analyze treatment adherence according to patients' clinical and socio-demographic characteristic in a priority city for TB control in Brazil.

Design/methods: Exploratory study conducted in São José do Rio Preto between November 2011 to October 2012. A total number of 106 TB patients in treatment for at least 3 months or more, aged above 18 years, outside prisional system and without limits of cognitions. For data collection, a structured questionnaire, based on the multidimensional concept of adherence as described in the WHO 'Adherence to long-term therapies: evidence for action' of 2003. In this study, only the aspects related to patients were analyzed. The questionnaire is composed by a Likert 9-scale questions from zero, being this the worst classification, to nine, the best classification. Cluster analysis was used for the definition of 2 groups of adherence (cluster 1) and non-adherence (cluster 2). The association of both cluster with the clinical and socio-demographic TB patients was tested with the
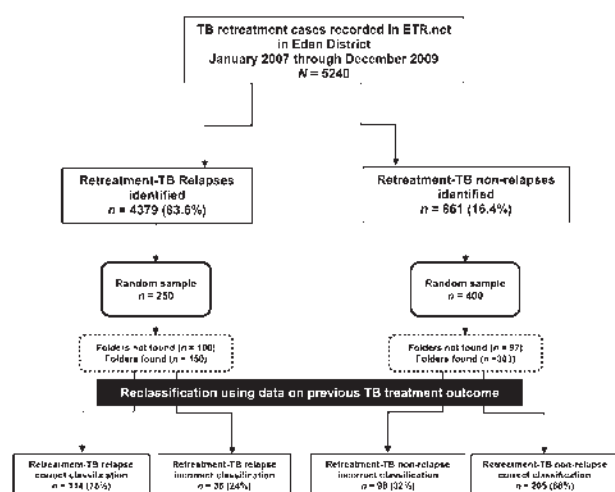
multiple correspondence analysis followed by residual analysis.

Results: The cluster 1 (adherence) presented association with male gender, age range from 60 to 79 years, no schooling, employed, without HIV co-infection, without use of alcohol or drugs and presence of co-morbidity with chronic conditions. Cases from cluster 2 (non-adherence) presented association with female gender, age range from 18 to 39 years, with more than 15 years of study, unemployment, co-infected with HIV, alcohol and drug and absence of co-morbidities.
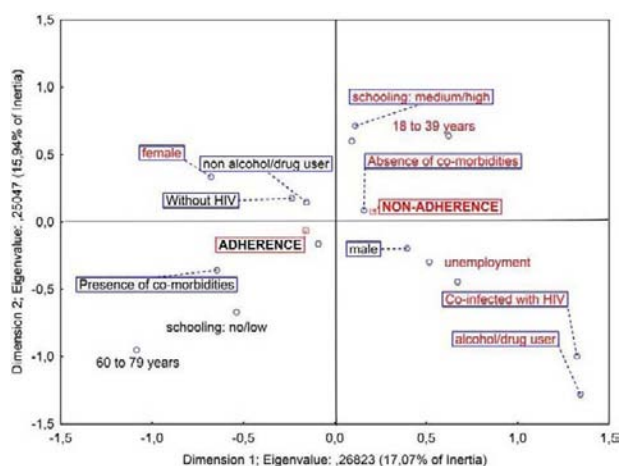
Figure Factorial plan for the patients' clinical and socio-demographic variables according to treatment adherence, São José do Rio Preto, Brazil, 2012.

Conclusion: Results show that people with chronic condition present more predisposition for treatment adherence, alerting health teams to observe TB patients characteristics that highlight vulnerabilities—such as unemployment, younger age and co-infection with the HIV. Possibilities in prioritizing this group of patients are needed in order to achieve less drop-outs during follow-up.

PC-744-02   Treatment adherence in a priority city for tuberculosis control, Brazil, 2012

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Background: The degree of adherence to the therapeutic regimen for tuberculosis (TB) is directly related to disease control effectiveness. In Brazil, about 9% of TB patients do not complete treatment. Our country has not yet reached the 5% drop-out goal established by the World Health Organization (WHO). WHO recognizes, as some of the elements to treat-

ment adherence, the knowledge, attitudes, practices, as well as patients' empowerment.

Aim: To analyze indicators of TB adherence to treatment.

Design/methods: A descriptive study, survey type, conducted in São José do Rio Preto, a priority city for TB control in Brazil. The study included 106 patients, of a total of 165 treated between November 2011 to October 2012, aged over 18 and outside the prison system. To collect data, a structured questionnaire was used, based on adherence multidimensional concept described by WHO in 'Adherence to long-term therapies: evidence for action' (2003), with Likert response scale (0 to 8). Adherence indicators were created by the mean scores of all respondents sum to each item of the instrument, and they were considered unsatisfactory (0–2), regular (3–5) and satisfactory (6–8).

Results: The indicators classified as unsatisfactory for treatment adherence in the municipality were: searching for information about TB (mean 2.6) and participation in support group (mean 2.7). The indicators considered as regular were: patient's knowledge about TB (mean 4.7) and its treatment (mean 5.2), participation in decisions related to treatment (mean 5.8) and dedication of time to the care of their own health (mean 5.5). The satisfactory indicators were: attending medical appointments (mean 8.4), drug intake as oriented by health professionals (mean 8.4), the search for a health service when they have questions about the treatment (mean 7.8) and seeking support to continue treatment (mean 7.9).

Conclusion: Adherence is centered on attending medical appointments and intake of medicines as directed. The weaknesses observed for adherence could warn the need patients empowerment, participation in making decisions about treatment, seeking information about the disease, participating in support groups, and also encourage patients to support their own health.

PC-745-02   Evaluation of tuberculosis care in the public health sector in Brazil

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Background: Tuberculosis (TB) treatment in Brazil has been decentralized to Primary Health Care (PHC) since 2004 as part of the national strategy to control TB. PHC arrangements related to the structure and process of care influences TB therapeutic success, requiring researches to evaluate the incorporation of TB control actions in PHC setting.

Aim: To analyze PHC services' performance to TB treatment in a large city of Brazil.

Method: Operational research conducted in São José do Rio Preto (SJRP) São Paulo State. A questionnaire on PHC evaluation to TB care was applied to 239 health care workers (physician, nurse, practical nurse and community health worker) from June to December 2011. Nine indicators were created (5 related to PHC structure and 4 of TB process of care) to evaluate TB care in PHC. Considering the differences between the health services, a standardized variable Z was calculated to PHC services evaluation in 5 priority cities for TB control of a multicentre study, including SJRP. Thus, the comparison unit (Z) was accepted as a measure to calculate indicators that were classified as unsatisfactory (lower than -1), good (between -1 and 1) and very good (above 1).

Results: We classified as unsatisfactory ($Z < -1$) the structure indicators 'staff training' and 'access to medical records' and the process of care indicators 'DOT (directly observed therapy)' and 'TB activities in the community'. The structure indicators 'material resource' and 'articulation with other services' and process of care indicator 'TB information' were classified as good. The best evaluated indicators were 'staff involved with TB treatment' and 'reference/counter reference' (Figure).
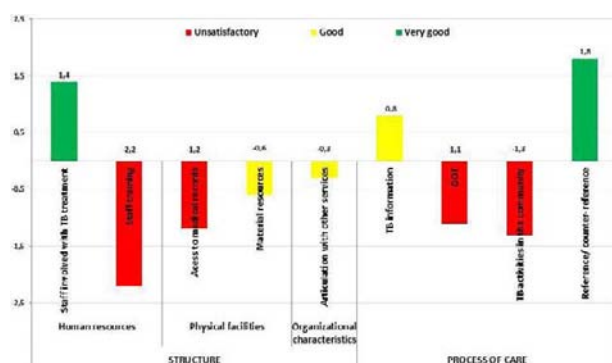
Figure Performance indicators for PHC services according to the evaluative component (Structure and Process of care), São José do Rio Preto, Brazil, 2011.

Conclusion: The results show that the main barriers related to PHC for TB control in the study site are related to the human resources qualification and their access to the patients' records. Other barriers are related to the provision of DOT and TB activities to the community. These weaknesses should be highlighted to improve PHC responsibility and effectiveness for TB control.

PC-746-02   Sputum transportation improving access to laboratory services in Chadiza District of the Eastern Province of Zambia

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Background: Access to laboratory services in general and sputum examination for tuberculosis diagnosis in particular has been a major challenge in the sub-Saharan Africa. Eastern Province of Zambia had 53% of pulmonary TB cases notified in 2012 as being sputum smear positive for TB (Eastern Province TB report). In Chadiza District of Eastern Province of Zambia, 410 patients who were being investigated for TB had sputum examination in 2008 of which 28 were found to have smear positive TB. In 2009, Eastern Provincial Health Office in partnership with Riders for Health, a UK registered charity operating in Zambia started a program to provide courier services for sample transportation in general and sputum specimens in particular from all the 16 rural health facilities of Chadiza District to the hub laboratory and transporting results back to the health facilities for clinical decision making.

Objective: To establish a 'sample transport system' in Chadiza District so as to reduce the turnaround time (from collection of samples to the receipt of the results) for sputum examination from 7 days in 2008 to 3 days by 2012.

Intervention and method: Riders for Health and Ministry of Health signed a memorandum of understanding (MOU) for Riders for Health to support transportation of samples from 16 health facilities to the hub laboratory and transportation of results from the hub laboratory back to the referring health facilities. Riders for Health provided 4 motorbikes, 4 couriers, fuel, spares, maintenance and repair of the motorbikes. Training of riders was conducted and included transportation and safe handling of samples. All health facilities were given the schedule when the riders (couriers) were to visit their facilities and when the results would be received.

Results: Sample transport using motorbike courier service increased the number of patients being investigated for TB using sputum examination from 410 in 2008 to 1064 in 2012, while the turnaround time

Table Chadiza District TB data, 2006–2011

Year	Patients investigated for TB using sputum examination	No. of smear-positive patients
2006	204	14
2007	239	20
2008	410	28
2009	958	39
2010	1115	40
2011	1571	31
2012	1064	22

for sputum examination results reduced from 7 days to 3 days from collection to receiving of the results.
Conclusions: Having an established courier system for sample transportation reduces the turnaround time for sputum examination, increasing the number of patients investigated for TB using sputum examination.

WHO IS AT RISK WITH TUBERCULOSIS?

PC-747-02   Where is tuberculosis transmitted in a South African township? Insights from social contact and environmental data

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Background: There are few data to inform where tuberculosis transmission occurs in high burden communities. Due to the role of casual contacts in tuberculosis transmission, social network analysis and molecular epidemiologic data provide limited insights into transmission patterns in these settings. We aimed to evaluate the role of social contact patterns and indoor environments in tuberculosis transmission in a high burden setting.
Methods: This study was performed in a peri-urban township near Cape Town, South Africa. We created an age-structured model of tuberculosis transmission, utilizing extensions to the Wells-Riley model of tuberculosis transmission in indoor settings, to describe transmission patterns in an endemic community. This approach uses exhaled carbon dioxide as a natural tracer gas to assess ventilation. We drew upon detailed social interaction data and carbon dioxide measurements from common indoor settings, including homes, schools, workplaces and public transportation. We incorporated age-stratified data on tuberculosis notifications and fit the model to data on latent tuberculosis prevalence by age in this community.
Results: Over 97% of indoor contact-time occurred in five locations: own households, other households, schools, workplaces and public transit. Median carbon dioxide levels were highest in schools and public transit, followed by homes and workplaces. The majority of tuberculosis transmission was projected to occur outside of one's own households, for all age groups (weighted mean percentage in own households: 23%). Due to poor ventilation and high indoor contact rates, schools accounted for up to 35% of tuberculosis infections in children (Figure); however, the low prevalence of smear-positive tuberculosis in this age group limited infection risk. By contrast, despite lower numbers of contacts in workplaces, assortative mixing among adults with high rates of smear-positive tuberculosis contributed to high levels of transmission in this environment.
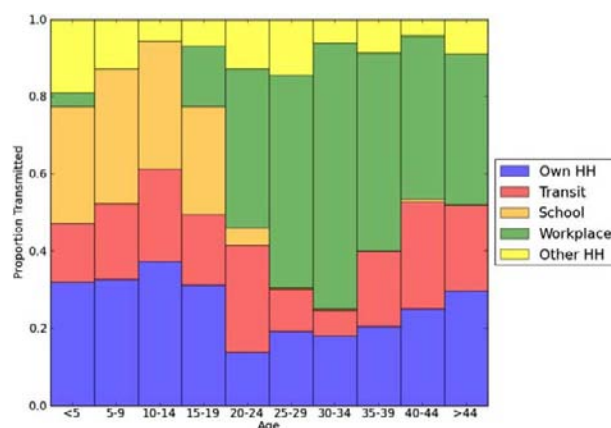
Figure   Estimated proportion of tuberculosis infections acquired in each setting, according to age group. HH = household.

Conclusions: The majority of tuberculosis transmission occurred outside of households, which may have implications for contact investigations. Public transportation is an important mechanism for transmission between age groups, which disseminates and sustains tuberculosis transmission. Integrating social contact and environmental data may yield new insights for understanding transmission dynamics of tuberculosis.

PC-748-02   Case-control study: why smear-positive tuberculosis cases remained undiagnosed until the second prevalence survey in Cambodia

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Background: The second national TB prevalence survey in Cambodia was successfully conducted in 2011 and identified 103 cases with smear-positive TB. The TB patients detected in the survey were referred to nearby DOTS centers for treatment. A research questions is why TB cases detected in the survey remained undiagnosed until the survey time, while TB cases notified to the NTP passively sought medical attention in line with the conventional DOTS strategy.
Objective: To examine what differences in demographic, socio-economic and clinical characteristics there are between actively detected cases through prevalence survey and passively detected cases through routine DOTS services in Cambodia.
Methods: A matched paired case-control study with 1 to 2 was conducted. The cases were 103 smear-positive pulmonary TB cases identified by the prevalence survey period between December 2010 and September 2011. Controls were selected from smear-positive TB cases detected by routine DOTS services

in the same commune as a case. Conditional logistic regression model was performed by univariate and multivariate analysesto examine odds ratios of being 'case' compared to being 'control'.

Results: 95 (92%) cases of 103 TB cases detected in the survey and 190 controlswere interviewed. Age $\geqslant$ 55 years and had significantly greater odds ratio of 1.92 and smear grade $\geqslant$ 1+ had significantly lower odds ratio of 0.12 as well as 8 TB related symptoms by the univariate analysis. Previous TB history became significant with the odds ratio of 2.02 by the multivariate analysis.As a result of repeated multivariate analyses, 7 variables were selected as being statistically significant; age $\geqslant$ 55 years (3.14 odds ratio), smear grade $\geqslant$ 1+ (0.12 odds ratio), cough $\geqslant$ 28 days (0.07 odds ratio), haemoptysis (0.06 odds ratio), weight loss (0.33 odds ratio), night sweat (0.21 odds ratio) and previous TB history (50.8 odds ratio).

Conclusion: TB related symptoms are one of the greatest factors to drive TB patients to seek medical care. The NTP should strengthen case detection among the middle-aged and elderly and TB patients without TB suspected symptoms through active case detection approach and prevention of additional transmission of TB in the community, sustaining the current DOTS strategy.

PC-749-02   Risk factors for adult in-patient mortality due to tuberculosis in Pune, India

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Background: India has the highest burden of tuberculosis (TB) globally, and understanding risk factors that contribute to poor TB outcomes is a high national and global health priority.

Design/methods: A retrospective chart review was conducted of all adult patients (18 years and above) admitted with a diagnosis of active pulmonary (PTB) or extra-pulmonary TB (EPTB) to Sassoon General Hospital (SGH)—Byramjee Jeejeebhoy Medical College (BJMC), between January 1 and July 31 2009. Univariate and multivariate logistic regression was performed to evaluate risk factors associated with in hospital all-cause mortality.

Results: Of 173 patients admitted with TB who had accessible records, 120 (69.4%) were male and 57 (32%) were HIV-positive. The median age was 36.5 years (IQR 30–48 years) and 132 (76.3%) were PTB, 31 (13.7%) were EPTB. The total number of MDR cases was 15, all of whom were already being treated for active TB at the time of admission. Median days hospitalized was 5 (IQR 2–16). Fifty one (28.7%) died during hospitalization. Male sex (ad-

justed odds ratio (AOR) 3.71, 95%CI 1.21–11.4), unit increase in respiratory rate (AOR 1.38, 95%CI 1.13–1.68), admission for less than seven days (AOR 5.54, 95%CI 2.11–16.2, $P = 0.001$) were significantly associated with all-cause in-hospital mortality. HIV co-infection (AOR 2.29, 95%CI 0.878–6.05, $P = 0.094$) and presenting as a new previously undiagnosed case of TB (AOR 5.30, 95%CI 0.861–32.6, $P = 0.072$) were associated with mortality but did not reach $P < 0.05$ statistical significance.

Conclusion: We observed 29% all-cause inpatient mortality among adult TB cases and major risk factors associated with all cause-mortality were male sex, unit increase in respiratory rate, and admission for <7 days.

PC-750-02   Risk factors associated with tuberculosis resulting from recent transmission of *Mycobacterium tuberculosis* of different RFLP lineages in Brazil

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Background: Many molecular epidemiology studies have been conducted to identify risk factors for clustering of tuberculosis (TB) cases in the population. Our aim was to determine if predominant cluster patterns of DNA fingerprinting of *Mycobacterium tuberculosis* can be predicted using symptoms, signs, and RD^{Rio} genotype.

Design/methods: Case control study of new TB cases in the metropolitan area of Vitoria, in Brazil between 2000 and 2010. Cluster patterns of TB isolates based on IS 6110-RFLP analysis were compared to TB cases with identical DNA fingerprints were used to develop a visual presentation of epidemiologic links between cases. A big cluster was considered when 10 or more patients have the same RFLP genotype. Small cluster was defined when 9 or less patients have the same RFLP genotype. To better show the relationship between the big clusters, small clusters and unique patterns and families in the metropolitan area we build two models (Model 1 and Model 2). Epidemiologic data from the Brazilian Surveillance system was reviewed. The logistic regression analysis method was used to compare the big cluster with demographic and clinical characteristics.

Results: Our results showed that among 980 strains there were seven big clusters circulating in the metropolitan area of Vitoria, Brazil. Among those, named number family ES14, had the majority of clustered

strains. The RD^Rio genotype is 100% present in all big clusters. The multivariate model showed that LAM family and RD^Rio genotype was the strongest risk factor associated with clustering in Model 1 and Model 2. AFB smear results were also found to be associated with clustering in both Model 1 and Model 2. **Conclusion:** This analysis demonstrates that to belong to LAM family, to be of RD^Rio genotype and have AFB smear positive were identified as risk factors for clustering in different models. These findings may help adjust TB control and contact tracing strategies.

PC-751-02   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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Background: Tuberculosis (TB) related death may be preventable, especially in developed countries. This study aims to identify risk-factors and estimate the mortality burden among treated TB patients in Israel.
Design/methods: Death certificates and/or last hospitalization records of all TB fatalities between 2000 and 2010 were reviewed. TB-fatalities were divided into TB-associated and non-TB associated deaths to calculate the case fatality rate (CFR) and additional mortality measures.
Results: From 4555 TB patients reported during the follow-up period, 447 died during treatment (average CFR 9.8%, annual range 4.7–14.3%). Comparing to patients who were diagnosed with TB and survived, those who died during treatment were more likely to be 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-coinfected (39, $P < 0.01$) and had multi drug resistant (MDR) -TB (34, $P < 0.01$). In multivariate analysis, being male, older age, HIV-coinfection and MDR were factor predicting all-causes mortality. From all 447 fatalities, 336 (75.2%) were TB-associated deaths (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%) were born in Europe/North America, 27 (8.0%) HIV-coinfected 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). **Conclusion:** Being a male, older age, HIV-coinfection and MDR-TB were found risk factors associate with TB mortality in our study. Most of these risk factors can be identified in the early stages of treatment, and followed up during the treatment period to decrease TB-associated death.

PC-752-02   *Mycobacterium tuberculosis* infection incidence and social contact patterns in Zambia and South Africa

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Background: Disease caused by *Mycobacterium tuberculosis* infection remains a major public health problem. However, *M. tuberculosis* infection incidence cannot be reliably measured because of the lack of a test of recent infection. In order to estimate gender and age specific *M. tuberculosis* infection incidence, we used a combination of social contact pattern and disease prevalence data on adults, and tuberculin skin test incidence data on children in the 24 Zamstar communities in Zambia and South Africa.
Design/methods: Cross-sectional face-to-face surveys of adults ($\geqslant$18 years) were conducted in 16 communities in Zambia and 8 communities in the Western Cape, South Africa. 'Close' (shared conversation) and 'casual' (shared indoor space) contacts were enumerated. Adult *M. tuberculosis* infection incidence was estimated using relative rates of contacting adults by age and empirical estimates of infection incidence among schoolchildren and disease prevalence in adults (culture positivity for *M. tuberculosis* in a single respiratory sample) in these communities.
Results: 3528 adults participated in the social contact survey. The reported community mean close and casual contact rates were 4.9 (95%CI 4.6–5.2) and 10.4 (95%CI 9.3–11.6) contacts per adult per day, respectively. Overall community mean close contact rates were higher for adults in larger households and in rural areas. Close contact rates with children were higher among 26–45 years olds, women, adults in larger households and South Africans. There was strong evidence of within age-group and within gender mixing of close contacts. Estimated *M. tuberculosis* infection incidence in adults was two to five times higher (2–6% per year) than was empirically measured in children. 50% or more of infection in children may be due to contact with males, as was infection in women of all ages. In adolescent and adult men, most infection was due to contact with other men.
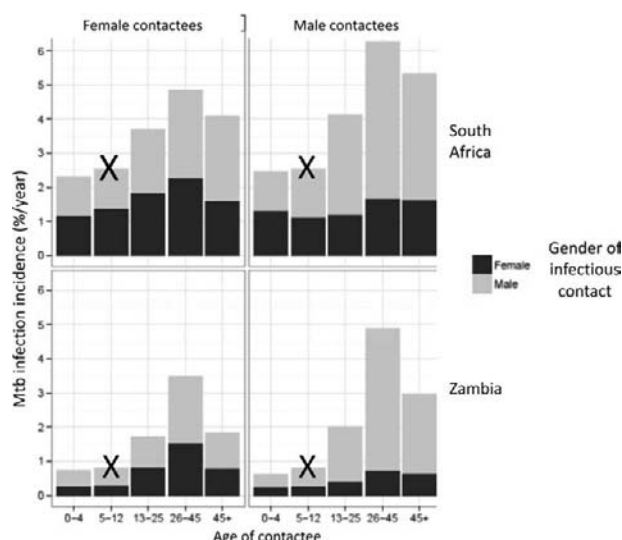
Figure Estimated *M. tuberculosis* infection incidence (%/year), by sex of infectious contact (dark bars = infectious females, light bars = infectious males), sex of contactee (columns), age and country (rows). Crosses show empirical estimates of infection incidence among schoolchildren.

Conclusion: Strong within age-group mixing imply ARTI estimates based on TST surveys in children may underestimate *M. tuberculosis* exposure in adults. Care and control of TB in males is critical to protecting men, women and children from TB disease.

PC-753-02   Unfavorable outcomes and associated risk factors in a cohort of tuberculosis patient treated in Cuba, 2009–2010

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Background: Cuba, is one of the countries of the Americas with lower incidence of tuberculosis (TB), and orientates her efforts for the elimination of the tuberculosis like health problem public. In the last years the successful outcomes rates oscillated around 90% in Cuba. Nevertheless, some patients with active TB still die, default or failure while on treatment for their disease. The objective of the study is to determine the magnitude and identify risk factors associated with TB case unfavourable outcomes in Cuba, in order to eventually promote a further increment of the successful rate.
Methods: Conducting a retrospective study, outcomes for the TB cases of cohorts 2009–2010, as notified by the TB programme, were identified. Data was obtained by assessing medical records, epidemio-

logical and treatments cards of TB patients registered from January 2009 to December 2010 who started the anti-tuberculosis treatment. Data on age, sex, type of TB, place and technique of diagnosis, comorbidity and HIV infection status, alcoholism, penitentiary incarceration, diagnosis and treatment delay, date of death were recorded. Bivariate and multivariate analyses were performed.
Results: From a total of 1607 registered TB patients, we excluded 23 (1.4%) with postmortem diagnosis and 55 (3.4%) with non-tuberculosis mycobacterium. Of 1529 eligible, 1372 (90%) were successfully treated, 103 (6.7%) died, 17 (1.1%) failed and 37 (2.4%) default the treatment. Out of 1529 who started the treatment 1173 (77%) were male, 1416 (93%) were new cases, 972 (64%) were pulmonary TB (PTB) acid fast bacilli (AFB) positive, 367 (24%) were PTB AFB negative and 190 (12%) were extrapulmonary TB. Associated risk factors with unfavourable outcomes were HIV positive (RR 3.4; 95%CI 2.4–4.8), previous anti-tuberculosis treatment (RR 2.4; 95%CI 1.7–3.6), age 65 years or over (RR 2.3; 95%CI 1.1–2.6) and male sex (RR 2.3; 95%CI 1.4–3.8). Just the same in multivariate analysis were statistically significant HIV positive (RR 5.6; 95%CI 3.3–9.4), previous anti-tuberculosis treatment (RR 2.9; 95%CI 1.7–4.7), age 65 years or over (RR 2.3; 95%CI 1.1–5.1) and male sex (RR 2.0; 95%CI 1.1–3.4). A stratified analysis in PTB AFB positive cases showed delayed diagnosis attributable to look for medical care attention and an increased risk of unfavourable outcomes in them.
Conclusions: The majority of unfavorable outcomes were dead, although with low levels. The successful of treatment could still improve if we optimize the strategies for an early diagnosis, opportune treatment and adequate follow up of specific groups, with special attention of HIV and elderly patients.

PC-754-02   Incidence of smear-positive tuberculosis in Dabat, northern Ethiopia

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Objective: To determine the incidence of smear-positive tuberculosis (TB) in Dabat District, northern Ethiopia.
Design/methods: Using a population-based longitudinal design, a TB surveillance system was initiated among 46 165 residents at the Dabat Health and Demographic Surveillance System site. Trained field workers visited each household every third month and interviewed all individuals aged ⩾14 years using a uniform questionnaire to detect suspected cases of TB (cough ⩾15 days), at which time two sputum

(spot-morning) samples were collected for smear microscopy.

Results: A total of 281 820 person-months were observed during the 1-year period, which generated 74 smear-positive TB cases. The incidence of smear-positive TB was calculated at 311 per 100 000 person-years (95%CI 240–382). Higher rates were observed among females (incidence rate ratio [IRR] 2.08, 95%CI 1.24–3.52), persons with no schooling (IRR 2.74, 95%CI 1.11–6.78) and urban residents (IRR 2.39, 95%CI 1.39–4.12).

Conclusion: The incidence of smear-positive TB is high in Dabat District, suggesting a high risk of transmission in the communities. TB control programmes thus need to improve case-finding mechanisms at the community level in Ethiopia, with greater emphasis on risk groups.

PC-755-02   Gender-specific prevalence of known risk factors for tuberculosis infection in Karachi, Pakistan

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Background: The worldwide male:female ratio of tuberculosis (TB) patients is estimated to be roughly 1.9, indicating that there are almost twice as many smear-positive TB cases in males compared with females. Pakistan has the second lowest ratio (1.07) of the 22 high-burden countries and the reasons behind the higher rates of TB among females are not known. We investigated this unusual epidemiology to determine the gender-specific prevalence of TB risk factors.

Method: A sample of 300 TB participants, 150 males and 150 females, were recruited for this study at the largest TB clinic in Karachi, Pakistan. Informed consent was obtained from all participants and was followed by a standardized Urdu-language questionnaire assessing demographic, behavioural, and medical risks factors for TB. Questionnaire data was entered using standard double data entry, reconciliation and cleaning procedures.

Results: Independent and significant risk factors reported by women were inadequate sun exposure, insufficient dairy product consumption and observing purdah (wearing all-enveloping clothes). Males and females did not report significantly different exposure to known TB contacts, however males were significantly more likely to have been in touch with contacts while they were symptomatic, such as while caring for and living with contacts. Females reported significantly higher rates of spending time (as a patient or as staff) at hospitals.

Discussion: While males and females do not report

Table Prevalence of risk factors for tuberculosis

	Male (n = 150) n (%)	Female (n = 150) n (%)	P value
Sun exposure			
<5 min/day	25 (16.9)	78 (52.0)	<0.001
⩾5 min/day	123 (83.1)	72 (48.0)	
Milk consumption			
No milk consumption	4 (2.7)	44 (29.3)	<0.001
1 Glass or more/day	145 (97.3)	106 (70.7)	
Vitamin consumption	31 (20.7)	95 (63.3)	<0.001
Purdah	0	82 (54.7)	—
Potential exposure due to high risk settings			
Worked or spent time in hospital	9 (6.0)	35 (23.3)	<0.001
Worked or spent time in prison	5 (3.3)	0	0.024
Drug or alcohol rehabilitation centre	2 (1.3)	0	0.156
Potential exposure due to contact with TB patients			
Contact with symptomatic TB patient	64 (42.7)	34 (22.7)	<0.001
Live in same household	61 (40.7)	24 (16.0)	<0.001
Care for TB patient	51 (34.0)	25 (16.7)	0.001
Use the same bedroom	61 (40.7)	20 (13.3)	<0.001

significantly different exposure to known TB patients, females report significantly fewer close interactions such as caring for, cohabiting, and sharing a bedroom with known TB patients. On the other hand, females were almost 4 times more likely to report spending time in a hospital setting than males, suggesting that females may be contracting TB infections in this medical setting while males do so through household and/or work contacts. Females also report significantly less exposure to sunlight and less consumption of dairy than males, indicating that vitamin D deficiency may play a role in TB disease progression in females. It is possible that the excess of female TB patients in Pakistan is due to nosocomial infections and socio-cultural factors limiting female exposure to important vitamin D sources.

PC-756-02   Indoor air pollution from solid fuel and tuberculosis: an updated systematic review and meta-analysis

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Background: Evidence on the relationship between indoor solid-fuel combustion and tuberculosis has been limited and controversial. We carried out an updated systematic review and meta-analysis on the effect of exposure to solid-fuel combustion for tuberculosis.

Design/methods: We searched for English and non-English articles using PubMed and EMBASE up to

February 28, 2013. We included randomized controlled trials and observational epidemiological studies, including cohort studies, case-control studies, and cross-sectional studies that reported the association between indoor air pollution from using solid fuel and tuberculosis. Two reviewers independently extracted the information from included studies and assessed the risk of bias of these studies using pre-defined criteria. The effect sizes of eligible studies were pooled using random-effects model; the heterogeneity across studies were quantified using I-squared statistics. We conducted subgroup analysis and meta-regression to examine whether the summary effect size varied substantially by important study characteristics or quality factors.

Results: We identified 15 studies (10 case-control and five cross-sectional) on solid-fuel use and active tuberculosis and one on solid-fuel use and latent tuberculosis infection. The summary odds ratio from case-control and cross-sectional studies were 1.17 (95%CI 0.83–1.65) and 1.62 (0.89–2.93) respectively, with substantial between-study heterogeneity (I-squared 56.2% and 80.5% respectively; Figure). The assessment of risk of bias showed that most of the studies had high risk of bias in the domain of exposure assessment and selection of controls, and 40% of the studies did not account for any measure of socioeconomic status. Subgroup analysis and meta-regression analysis did not identify any study-level factors that could explain the observed heterogeneity.

Case-control studies
Perez-Padilla 2001 — 2.20 (1.13, 4.30) 10.98
Crampin 2004 — 0.60 (0.31, 1.15) 11.27
Shetty 2006 — 0.90 (0.46, 1.76) 10.97
Garcia-Sancho 2009 — 3.30 (1.06, 10.29) 6.10
Behera 2010 — 0.60 (0.21, 1.70) 6.87
Pokhrel 2010 — 1.21 (0.48, 3.05) 7.93
Gninafon 2011 — 1.40 (0.71, 2.75) 10.91
Kan 2011 — 1.08 (0.62, 1.88) 12.72
Lakshmi 2012 — 3.14 (1.15, 8.57) 7.18
Patra 2012 — 0.76 (0.51, 1.14) 15.06
Subtotal (I-squared = 56.2%, p = 0.015) — 1.17 (0.83, 1.65) 100.00
with estimated predictive interval (0.43, 3.19)

Cross-sectional studies
Gupta 1997 — 2.54 (1.07, 6.03) 18.44
Mishra 1999 — 2.58 (1.98, 3.37) 28.61
Kolappan 2009 — 1.70 (1.00, 2.89) 24.39
Mengersen 2011 — 0.17 (0.00, 5.79) 2.59
Saha 2011 — 0.84 (0.54, 1.31) 25.96
Subtotal (I-squared = 80.5%, p = 0.000) — 1.62 (0.89, 2.93) 100.00
with estimated predictive interval (0.22, 11.91)

NOTE: Weights are from random effects analysis

Biomass reduces TB risk   Biomass increases TB risk

Conclusion: Our results suggested that the level of quality of evidence for the association between exposure to combustion of solid fuels and TB was very low. Given the high prevalence of solid fuel combustion in developing countries where TB is most concentrated, high quality studies are badly needed to clarify this association and to estimate the impact of the problem.

PC-757-02 Tuberculosis deaths: case structure in Moscow City, Russia

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Background: Moscow city has one of the lowest levels of TB mortality rate in the Russia (4.2 per 100K, 2011). The Russian dispensary follow-up permits to provide routine analysis history of disease between TB registration and death for separate evaluation of different mortality components, differing on time between TB registration and TB death: groups of post-mortem detected TB cases (never been registered before death -PM) and cases who died from TB during the follow-up (FC), which include who died less 1 month after TB registration (D1M), less 1 year (D1Y) and who was in register more 1 year before death (M1Y). PM and D1M reflect problem of late detection, which defines infection impact on population during certain period. D1Y and M1Y indirectly associate with treatment effectiveness of incident and re–treatment (chronic) cases. Information about characteristics of TB death cases in these groups can help to define specific measurements to decrease every of these mortality components.

Design/methods: Three years 2010–2012 TB deaths data including 1468 cases (391 in 2012) were analyzed based on death certificates data saved in the mortality register. Socio-demographic data and circumstances of death registration were used for analysis.

Results: TB death cases include 38.4% of PM, 16.3% of D1Y (including 4.3% of D1M) and 40.5% of M1Y.As compared with FC, level of PM was higher among died non-Moscow residents—77% (OR 16; 95%CI 13-21), homeless—79% (OR 10; 8–14), among died outside of in-patient hospital—38.2% (OR 2; 1.5–2.8), women—47% (OR 1.4; 1.1–1.8). Age median for PM (46) was less than for FC (51, $P < 0.05$). For FC deaths, analysis showed that frequency of D1M higher in hospital—8.7% (OR 4.2; 1.3–13.8) and among residents—8.7% (OR 12; 2–84). Median of age (61) for D1M is more than for other FC (51, $P < 0.05$). D1Y group of TB deaths is more often among non-Moscow resident 45.9% (OR 2.4; 1.6–3.6), arrived to Moscow from other Russian regions—58.3% (OR 4; 2–7), died in hospital 33.2% (OR 7; 3.5–14) and women 40.6% (OR 2; 1.4–2.8). Level autopsy did not differ between the groups.

Conclusion: TB control measures for decrease TB mortality have to be specified according to particularities of TB mortality components, defined based on time between TB registration and TB death. These mortality components are characterized by different demographic groups, places of death and history of inhabitation, that should be taken into account for monitoring TB mortality.

PC-758-02   Are women at higher risk of tuberculosis? An epidemiological study of prevalence and risk factors for tuberculosis in Khyber Pakhtunkhwa, Pakistan

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Objective: To explore the higher incidence of tuberculosis in adult females in the province of Khyber Pakhtunkhwa, Pakistan, and to describe the epidemiological characteristics of confirmed TB cases in Khyber Pakhtunkhwa by age, gender, nationality, geographical location and disease type for 2002 to 2010. **Design/methods:** A descriptive epidemiological study of tuberculosis in the province of KPK, Pakistan between 2002 to 2010. Research provides important data regarding the diseases burden and to confirm that women are at a higher risk for TB in the region. We retrospectively collected data for all registered TB patients between 2002 and 2010 in using data from the National TB Control Programme (NTP) in KPK, Pakistan. We analysed the data to show the distribution of TB by age, gender, type of disease, geographical location and treatment outcome. We also describe the outline of a study to investigate the risk factors associated with the increased incidence and prevalence of TB in this area of Pakistan.
Results: Total of 69 387 new TB patients were reported in the data set, with the prevalence of TB 57% female and 42% male. There was a significant variation in the geographical distribution of TB between different distrcits—reflecting the population distribu-

tion. However, there were also marked gender differences in distribution of new cases of TB in women ranging from 78% in Khoistan to 52% percent in karak. In more than half the districts, women accounted for over 60% of newly diagnosed TB cases. **Conclusion:** Our results confirmed the increased incidence and prevalence of TB in women. We will discuss the likely reasons for this and the implications for TB control programs.

PARTNERSHIPS IN TUBERCULOSIS CONTROL

PC-759-02   Advocacy strategy to engage private practitioners of Indian systems of medicine to adopt DOTS

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Introduction: National Tuberculosis Control Programme in India is implemented through a structured public health system with support from non-governmental agencies for community involvement and multi-sector coordination. Project Axshya is a civil society initiative to strengthen countries Revised National Tuberculosis Control Program by engaging communities and community care providers. Though programme strategies have discussed about involving professionals from alternative systems of medicine, e.g., ISM (AYUSH doctors), only a few federal states have implemented the strategies. Kerala state piloted strategies to involve practitioners of Indian System of Medicine to enhance the performance of RNTCP. The paper here documents the experiences and way forward.
Method: An intervention was planned with support of Project Axshya to train private practitioners from ISM of Medicine in 2011, process facilitated by Catholic Health Association of India. Following this, a policy was drafted to engage practitioners in TB care and control. As part of intervention a model district (Kollam) was selected where, about 40 practitioners were trained and their performance was monitored over a period of one year by Project Axshya team.
Result: The trained private practitioner's clinics were notified as DOTS center by State TB Officer on 14 July 2012. Over the period of six months about 300 TB symptomatic were referred out of which 13 turned positive. The model received mention in ISM associations, their magazines, state chapters, and media. As a result Association encouraged 70 ISM Doctors to be trained on RNTCP in the district. However, the major challenge was to overcome the policy regulation of practice that withholds the practitioners
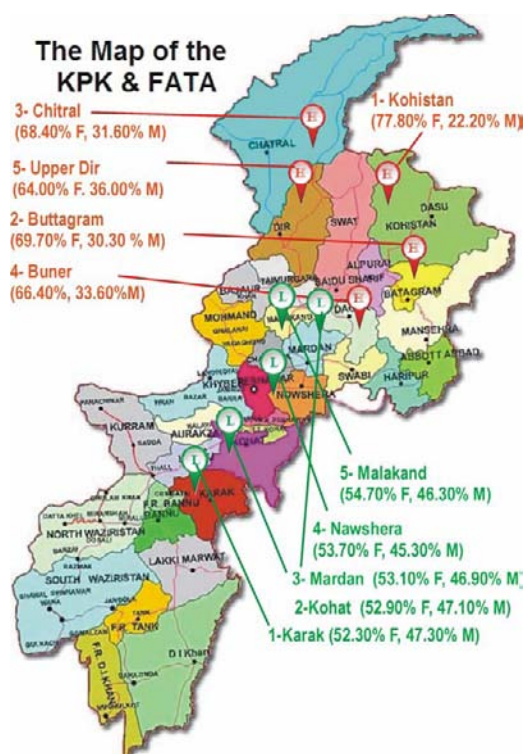
Figure State Tuberculosis Officer, Government of Kerala, recognising ISM Hospitals (AYUSH) as RNTCP DOT centres.

Key: Categorical variables of structure component. **V1**: Nurse trained (last 3 years); **V2**: Practical nurse trained (last 3 years); **V3**: Physician trained (last 3 years); **V4**: Training for TB control offered by epidemiologic surveillance (last 12 months); **V5**: Training for TB control offered by PHC services (last 12 months); **V6**: Access to TB reporting form; **V7**: Access to medical records; **V8**: Access to daily DOT record; **V9**: Access to follow-up data book; **V10**: Sputum smear test form; **V11**: Sputum culture form; **V12**: Articulation with other services – co-infected patient; **V13**: Articulation with other services – difficulties to conduct DOT; **V14**: Agreement between TB patient and health care workers about DOT place; **V15**: Agreement between TB patient and health care personnel about DOT schedule; **V16**: Conducting DOT at TB patient home; **V17**: Conducting activities routinely in the community to TB control.

from adopting DOTS (allopathic medicine) and starts DMC in their Nursing Homes.

Conclusion: Advocacy with ISM practitioners under TB control strategy yields better reach, resulting in increased awareness to identify TB. Can be replicated in other districts of the state/country.

PC-760-02 Family health units and basic health units: assessment of tuberculosis treatment in Brazil

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Background: In Brazil, Tuberculosis (TB) Control Program recommends that TB treatment should be made at Primary Health Care (PHC) settings, one of the pillars of public health system and the main gatekeeper for health care. PHC services are composed by: Family Health Units (FHU)—oriented towards family and community care—and by Basic Health Units (BHU)—which are more focused on individual needs.

Aim: To assess BHU and FHU for TB treatment in Brazil.

Method: Cross-sectional study conducted in 2011 with 81 health care workers from BHU and 157 from FHU of São José do Rio Preto, a priority city for TB control in Brazil presenting 24% of its population coverage by FHU. Data collection was conducted by interviews using a structured questionnaire elaborated to evaluate TB care in those settings. Multiple correspondence analysis was used to identify associations between each service and categorical variables.

Results: FHU were associated with conducting training in TB care for health care personnel in the last 3 years; training in TB control offered by epidemiological surveillance and by the FHU itself; access to records (TB reporting form, medical records, daily DOT (Directly Observed Therapy) record, follow up data book); availability of sputum smear and sputum culture forms; articulation with other services when patient is co-infected with HIV/aids and presents difficulties to conduct DOT; agreement between TB patient and health care personnel about DOT place and schedule; and conducting activities routinely in the community to TB control. The BHU was associated with the opposites characteristics assessed, that is the non-accomplish of them (Figure).

Conclusion: Differences in the performance of the two modalities of PHC services for TB control were observed, highlighting the low performance of BHU for TB surveillance actions and indicating the main barriers to the effective incorporation of the TB program in these services. The results show challenges for effective decentralization of TB control activities as well as for expand and strengthen FHU coverage.

PC-761-02 Evolving strategies for addressing MDR-TB in Mumbai, India

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Background and challenges: Mumbai, economic capital of country having 12.4 million population stacked in 438 sq.kms. with thick population density. More than 60% resides in slums with unhygienic, unsanitary conditions and poor air ventilation. Slum house

of approximately 100 sq.ft. accommodates 5–6 persons. Till 2010, Mumbai had no certified diagnostic facility to diagnose MDR-TB. The magnitude of MDR-TB was based on clinical assumptions. 2010 onwards limited facilities were available which could not reveal the actual facts.

Year	TB cases	Retreatment cases	MDR-TB
2010	29 685	9606	53
2011	29 212	8666	181
2012	30 828	9633	2429

In Jan. 2012, private sector study revealed MDR-TB cases are more than estimated. Municipal Corporation of Greater Mumbai (MCGM), Central TB Division, Delhi took cognizance. The diagnostic and treatment facilities augmented to address the serious challenge of spread of MDR-TB. With this scenario, is Mumbai experienced different MDR-TB epidemic and has more challenges to face? Answer may be yes but needs to be substantiated with evidence.

Response: MCGM alongwith Central TB Division initiated process of strengthening diagnostic and treatment facilities, which included: 1) upscaling of the laboratory (lab) capacity—increasing lab capacity per day from 15 to 50 samples at Hinduja Hospital and from 10 to 60 samples at J.J. Hospital. Installing 2 GeneXpert machines at dense slum locality Hospitals (Dharavi and Govandi); 2) lab notification issued to private labs and doctors for reporting MDR-TB cases; 3) changing referral criteria for MDR diagnosis to criteria C, i.e., previously treated TB cases at diagnosis, any follow up +ve, HIV-TB co-infected, pulmonary TB contacts of known MDR-TB cases; 4) augmented DR TB treatment facilities from 22 to 150 beds at TB hospital and number of DOTS centers from 998 to 1631 increased; and 5) training of health care workers for DR TB.

Results: In 2012, MDR-TB suspects screened were 10 323, diagnosed were 2229 and put on treatment were 2276. DR TB treatment capacity increased thru physical facilities at TB Hospital. Trained 479 doctors in DR TB. Private lab and doctors started reporting, diagnosed cases reported are 2370.

Conclusions: Mumbai TB Program has aggressively addressed MDR-TB issue, however, looking at the population density, failure of cases in drug sensitive TB, there is need to further strengthen the services for diagnosis and treatment involving comprehensively both public and private sector.

PC-762-02   Recherche de cas additionnels de tuberculose dans les pharmacies au Burkina Faso : acceptabilité des principaux acteurs et leçons tirés

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Contexte : L'incidence de la tuberculose au Burkina Faso est de 57 cas pour 100 000 habitants. L'Automédication y est très courante et l'officine pharmaceutique est très souvent un des premiers points de contact pour beaucoup de patients. Cette situation est une opportunité pour renforcer la recherche de la Tuberculose dans la communauté. A cet effet, le PAMAC en Collaboration avec le PNT a obtenu du partenariat STOP TB (OMS) un financement pour le renforcement de la lutte contre la TB dans les pharamcies.

Objectifs : Identifier ces cas de suspects de tuberculose en automédication dans les officines pharmaceutiques de Ouagadougou et de Bobo-Dioulasso et les orienter vers les centres de diagnostic et de traitement de la tuberculose.

Intervention : Le personnel de la pharmacie à l'aide d'un algorithme, recherche les symptômes de la tuberculose, notamment la toux de plus de 14 jours chez les clients se présentant en auto-médication dans les pharmacies. Si le client répond à ces critères, il lui prodigue des conseils et le réfère vers un CDT avec une carte de référence.

Résultats : Une bonne adhésion des pharmacies. 131 pharmacies sur 155 des deux villes (84,5%) ont adhéré au projet. 339 auxiliaires de ventes formés à la détection des cas de TB, 46421 clients touchés. 821 clients, (2%) référés vers les C DT Tuberculose. 361 (39%) soumis à un examen de crachat BAAR et 17 cas de TPM+ et 1 Cas de TMP- ont été détectés.

Conclusion : Cette initiative montre que les pharmacies sont disposées à apporter leur contribution à la lutte contre la TB à travers la recherche de cas parmi leurs clients. Leurs adhésion contribue également améliorer les taux de détection des patients TB dans les contextes où l'automédication est le premier réflexe des patients. Cette initiative pourrait être reproduite dans les régions à haute prévalence de la tuberculose car elle pourrait contribuer à améliorer la détection précoce de la tuberculose. Elle pourrait également favoriser des réflexes de références de certains clients des pharmacies vers des services adaptés pour leur prise en charge.

PC-763-02   Situacion epidemiologica de nativos afectados por tuberculosis en Paraguay

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Objetivo: Describir las caracteristicas de la poblacion nativa con tuberculosis en el Paraguay.
Metodos: Estudio retrospectivo, observacional, descriptivo de la base de datos del Programa Nacional de Control de la Tuberculosis. Fueron analizados los pacientes nativos de todas las regiones sanitarias del pais que iniciaron tratamiento para tuberculosis a partir del 1 de enero al 31 de diciembre de 2012.
Resultados: Un total de 563 (20,82%) pacientes nativos con tuberculosis fueron diagnosticados e iniciaron tratamiento, de los cuales 266 (47,24%) mujeres y 297 (52,75%) hombres, el promedio de edad fue 22 ± 6 años. Presentaron tuberculosis pulmonar 525 (93,25%) pacientes, 366 (52,75%) pacientes presentaron baciloscopia positiva. La distribucion departamental evidencio una mayor proporcion en el departamento de Presidente Hayes (chaco paraguayo) con 155 (27,53%) casos. La etnia con mayor numero de casos fueron los Mbya Guarani 106 (18,82%) pacientes. Se registraron 5 casos de coinfeccion TB-HIV y 23 muertes.
Conclusion: Los datos de nuestro estudio indicaron que la presentacion de tuberculosis pulmonar en nativos es mayor, la edad de mayor afectacion por tuberculosis es la edad productiva, la region con mayor numero de casos sigue siendo la zona sur de la region occidental del pais.
   Necesitamos seguir fomentando el fortalecimiento de una vigilancia mas estrecha, asi como la estrategia de comunicacion entre el equipo de salud y la poblacion nativa.

PC-764-02   Health seeking for tuberculosis symptoms in Dong Tap and An Giang provinces, Viet Nam: the importance of the private sector for increasing case detection

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Background: Viet Nam is one of 22 countries identified as having the highest global burdens of disease from TB. PSI/Viet Nam is collaborating with the Viet Nam National TB Program, Departments of Health and other partners to implement a public-private mix approach to increase private provider contributions to national TB control objectives. This paper presents findings from a household survey collecting data on health seeking behaviors among those with symptoms of TB in the last 6 months. This information is key for developing successful strategies for increasing TB case detection in Viet Nam.
Design/methods: 580 men and women reporting a long-lasting cough in the past two weeks, in An Giang and Dong Tap provinces, were surveyed. Twenty-one villages were selected using probability proportionate to population size. Households were selected using simple random sampling and one person meeting the inclusion criteria—long lasting cough of at least two weeks in the past 6 months—was recruited.
Results: The majority of respondents were in the lowest two wealth quintiles (64.4%). A quarter of respondents (25%) did not seek any care for their TB symptoms; 16.8% of respondents suspected that they may have TB. A little over half of respondents have health insurance (56%). Among those seeking care, the majority (73.4%) sought care first in pharmacies. 80% continued to a second source of care, with private clinics being the most common outlet (44.7%), followed by provincial (16.6%) and district (12.2%) public hospitals. Provider expertise (70.4%) and convenience (51.8%) were the two most commonly cited reasons for choosing private clinics. Those with health insurance were more likely to first seek care at public health facilities (16.7%, 3.7%). The odds of seeking care were higher among respondents who suspected that their symptoms may indicate TB (AOR 3.8); and those who had health insurance (AOR 2.5).
Conclusion: Findings confirm that people with TB symptoms in Viet Nam often seek care at pharmacies and private health clinics. This indicates an important role for private sector involvement in increasing TB case detection in Viet Nam. Boosting provider skills to detect and refer TB cases should be a key part of this strategy, together with efforts to raise awareness of symptoms and the importance of seeking healthcare to ensure early diagnosis among populations at risk.

PC-766-02   National Tuberculosis Control Program–private practitioner partnership: perceptions, preparedness and the role that they choose

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Aim: One of strategies of the national tuberculosis (TB) control program (NTP) is to strengthen partnership with private sector. The partnership is important in TB control acceleration. An agreement had been made between the Governor of Bali and the Chairman of the Indonesian Medical Doctors Association (IMDA) to encourage the role of private practitioners (PPs) in NTP. We determined perceptions, preparedness of PPs and the role that they choose in NTP.
Methods: This was a descriptive cross-sectional study, conducted in the fourth quarter of 2012. Populations

were all PPs (general practitioners and specialists) in Bali Province. Samples were obtained from PPs who attending the disseminations of international standards for tuberculosis care (ISTC) in each district/city and willing to completing a questionnaire. Before completing the questionnaire, they described about the agreement and partnership program. Data were analyzed descriptively.

Results: 145 of 225 (64.4%) participants complete the questionnaires. The mean of age was 37.5 years old. The proportion of men was 54.5% and women 45.5%. Most of private practitioners (92.4%) were general practitioners and 7.6% specialist. Most of them have good perceptions to the partnership programs, where 95.2% answered the program was appropriate to their hopes and 95.2% answered this program will be able to motivate them to have a role in TB control program. Furthermore almost all practitioners (99.3%) answered ready to have a role. Of 144 PPs who were ready to have a role, 80 (55.5%) chose the first role or finding presumptive TB cases, 40 (27.8%) chose the second role or diagnosis of TB and 24 (16.7%) chose the third role or to ensure the compliance of treatment, curing, recording and reporting.

Conclusion: Private practitioners have a good perception and preparedness. They have decided their role in TB control programs. This result should be followed by a positive response through implementation of the agreement continuously.

PC-767-02   Improving tuberculosis case detection in Mandalay region by establishing innovative links to private sector providers

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Background: Myanmar is one of 22 highest tuberculosis (TB) burden countries in the world. Population Services International (PSI)—Myanmar has been providing TB diagnosis and treatment services through PPM (Public Private Mix) DOTS program in the franchise network of Sun Quality Health (SQH) clinics since 2004. According to prevalence survey conducted in 2009–2010, the higher TB burden was seen in urban areas where population density was higher compared to rural areas. PSI–Myanmar had added innovative linkage by interpersonal communicators (IPCs) and by informal health providers (pharmacy) in eight townships of Mandalay region during October 2011–September 2012 period. This innovative linkage aimed to find additional TB cases in high density, high prevalence urban settings through active case finding activities by IPCs and private pharmacies.

Intervention: 9 IPCs and 78 trained pharmacies are involved in the Mandalay project. During project period, IPCs conduct health talk session on TB, detect suspected cases and refer them to laboratories and treatment centres where free services are available for TB cases. The trained pharmacies in urban areas also identify people with the symptoms of TB among their clients and refer them to TB diagnosis and treatment centres.

Results: We compare the total TB cases detected in eight project townships, Mandalay region during twelve months before and after the start of innovative linkage. The percentage changes of TB cases detected between two periods in each township vary from 61% increased to 154% increased (Table). The only one township show 3% decreased. The overall increased TB cases detection by new approach is 83% of detected TB cases of prior program year (October 2010 to September 2011). The contributions by this linkage with private sector range from 21% to 68% of total detected TB cases in each township.

Table Comparison of TB case detection before and during innovative linkage with private sector

Township	No. of TB cases registered before program (Oct 2010– Sept 2011)	No. of TB cases registered during program (Oct 2011– Sept 2012)	No. of TB cases contributed by linkage	% Change
Amarapura	270	488	138	81
Madaya	77	177	100	130
Meikhtila	167	302	135	81
Myittha	70	154	61	120
Patheingyi	41	71	48	73
Sintgaing	13	33	17	154
Tada U	34	33	7	−3
Wundwin	128	206	57	61
Total	800	1464	563	83

Conclusions: The one of the national strategic plans of National TB Program (NTP) in Myanmar is intensified case finding in the community. The active case finding by interpersonal communicators and private pharmacies have remarkable outputs in the most of townships. The lowest percentage change townships (Tada U, Wundwin and Patheingyi) are low population density compared with others. In future program, a changed case finding strategy, including site selection based on population density, helped lead to the success.

ABSTRACT PRESENTATIONS
SUNDAY
3 NOVEMBER 2013

ORAL PRESENTATION SESSIONS

UPFRONT AND CLOSE: CONTACT INVESTIGATIONS AMONG THE HIGH RISK

OP-247-03   Tuberculosis contact tracing in Viet Nam

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Background: Close contacts are a high-risk group for developing tuberculosis (TB). Currently it is unknown how contact screening for TB is currently practiced in Viet Nam. This study aim at assessment of current TB contact tracing practices in Viet Nam.
Design/methods: Assess 2008 data from the national TB program from nine randomly selected districts of three large cities in Viet Nam and interview of household members of smear positive TB patients.
Results: From the list of smear positive TB patients registered in 2008 in 9 selected districts in Hanoi, Ho Chi Minh city, and Da Nang, household members (including TB patients) of 1091 smear positive TB patients were identified and interviewed in this study. Total of household contacts recorded were 4118 including 293 children under five years of age, of which 474 contacts (11.5%) went for a health check. Only 5.5% children that were less than 5 years old were taken for a health check. Sputum examinations were performed on 374 contacts among the 474 contacts who went for screening, 27 pulmonary TB patients were detected of which 20 were smear positive. The proportion of TB detected among all household contact in this study was about 0.7% (656 cases/100 000 contacts).
Conclusion: The found low proportion of contacts that went for TB screening shows the limitation of contact tracing with a passive approach that is currently practiced in Viet Nam. Active case finding for close contacts of infectious TB cases is recommended to intensify case detection.

OP-248-03   Active contact identification and screening for drug-resistant tuberculosis in the context of universal access to DST with Xpert: Khayelitsha, South Africa

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Background: Direct transmission is driving the drug-resistant tuberculosis (DR-TB) epidemic. Screening of close contacts of DR-TB cases initially and thereafter at regular intervals is recommended by WHO and others, with the assumption that drug susceptibility testing (DST) is not routine and contacts should be prioritized for DST. However, contact identification and repeat screening is resource intensive and all individuals with presumptive TB now receive DST through the GeneXpert roll out in South Africa. To determine the role of contact screening in this setting, we assessed DR-TB burden and time to diagnosis among contacts in a decentralized DR-TB programme.
Intervention: Close contacts were identified by a trained counselor during a home visit. Children aged ≤5 years, were referred for clinical assessment, with specialist follow-up. Contacts aged >5 were TB symptom screened during the initial home visit, or on later visits, and, if symptomatic, were counseled on care seeking and offered sputum screening. Due to a lack of resources, repeat screening at regular intervals was not done routinely.
Results: Between Jan 2008 and Dec 2012, 984 adult confirmed pulmonary DR-TB (rifampicin resistance) cases were diagnosed. In total 2778 contacts were identified, linked to 701 index cases; 90% were household contacts. Among 617 paediatric contacts, 38 (6.2%) were diagnosed with DR-TB, predominantly presumptively. To date, 52 (2.4%) DR-TB cases have been diagnosed among 2161 contacts aged > 5. A further 13 DR-TB cases were retrospectively determined as contacts, but were not identified initially. Of the 38 pediatric cases, 23 (61%) were diagnosed within 4 months of index case diagnosis, whereas only 7 of 52 (13%) older cases were diagnosed within 4 months.
Conclusions: DR-TB burden is substantial among DR-TB close contacts, particularly in young children. Identification and rapid assessment of children is crucial to diagnosing DR-TB. In contrast, few older contacts were diagnosed with DR-TB upon initial screening; the majority subsequently detected following passive presentation. Resources should focus primarily on initial identification and education of all DR-TB contacts, with active follow up of those <5 years. Repeat active screening of contacts at sparse intervals in the context of GeneXpert roll out is unlikely to be resource efficient. In this setting, priority should

be given to identification of all contacts, referral of pediatric contacts, and education for all contacts to seek care if symptoms develop at any time.

OP-249-03   Yield of contact investigations in the Netherlands after notification of infectious tuberculosis on flights after change of protocol

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Background: Until 2010 Dutch public health authorities assigned to investigate TB transmission by potentially infectious passengers on incoming flights to Dutch airports, were applying criteria as formulated in the WHO guideline 'Tuberculosis and air travel' (3rd ed., 2008). Main criteria for initiating a CI were: flight duration $\geq$ 8 hrs and the patient likely to have been infectious at the time of travel. This resulted in a considerable number of CIs per year. The implementation of these is very time consuming and the yield was very low.

In 2010 the new ECDC guidance 'Risk assessment guidelines for diseases transmitted on aircraft' (2009) was implemented. The main difference between the ECDC and the WHO guideline is the requirement, that there is evidence of transmission in other settings, such as transmission to household members or other close contacts, before launching a CI among fellow passengers. The expectation was that this would result in a lower number of CIs and a higher yield.

Design/methods: Data were routinely collected from all notifications of cases of infectious tuberculosis on incoming flights in the period 2008–2012 and retrospectively analyzed. Limitation of the collection and the analysis is that only the results of investigations conducted in the Netherlandsare known. Many passengers on flights to the Netherlandsare in transfer to foreign destinations. In case of a CI, their information is forwarded via the Dutch focal point for the International Health Regulations to the focal point of their country of residence. No feedback is received on these CIs abroad, but, presumably, these would be similar to what is found in the Netherlands.

Results: Application of the ECDC Guidance resulted in a considerable lower proportion of notifications being followed by CIs, from on average 43% in the period 2008–2010 till 20% in the period 2011–2012. But although this more focused approach was chosen, the yield has not increased.

Conclusion: After evaluating the data we decided to continue the approach as advised in ECDC guideline, but the question is warranted whether this type of investigation should be continued, considering all the efforts involved. As already stated in the WHO guideline: '. . . the role of air travel-related transmission of TB is minimal compared with the overall transmission of TB worldwide'.

OP-250-03   Concurrent and former tuberculosis episodes among household contacts of new pulmonary tuberculosis cases

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Background: Household contact (HC) investigation allows detection of latent infection and active TB cases. If infected HC are started on prophylaxis, the risk of activation is lower. Putting active cases on treatment decreases the length of exposure of other household members. We determined the occurrence of TB among HC of new smear-positive cases diagnosed in a high incidence district in Lima, Peru.

Methods: We enrolled adults with a first episode of smear-positive pulmonary TB, the index cases, in North Lima from March 2010 to December 2011. We enumerated their HC and ascertained their sex, age, relationship, former and concurrent diagnosis of TB. A HC was defined as a person sleeping under the same roof and sharing cooking facilities. We defined as a former TB episode any previous TB treatment in a HC completed or interrupted before the diagnosis of the IC. A concurrent episode of TB was defined as receiving TB treatment when the index case was diagnosed or being started on it within 60 days.

Results: The 1225 index cases reported 5683 HC, a median of 4 (IQR 3–6). Their median age was 24 years (IQR 12–40), 12.4% were under five and 51.0% were female. Siblings (26.1%), offspring (18.6%) and parents (17.7%) were the most frequent HC. At diagnosis of the index case, 91.5% of the HC had never had an episode of TB, 6.9% were former TB cases, of which 46.4% (183) were diagnosed in the last 5 years. Concurrent TB was reported in 1.6% of the HC. On the other hand, 27.7% of index cases reported at least one concurrent or former TB episode among HC and 9.1% had two or more HC with any episode of TB. TB prophylaxis was reported by 6.5% (22/339) of index cases that had had a HC with TB.

Conclusion: TB control guidelines in Peru encompass HC investigation, with a focus on children, but are not well adhered to. The frequency of households with several members concurrently or formerly affected by TB highlight the need to comply with this policy.

OP-251-03   Active and latent tuberculosis among household contacts of tuberculosis patients in Tbilisi, Georgia

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Background: Contact investigations among close contacts of persons with active pulmonary tuberculosis (TB) patients is useful to detect TB disease earlier (active TB case finding) and prevent progression from latent TB infection (LTBI) to active TB. The purpose of this study was to determine the incidence and prevalence of active TB disease among household (HH) contacts of active pulmonary index TB cases in Georgia.

Design/methods: All HH contacts of active pulmonary TB cases registered in 2010–2011 were evaluated for active TB based on clinical symptoms when they presented to the National Center for Tuberculosis and Lung Disease. After ruling out active TB, nurses also screened contacts for LTBI using Mantoux methods for tuberculin skin testing (TST). Children aged ⩽5 years who were contacts of non MDR–TB cases were offered 6-month isoniazid preventive treatment.

Results: 700 household contacts of 304 index patients were enrolled. Out of 700 contacts, 20 (2.9%) developed active TB during the baseline period. A total of 32 contacts of 31 index patients developed active TB disease during follow-up. Mean follow-up time was 1.7 person years (SD 0.4). The incidence rate of active TB disease among HH contacts was 2628 per 100 000 person years (95%CI 1828–3665 per 100 000 person-years). The incidence of active TB was higher among contacts of index patients who were AFB sputum smear (SS) positive (>2+) compared to those contacts of index cases who were AFB SS <2+ (rate ratio 1.64 (95%CI 0.75–3.59). Among HH contacts who received TST (330 of 700), 53.5% (CI 48.2%–58.9%) had LTBI. Among 18 of 118 (15.3%) children ⩽5 years old who received LTBI treatment, none developed active TB disease.

Conclusion: High rates of active TB and LTBI were found among HH contacts of active TB cases in Tbilisi, Georgia. Conducting HH contact investigations of active pulmonary TB cases is an effective strategy for active TB case finding and should be enhanced and expanded in Georgia. Future investigations are needed to describe transmission dynamics and determine whether TB infection among HH contacts results from transmission inside or outside the HH.

MOLECULAR DIAGNOSTICS FOR TUBERCULOSIS

OP-252-03   Multiplex real-time PCR and melting curve analysis to detect mutations in multidrug-resistant *Mycobacterium tuberculosis* clinical isolates

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Background: Rapid detection of multidrug-resistant tuberculosis (MDR-TB) cases is an important issue in order to prevent the transmission of resistant strains and to begin effective treatment regimens. The purpose of this study is to detect the mutations causing resistance to isoniazide and rifampicin in *Mycobacterium tuberculosis* isolates by using multiplex real-time PCR and melting curve analysis. By using this method, resistance to isoniazide and rifampicin can be detected by two PCR assays in about two hours.

Design/methods: In this study, we used custom made primers and probes. For detection of rifampicin resistance we used two probes (RpoP1 and RpoP2) for rpoB 81-bp rifampicin resistance determining region (RRDR) in a tube. For detection of isoniazide resistance, we used two dually labeled probes for *kat*G315 and *inh*A promoter sides in a tube. For DNA isolation, Roche High Pure DNA Template Kit was used. Roche three-channel Light Cycler instrument was used for real-time PCR and melting curve analysis. Asymmetric PCR was performed. By this way, more single-strand amplicons were obtained. In order to avoid the hydrolysis of TaqMan probes and to keep them intact during the amplification we used aTaq polymerase without 5′ nuclease activity. Both multidrug resistant isolates and drug sensitive isolates were used in this study.

Results: The average temperatures of *M. tuberculosis* H37Ra were 66.34°C for RpoP1 and 71.28°C for RpoP2. The isolates that yielded different temperatures than those of *M. tuberculosis* H37Ra were evaluated as rifampicin resistant. The average temperatures of *M. tuberculosis* H37Ra was 58.07°C for both InhA promoter and KatG315 probes. The isolates with *kat*G 315 and *inh*A promoter mutation, showed average temperaturesat 45.43°C and 52.98°C respectively. These are the preliminary results of our study.

Conclusion: This method provided a new way to rapidly detect multidrug-resistant mutations in *M. tuberculosis*. Compared to fluorescence resonance energy transfer (FRET) melting curve analysis and high-resolution melting curve (HRM) analysis, we used fewer probes, which were labeled with the same fluorophore. Multiplex real-time PCR with TaqMan probes is a rapid and useful method for detecting MDR *M. tuberculosis* isolates.

OP-253-03   Comparative analysis of Magicplex™ TB/MDR Real-Time Test and GenoType MTBDR*plus* in detecting INH and RMP resistance directly from sputum samples

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Aim: We evaluated Real-Time PCR based Magicplex™ TB/MDR Real-Time Test (Seegene Inc., Seoul, Rep. of Korea) for detecting resistance to INH and RMP from sputum of tuberculosis patients and compared with GenoType MTBDR*plus* (Hain lifescience, Germany).

Design/methods: Sputum samples ($n = 167$) banked in Tuberculosis Specimen BioBank established in Masan National Hospital were randomly selected. Selected sputum samples were applied to smear examination, DNA extraction and *M. tuberculosis* isolation. Then extracted DNAs were applied to two molecular methods, Magicplex™ TB/MDR Real-Time Test and GenoType MTBDR*plus*, to detect the mutations in both *inh*A and *kat*G, and *rpo*B genes known to be associated with INH and RMP resistance, respectively. *M. tuberculosis* isolates were applied for conventional culture based DST (proportion method) which was considered as the gold standard. Sen (sensitivity) and Spe (specificity) of the two tests to detect the drug resistant associated mutations from sputum were comparatively analyzed.

Results: Among 167 sputum samples, 137 were culture positive and were employed in this study; 30 samples were culture negative or contamination thus excluded. With DNAs extracted from sputum ($n = 137$), Sen and Spe for INH resistance using Magicplex™ were 88.1 and 97.1%, respectively, while MTBDRplus were 91.0 and 75.0%, respectively. For RMP resistance, Magicplex™ showed 85.1 and 98.6%, respectively, while MTBDR*plus* showed 88.1 and 84.3%, respectively. When the 137 samples were divided into two groups depending on the smear levels; 19 were smear negative (or scanty), and 118 were smear positive group with the levels of 1+ to 3+. In smear negative group, Magicplex™ supported lower Sen for INH and RMP than MTBDR*plus* (54.4 and 45.5% vs. 100 and 72.7%, respectively). However, Spe for INH and RMP using Magicplex™ (87.5 and 100%, respectively) were higher than those using MTBDRplus (12.5 and 25.0%, respectively). In smear positive group, Sen and Spe for INH and RMP using Magicplex™ were higher than 92.9%, while using MTBDR*plus* were ranged from 85.5 to 91.9%.

Conclusion: Magicplex™ showed excellent diagnostic performance to detect INH and RMP resistance from sputum samples of pulmonary TB patients. However, it is necessary for Magicplex™ to increase sensitivity in smear negative samples.

OP-254-03   MDR-TB and simultaneous detection of *rpo*B, *kat*G and *inh*A mutation genes by Genotype® MTBDR*plus* assay in clinical specimens in Rwanda

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Background: Genotype® MTBDR*plus* Assay (Hain Lifescience GmbH, Nehren, Germany) is a new molecular technique which can simultaneously identify mutations in *Mycobacterium tuberculosis* genes associated with resistance in rifampicin (R) and isoniazid (INH). We assessed mutations and multidrug-resistant tuberculosis (MDR-TB) in new and retreatment patients.

Design/methods: A laboratory based analysis of clinical specimens was conducted at Rwanda National Reference Laboratory (NRL) over a period of 2 years (2011 to 2012) using GenoType® MTBDR*plus* test a line probe assay that detects mutations in catalase-peroxidase gene (*kat*G), in the promoter region of inhA and the 81-bp hot-spot region of the *rpo*B genes. Specific binging pattern indicated mutant strains either by deletion of a wild-type probe or staining of a mutant probe. Statistical analyses were performed using Epi Info version 3.5.3. P values were derived from χ^2 test and P value of < 0.05 was considered as evidence of a significant difference.

Results: Out of 115 MDR-TB patients, 4.1% were new patients and 8.8% retreatment patients. In retreatment patients, relapse cases account for 57.8% (55/96), failure 17.7% (17/96) and default 5.2% (5/96). Out of all mutations in *kat*G gene for isoniazid resistance, the most frequent mutation found on *kat*G gene was deletion of wild-type S315 region of *kat*G (85.8%). *kat*G MUT 1 designated to assess the AGC-to-ACC (S315T) and *kat*G MUT T2 used to assess the AGC-to-ACA (S315T) mutations was found to be 95.8% and 1.7% respectively. For rifampicin resistance, *rpo*B genes mutations were detected including *rpo*B MUT D516V, *rpo*B MUT H526Y, *rpo*B MUT H526D, and *rpo*B MUT S531L. The *rpo*B MUT 3 (*rpo*B S531L) was found to be the common representing 88.3% of all mutations in *rpo*B gene. Most MDR TB cases (75.8%) diagnosed with HIV were among retreatment patients whereas in new patients, MDR TB co-infected HIV patients were found in 24.2%. However, there was no significant relationship between HIV status and the treatment history ($P > 0.05$).

Conclusion: GenoType® MTBDR*plus* assay detected isoniazid and rifampicin resistance the two powerful drugs used to treat TB patients by detecting mutations in either *rpo*B, *kat*G, and *inh*A genes. There was no significance difference in new and previously treated

patients ($P > 0.05$). More effort should be put in MDR-TB co-infected with HIV to control the spread of TB HIV co-infection.

OP-255-03   Automation of multidrug-resistant tuberculosis PCR diagnostics

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Introduction: TB diagnostics based on PCR is widely used in phtisiology. Complicated process of MTB DNA extraction from clinical samples and following manipulations with DNA during the PCR mixture preparation when done manually limit the number of assays performed by a bacteriology lab.
Aim: Molecular MDR TB diagnostics consisted of DNA extraction from clinical samples, MTB detection assay and determination of rifampicin and isoniazid susceptibility in MTB DNA-positive samples. The automation of the most labour-intensive steps of PCR diagnostics including DNA extraction, PCR mix preparation, sample DNA addition was fulfilled using a robotic platform.
Materials and methods: We used the inactivating reagent A, which allowed to liquefy sputum and completely inactivate MTB without losing DNA. As a robotic platform we choose Tecan Freedom Evo 150 (Tecan, Switzerland). For automated DNA extraction we used a protocol with magnetic particles.
Results: The optimal protocol and the design of the worktable to prevent cross-contamination during DNA extraction were developed. The comparison of DNA extraction results showed that the efficiency of DNA extraction from clinical samples in the automated system was not lower than that of manual extraction. MTB detection assay LOD was 25 CFU. The development of assay based on real-time PCR for detection of mutations in MTB genome allowed MDR diagnostics by RMP and H susceptibility testing. From January 2012 we performed 4477 assays for 1248 patients with new TB cases. In 904 patients (72.4%) at least 1 sample was PCR-positive. From January 2013 we determined susceptibility to RMP and H using real-time PCR in 155 TB patients. Out of these 155 cases 87 were MDR, 46 were sensitive to RMP and H, 20 samples were RMP-sensitive, H-resistant, 2 samples were RMP-resistant, H-sensitive. Eighty-six out of 155 samples, which grew in liquid media (BACTEC MGIT 960), showed complete agreement of RMP and H susceptibility test results obtained by both molecular genetic technique and cultural method.
Conclusion: The automated assay for detection of *M. tuberculosis* DNA and rifampicin/isoniazid susceptibility testing takes one day, allows determining a cohort of MDR TB cases and early beginning adequate chemotherapy.

OP-256-03   Multicenter evaluation of MAS-PCR for detection of rifampicin-resistant *Mycobacterium tuberculosis*

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Background: Rapid detection of multidrug-resistant *M. tuberculosis* (MDRTB) is one of the key components of tuberculosis (TB) control. Molecular-based methods have been shown to be promising for TB diagnosis, particularly for detection of MDRTB. They provide a rapid and high-throughput result, with variable cost depending on method used, reagents and equipment requirements. PCR-based methods are inexpensive, simple and practical for use in routine molecular laboratories. The MAS-PCR was developed based on detection of wild type sequences of the *rpo*B at codon 516, 526, and 531.

The objective of the study was to evaluate this method for detection of rifampicin-resistant *M. tuberculosis* directly from sputum samples.
Design/methods: We conducted a retrospective study in five different laboratories located in two countries, Thailand (Drug-Resistant Tuberculosis Research Laboratories, Siriraj Foundation, Mahidol University; Bureau of Tuberculosis, and Chest Diseases Institute of Thailand, MOPH, Nonthaburi) and China (National Tuberculosis Reference Laboratory, China CDC, Beijing and Yunnan Provincial Center for Disease Control, Yunnan). Simulated sputum samples consisting of 100 rifampicin-resistant and 100 rifampicin-susceptible *M. tuberculosis* samples were prepared, blinded and sent to each laboratory for performing the MAS-PCR. We compared the test results with the Genotype MTBDR Plus assay (Hain Lifescience, Germany), DNA sequencing and drug susceptibility testing.
Results: All tested samples ($n = 200$) were obtained from three sites. Two remaining sites performed only 195 and 160 samples respectively. Only the readable results were evaluated by comparison with the results of drug susceptibility testing and DNA sequencing. High false positive rates were found in two sites, with 21% combined. The false negative rates were between 3.5% and 9.4%. Major discordant results came from the presence of non-specific bands around the position of the specific band of codon 526, leading to misinterpreting the result as resistance. Overall, the method showed 82%–100% sensitivity and

56%–100% specificity among these three labs. Comparison with results of the Genotype MTBDR*plus*, MAS-PCR showed 100% concordant results.

Conclusion: MAS-PCR is a rapid and simple method that can be used for screening of rifampicin-resistant *M. tuberculosis* strains in clinical samples. Limitation was found when the method is performed and interpreted with inexperienced laboratory personnel.

BABIES, MOTHERS, ADOLESCENTS AND STIGMA: FAMILY ISSUES IN TB-HIV

OP-257-03 'There is no need for us to say anything': self-reliance and secrecy among MDR-TB-HIV co-infected patients and their family caregivers in Mumbai, India

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Background: Management of multidrug-resistant tuberculosis (MDR-TB) in HIV-infected patients necessitates strict adherence to a 20 month regimen of daily directly-observed-treatment (DOT) with a high number of toxic drugs and injections and antiretroviral treatment for life. Physically extremely demanding, this regimen places a high burden of care on family members, yet little is known about their roles, experiences, and needs in supporting patients on treatment. Against the backdrop of limited public sector access to timely diagnosis and treatment for MDR-TB, a Médecins Sans Frontières (MSF) clinic in Mumbai, India has been offering a comprehensive package of free services for MDR-TB and HIV care including counseling for family caregivers since 2007. This cohort offers rare insights into family dynamics of those affected.

Methods: Qualitative study using in-depth interviews with 12 MDR-TB-HIV co-infected patients from the MSF cohort, 5 family caregivers and 10 formal care providers. Data were thematically analyzed along the physiological, psycho-social, and structural impact of patients' treatment-seeking behaviour on their immediate social surroundings.

Results: Patients and family members are financially and emotionally depleted by the time they access the MSF clinic. Being on treatment is experienced as debilitating, due to treatment side effects. Patients require considerable physical care and emotional support from family caregivers, many of whom take on additional social and economic responsibilities of patients. Spouses play an active role in helping the patient adhere to treatment; when this support is non-existent or withdrawn, patients weaken considerably, losing hope and the will to continue treatment. Family caregivers also expressed the detrimental effects of mental stress and stigma on households, yet tended to carry the burden of care on their own. External support, including MSF counselors, was rarely accessed to discuss personal concerns and anxieties.

Conclusions: Due to stigma for both TB and HIV, as well as a sense of familial duty, family caregivers of co-infected people strive to be self-reliant and reluctant to seek help outside the family. They assume a high physical, social, and emotional burden of care. In the current absence of safer and shorter treatment regimens, treatment support strategies that draw on the use of family caregivers need to be adapted in this cultural context.

OP-258-03 Prevalence and predictors of pulmonary tuberculosis in antenatal clinics in Lusaka, Zambia

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Background: Tuberculosis (TB) is highly prevalent in sub-Saharan Africa. Previous studies show that it is an important cause of maternal and infant morbidity and mortality. We screened pregnant women in 3 Lusaka antenatal care (ANC) clinics to estimate TB prevalence.

Design/methods: As part of a pilot program, women >18 years of age attending their first ANC visit were offered HIV testing and TB symptom screening. We asked all HIV-infected women (regardless of symptoms) and symptomatic HIV-negative women to submit sputum. Two sputum samples were examined with LED fluorescence microscopy and one was cultured with liquid and solid culture. Patients found to be smear or culture positive were initiated on TB treatment through the National TB Program. The study received ethical approval from the University of Zambia and the University of Alabama at Birmingham.

Results: From November 2011 to October 2012, 5033 women were offered TB symptom screening and all accepted. 1422 (28%) met criteria for sputum examination; of these, 1152 (81%) submitted sputum and had valid culture results. Seventeen women (1.5%) had culture-confirmed TB; only 2/17 (12%) were smear-positive. Among women with culture results, 10/664 (1.5%) HIV-infected and 7/488 (1.4%) HIV-uninfected women had TB. Using denominators from the entire cohort, this translates to a detected prevalence of 1170/100000 (95% confidence

interval (CI), 560–2140) among HIV-positive and 167/100 000 (95%CI, 40–340) among HIV-negative women. Fifty percent (5/10) of HIV-infected TB patients were asymptomatic.

Conclusion: Among HIV-infected women, the TB prevalence was approximately 3-fold greater than the national prevalence of 352/100 000, highlighting a need for routine screening. Symptom screening would have identified only half of the HIV-positive TB cases, suggesting this method is insufficient for TB detection in these women. The prevalence among HIV-negative women was much lower, but may be underestimated because we only cultured symptomatic women. This also precludes us from evaluating the sensitivity of symptom screening in HIV-negative women. While screening uptake was high, operational challenges included inability to produce sputum and culture contamination. Our results support the need for sensitive, inexpensive TB diagnostics and routine screening in HIV-infected pregnant women. Further evaluation is needed for HIV-negative women.

OP-259-03 Drug-resistant tuberculosis: a global perspective on diagnosis and treatment among antiretroviral treatment programs in lower-income countries

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Background: Tuberculosis (TB) is a major public health problem, particularly in the context of HIV and multidrug resistant (MDR) TB. Strategies to control drug resistant TB include prompt identification of drug resistance and provision of adequate treatment. We describe the availability and use of drug resistance detection methods as well as MDR-TB treatment in antiretroviral therapy (ART) programs from lower-income countries.

Methods: We surveyed ART programs participating in the International epidemiologic Databases to Evaluate AIDS in Africa, Asia, the Caribbean, Central and South America in 2012. TB data was collected on the characteristics of participating ART programs and on HIV-infected TB patients seen during the study period by web-based questionnaires.

Results: We included 47 ART programs treating HIV-infected adults from 26 countries: 34 (72%) in Africa, 7 (15%) in the Caribbean, Central and South America, and 6 (13%) in Asia. Drug susceptibility testing (DST) was available in 36 (77%) ART programs on

Table Tuberculosis treatment practices in 47 antiretroviral therapy programs, overall and by geographical regions

ART program characteristic	All (n = 47)	Asia (n = 6)	Caribbean, Central and South America (n = 7)	Southern Africa (n = 14)	West, Central and East Africa (n = 20)
Treatment in line with NTP recommendations					
Strictly	40 (85.1)	4 (66.7)	5 (71.4)	11 (78.6)	20 (100)
Somewhat modified	7 (14.9)	2 (33.3)	2 (28.6)	3 (21.4)	0
Directly observed therapy*					
Never	11 (23.4)	2 (33.3)	2 (28.6)	5 (35.7)	2 (10)
During intensive phase	16 (34)	2 (33.3)	1 (14.3)	5 (35.7)	8 (40)
During the whole treatment duration	20 (42.6)	2 (33.3)	4 (57.1)	4 (28.6)	10 (50)
TB drug supply shortage in the past or present					
Never	28 (59.6)	6 (100)	5 (71.4)	7 (50)	10 (50)
At least one shortage	19 (40.4)	0	2 (10.6)	7 (50)	10 (50)
MDR-TB treatment					
Available†	26 (55.3)	5 (83.3)	4 (57.1)	5 (35.7)	12 (60)
Patient referred elsewhere	7 (14.9)	0	1 (14.3)	3 (21.4)	3 (15)
No specific regimen reported	14 (29.8)	1 (16.7)	2 (28.6)	6 (42.9)	5 (25)

* Directly observed treatment reflects its general use at the participating sites, irrespective of drug resistance.
† Sites with MDR-TB treatment available include sites with an MDR-specific regimen and sites using individualized regimens for the treatment of MDR-TB.
NTP = National Tuberculosis Program; TB = tuberculosis; MDR = multidrug-resistant.

site or within 50 km. HAIN GenoType MTBDR*plus* was available in 24 (51%) programs on site or within 50 km; 16/24 sites (67%) reported using it in case of suspected drug resistance. GeneXpert MTB/RIF was available in 23 (49%) programs on or off site. Directly observed therapy (DOT) as part of routine TB management was used by 36 sites (77%) during the entire treatment or the intensive phase only, and never used by 11 sites (23%). Nineteen (40%) sites used 19 different MDR-specific regimens, 7 (15%) sites individualized regimens, 7 (15%) sites referred MDR patients elsewhere and 14 (30%) sites did not report any MDR-specific regimen. At least one TB drug supply shortage was reported by 19 (40%) sites (Table). At the patient level, we observed that DST was used to diagnose TB in 158/719 (22%) HIV patients recruited at sites with access to DST. GeneXpert MTB/RIF and GenoType MTBDR*plus* were used in 21% and 15% of patients from sites with access to these tools, respectively. Where available, DST was less frequently performed among patients visiting rural than urban programs (0% and 24%, $P = 0.016$), while GeneXpert MTB/RIF was mainly used in peri-urban sites ($P = 0.007$) and GenoType MTBDR*plus* exclusively in urban sites ($P < 0.001$).

Conclusions: Key elements for controlling MDR-TB urgently need to be expanded in ART programs in lower-income countries, particularly drug resistance diagnostic capacity, DOT practices, adequate treatments and uninterrupted TB drug supply.

OP-260-03 Outcomes of isoniazid prophylaxis among HIV-infected children in routine clinical settings in Kenya

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Background: In 2011, the TB and HIV control programs in Kenya, started IPT implementation in selected HIV care clinics in public hospitals. The purpose was to gain local programmatic experience that would inform widespread IPT scale-up in HIV care clinics. We report the rates of treatment completion, loss-to-follow up, development of adverse drug reactions, TB disease and mortality among the HIV-infected children during the 6 months of isoniazid prophylaxis therapy (IPT).

Design/methods: We conducted a retrospective patient record review of all HIV-infected children enrolled in HIV care started on IPT in September 2011 and who had completed by November 2012 in three HIV care clinics in Makueni, Kangundo and Makindu District Hospitals of Eastern Province, Kenya. Eligibility for IPT in these facilities was determined by screening for TB using a nationally developed standard symptom questionnaire. During scheduled monthly follow-up clinics, TB screenings, clinical evaluation for adverse drug reactions, reinforcement of adherence counseling and filling of the IPT register were conducted as part of routine HIV care.

We retrieved the information on the study variables using the facility IPT register between December 2012 and January 2013. Data analysis was analyzed using Epi-Data software and done in relation to the study objectives.

Results: Out of 606 children started on IPT, 556 (91.7%) successfully completed while 20 (3.3%) completed with some treatment interruptions. Cumulatively, 30 children (4.9%) did not complete; four children (0.7%) were lost-to-follow, 4 (0.7%) were discontinued due to treatment interruptions, 2 (0.3%)

Figure Flow chart showing IPT implementation and outcomes.

developed adverse drug reactions up, 1 (0.165%) developed a chronic cough, 1 (0.165%) was transferred to non-IPT site and 18 (2.97%) developed TB including 2 (0.3%) who eventually died. TB was diagnosed in a median time of 3 weeks (interquartile range 2–16 weeks) post-IPT initiation. The median CD-4 cell count for those aged 1–4 years who developed TB disease was 1023 cells/ml[3] (interquartile range; 375–1432 cells/mm^{3}) while for those 5–14 years was 149 cells/ml[3] cells (interquartile range; 16–332 cells/mm^{3}). Isoniazid resistance was not detected in the four culture confirmed tuberculosis cases.

Conclusion: The high treatment completion, low loss-to-follow up rate and few adverse drug reactions affirm the feasibility of IPT provision to HIV-infected children in routine HIV care settings.

OP-261-03 Poor outcomes in a cohort of HIV-infected adolescents undergoing treatment for multidrug-resistant tuberculosis in Mumbai, India

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Background: Little is known about the treatment of multidrug-resistant tuberculosis (MDR-TB) in HIV-co-infected adolescents, while data from other chronic diseases suggest the need for special interventions in this age-group. This study aimed to present the intermediate outcomes of HIV-infected adolescents ages 10–19 years receiving second-line anti-TB treatment in a Médecins Sans Frontières (MSF) project in Mumbai, India.

Design/methods: A retrospective review of medical records of 11 adolescents between July 2007 and January 2013 was undertaken. Patients were initiated on either empirical or individualized second-line ambulatory TB-treatment under direct observation.

Results: The median age was 16 (IQR:14–18) years and 64% were female. Five (46%) adolescents had pulmonary-TB (PTB), three (27%) extrapulmonary disease (EPTB) and three (27%) had both PTB and EPTB. Median CD4-count at the time of MDR-TB diagnosis was 162.7 cells/μl (IQR 84.8–250.5). By January 2013, eight patients had final and 3 had interim outcomes. Positive results were seen in four (36.5%) patients—one was cured and three were still on-treatment with negative culture. Seven patients (64%) had poor outcomes: four (36.5%) died and three (27%) defaulted. Three of the patients who died never started on antiretroviral and/or TB-treatment and one died 16 days after treatment initiation. Two
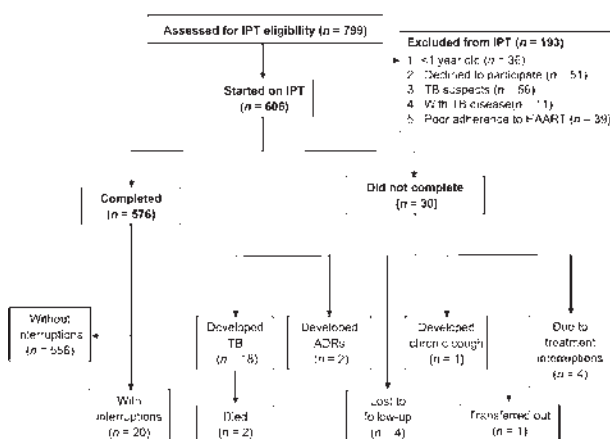
of the defaulted patients died soon after default. All patients (100%) on-treatment experienced adverse events: two required permanent discontinuation of the culprit drug and two were hospitalized due to AEs. No patient required permanent discontinuation of the entire second-line TB or antiretroviral regimens.

Conclusion: Early mortality and mortality after default were the most common reasons for poor outcomes in this study. Early mortality suggests the need for rapid diagnosis and prompt treatment initiation, and adolescents might benefit from active contact-tracing and immediate referral. Default occurred at different times suggesting the need for continuous, intensified and individualized psychosocial support for co-infected adolescents. Operational research among co-infected adolescents will be especially important in designing effective interventions for this vulnerable group.

IDENTIFYING BARRIERS TO THE TREATMENT AND PREVENTION OF TUBERCULOSIS IN CHILDREN

OP-262-03   Increasing pediatric tuberculosis detection: moving from guidelines to implementation

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Background: Globally, pediatric TB is under diagnosed, leading to unnecessary childhood deaths. In 2011 in Tanzania, there were 4968 (NTLP data report) TB case notifications in children under 15 years of age, accounting for 8.4 percent of the total new case notifications. However, the true magnitude of TB disease among children in Tanzania is likely much greater due to difficult in diagnosing TB in children. The Tanzania Ministry of Health worked with partners to develop a comprehensive pediatric TB program to increase TB detection and improve management of TB among children in an effort to reduce the child mortality and morbidity caused by TB disease.

Methods: With funding from the United States Agency for International Development, PATH, Dartmouth College and other partners have supported the Ministry of Health and Social Welfare's National TB and Leprosy Program to develop national pediatric TB guidelines and pilot training materials for health care workers from May 2010 to March 2012. Between June 2012 and March 2013, PATH and NTLP, trained trainers and health care workers on pediatric TB management. Work plans were developed to increase case detection in children. The trained personnel were

visited on a monthly basis to provide additional mentorship.

Results: The pediatric TB guidelines were implemented in all health facilities in which 49 trainers and 481 health care workers were trained. Findings from the supervision show that screening for TB infection in children is being practiced in those health facilities with trained health care workers.

There has already been notable increase in the number of children suspected, screened, and diagnosed with TB. As an illustrative example, the chart below shows more than doubling in the number of children diagnosed with TB from the previous year in four hospitals. We will be able to report on regional level data later in 2013. In addition, community based organizations have been engaged to assist with tracking lost-to-follow-up children.
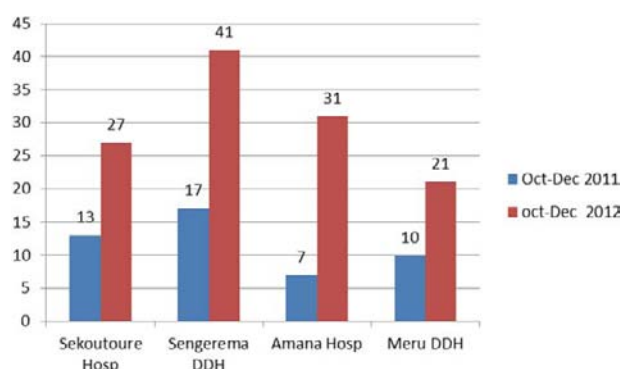
Figure   Number of children diagnosed with TB in 4 hospitals.

Conclusions: The introduction of new pediatric TB guidelines and accompanying training, routine supportive supervision and mentorship for health workers has improved TB case detection among children. Future work should also take advantage of existing community innovations (use of drug sellers, traditional healers, community based distributor) to improve case detection.

OP-263-03   Health system gaps in the management of childhood tuberculosis in Bangladesh: findings from a rapid assessment

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Background: According to the Bangladesh National Tuberculosis Control Program (NTP), the reported prevalence of childhood TB among all cases is 2.8%. This is considerably low compared to 11% of all cases in other high-burden countries. Contrary to NTP estimate, studies conducted by the Damien Foundation and icddr,b have shown a far greater prevalence of childhood TB in Bangladesh. For understanding the causal factors behind low detection of childhood

TB, it is essential to gather evidence-based information on existing capacities and resources of the service delivery system. For this, we conducted a rapid assessment during April–August 2011 at selected primary healthcare facilities to identify gaps in childhood TB management in terms of supply-side inputs, processes and outputs, and identify modifiable determinants of gaps pertinent to capacities and resources.

Methods: Nineteen primary healthcare outlets of NTP partner organizations were purposively chosen from urban and rural areas. Key informant interviews, facility inventories, review of service statistics and documents were conducted. Service statistics reviewed were pertinent to the year prior to the assessment. Information collected was organized by manual coding into themes and subthemes for thematic analysis. Triangulation of data derived from different sources was carried out to validate information.

Results: Proportion of childhood TB managed was substantially low (4%) compared to adult TB cases (96%). Surprisingly, no case of TB was detected in under-five children. In Dhaka, children were diagnosed at the tertiary-care facilities and showed up at study clinics for receiving anti-TB drugs. Service providers had no training on childhood TB management depicting a knowledge gap. The IEC materials displayed and used were all focused on adult TB. Shortage of supplies for Mantoux test and radiology was observed. Contact tracing and preventive therapy were not routinely practiced.

Conclusions: Considerable gaps in the capacity of workforce, information dissemination, and diagnostics were identified. Determinants attributable to gaps were lack of training, IEC materials specific to childhood TB, and diagnostic tools. Based on the hypothesis generated through this assessment, we recommended undertaking of an implementation research to develop, test, and scale up appropriate interventions.

OP-264-03   Barriers to care preventing tuberculosis-exposed newborns from completing therapy

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Background: High-risk tuberculosis (TB) -exposed newborns were evaluated for health system-, maternal-infant- and socio-economic factors associated with completing TB therapy.

Methods: A prospective cohort study, conducted at Tygerberg Hospital, Cape Town, South Africa, from January 2011 through June 2012, followed TB-exposed newborns requiring TB therapy to 6 months of age. The primary determinant, appropriate TB therapy referral was defined as evidence of a TB clinic referral letter or prescription of TB therapy. Maternal, infant and socio-economic characteristics were evaluated at baseline. The primary outcome, completed TB therapy (defined as isoniazid preventive therapy (IPT), TB treatment for 6 months or 3 months of IPT with a negative tuberculin skin test) was measured at 6 months. Data was collected from maternal-infant folders and standardized caregiver interviews. Logistic regression was used to determine odds ratios.

Results: Fifty-six TB-exposed newborns were included (63% HIV-exposed); 53 receiving IPT and 3 TB treatment. Forty-four of 56 (79%) were followed to 6 months and 12 were not retained; 1 died, 4 withdrew and 7 were lost to follow-up. The median gestational age was 36 weeks (IQR 36–39 weeks) and median birth weight 2120 grams (IQR 1528–2866 grams). Twenty-nine of 44 (66%) infants completed TB therapy with standard study protocol measures. Appropriate TB referral was associated with completion of TB therapy; unadjusted odds ratio of 3.6 (95%CI 1.0–13.5). Multivariable adjustment for maternal, infant and socio-economic factors did not alter this association 3.4 (95%CI 0.9–13.4).

Conclusions: Appropriate TB referral could aid to ensure TB therapy is completed in TB-exposed newborns in high burden settings.

OP-265-03   Isoniazid preventive treatment in two districts of Tamil Nadu, India: does practice follow policy?

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Background: India's Revised National Tuberculosis (TB) Control Programme recommends screening of all household contacts of smear-positive TB cases. For contacts aged <6 years without TB disease, daily isoniazid (INH) preventive treatment (IPT) is recommended for 6 months. Among sputum smear-positive patients registered for TB treatment during January–June 2012 in Krishnagiri and Tiruvalur districts of Tamil Nadu, India, we determined the proportion of pediatric household contacts who initiated and completed IPT, and determined the reasons for non-initiation and non-completion.

Design/methods: Among 1513 sputum smear-positive index patients, 691 were randomly selected and interviewed to identify all household contacts <6 years of age. Questions were asked to assess the processes of TB screening among their child contacts, IPT initiation and reasons for non-initiation and non-completion

of IPT. To rule out active TB and assess IPT eligibility, all children were evaluated by medical examination, review of signs and symptoms, chest radiograph, and when available, sputum smear microscopy.

Results: Amongst 271 pediatric contacts identified to be living with 691 index patients, 218 (80%) were evaluated and 9 were diagnosed with TB. Of 209 eligible contacts, 70 (33%) were initiated on IPT, and 16 (23%) completed a full course of IPT. Of 139 contacts eligible but did not initiate IPT, 5 became subsequent TB cases. The main reasons for non-initiation of IPT included: no initial home visit by the field staff (19%), home visit by field staff but no information about IPT provided (61%), informed about IPT but no INH was provided (11%), INH provided but not consumed due to daily pill burden (9%). Fifty-four patients who started IPT did not complete, including 6 who developed TB during IPT. The main reasons for not completing IPT included: INH not provided (51%), daily pill burden (27%), treatment related side effect (11%), and death or migration of the index case (11%).
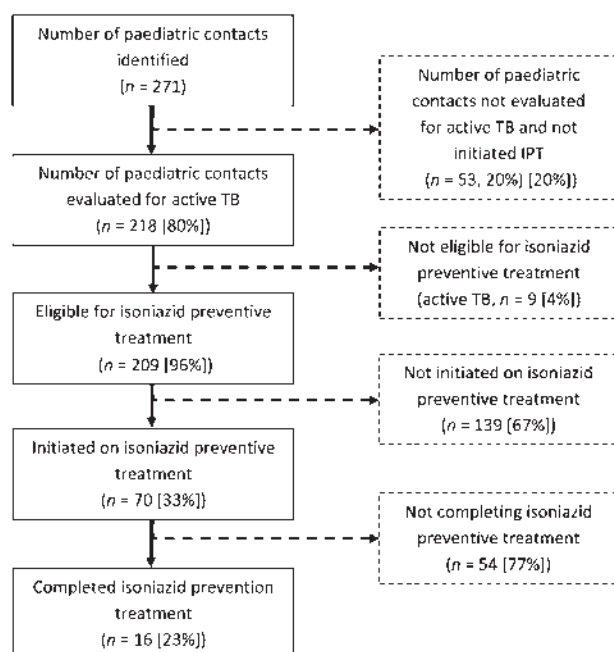
Figure Paediatric tuberculosis contacts identified, screened, and initiated isoniazid preventive treatment (IPT) and completing IPT in Krishnagiri and Tiruvalur Districts, India 2012.

Conclusion: While household contact investigation identified eligible contacts, IPT initiation and completion was low. These data represent a missed opportunity to prevent future TB cases. Major gaps for non-initiation may be corrected by training, improved logistics and enhanced supervision and monitoring. Moreover, because daily pill requirement was noted as a barrier, a newer once-weekly, 12-dose regimen may improve both treatment initiation and completion and should be evaluated for use in India.

OP-266-03   Ending child deaths from drug-resistant tuberculosis: lessons from the Sentinel Project

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Background and challenges to implementation: Despite advances made against tuberculosis (TB) and recent calls to achieve zero TB deaths and suffering, children continue to be left behind. TB in a child is a sentinel health event that signals ongoing transmission in that child's community. The experiences of children with drug-resistant TB (DR-TB) in particular, identify gaps in programs, policies, and practices that are failing. The Sentinel Project on Pediatric Drug-Resistant Tuberculosis and Treatment Action Group (TAG) reached out to colleagues around the world who submitted stories of children affected by DR-TB. Here, we present the actionable gaps in programs, policies, and science identified through the collection of 62 stories from 38 countries.

Intervention or response: Between January 2012 and March 2013, the Sentinel Project on Pediatric Drug-Resistant Tuberculosis and TAG reached out to a global community of stakeholders to collect information about the experiences of individual children affected by DR-TB. We requested either drafts of stories or responses to a structured questionnaire made available in four languages. Through a review of the gathered materials, we identified gaps in current programs, policies, and science and then categorized these by theme: (1) prevention, (2) diagnosis, or (3) treatment, care and support. We then developed recommendations to address these gaps.

Category	Recommendations to address TB in children: what we need
Prevention	A more effective vaccine to prevent all forms of TB and provide lasting immunity
	Development and delivery of preventive therapy (with child-friendly formulations) for individuals exposed to patients with DR-TB
	Improved infection control in TB clinics and hospitals
	Community education about how to prevent TB transmission
Diagnosis	Application of a family-centered approach to screening for TB that includes screening of all child contacts of patients with DR-TB
	Improved referral systems and follow-up for child contacts
	Improved training for clinicians and community health workers to detect TB in children
	Improved clinical evaluation guidelines
	Better tests to detect TB and drug resistance in children, specifically point-of-care tests that are rapid and do not rely on sputum specimens
	Streamlined communication strategies between diagnostic labs and health care providers and patients
Treatment	Implementation of a patient-centered approach to care that provides comprehensive services and psychosocial support to children with DR-TB and their families
	Delivery of DR-TB treatment regimens for children that promise the best chance of cure, including the use of empirical regimens in patients without bacteriologic confirmation or who are awaiting DST results
	Integration of care with other health programs, including migrant services, HIV services, and existing child health programs
	Child-friendly formulations of TB drugs that have a low pill burden, are easier to ingest, taste better, and do not require injections
	Faster-acting, more tolerable drugs with fewer side effects
	A steady and reliable supply of TB drugs

Results and lessons learnt: By March 2013, we gathered 62 stories from 38 countries and identified a series of recommendations for actions required to improve prevention, diagnosis, and treatment of childhood DR-TB. These recommendations draw attention to children with DR-TB and offer the global TB community specific areas on which to focus their attention and efforts in order to prevent child deaths and suffering from all forms of TB.

Conclusions and key recommendations: Stories of individual children with DR-TB are invaluable sources of information. Gaps in science and action can be readily identified by a review of stories gathered through a network of global stakeholders. Zero TB deaths, new infections, and suffering in children will remain elusive until we address the identified gaps in programs, policies, and science. These gaps will only be addressed with increased political will and investment in tackling all forms of TB in children.

HUMAN CAPACITY DEVELOPMENT: THE BASIS OF GOOD PROGRAMMES

OP-267-03   Advice about contraception to female tuberculosis patients and LTBI patients

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Background and challenges to implementation: The Dutch guidelines advise alternative contraception for women with active TB and LTBI, receiving rifampicin treatment, who use oral contraception. Using condoms and prescribing a higher dosage, are the given alternatives for oral contraception. Patients have to be informed about interference of TB medication by their physician. One of the questions on the Dutch nurses case history, refers to oral contraception.

A female patient asked an alternative contraception for condom use. She preferred oral contraception. We consulted colleague nurses and TB-physicians and looked for guidelines on the internet. We received different and sometimes contradictive advices.

Intervention or response: A questionnaire was sent to all public health TB-nurses (70) and TB-physicians (31) and to all TB-physicians (4) from the Dutch Tuberculosis Centers. Additionally we informed all participants by e-mail to motivate participation. The results have been sent back within 3 weeks. We analysed the results in Excel. The results will be shared with all participants.

Additionally, 6 TB-nurses and 1 TB-physician have been interviewed about 9 pregnant patients in 2011.

Results and lessons learnt:
- 60 nurses and 26 physicians have sent in the questionnaire. (Not) surprisingly there was not much consensus.
- 31% of the physicians and 47% of the nurses would like to have more information or an additional directive about alternative contraceptives.
- A fact sheet about alternative contraception methods has been developed.

Conclusions and key recommendations:
- Both physicians (27%) and nurses (37%) often recommend as only alternative method, the use of condoms.
- Most physicians (54%) and nurses (57%) discuss the subject no more than once during the treatment.
- Cultural aspects, religion, health literacy and personal beliefs and preferecences from the patient and her partner influence their choice for a contraceptive.
- All women of fertile age should get an advice about contraception.
- Mention different contraceptive methods. Give an advice that is suitable for the woman.
- Discuss it at least twice with the patient; the first time to inform and advise the patient and the second tim to ask if she found a found a solution or to repeat the message.
- Pregnancy should be avoided in patients with MDR-TB and XDR-TB and during the first months of TB treatment.

OP-268-03   Evaluation of a tuberculosis infection control training and implementation package for HIV clinics and outpatient clinics in resource-limited settings, Zambia

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Background and challenges to implementation: Crowded antiretroviral treatment (ART) clinics in sub-Saharan Africa are high-risk locations for transmission of tuberculosis (TB). An implementation package was developed to train HIV clinic staff on TB infection control (TBIC) concepts and included a training video, risk assessment and planning tools, and job aids. The objective of this evaluation was to collect facility-level data at baseline and at 1-year to evaluate the ability of healthcare workers trained with the package to improve TB IC measures.

Intervention or response: In September 2011, training was provided for healthcare workers and supervisory staff from 8 ART clinics in 4 provinces of Zambia. The facilities were assessed at baseline and subsequently reassessed in September 2012 with a

32 item risk assessment tool to document changes in TB infection control practices. Health care workers were interviewed to determine implementation barriers.

Results and lessons learnt: Of TB infection control risk reduction activities measured at baseline and follow-up at the 8 clinics, there was an overall increase in implementation of the 32 measures from 31.0% to 56.1%. Implementation of categories of controls also increased: managerial (42.1% to 61.4%), administrative (25.0% to 56.3%), environmental (35.7% to 69.2%), and personal protective equipment (PPE) (3.7% to 11.1%). There was a significant increase at $P < 0.05$ in clinics complying post-intervention on 7 of 32 indicators on the risk assessment: facility design and patient flow assessed; TBIC training for all staff done; coughing patients separated and fast-tracked; supplies available for coughing patients; staff receive an evaluation for TB annually; confidential log is kept of all staff diagnosed with TB; and surgical masks available and worn by coughing patients. 22 trainees completed a 44-question pre-/post-test; their scores improved by an average of 3.5 questions. At 1-year, healthcare workers were interviewed on what could be done to increase implementation of TBIC and stated the need for supervision, staff training and community sensitization, as well as supplies and support from management, including a budget for TBIC activities. Of those trained 57% stated that they had received a TB IC supervisory visit.

Conclusions and key recommendations: A structured TB infection control training package resulted in improved healthcare worker knowledge and practices at 1-year following the training. Support from facility management as well as ongoing supervision is important for program sustainability.

OP-269-03 Training and practice improvement following ICN Training for Transformation in Indonesia: impact, facilitating and hindering factors

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Background: The International Council of Nurses (ICN) with the Indonesian National Nurses Association (INNA) ran courses in March 2010 and November 2011 to train nurses as trainers in the care of people affected by TB. Before the course, the nurses expressed commitment to each train at least 10 nurses and 10 allied health personnel after the TFT. In November 2012, the nurses attended a review which included an evaluation survey.

Aims: The survey aimed to describe the impact of the TFT and identify facilitating and hindering factors.

Methods: A self-administered questionnaire was used which was developed using information from previous evaluations, review workshops, feedback from trainers and national nurses associations.

Results: Of the 55 nurses trained in 2010 or 2011, 29 (53%) answered the tool. Majority (62%) were females. The nurses reported training a total of 2094 people including 642 nurses, 797 students, and 574 community members including community leaders and teachers—an average of 72 training contacts per nurse originally trained. Since the TFT, all developed health education materials, 21 (72%) reported seeing an improved attitude among nurses towards people affected by TB, 23 (79%) reported reduced stigma among service users, 12 (41%) engaged community organizations. Many reported a higher level of confidence when talking to colleagues (97%) and superiors (90%) about TB, advocated for improved emotional support for patients (86%) and for improved TB infection control measures in their work settings (69%), and 26 (90%) have been given more responsibility regarding TB. Some (41%) conveyed that other personnel working in the TB control programme did not think they should do training. The most important factor which helped majority (72%) of the nurses to train others were motivation (31%), funding support (28%), time (28%), and management/stakeholder support (21%). The biggest barriers identified were financial (55%) and stakeholder (31%) support, human resource limitations (7%) and time (17%).

Conclusion: The nurses exceeded expectations in terms of the number of people trained. Positive changes in attitude towards people affected by TB and initiatives to improve nursing practice were reported. Collaboration with the NTP and other partners is needed to sustain the facilitating factors, address barriers and integrate the TFT trained nurses' role and activities to the TB prevention and control initiatives in Indonesia.

OP-270-03 Preparedness for task shifting of TB-HIV services: an exploratory study among community health workers in the Free State Province, South Africa

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Background: In South Africa the advent of task-shifting and the primary health care (PHC) re-engineering strategy with its emphasis on multi-trained and skilled outreach teams necessitates consideration

of the preparedness of community health workers (CHWs) to provide a variety of TB-HIV services. The objective of this exploratory research was to assess and describe CHWs' preparedness—namely their training, knowledge and attitudes—to provide TB-HIV services.

Design/methods: Interviews were conducted with 206 CHWs at 28 clinics in three sub-districts in the Free State Province. Uni- and bivariate analyses were performed. Findings include statistically significant correlations between the types of CHWs and their sub-district location, on the one hand, and their TB-HIV-related training, knowledge and attitudes, on the other.

Results: Large majorities the CHWs had not received basic training in HIV counselling and HIV testing and a large minority had not received basic training in TB/DOT support. Large majorities had not received any follow-up training in HIV counselling, HIV testing, and TB/DOT support. In respect of the TB-HIV knowledge items assessed, a large majority were knowledgeable, but a small minority were ignorant about important facts related to TB-HIV. Lay counsellors were found to be statistically significantly more knowledgeable about TB-HIV than TB/DOT supporters ($U = 2074$; $P = 0.04$) and other CHWs ($U = 523$; $P = 0.00$). While majorities (strongly) disagreed with stigmatising statements about people with TB-HIV, minorities (strongly) agreed with certain stigmatising assertions. The sub-district location of CHWs was statistically significantly associated with their attitudes towards people with TB-HIV, with CHWs in rural sub-districts being more likely to harbour stigmatising attitudes.

Conclusion: In the context of PHC re-engineering, this exploratory research suggests that CHWs' TB-HIV training, knowledge and attitudes need to be improved if integrated TB-HIV services are to be successfully task-shifted to them in line with policy recommendations.

OP-271-03   A study to compare the opinions of RNTCP managers and nurse educators about the involvement of nurses in tuberculosis control in India

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Introduction: India has a high burden of TB MDR TB, and HIV. The stop TB partnership global plan estimates that one million MDR TB patients will need to be detected and put on treatment between year 2011–2015 globally. This plan also aims that 75% MDR TB will be treated successfully. To achieve these targets the right number of people, with right skill, in right places at right time are needed. India is preparing approximately 225 000 nurses by various nursing institutions in different cadres apart from already registered nurses.

Aim: This study was done to assess the opinion of both RNTCP managers and nurse educators on the involvement of nurses in tuberculosis care and the associated training needs.

Materials and methods: One semi structured opinionnaire constructed for the study was used to collect the data from RNTCP managers and nurse educators. Content validity and reliability was established before data collection. The tool had three parts starting from broad question to specific questions. χ^2 and exact test were used using SPSS with confidence interval of 95%.

Results: Though there was 100% agreement that nurses should be trained to involve in RNTCP for tuberculosis control, statistically significant differences of opinion were found when the tool narrowed down on training aspect related to content and skill. Nurse educators had a broader view of training than the RNTCP managers. 70% of nurse educators and 46% of RNTCP managers felt that DOTS strategy should be taught to nurses. As for DOTS Plus strategy only 40% of RNTCP managers said yes against 70% of nurse educators. Only 50% of RNTCP managers agree that nurses should be oriented to RNTCP whereas 90% of nurse educators thought they should. More specifically there was strong support (90–100%) for nurses to identify side effects, implement ACSM and provide patient counseling.

Discussion: The potential role of nurses in TB care and management may be limited by a lack of understanding of the broad nature of the nursing role. The Indian Nurse Training curriculum is oriented to equip nurses with skills of problem solving, critical thinking, decision making, health education, advocacy, creativity, communication, empathy, interpersonal relations and self awareness: the same qualities required by Senior Treatment Supervisor in RNTCP.

Conclusion: The potential of nursing workforce could be more effectively utilized for tuberculosis control.

TUBERCULOSIS IN THE WORKPLACE

OP-272-03   Cost-effectiveness of IGRAs and chest X-ray for tuberculosis screening of health care workers with and without diabetes and tobacco smoking

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Background: The prevalence of tuberculosis (TB) in healthcare workers (HCWs) is higher than that of the

general population. Interferon-gamma release assays (IGRAs); QuantiFERON-TB® Gold In-Tube (QFT) and T-SPOT®.TB (T-SPOT), are new alternatives to the tuberculin skin test (TST) to detect latent tuberculosis infection (LTBI) with higher specificities than that of TST. This study aimed to assess the cost effectiveness for TB screening of HCWs with and without diabetes mellitus (DM) and tobacco smoking using IGRAs compared to TST and chest X-ray (CXR).

Design/methods: We constructed Markov models of six strategies; QFT, T-SPOT, TST, TST followed by QFT, TST followed by T-SPOT and CXR. HCWs of 30-year olds with and without DM and tobacco smoking were chosen as a hypothetical cohort followed to 60 years using a societal perspective. Incremental cost per quality adjusted life year (QALY) gained ratios were compared. All costs and clinical benefits were discounted at a fixed annual rate of 3%.

Results: In base-case analysis of HCWs, QFT strategy yielded the greatest benefits at the lowest cost (HCWs: US$750.75, 21.09 QALYs, HCWs with DM: US$969.15, 21.08 QALYs, HCWs with tobacco smoking: US$922.75; 21.06 QALYs,) [year 2012 values]. CXR strategy was the least cost-effective. Cost-effectiveness was sensitive to BCG vaccination rate. TST strategy was more cost-effective than QFT strategy at the willingness to pay level of US$50000/QALY gained only when BCG vaccination rate was less than 0.02 (HCWs), 0.18 (HCWs with DM) and 0.32 (HCWs with tobacco smoking).

Conclusion: The QFT strategy yielded the greatest benefits with the lowest cost for TB screening of HCWs with and without DM and tobacco smoking. Using IGRAs for TB screening of HCWs with and without DM and tobacco smoking should be recommended on the basis of the cost-effectiveness.

OP-273-03   Tuberculosis screening campaign and control measures to reduce transmission of occupational tuberculosis in health workers at the flagship public hospital of Mozambique

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Introduction: In crowded Mozambican hospitals, HIV drives transmission of nosocomial tuberculosis (TB). Health workers (HW) exposed on the job suffer morbidity, absenteeism and even mortality. Underfunded hospitals lack effective TB control programs. At Maputo Central Hospital (MCH), the flagship hospital of the Mozambican public health system, numerous cases of TB and at least 3 cases of multi-drug-resistant (MDR) -TB occurred among HW in 2010. At this time, there was no TB control office, no screening or reporting of TB in HW, and no plan to control in-hospital TB transmission. The recently chartered TB control committee has not yet fully implemented a TB control program. A pilot to determine the point prevalence of HIV and TB in HW and gather baseline incidence data was conducted.

Methods: The TB control committee chartered in late 2011 executed a publicity campaign with posters and departmental trainings advocating early identification, triage, and treatment of TB suspects, cough etiquette and appropriate mask use. In April 2012 a pilot screen for HIV and active TB was conducted in the medicine department. Twelve months after the initial screen, physicians in the medicine department who treat TB were surveyed.

Results: Of 156 HW screened in the pilot, 17% were HIV positive and 1 case of active TB was identified. Four additional symptomatic cases presented to TB control personnel in the following months. At the end of 12 months, twenty cases of active TB in HW were reported: 19 new cases and one re-treatment. Three new cases (16%) were MDR-TB. Fourteen were pulmonary, 5 extrapulmonary, and one was both. Thirteen were smear-positive, 3 smear-negative, and 4 did not provide samples. Four were HIV+, 10 HIV−, and 6 had unknown HIV status at the time of the survey. Given this information, the hospital director pledged to support the designation of TB office space, administrative support for early triage, isolation and treatment of TB suspects and further to renovate ventilation and add upper-room Ultraviolet Germicidal Irradiation (UVGI) fixtures in high-risk areas. Funds for a dedicated TB-control nurse to oversee implementation and adherence were further requested.

Future plans: The two-phase implementation of a UVGI installation and a triage-isolation protocol in urgent care is outlined in the figure. In a move toward annual screening of HW, a pilot to screen 500 HW for active and latent TB, funded by UCSD Center For AIDS Research, will start in May 2013.

OP-274-03   Analysis of the prevalence of tuberculosis among health care workers in Guangxi, 2007 to 2011

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Background: To analyze the tuberculosis (TB) case among health care workers in Guangxi, and provide evidence for intensifying control of TB infection.

Design/methods: Applied the systematic review methods, and investigated the situation of TB case among health care workers from 2007–2011.

Results: During the 5 years, there ware register 710 TB case whose profession was health care. The reported incidence among health care workers in TB control institutions (0.8%) is higher than the other (0.31%), $P < 0.01$. The reported incidence among health care workers come from west and north area (0.35%) is higher then those come from east and south area (0.23%), $P < 0.01$. The Logistic regression analysis on the influence factor show that: institution and area are the risk factor. Only 46.20% those who present TB symptoms can go and see doctors.

Conclusion: It must developing a TB control strategy for supervise and manage health facility. In the meantime, it is imprudent to support backward area and provide training to raise health care workers' awareness.

OP-275-03   Latent tuberculosis and within-subject variability of IGRA in Danish health care workers

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Background: Health care workers (HCWs) treating patients with tuberculosis (TB) are at risk of becoming infected. Hence periodical screening of HCWs is a part of TB control programs in low incidence countries. Evidence of the utility of interferon gamma release assays (IGRAs) in diagnosing latent TB is growing. The use of IGRAs for serial testing is complicated by lack of data on optimal cut-off. But because of a substantial within-subject variability the use of an uncertainty zone (for instance between 0.2 and 0.7 iU/ml) has been suggested.

Aim: The aim of the study was to estimate the prevalence of latent tuberculosis and the within-subject variability of IGRA among health care workers with known exposure to TB at work in a TB low incidence country.

Methods: Employees working at the pulmonary ward, intensive care unit and as radiographers in Gentofte Hospital in Copenhagen (approximately 150 treated TB patients/year) were invited to participate. They completed a questionnaire and blood samples for IGRA-testing (QuantiFERON®, cellestis (QFT)) were drawn twice with an interval of two weeks.

Results: 168 persons participated. In 9 participants (5.4%) both QFT tests were positive. Six of these participants had no history of TB exposure other than at work. One had previously been treated for pulmonary TB, which was presumed work-related. Two of them had been living in TB high incidence countries. The first test of one participant, who had been living in a TB high incidence country, was posi-

tive, the second test was inconclusive due to a technical error.

8 participants (4.8%) had inconsistent tests (the first test was negative and the second positive in 6 participants and the first test was positive and the second negative in 2 participants). All but two of the participants with inconsistent tests had at least one result within the suggested uncertainty zone. Only one of the participants with two positive QFT tests had a test result within the zone. 132 had two negative QFT, 6 had one negative end one indeterminate test. 11 participants, who only got tested once, had a negative QFT.

Conclusion: HCWs have an occupational risk of becoming latently infected with TB. In our study we found that 5.4% of the participants were latently infected. 4.8% had inconsistent results. How, and under which circumstances, IGRA tests can be used to screen healthcare workers for latent *M. tuberculosis* infection awaits further studies on IGRAs used for serial testing.

OP-276-03   Tuberculosis in special setting-developing partnerships with the garment industries in Bangladesh

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Background: The Bangladesh garment manufacturing sector is a significant employer employing nearly 4 million workers. More than 80% of whom are poor young women, migrated from rural and work long hours in a confined environment. They are vulnerable to TB, both directly due to higher risk of infection as a result of high concentrations of people in the workplace, and indirectly due to job loss as they are perceived as a workforce threat. We, therefore, developed a sustainable TB workplace model with garment factories to reduce the TB burden in their workforce.

Design/methods: We used operational research to develop and evaluate a mechanism for effective and sustainable TB control in 60 garment factories of Dhaka city. We evaluated the project using quantitative and qualitative measures: changes in TB outcomes were calculated using standard indicators based on factory and DOTS centre records; changes in TB care-seeking behaviour were assessed using semi-structured in-depth interviews. Quantitative data were analysed using SPSS, version 14.0 and Microsoft Excel. Qualitative data were systematically analysed using a thematic approach based on predefined and emergent themes relevant to the study objectives.

Results: The project brought positive changes in knowledge, attitudes and practices of managers, workers and health care provides on TB care and control. During 2008–2010, a total of 3372 workers from a workforce of 69 000 were examined for sputum microscopy and 598 were diagnosed with smear positive TB, 145 of which received care at their workplace—the overall treatment success rate was 100%. The remaining 453 smear-positive TB cases continued to receive TB treatment from the NGO-run DOTS centres after being diagnosed with TB. Recording and reporting of those cases was made through the NTP. The overall treatment success rates of those partner NGOs varied between 85% and 89%. 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: It is feasible to engage garment sector in TB control activities, and thereby increase case notifications, improve treatment outcomes amongst garment workers. This approach is now being scaled up across other garment factories in Bangladesh.

AROUND THE WORLD WITH TUBERCULOSIS AND DIABETES MELLITUS

OP-277-03   Response to treatment by patients with tuberculosis and diabetes mellitus under a routine program setting in India

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Setting: Diabetes mellitus (DM) is emerging global public health problem which can increase the risk of tuberculosis and adversely affect TB treatment outcomes. A descriptive study was carried out in a cohort of TB patients registered at Lok Nayak Clinic in a tertiary health facility in Delhi, India.

Methods: A descriptive study was carried out reviewing records and reports of the Revised National TB Control Program (RNTCP). The setting was a chest clinic at a tertiary care teaching hospital in New Delhi, which has been implementing TB control activities for the last 10 years. The clinic has a catchment population of 0.5 million, and was one of the collaborating centers for the TB-DM bi-directional pilot project. All adult TB patients diagnosed and registered from 15 February to 30 September 2012, were included in the study. Patients were first screened for known DM, and in the remainder blood tests were carried out using glucometers and test strips as previously described. Patients were diagnosed with DM if the fasting blood glucose (FBG) ⩾ 126 mg/dl,

in line with WHO guidelines. Regardless of DM status, all patients were treated with standardized TB treatment according to national guidelines, and were followed until the end of treatment.

Results: There were 458 registered TB patients in the study out of which 226 (49%) were males and 232 (51%) were females. The mean age of the study population was 32 years (IQR 20–42). Nearly 66 patients (14.5%) were found to be diabetic. The TB patients with DM and without DM were compared for the variables like sex, age, disease classification, type of TB, HIV status, smoking status, sputum smear conversion and treatment outcomes (Table). Only variables with age above 40 years and disease classification with pulmonary tuberculosis were found to be statistically significant.

Conclusion: In this study, we found that it was feasible to routinely screen all TB patients for DM. There is no significant difference in sputum smear conversion and treatment outcome among diabetic and non diabetic group. The prevalence of DM was found to be higher among patients aged above 40 years and with pulmonary tuberculosis. To conclude, it is feasible to routinely screen all TB patients for DM under programmatic settings. The TB-DM patients should be closely monitored for better treatment outcomes.

OP-278-03   Diabetes mellitus, hemoglobin A1c and tuberculosis disease characteristics in new adult pulmonary tuberculosis patients, Tbilisi, Georgia: a prospective cohort study

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Background: Diabetes mellitus (DM) and TB co-infection is an increasing global public health problem, but limited data exists on the association of DM and TB in the Caucasus region. The purpose of our study was to estimate the prevalence of DM and pre-DM among TB patients in the country of Georgia and estimate the effect of DM on TB clinical presentation and 2-month smear conversion.

Design/methods: Eligible participants included all new TB patients aged >34 years. Patients were enrolled from October 2011 to February 2013 at the Georgia National Center for TB and Lung Disease in Tbilisi. A rapid hemogloblin A1c (HbA1c) test from capillary blood was performed and was used to define DM (⩾6.5%), pre-DM (⩾5.7–6.4%), and normal glucose (<5.7%). Interviews along with medical chart and laboratory data abstraction were performed to measure clinical symptoms at presentation and to assess 2-month AFB status. Bivariate and multivariable logistic regression analyses were used

to determine associations between DM, pre-DM, and participant traits.

Results: Of 393 eligible participants, 224 enrolled. Most participants were male (74.6%), had completed high school (63.4%), and median age was 49 years. Prevalence of DM was 14.3% (95% confidence interval [CI] 10.2–18.9%) and pre-DM prevalence was 19.2% (95%CI 14.0–24.4%). Multidrug-resistant TB was common (17.9%) and HIV co-infection was low (3.8%). Compared to participants with normal glucose, those with DM had higher median body mass index (23.2 vs. 20.9), were more likely to be AFB smear positive (90.6% vs. 69.4%), and more often reported cough (93.1% vs. 73.6%) and hemoptysis (44.8% vs. 20.1%) at the time of diagnosis (P value <0.05 for all comparisons). In multivariable analyses, patients with TB and DM were more likely to have hemoptysis (adjusted odds ratio [aOR] 3.2, 95%CI 1.4–7.5); those with TB and DM/pre-DM were more likely to have cough (aOR 3.2, 95%CI 1.2–8.1), higher sputum AFB smear grade (aOR 2.2, 95%CI 1.0–4.0) and cavitary pulmonary disease (aOR 2.3, 1.0–5.0) compared to participants with normal glucose. Of 158 participants with completed 2-month AFB sputum smear, 30.4% were positive, including 38.9% with DM/pre-DM and 25.9% without DM, the difference was not significant.

Conclusion: Adults with new pulmonary TB in Tbilisi, Georgia with DM and pre-DM had more severe clinical disease at the time of diagnosis, but we did not detect a significant difference in 2-month AFB smear conversion. Additional longitudinal data is needed to determine if DM or pre-DM affects TB treatment outcomes in the country of Georgia.

OP-279-03   Association of tuberculosis and diabetes mellitus in urban Tanzania

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Background: Diabetes mellitus (DM) increases the risk of tuberculosis (TB) reactivation. However, only few studies have been conducted in sub-Saharan Africa, where the high incidence of TB is associated with HIV infection and where a sharp rise in the prevalence of DM is observed. We analyzed the cross-sectional link between TB, DM and HIV infection in Tanzania.

Design/methods: We conducted a case-control study between July 2012 and March 2013. Adults with TB diagnosed in 2 hospitals of the Kinondoni District in Dar es Salaam were included in the study. Healthy volunteers, free of infection and/or trauma and without past history of TB, were recruited among people accompanying patients at the outpatient department of one of these hospitals. They were screened for HIV and DM using fasting capillary glucose and 2 hours capillary glucose measured by a plasma-calibrated glucose meter (GlucoPlus™, Dibcare). DM was defined according to the American Diabetes Association. Independent predictors of DM among TB patients were identified by multivariable logistic regression analysis using Stata software (StataCorp, College Station, TX, version 11.2).

Results: Overall, 292 patients with TB and 125 healthy volunteers were included. Compared to controls patients with TB were more often male (64 vs. 35%; $P < 0.001$), had a lower body mass index (19.6 vs. 29.1; $P < 0.001$) and a higher prevalence of HIV infection (32 vs. 13%; $P < 0.001$). The prevalence of DM was higher among TB patients (7 vs. 3%; $P = 0.14$). Half of the diabetic cases were diagnosed by the 2 hours glucose only. TB cases presented significantly more often glycemic disturbance than controls (prediabetes and DM; 51 vs. 9%; $P < 0.001$).

Among TB cases, predictors of DM were advanced age (adjusted odds ratio aOR [95%CI] 1 [1–1.1]) and HIV infection (aOR [95%CI] 2.9 [1.1–7.2]) independently of combined antiretroviral therapy (Table).

	TB cases with DM $n = 20$ (7%) n (%)	TB cases without DM $n = 272$ (93%) n (%)	Factors associated with DM bivariate/ multivariable analysis	
			OR (95%CI)	P value
Age, years, mean ± SD	45 ± 11	36 ± 13	1 (1–1.1)/ 1 (1–1.1)	0.006/ 0.007
Male sex	9 (45)	170 (65)	2.3 (0.9–5.7)	0.08
Body mass index, mean ± SD	20.1 ± 4	19.6 ± 4.7	1 (0.9–1.1)	0.6
Waist size	76 (10)	73 (9)	1 (1–1.1)	0.2
Hip size	89 (10)	88 (9)	1 (1–1.1)	0.6
HIV infection or unknown HIV status	12 (60)	94 (35)	2.8 (1.1–7)/ 2.9 (1.1–7.2)	0.03/ 0.04
High blood pressure	3 (15)	16 (6)	2.7 (0.7–10.2)	0.1
Tuberculosis status				
Pulmonary smear positive	13 (65)	177 (66)	Ref.	Ref.
Pulmonary smear negative	5 (25)	67 (25)	1 (0.3–3)	1
Extra-pulmonary	2 (10)	23 (9)	1.2 (0.3–5.6)	0.8

Conclusion: Glycemic disturbance is significantly higher among patients with TB despite substantially lower BMI. HIV infection is overrepresented among TB cases with DM. The longitudinal characterization of DM epidemiology among TB patients as well as the identification of an optimal DM screening method in the TB setting are of public health relevance to improve the management of DM and TB in this population.

OP-280-03   The association of diabetes and tuberculosis: risk of active disease among household and community contacts suffering from diabetes mellitus

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Background: DM triples the risk of developing TB. Moreover, people with DM are more likely to fail treatment and more likely to die during treatment compared to those without DM. In Mexico, where the burden of DM is relatively high, it is a significant contributor to the number of cases of TB. Very few studies have sought to determine the risk of active TB among patients with DM who are HC of pulmonary TB patients. Furthermore, there is a lack of international consensus regarding strategies to prevent transmission of TB to patients with DM within the household.

Objective: To determine the risk of active TB among individuals with DM who share the household with pulmonary TB patients.

Methods: From 2001–2010, we collected epidemiological and clinical information from pulmonary TB patients and their HC and CC in the Orizaba Health Jurisdiction in Veracruz State, Mexico. Follow-up was performed to ascertain the development of active TB among contacts. Sputum samples were processed for *M. tuberculosis* following standardised procedures, and the isolates were genotyped and compared using IS6110-based restriction fragment-length polymorphisms (RFLP) and spoligotyping if the isolate's IS6110 RFLP patterns had fewer than 6 bands. We constructed random effects logistic models, which take into account the clustering of contacts within households, to assess the association between contacts with DM and their development of active TB.

Results: The prevalence of DM among 458 TB patients, 900 HC and 889 CC was 29.64%, 6.67% and 5.40%, respectively. The contacts were followed for a median of 91.26 months (range, 79.9–100.8); 30 individuals were diagnosed with TB during follow-up, (22 HC and 26 within 5 years after diagnosis of the index case). The adjusted odds ratio (aOR) of developing active TB among contacts with DM was 5.45, 95%CI 2.11–14.12 among all contacts; aOR 9.17, 95%CI 3.26–25.77 among HC; and aOR 17.69, 95%CI 5.06–61.87, among contacts developing TB with the same genotype as the index case. Models were adjusted for the age of the contact and the degree of exposure to the index case.

Conclusion: It is necessary to evaluate the need for recommendations to prevent TB in individuals with DM, particularly those who are exposed to pulmonary TB in the household.

OP-281-03   Population-level epidemiology of tuberculosis and diabetes mellitus in the context of epidemiological and economic transition

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Background: The global burden of type II diabetes mellitus (DM) is rising, with majority of adult cases expected to occur in low and middle-income countries. These countries are undergoing rapid demographic and epidemiological transition but still have a high burden of communicable diseases including tuberculosis (TB). The link between DM and TB has been recognized and increasingly more focus on the interaction between DM and TB is required.

We aimed to explore crude correlations between TB and DM at country and global regional levels.

Design/methods: We utilized 2008 WHO country data on TB incidence and DM prevalence (the most recent year for which DM data is available). Countries were classified using WHO regions. African countries were grouped using Global Burden of Disease sub-regions. Data on Gross National Income (GNI) per capita (an economic and epidemiological transition proxy) was obtained from the World Bank for 2004–2008. Correlations were calculated using Spearman's rank correlation coefficient.

Results: A significant positive correlation was found between TB and DM in Europe but a negative correlation was found in the Americas (non-significant in other regions; Figure).

We also compared the average change in gross national income (GNI) from 2004–2008 to DM prevalence and found a positive correlation between GNI growth and DM prevalence in the African and Eastern Mediterranean regions, but a negative correlation in Europe. Within Africa, there was a significant association between GNI growth and DM prevalence in Eastern and Central African, but not in Southern and Western African countries, where GNI growth was slower between 2004–2008. One hypothesis is that beyond a certain level of GNI and/or GNI growth, additional income can be used to address chronic
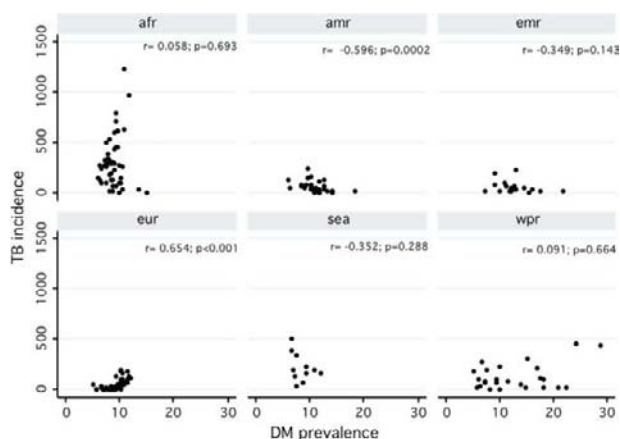
diseases of lifestyle associated with development. By contrast, less developed countries are less equipped to address these emerging NCD epidemics resulting in a rise in DM prevalence accompanying GNI growth. **Conclusion:** The non-significant correlation between TB and DM in regions outside of Europe and the Americas suggests that TB burden is driven by other factors such as HIV-infection and social determinants in less developed countries. This highlights that the association between TB and DM is heterogeneous at the population level and worthy of further evaluation across different high TB burden settings, to adequately assess the impact of epidemiological and economic transition on the TB burden.

EXPLORING TUBERCULOSIS RISK FACTORS

OP-282-03   Air pollution and pulmonary tuberculosis among a population-based sample of Northern California residents

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Background: Ecologic analyses, case-case comparisons and animal experiments suggest a positive association between air pollution and tuberculosis. No previous epidemiologic studies have examined this hypothesis in a large population-based sample, which would yield results that are more applicable to the general US population. We evaluated the association between ambient air pollutants and active pulmonary tuberculosis (PTB).
Design/methods: A nested case-control study was conducted among members of Kaiser Permanente Northern California. All cases of active PTB diag-

nosed from 1996–2010 ($n = 2309$) were matched to two controls ($n = 4604$) by age, gender and race/ethnicity. Average individual-level concentrations of carbon monoxide (CO), nitrogen dioxide (NO_2), sulfur dioxide (SO_2), ozone (O_3), and particulate matter with aerodynamic diameter <2.5 μm ($PM_{2.5}$) and 10 μm (PM_{10}) for two years prior to diagnosis/entry into the study were estimated based on home address.
Results: In single-pollutant, adjusted conditional logistic regression models, the odds ratio (95% confidence interval) was 1.50 (1.15, 1.95) for the association between the highest CO quintile (vs. lowest); corresponding estimates were higher among never (1.68 (1.26, 2.24)) than ever smokers (1.19 (0.74, 1.92)). In contrast, NO_2–PTB associations were higher among ever (1.81 (1.13, 2.91)) than in never smokers (1.29 (0.97, 1.71). O_3 was inversely associated with PTB for both smokers and nonsmokers. No consistent patterns were observed for other pollutants. Findings from multi-pollutant models were similar.

Table   Adjusted* odds ratios and 95% confidence intervals for the associations of pulmonary tuberculosis and quintile increase in ambient criteria air pollutants concentrations, 0–24 months, among all cases and matched controls nested within the 1996–2010 KPNC membership, and stratified by smoking status (ever vs. never smokers)

Air pollutant	Quintile	All	Never smokers	Ever smokers
24 h NO_2 (ppm)	1	ref	ref	ref
	2	1.17 (0.93, 1.46)	1.15 (0.89, 1.48)	1.24 (0.79, 1.97)
	3	1.17 (0.93, 1.48)	1.00 (0.77, 1.29)	1.66 (1.05, 2.63)
	4	1.27 (1.01, 1.61)	1.18 (0.91, 1.53)	1.57 (0.99, 2.49)
	5	1.42 (1.10, 1.84)	1.29 (0.97, 1.71)	1.81 (1.13, 2.92)
8 h O_3 (ppm)	1	ref	ref	ref
	2	0.92 (0.78, 1.10)	0.91 (0.74, 1.12)	0.94 (0.62, 1.43)
	3	0.95 (0.80, 1.14)	0.98 (0.80, 1.21)	0.88 (0.58, 1.33)
	4	0.71 (0.59, 0.85)	0.68 (0.55, 0.85)	0.76 (0.50, 1.17)
	5	0.66 (0.55, 0.79)	0.65 (0.52, 0.81)	0.66 (0.43, 1.02)
8 h CO (ppm)	1	ref	ref	ref
	2	1.04 (0.86, 1.24)	1.02 (0.82, 1.27)	1.08 (0.70, 1.66)
	3	1.19 (0.98, 1.45)	1.25 (0.99, 1.58)	1.10 (0.71, 1.70)
	4	1.33 (1.06, 1.68)	1.36 (1.05, 1.77)	1.30 (0.83, 2.05)
	5	1.50 (1.15, 1.95)	1.68 (1.26, 2.24)	1.19 (0.74, 1.92)

*Adjusted for the matching factors (age, gender, and race/ethnicity).

Conclusion: Among a population-based sample of Northern California residents, exposure to ambient CO was positively associated with PTB. This association requires confirmation in other US-based and international populations.

OP-283-03   Mass public transportation and tuberculosis transmission in a high incidence setting

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Background: Airborne transmission of tuberculosis (TB) may occur in extra-domiciliary settings, such as using public transportation. We evaluated if the use of mass public transportation (MPT) is associated with acquiring TB in a high incidence urban district in Lima, Peru.

Methods: A case control study was conducted in San Juan de Lurigancho district, the most densely populated district in Lima, with one million inhabitants. Consecutive newly diagnosed multidrug resistant TB cases, randomly selected drug-sensitive TB cases both with no history of previous treatment, and community controls were included from August to December 2008. Transport to go to work was used as the best description of transportation usage, as this is the most frequent reason for transportation. MPT was defined as using buses and minibuses for transportation and was included in statistical analysis using logistic regression, with other demographic, socio-economic and behavioral factors associated with TB. Crude and adjusted odd ratios (OR) and 95% confidence intervals were calculated to study the association between use of MPT and TB.

Results: Of the 220 subjects, 140 (63.6%) were TB cases. The overall use of MPT to go to work was 44.9%; 53.3% (72/135) among cases and 30.4% (24/79) among community controls. In the TB group: 25.7% (36/140) of subjects reported to have had a recent household contact, and 13% (18/139) reported to have had a workplace contact, corresponding figures for the community controls were 3.8% (3/80)

Variable	Community control (n = 80) n (%)	TB cases (n = 140) n (%)	Adjusted OR (95%CI)	P value
Age >50 years old	16 (20)	19 (13.6)	0.19 (0.04–0.97)	0.046
House income >1000 soles	18 (24.3)	16 (13.3)	0.18 (0.05–0.62)	0.006
Use of MPT to go to work	24 (30.4)	72 (53.3)	11.8 (1.45–96.07)	0.021
Household contact	3 (3.8)	36 (25.7)	26.37 (3.98–174.72)	0.001
Workplace contact	3 (4.1)	18 (13.0)	2.43 (0.43–13.56)	0.312

and 4.1% (3/73), respectively. Civil status, age, house income, time in the same work place, use of MPT to work, commute time to work, household and work place contact were associated to the outcome in bivariate analysis. Using MPT to go to work was independently associated to develop TB (OR 11.8, 95%CI 1.45–96.07, $P = 0.021$), in the multivariate analysis. Other significant results are summarized in the Table.

Conclusion: Using MPT to go to work is a risk factor for TB transmission in a high incidence area. Measures to minimize transmission risk during MPT use should be implemented.

OP-284-03   Tuberculosis and hepatitis C co-infection in Karachi, Pakistan

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Background: The burden of both tuberculosis (TB) and hepatitis C virus (HCV) in the general population of Pakistan ranks among the highest in the world. In a setting such as this, there is a dearth of literature examining the overlap of these epidemics. Unlike many high TB burden countries, the prevalence of HIV among incident TB infections in Pakistan is below 0.5%. Hence, comorbid diseases such as chronic HCV are becoming increasingly important in prevention and care of TB.

Methods: Data were abstracted from the medical records of all pulmonary TB patients registered at Indus Hospital who had HCV antibodies tested at initiation of TB treatment. Data were analyzed for three distinct populations: drug-sensitive patients residing in Karachi (DS-TB); drug-resistant TB patients residing in Karachi (DR-TB Karachi); and DR-TB patients residing in Sindh province outside Karachi (DR-TB Sindh). Additionally, HCV infection rates for the general population (no active TB disease) were calculated using published data from Indus Hospital Community Cohort recruited from Indus Hospital's catchment area. HCV co-infection rates were then compared to HCV rates in the general population by calculating age- and gender-adjusted odds ratios and 95% confidence intervals.

Results: Between Nov 2007 and Mar 2012, 1109 pulmonary TB patients were screened for HCV infection, resulting in the detection of 158 (14.2%) TB-HCV co-infected patients. Significant differences in HCV-positivity were observed between the 3 TB patient populations. The IHCC screened 547 individuals for HCV, yielding 52 (9.5%) infected individuals. After adjustment, the DS-TB and DR-TB Sindh populations were significantly more likely to be HCV

	n	No. positive (%)	OR (95% CI)	aOR (95% CI)
Age group				
10–24	655	42 (6.4)	ref	ref
25–39	501	66 (13.2)	2.21 (1.48, 3.32)	2.23 (1.48, 3.36)
40–54	290	63 (21.7)	4.05 (2.66, 6.16)	4.16 (2.72, 6.37)
≥55	210	39 (18.6)	3.34 (2.09, 5.31)	3.46 (2.15, 5.58)
Gender				
Male	719	100 (13.9)	ref	ref
Female	937	110 (11.7)	0.82 (0.62, 1.10)	1.03 (0.76, 1.39)
Program				
IHCC	547	52 (9.5)	ref	ref
DS-TB	811	112 (13.8)	1.53 (1.08, 2.16)	1.60 (1.11, 2.28)
DR-TB Karachi	173	17 (9.8)	1.04 (0.58, 1.85)	1.08 (0.60, 1.93)
DR-TB Sindh	125	29 (23.2)	2.88 (1.74, 4.76)	3.06 (1.82, 5.15)

infected than the general population [DS-TB: aOR 1.60 (1.1, 2.3); DR-TB Sindh: aOR 3.06 (1.8, 5.2)]. The DR-TB Karachi population had slightly trended towards higher odds of HCV infection which were not statistically significant.

Discussion: In Pakistan we identify three distinct TB populations with high rates of HCV co-infection, two of which have significantly higher rates than the general population. These findings raise important questions about the potential common exposure and/or immune impairment due to chronic disease. As the Pakistani population ages, complications from chronic HCV may adversely impact the management of TB in co-infected patients.

OP-285-03   The smoking status of tuberculosis patients modifies the risk of infection among their contacts

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Background: Smoking is a well-established risk factor for TB infection, progression and death. Although available evidence is limited, exposure to second hand smoke has also been identified as a determinant of TB disease. Previous studies, however, have not differentiated between any second-hand smoke exposure and exposure to smoking by a contact with active TB. Here, we address this question among a cohort of exposed household contacts.

Design/methods: Between September 2009 and August 2012, we identified and enrolled 5128 household contacts of 1609 patients with drug sensitive tuberculosis in Lima, Peru. Data was collected on active and second hand smoking status and other risk factors for infection specific to the index case, the household and the exposed individuals. Contacts under-

went tuberculin skin testing to determine TB infection status. We estimated the association between exposure to an index case who smoked and TB infection through multivariate modeling using the Poisson generalized estimating equation (GEE).

Results: Household contacts exposed to index TB patients who smoke were more likely to be tuberculin skin test positive than those exposed to non-smoking patients (RR 1.63, 95%CI 1.25–2.13). This effect was stronger among child contacts who were less likely to have been infected with TB prior to the household exposure (RR 2.19, 95%CI 1.39–3.45). After adjusting for smoking in the index case, we found that second hand smoke did not increase the risk of TB infection in this cohort.

Conclusion: TB patients who smoke may be more likely to transmit infection to their contacts. These data suggest that interventions designed to reduce smoking among those with active TB may not only improve patient outcomes but also minimize further spread of the disease, especially among children living in households of smokers.

OP-286-03   Risk factors for active tuberculosis infection after the treatment of latent tuberculosis in HIV-infected adults

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Background: The Soweto/Johns Hopkins Tuberculosis Prevention Trial showed that the shorter directly observed combination regimens isoniazid-rifapentine (once weekly for 12 weeks), and isoniazid-rifampin (twice weekly for 12 weeks) had similar efficacy to 6 months of daily isoniazid in treating latent tuberculosis in HIV-infected adults. The CDC (USA) now recommends the use of isoniazid-rifapentine for the treatment of latent tuberculosis infection. We studied the independent risk factors for incident tuberculosis infection after the treatment of latent tuberculosis infection in HIV-infected adults, as this may be of benefit in the design of tuberculosis prevention interventions.

Design/methods: We looked at sociodemographic and baseline clinical factors among 908 participants of the Soweto/Johns Hopkins Tuberculosis Prevention Trial. These participants completed at least 80% of their treatment regimen and were in the daily isoniazid for 6 months arm; isoniazid-rifapentine arm; and isoniazid-rifampin arm of the trial. We used survival analysis methods and Cox proportional hazard regression models. All multivariate Cox models were adjusted for age, sex, smoking status, alcohol

consumption, baseline viral load, baseline CD4, TST (PPD) result, BMI and study arm. Complementary log-log plots were used to check the proportional hazards assumption.

Results: The median age of participants was 30 years and all were of self reported black race. The median

Table Univariate and multivariate hazard ratios of incident active TB infection

Risk factor	Univariate analysis HR (95%CI)	P value	Multivariate analysis HR (95%CI)	P value
Age (per year increase)	1.03 (0.99–1.07)	0.119	1.02 (0.98–1.06)	0.435
Sex				
Male	REF		REF	
Female	0.56 (0.31–1.01)	0.055	0.94 (0.44–2.04)	0.880
Employment status				
Employment	REF		REF	
Lack of employment	1.78 (0.71–4.46)	0.216	2.05 (0.81–5.19)	0.131
Highest education level				
≥12 years of schooling	REF		REF	
<12 years of schooling	1.29 (0.72–2.28)	0.391	1.04 (0.56–1.94)	0.903
Living conditions				
House/flat	REF		REF	
Shack/shelter/other	0.91 (0.52–1.56)	0.723	0.98 (0.56–1.72)	0.941
Smoking				
Never	REF		REF	
Past/present	1.60 (0.95–2.72)	0.079	0.94 (0.46–1.92)	0.874
Alcohol use				
No use	REF		REF	
Use	1.99 (1.19–3.33)	0.009	2.07 (1.13–3.77)	0.018
Alcohol units per week ($n = 249$)*				
≤4 units per week	REF		REF	
>4 units per week	1.63 (0.74–3.59)	0.227	1.37 (0.57–3.31)	0.482
Years of alcohol use ($n = 249$)*				
≤8 years	REF		REF	
>8 years	1.74 (0.78–3.88)	0.175	1.33 (0.52–3.42)	0.549
Baseline CD4				
<500	2.44 (1.39–4.28)	0.002	1.91 (1.06–3.46)	0.032
≥500	REF		REF	
Baseline viral load				
≤4.2 log10 copies/ml	REF		REF	
>4.2 log10 copies/ml	3.84 (2.08–7.11)	<0.001	3.14 (1.64–5.99)	0.001
PPD (TST) result				
5–9 mm	REF		REF	
10–15 mm	2.15 (0.81–5.69)	0.125	1.92 (0.72–5.14)	0.192
>15 mm	2.90 (1.13–7.42)	0.027	2.71 (1.05–6.99)	0.039
BMI				
<18.5	1.48 (0.61–3.59)	0.389	2.18 (0.87–5.48)	0.096
18.5–24.9	REF		REF	
25–30	0.76 (0.38–1.51)	0.438	0.88 (0.44–1.75)	0.715
>30	1.03 (0.54–1.94)	0.936	1.43 (0.73–2.78)	0.299
Treatment arm				
Rifapentine - isoniazid	1.19 (0.61–2.31)	0.610	1.29 (0.66–2.52)	0.452
Rifampin - isoniazid	1.35 (0.71–2.60)	0.357	1.30 (0.67–2.50)	0.437
Isoniazid for 6 months	REF		REF	

All multivariate models were adjusted for age, sex, smoking status, alcohol use, baseline CD4, baseline viral load, PPD result, BMI, and treatment arm of study.
*Model included only participants who self-reported alcohol consumption.

follow up time was 3.73 years and the incidence of tuberculosis was 1.95 per 100 person years. Independent risk factors for incident tuberculosis infection from multivariate analysis include the following: A tuberculin skin test result of >15 mm vs. 5–9 mm (HR 2.71, 95%CI 1.05–6.99, $P = 0.039$); self reported alcohol consumption (HR 2.07, 95%CI 1.13–3.77, $P = 0.018$); baseline viral load greater than the median, i.e., 4.2 log10 copies/ml (HR 3.14, 95%CI 1.64–5.99, $P = 0.001$); and baseline CD4 cell count of <500 cell/mm^{3} (HR 1.91, 95%CI 1.06–3.46, $P = 0.032$).

Conclusion: Alcohol consumption was the only social factor that was statistically significantly associated with increased hazard ratio of incident tuberculosis. Our results suggest that discouraging (quitting) alcohol consumption, early treatment with HAART, and possibly longer duration of latent tuberculosis treatment for individuals with a very large tuberculin skin test (>15 mm) may be helpful in reducing the risk and incidence of TB in HIV-infected individuals.

TOBACCO CONTROL: ADVOCACY AND PROGRAMME IMPLEMENTATION

OP-287-03 Mayors' alliance accelerating sub-national smoke-free in Indonesia: lessons learnt

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Background: In Indonesia, smoking kills more than 200 000 people every year. About 80% of Indonesian households are exposed to SHS every day. Smoking prevalence in males was 67% and in females was 2.7%. Indonesia has not ratified the Framework Convention on Tobacco Control (FCTC) yet and also absence of a comprehensive tobacco control law at national level, however, government regulation on tobacco control was passed in 2012 which includes provision of smoke-free and pictorial health warning.

Objectives: To share lessons learnt in smoke-free implementation through Mayors Alliance.

Methods: To gain sub-national political will for smoke-free policy, Mayors' alliance was established early 2011. Local evidences were built, and policy advocacy tool kits and guideline were developed. Periodic follow up meeting is carried out. An approach called 'Mayor-talks–Mayor' carried out which included one to one meeting, visit city to city and share lesson learnt and policy communication and declaration.

Results: Initially the alliance was joined by 12 mayors and the Governor of Jakarta in January 2011. It

has been expanded to 59 cities in 2012. Fourteen cities and four provinces are being implemented 100% smoke-free policy. Substantial number of cities and districts are on progress to develop smoke-free policy. The Alliance contributed MOH to endorse a joint Ministerial Decree on smoke-free policy in 2011 and adoption of health regulation in 2012.

Conclusions: Mayors with their unified efforts demonstrated a successful model of smoke-free implementation at sub-national level and the Alliance became an important partner of MOH to expand smoke-free.

OP-288-03   Cigarette smoke induces DNA damage and inhibition of function in alveolar macrophage

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Background: Cigarette smoke is a major risk factor for pulmonary diseases. Alveolar macrophages (AM) phagocytize microorganisms, produce reactive oxygen species (ROS) and play an important role in immunological surveillance for the lung. In previous studies, we demonstrated tobacco smoking inhibits immune functions in AM. However, the mechanism of inhibition of immune function in AM is not well defined. In this study, we investigated whether DNA damage of AM relates to inhibition of immune functions.

Methods: C57Bl/6 mice (female, 8–10 weeks) were exposed to 20 cigarettes/day during 10 days with Hamburg II smoking machine. After exposure, AM were obtained by bronchoalveolar lavage (BAL). Surface antigen expression, phagocyte activity and production of ROS of AM were analyzed by FACS. The ultrastructure of AM was analyzed by TEM. DNA damage was analyzed by Comet assay.

Results: Expression of surface antigens (CD11, Class II, CD14 and TLR2) on AM were significantly ($P <$ 0.05) suppressed in smoked mice (S) as compared with non-smoked mice (NS). Inclusion bodies of high density were observed in AM from S. Phagocyte activity of AM was significantly inhibited in S. Production of ROS in AM was significantly increased in S. DNA damage in AM was significantly increased in S.

Conclusion: These results suggest the inhibition of immunological function of AM may be due to DNA damage caused by increased ROS with the appearance of inclusion bodies in AM by smoke exposure. Such inhibition by DNA damage of AM could be closely associated with the risk of increasing microbial infection in the lung.

OP-289-03   Field-based study in seven states of India to evaluate and recommend an effective, strong pictorial health warning on tobacco product packages

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Background and challenges to implementation: Tobacco product packages are effective mediums for informing current and potential users about the harmful impact of tobacco use. Research evidences exist to prove that effective warning labels increase knowledge about risks associated with smoking and can influence future decisions about smoking. Large and graphic warnings can motivate tobacco users to quit, discourage nonsmokers/non-users from initiating and keep ex-users from starting again. The Indian Tobacco Control Act, (COTPA) 2003 provides for placement of pictorial health warnings on all tobacco products covering 40% of the principal display area in the front panel of the pack. It also provides for rotation of the warnings every 12 months or earlier as prescribed by the parliament.

Intervention or response: A qualitative study was carried out by Voluntary Health Association of India (VHAI) with the support of its state chapters, through focus group discussions and individual interviews. The main objective of this study was to explore and gather public opinion regarding the new shortlisted set of pictorial health warnings presented by the ministry of health and family welfare, and assess feedback on the range of messages conveyed through these warnings. Focused group discussions (FGDs) were carried out with different sets of respondents in the rural and urban areas of 7 states representing all four regions in India (viz-Arunachal Pradesh, Bihar, Orissa, Uttar Pradesh, Madhya Pradesh, Andhra Pradesh and Kerala). The sample size of the study in each of the states was 100. The participants were segregated into 3 different groups of women, men and youth. Possible suggestions for improving/modifying the warnings also formed a part of this discussion. Structured individual interviews were also conducted with tobacco users, non users and retailers of all tobacco products to assess their opinion towards the pictorial health warnings and its impact.

Results and lessons learnt: As a result of the study, out of the 11 pictures, one warning showing a cancer-affected mouth, which was recommended by maximum respondents during the field testing, was notified by the Ministry of Health and Family Welfare, Government of India.

OP-290-03   E-cigarette: an emerging public health challenge in India

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Background: Numerous webpages in Indian internet media are popping up e-cigarette's advertisments. These advertisements claim the e-cigarettes to be health friendly and protecting people from the second hand smoke and an economical option. With an aim to explore the list of e-cigarette brands available in India, understanding their distribution network and marketing tactics, researchers did the internet search.

Design/methods: Researchers performed the keyword search on search engine 'google' in March, 2013. Brand websites were examined for specifics about each product (flavor and nicotine strength option), ingredients in their products, claims about the products whether they were safer than conventional cigarettes. Besides this, the distributors and kiosk/outlets selling these products were also searched for.

Results: Total 68 brands of different flavor (12 types) and different nicotine strengths (9 types) of the e-cigarettes were found. In most brands (92%) the ingredients of the e-cigarettes were found, with most common ingredients being nicotine, propylene glycol, water and flavor. Near 30% brands explicitly declared that their product could not be used as a smoking cessation device, 10% claimed it useful for the cessation and rest did not mention anything. 90% of the brands claimed their product to be healthier and safer to the conventional cigarettes; none declared it unsafe to health. Most brands (93%) advertised their product to suitable to use in places where conventional tobacco products are hard to use. 76% of brands claimed their products an economical option than the conventional cigarette. All websites except five have an open access to the visitors including minors (aged less than 18 years). Near half of the websites gave their distribution details in the websites. 10 websites offer free shipping services, 23 websites offers the web chat options for marketing the products.

Conclusions: E-cigarette are the new emerging public health challenges in India. The claims (especially healthier option and useful for cessation) of the websites marketing these products are questionable and needs further research. The advertisement on the internet is violation of Indian tobacco control legislation, and warrants stronger enforcement.

OP-291-03   Unravelling India's tobacco epidemic: priorities and recommendations for the second round of Global Adult Tobacco Survey (GATS)

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Background: The Global Adult Tobacco Survey (GATS) is the first comprehensive nationally representative data on tobacco use behaviors of civilian, non-institutionalized individuals aged 15 years and older. The objectives of the GATS India were to: measure the impact of tobacco control efforts; and systematically monitor adult tobacco use. GATS was initiated in May 2008 and data released in 2010. GATS has informed national and state level policymakers in focusing their attention on specific tobacco-related challenges. The objective of this study was to highlight methodological issues with respect to GATS and thereon recommend measures that need to be taken to improve the next round of GATS. The topics covered include objectives, indicators, choice of sample size and representation, quality assurance, and analysis.

Design/methods: A small group consultation of tobacco control advocates deliberated upon the objectives of GATS, tobacco control indicators chosen, choice of sample size and representativeness, relevance of exclusion criteria, quality assurance measures, data inconsistencies and data analysis and its interpretation. Results of these are presented here.

Results: GATS has presented a comprehensive picture of the tobacco use prevalence in India. However we find the following limitations in the GATS:

1 Sampling strategy: The primary sampling units (PSUs) selected using probability proportional to size (PPS) sampling are not nationally representative when matched with age and gender data of Census of India (2001) and Census population projections for 2009–10. In addition the sample size is insufficient to make state level estimates and there is under-representation of the 15–18 years age group due to selection criteria.

2 Quality assurance mechanisms are unclear, especially information regarding field testing of questionnaires in local languages, editing, imputation and triangulation errors.

3 There are also gross errors in computation.

4 There is irrelevant and redundant information that has limited application.

5 There are also ethical concerns about research agencies hired for data collection that have working relationships with the tobacco industry.

Conclusion: GATS is an invaluable tool to design strategies against the tobacco epidemic. This research

has identified some limitations and proposes corrections that can be incorporated in the next rounds. An inclusive and consultative process can aid this.

OP-292-03 Tracking investments by financial institutions in tobacco companies: a possible endgame strategy

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Background: Roughly €3 trillion in assets and investments are managed by socially responsible investment (SRI) funds worldwide which motivate institutional investors to take a more stringent view on ethical investing. Ethical investing include not investing in tobacco industry or its stocks. Tobacco is a cross-cutting area where such investments are forbidden. Tracking investments made by governments and private financial investors in the tobacco sector can influence in mitigating the proliferation of the industry in the future.
Methods: This research examines investments made by the largest private banks in the world which conform to SRI standards using customised, paid for banking databases from 2002 to 2012.
Results: The analysis finds that 42 of the top 50 global bank invest and support tobacco industry domestically and in offshore projects.
Conclusion: Definition of socially responsible investments within the perspective of screening tobacco investments is perceived variably by financial institutions. Also in the absence of a watchdog institution and few disincentives for truant behaviour, investors continue to invest tobacco companies. Tobacco control advocates need to monitor investments made by large banks and institutions in tobacco industry and ensure that banks which have committed to SRI codes conform to them. More stringent monitoring to adherence of SRI principles and reducing access of public and private funds by tobacco industry is a potential strategy for the global endgame of tobacco.

OP-293-03 Relevance of correcting manufacturing costs of tobacco products to make tobacco taxes effective: an example from India

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Background: Tobacco and tobacco products are extremely affordable and widely accessible to all in India. As in much of South Asia, the entire lifecycle of tobacco products is subsidised—with low minimum wages for workers, heavy subsidies on input materials, and tax waivers for manufacturers. Such incentives keep production costs of tobacco products low, making them highly affordable to its users and profit-

able to its manufacturers. These factors driving the lifecycle of tobacco and facilitating its production also limit the effectiveness of demand-side strategies to combat the prevalence of tobacco use. Increasing taxes, in particular, fails to induce any perceptible changes on retail prices of tobacco products. As input and manufacturing costs are kept artificially low, even significant tax increases do not translate into corresponding price increases. At the same time, governments are often reluctant to increase taxes drastically as it appears unethical to benefit from sin taxes.
Design/methods: This poster presents conclusive arguments that taxes will be effective only if several corrections are made across the supply side of the product lifecycle. Using published secondary data, analyses of cost to manufacture and market, and retail price are measured for the most popular forms of smoked (bidis) using regional brands. Analysis of each step within the product's life cycle is considered and the subsidies involved are identified and measured. The lifecycle approach helps identify potential points of intervention which can make demand-side strategies effective.
Results: Based on the analyses of three national brands, this analyses finds that bidi manufacturers have a cost margin of 40–55% which enables bidi companies to absorb minor increase in taxes and may choose not to pass it on to consumers. The lifecylce approach identifies points within it where subsidies and incentives can be targeted, which can help realise a full-cost cost for tobacco products like the bidi.
Conclusion: Taxation strategies will become more effective and efficient if corrections are made across the supply side of the product lifecycle to realise the full cost of the product. Lifecycle analysis can help identify hidden subsidies and incentives for the tobacco industry and can be a useful tool to raise manufacturing costs, which in effect can translate into higher retail price of tobacco product.

POSTER DISCUSSION SESSIONS

FCTC, MPOWER AND TOBACCO CONTROL POLICIES

PC-780-03 Do people restrict smoking at public places? Lessons learnt from four districts in Bangladesh

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Background: This paper analyses the knowledge and attitude of people regarding smoking restriction at public places under the Tobacco Control Act-2005, identifies the barriers in making the public places

smoke free, and explores the ways to overcome those barriers.

Methods: A cross-sectional household survey and in-depth interviews of key informants were employed to collect data. A total of 908 households and 27 key informants were interviewed in four districts in Bangladesh in 2012.

Findings: 48% (436/908, 95% confidence interval [CI] 46–50) households had at least one adult smoker, 68% (402/592) adult smokers smoked at home, while 73% (433/592) smoked at public places, even in front of children and pregnant women. Only 22.7% (206/908) respondents considered 'having smoke free public places' as their right. Though tobacco use is prohibited at any public places under the Tobacco Control Act-2005, 52.4% of the respondents have no idea about 'public place', while only 38% respondents knew about the penalty for smoking at public places. Only 12.5% people among all respondents believed that the law is being implemented properly. Inadequate human and financial resources, especially at the central National Tobacco Control Cell within the Ministry of Health and Family Welfare, inadequate understanding of roles, responsibilities and authority of a number of Taskforce Committee members in implementing the Act 2005, inadequate coordination, lack of commitment and their busy work schedule were reported as the main reasons for irregular meetings and mobile court operations and poor monitoring of tobacco control initiatives. There is no mechanism for sharing information on smoking restrictions at public places, leading to limited knowledge on the tobacco control law among mass population. Respondents suggested organizing taskforce committee meeting once in a month instead of quarterly meeting, to train the members, involve political leaders and elected members in the committee, formation of anti tobacco committee at ward level and including youth group in anti tobacco campaign, to allocate annual budget directly to taskforce committee to operate mobile courts regularly, and to earmark a proportion of taxes collected from tobacco sale to taskforce committees.

Conclusion: Developing a strategic policy framework combined with effective monitoring and supervision and partnership-building among stakeholders are crucial for enforcing smoking restrictions at public places.

PC-781-03　Media advocacy for the implementation of regulating smoking in films

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Background and challenges to implementation: India, the world's largest producer of movies produces more than 1000 movies a year in several languages.

Bollywood represents the Indian Hindi movie industry and the worldwide viewership for their movies is estimated to be about 3 million. Bollywood movie stars in India are public figures, have large fan followings and exercise tremendous influence on the behavioural attitudes of adolescents. One of the major influences on the uptake of teen tobacco use is the glamorization of tobacco use in movies and on television. Movies are seen as very influential for kids and teens.

Intervention or response: Using earned media to create pressure on policymakers and to put indirect pressure on the Government to ensure implementation of the rules notified by the Government of India which firmly intended to regulate the depiction of tobacco use in Films and Television w.e.f the prescribed date of implementation. The strategy was to ensure that news items or stories come out to attract the attention of the government and the public. To do so, VHAI decided to increase consumer awareness about the issue of smoking scenes in films through a sustained strategy of media engagement. We increased our interactions with the media, both on a one-to-one basis.

Results and lessons learnt: In order to sustain the media's engagement with the issue, over the period of time, about 8 to 10 press releases were shared with the journalists and this strategy of media advocacy resulted in nearly 40–45 stories in National and Vernacular Media during May to December 2012.

Conclusions and key recommendations: From November 2012 onwards, the new films screened at movie halls started showing the disclaimers' of 30 seconds each on the ill-effects of tobacco use with strong graphic pictures of cancer affected mouth, pictures on how smoking causes heart attacks, effects of second hand smoke, etc., both in English and Hindi that appeared in the beginning and during the interval of the movie.

PC-782-03　Smoke-free homes for tuberculosis patients: a randomised controlled trial

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Background: Exposure to second hand smoke from tobacco worsens outcomes in TB patients and increases the risk of TB transmission to others particularly children in the household. 'Tobacco Smoke Free Homes for TB patients' is a behavioural intervention that encourages TB patients to negotiate a smoke free environment within their homes. The aim of this study was to develop and evaluate its effectiveness.

Design/methods: It was a pilot individual randomised controlled trial where all non-smoking TB patients who were exposed to second-hand smoking in their homes were eligible. These were recruited from two TB hospitals in Pakistan. The behavioural intervention was developed using taxonomy of behaviour change techniques and participants were randomly assigned to receive either behavioural intervention alone (arm 1) or in combination with a telephonic text message to the smoker (s) in their homes, persuading them to implement smoking restrictions in home (arm 2). The primary end point was an absolute reduction in the exposure to second-hand tobacco smoke among TB patients determined by urine cotinine levels checked before and after the intervention.

Results: A total of 103 patients were recruited in the trial. A sizeable proportion of TB patients in both arms (57.69% [95%CI 38.39%–75.37%] in arm 1 and 61.53% [95%CI 42.08%–78.55%] in arm 2) being successful in securing a tobacco smoke free environment at home after two months. Absolute reduction was seen in 31 cases. There was also a relative reduction in second-hand tobacco smoke exposure in small number of patients (34.61% [95%CI 18.38%–54.11%] in arm 1 and 23.07% [95%CI 9.92%–41.95] in arm 2). The barriers in creating a tobacco smoke free environment at homes are the differences in the social status (based on age and gender) between smokers and TB patients.

Conclusion: Behavioural interventions are effective in helping TB patients to negotiate and creating a smoke free environment at home.

PC-783-03 Compliance with statutory pictorial health warnings in India: a sub-national survey in three districts of India

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Background: Pictorial health warnings (PHW) are an effective measure to inform about harms of tobacco use to youth and people with low awareness and to those with lower literacy rates. As per GATS 2010, majority of cigarette smokers (71%), bidi smokers (62%) and smokeless tobacco users (63%) noticed PHW on respective products packages. Among those who noticed PHW on packages, 38% of cigarette smokers, 29% of bidi smokers and 34% of smokeless tobacco users thought of quitting.

To assess the compliance to PHW specification of COTPA, the present study was conducted across three districts of Indore (MP), Patna (BH) and Shimla (HP) in India.

Design/methods: Cross-sectional surveys were conducted at tobacco vending shops/kiosks across iden-

tified districts in Jan–Feb 2013. These tobacco vending shops/kiosks were selected through a stratified sampling based on population proportionate to size (PPS). A pre-tested checklist, based on the criteria specified under provisions of India's Cigarette and Other Tobacco Products Prohibition Act (COTPA-2003) was used. Section 7 of COTPA mandate that no person can produce, supply, distribute or import any tobacco product without the PHW as notified by the Central Government from time to time. It is also stated that these specified PHW should be legible, prominent and conspicuous in size, colour and style as per section 8. Section 9 prescribes languages in which the test warning should be written.

The data was collected through checklist and analysed by a supervisor. Quality assurance of information was done through random checks and validation of data entry, and re-visit to select premises to confirm results entered in the checklist.

Results: Results show that all Indian manufactured cigarettes package displayed specified PHW. But ⩾70% foreign manufactured tobacco products imported in India either had no PHW or displayed PHW which wasn't as per the specification.

Results also shown that even though mostly bidis and chewing tobacco packs displayed the specified PHW but due to the different shape of packaging, i.e., conical, square etc. it was distorted in term of readability, style, size and prominence.

Conclusion: Results established that the imported tobacco control packages are not adhering with the Indian tobacco control law and it must be checked for the compliance at the point of entry.

It is also recommended that the Act need to be amended to specify the PHW for different shape of bidis and chewing tobacco packages.

PC-784-03 Localization of tobacco control regulations in 12 pilot provinces in the Philippines

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Background and challenges to implementation: The project is designed to achieve implementation across the Philippines of the national legislation entitled 'Tobacco Regulation Act of 2003 TRA)'. In the Philippine devolved setting, the local government units have low compliance with respect to national mandates. The ultimate goal is to achieve an effective implementation of a local ordinance on TRA in 12 selected provinces.

Challenges to implementation were as follows: variable readiness of political leaders in the local government unit, pressure from business establishments, opposition from tobacco industry.

Intervention or response: This is a quasi experimental study where an intervention of policy advocacy

with social marketing and community organizing was done in the 12 pilot provinces. Due to the limitation of financial resources, household surveys were conducted in only one province for both the 2010 (baseline) and 2011 surveys. A total of 300 respondents aged 18 and above were included in each survey.

Results and lessons learnt: Results of the survey showed that although there is no significant decrease in the prevalence of smokers from 2010 to 2011, there is a marked decrease in terms of the amount smokers usually spend per month for buying cigarettes. From spending Php 300.00 per month in July 2010, smokers spent an average of Php 162.00 per month in August 2011. There is also a significant decrease in terms of exposure to secondhand cigarette smoke in public transportation (from 67% to 47%), restaurants (41% to 28%) and government buildings (35% to 24%). There is also an increase in awareness of laws and ordinances that prohibit smoking in workplaces and enclosed public places from 70% in July 2010 to 89% in August 2011. High support for the policy prohibiting smoking also remained with 92% of Vizcayanos in favor of the policy in 2010 and 94% in 2011.

Conclusions and key recommendations: Comprehensive tobacco control policies, synergistically implemented with social marketing and community organizing, as well as, capability building of the local enforcers in a highly functional health system of a local government unit would lead to changes in knowledge, attitudes and behaviors towards tobacco use. In the long run, such policies could lead to a significant decrease in tobacco usage as well as reduce public exposure to the harmful effects of secondhand smoke.

PC-785-03   Smoke-free implementation in educational institutions with youth advocacy

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Background and challenges to implementation: Smoke free environment is a very important factor as it is a human right for all young people as tobacco is the world's leading killer causing about 57000 deaths a year only in Bangladesh. Although it is a growing trend for educational institutions worldwide to have some form of tobacco-free policy in place, Bangladesh had been legged behind to adopt such policies in all its educational institutions. The movement had been steered up with the passing of the Tobacco Control Act 2005 as it clearly defined the educational institutions smoke-free having direct effect. However, the reality even after 6 years had not been so much encouraging in comparison with other public places, as the obstacles remained within the educational institution management.

Intervention or response: SERAC-Bangladesh with

the support from WBB Trust identified root causes to the implementation problem and introduced advocacy initiatives like meetings, IPC, campaigns and local level policy pressure group formation with a motivating youth team. Starting with a sub-district of Mymensingh district in 2011, namely Ishwarganj tobacco control taskforce we advocated with the education department and made them understand the need of a 100% smoke-free environment in schools. Our reasoning was: 1) to ensure a SHS free learning environment for children and 2) to enhance learning the bad effects of tobacco use.

With a very limited resource we developed a communication strategy to reach maximum number of schools in the sub-district. Our strategy enhanced the knowledge of the key personnel to reach the goal (i.e., smoke-free). Firstly with our advocacy, the task force chairperson, i.e., the sub-district executive officer declared 100 educational institutions smoke free and later on after a couple of months the task force again with the support from the education department declared all primary schools in that area smoke free.

Results and lessons learnt: This instance had been replicated in another sub-district called Haluaghat, as the sub-district education department officer also declared all the educational institutions under his jurisdiction smoke free. This grassroots activism is now being scaled up by many other organizations in other districts.

Conclusions and key recommendations: We can term this activity as an exemplary initiative by young people and a bottom-up approach of smoke free implementation from grassroots to national or divisional level.

PC-786-03   Implementation and evaluation of a smoke-free policy in taxis in Tianjin, China

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Background and challenges to implementation: China is the world's largest producer and consumer of tobacco. This paper describes the success experience in Tianjin, the third largest city in China, in the implementation and evaluation of a smoke-free policy in taxis.

Intervention or response: The 2008 'Public Notice on Smoking Ban in Taxis' was implemented using by law enforcement personnel, and a city-side public education campaign. A before-after comparison study evaluated the effectiveness of the by-law. Air quality was measured comparing taxis with other public places.

Results and lessons learnt: During the two years after implementation of the Public Notice, 11.4% of the taxis in Tianjin were monitored for compliance, 85.0% of the drivers and 54.0% of the city residents received smoke-free information from the public education campaign. The percentage of smokers in taxi drivers decreased by 9.5% after the smoke-free policy. Other major indicators also showed favorable shifts towards smoke-free taxis. In 2010, 39.8% of the taxis had a PM2.5 level that met the standard recommended by the World Health Organization.

Table A comparison of the characteristics of taxi drivers and their work environment before and after implementation of Public Notice on a Smoking Ban in Taxis effective April 29, 2008, Tianjin, China

Characteristics	2008 before survey ($n = 460$) % (95%CI)	2010 after survey ($n = 460$) % (95%CI)	χ^2	P value
Taxi driver				
Is a smoker	57.2 (50.5, 63.9)	47.7 (43.4, 52.0)	5.38	0.02
Smokes in taxis	25.2 (17.4, 33.0)	7.6 (4.3, 10.9)	21.71	0.00
Advises passengers not to smoke in taxis	17.8 (12.6, 23.0)	96.0 (94.3, 97.7)	470.62	0.00
Supports smoke-free environment in taxis	87.0 (82.5, 91.6)	91.2 (88.8, 93.6)	2.93	0.09
Thinks smoking is negative to the business	84.1 (79.2, 89.1)	81.9 (78.6, 85.2)	0.53	0.47
Taxi				
Has cigarette ends or ash in taxi	77.0 (71.2, 82.7)	15.3 (12.2, 18.4)	256.85	0.00
Has anti-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

n = sample size; CI = confidence interval.

Conclusions and key recommendations: The success of smoke-free policy in the taxi sector in Tianjin is associated with effective policy development and enforcement, comprehensive public education, and collaboration of multiple stakeholders. The experience could be applied to other sectors and industries.

PC-787-03   Lessons from the trenches: advocating for plain packaging in India through research

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Background: Over one million Indians die every year from smoking alone; another 100 million Indians will die prematurely in decades to come due to tobacco that has already been consumed. India's tobacco control legislation needs to go much further. Towards this end, the Union South-East Asia (USEA) office coordinated a scientific policy engagement process along with two NGO partners as part of the Australia-India Institute Taskforce on Tobacco Control. We argued for introduction of plain packaging in India since Australia is the first country to legislate plain packaging in December 2012. We seek to make the consumption of tobacco products unattractive by introducing plain packaging in India. This is a far-reaching and innovative public policy proposal which can dramatically reduce smoker initiation in one of the world's largest growing markets and make pack warnings on tobacco very effective by showing illiterate smokers visually and graphically the aftereffects of tobacco consumption.

Intervention: We contributed to the research, and dissemination of a Policy Document advocating the introduction of plain packaging. This has been noticed internationally: in July 2012, we presented this Policy Document officially to the Governments of India and Australia, respectively. A legal intern extended the work of the Policy Document by analyzing India's existing Bilateral Investment Treaties and International Investor Agreements; this paper has been accepted for publication in Economic and Political Weekly, one of India's most prestigious peer-reviewed public policy journals with wide readership amongst India's policymakers and academics as well as internationally. A USEA team also met a Member of Parliament who introduced a Private Member's Bill advocating the introduction of Plain Packaging. Copies of the Policy Document have been disseminated to a number of key stakeholders internationally. This has kindled much interest in India's public policy proposal in this arena of tobacco control.

Lessons learned: Sustained research, continuous advocacy, building up an India-specific body of research combined with dissemination and engagement with political stakeholders are key components of introducing changes in public health legislation. This Policy Document also builds our credibility with Indian politicians, policy makers and public health advocates globally as well building a strong case for policy change in India based on solid research.

Conclusions: Transparent engagement with the Indian political system for public health goals remains welcome, if we provide research-based and policy-orientated content that speaks to Indian interests. The USEA's presence in various districts and states of India for its current work on advancing tobacco control, support of the governments' tuberculosis control programme and its providing technical assistance authenticates our its credentials.

PC-788-03   The role of NGOs in increasing public awareness of tobacco industry intervention in Bogor City

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People of Bogor generally are not aware of tobacco industry intervention, because the intervention is designed to give a good impression and to build better society. The intervention are scholarship, social works, tobacco advertisements, and many more. Therefore, the role of NGO is really needed to increase public awareness on the danger of tobacco industry intervention. Tobacco industry keep promoting its' products rapidly. More over, teenagers become its' main target for promoting tobacco. Advertisement, promotion, sponsorship are most effective way for tobacco industry to market its product. There is also Corporate Social Responsibility (CSR) as its' tactic to get attention and positive impression from society. Most of people do not realize that CSR includes into an intervention. Besides it, tobacco industry had a lawsuit to Bogor city government on Smoke Free Area Local Regulation No. 12 of 2009 to Supreme Court on December 27th 2013, but the case was rejected. No Tobacco Community which is concern on Smoke Free Area Local Regulation in Bogor city also got a lawsuit from tobacco industry at Bogor City court in 2011–2012. In 2013, tobacco advertisement is forbidden in Bogor City. It is also a result from No.TC's effort to push Bogor City government to ban it. Because a loss of tobacco advertisement is just a commitment from Bogor City government or not in a written form, No.TC keeps increasing public awareness on the danger of tobacco advertisement. No.TC also works together with other organzations to gain support from public on written regulation of 100% tobacco advertisement banning, so that the Mayor of Bogor will issue written regulation about tobacco advertising as soon as possible. To fight tobacco industry intervention in Bogor City, NGOs must work together with government to cut and prevent early smokers to in achieving 100% Smoke Free Bogor City.

PC-789-03   Smokeless tobacco in South Asia: a policy review

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Background: Almost a fifth of world's tobacco is consumed in the form of smokeless products, mainly by people living in South Asia. This poses a major threat to public health. We ascertained the extent to which existing policies adequately address smokeless tobacco consumption in Bangladesh, India, Nepal and Pakistan.

Design/methods: We conducted a policy gap analysis on four aspects: (a) information and surveillance, (b) fiscal and taxation, (c) product regulation, and (d) service provision. Based on this framework, a questionnaire was developed and used to gather information from a number of policy makers and civil society organizations in the four countries. Findings were collated, analysed, and synthesised into five major themes.

Results: The analysis found that with the exception of few good examples, existing policies in South Asian countries are either inadequate or poorly implemented to have any significant impact on the consumption of smokeless tobacco. There are several gaps in the systematic gathering of information for effective policy formulation and communicating health hazards of smokeless tobacco to general public. There are some good examples including bans of some SLT products in certain states in India. However, a comprehensive approach to restrict and regulate the production, distribution, marketing and sale of smokeless tobacco, lacks in general. Where legislation and appropriate policy framework exist, there are gaps in implementation strategies and enforcement plans. Compared to cigarettes, smokeless tobacco products are taxed at very low rates. Tax evasion and weak administration is common. With the exception of India, where cessation services are available in certain districts, and Bangladesh where a few pilot clinics exist, such services are not available in public sector.

Conclusion: Smokeless tobacco consumption is a major threat to public health especially in South Asia. Our study highlights opportunities to tackle this threat through effective policy formulation and implementation in Bangladesh, India, Nepal and Pakistan.

PC-790-03   Evaluation of local regulations (Perda No. 5/2008) for smoke-free areas in Surabaya, Indonesia

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Background: Tobacco consumption kills one person every ten seconds. Smoking is not only dangerous for the smoker but also for other people around the smoker called passive smokers. Since 1981 harmful effect of cigarette smoke for passive smoker already proven. For that reason as a protection people from cigarette smoke, since 2008 Surabaya city have a local regulation for smoke free area, it's called Perda no. 5/2008. The places categorized as 100% smoke free areas are playgrounds, education and health facilities, worship areas, as well public transportation. And, for public places and working places categorized

as not fully smoke free areas because the places have to provide smoking room. After two years implementation, the regulation has to be evaluated and the results can describe the compliance of it.

Design/methods: The research was cross-sectional study with cluster random sampling. Surabaya district was divided into five areas, and then chosen 8 (eight) sub-districts with sample size were 1001 facilities. Data was analyzed descriptively and presented based on seven categories of facilities as the local regulation.

Results: As many 82.5% of the facilities showed no body smoke in the areas such as playing ground, education and health facilities, worship places, public transportation, working places and public places. At public and working places categorized as not fully smoke free areas were found smokers (68.6%), ashtray (69.9%), cigarettes smoke smelt (63.8%), cigarette butt (59.4%) and cigarette advertisement (87.1%). There was still 14.1% of all facilities found cigarette seller in those areas, most of them (63.8%) categorized as not fully smoke free areas. Only 17.5% of facilities put signing of no smoking as stated in the regulation.

Conclusion: Implementation of local regulation of smoke free area in Surabaya city has run quite well. The recommendation to optimize the implementation of it was to enforce sanctions, to put no smoking sign as stated the regulation, and to do socialization of the local regulation routinely, as well to give appreciation for facilities that implemented properly the local regulation.

PC-791-03 Impact of forceful policy advocacy and enforcement mechanisms in Himachal Pradesh to counter tobacco industry tactics

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Background: There is a high prevalence of tobacco consumption in Himachal Pradesh (India), 21.2% adults consume tobacco. It is neither a state wherein any agricultural production of tobacco is done nor any tobacco manufacturing industry is present. But yet Himachal posed a threat to tobacco industry after the successful declaration of Smoke Free Shimla and HPVHA's campaign of Smoke free Himachal Pradesh

Challenges: Effective implementation of smoke free laws campaign resulted in tobacco industry's desperate countering tactics by establishment of a biri rolling unit amongst women of self help groups, provision of incentives to tobacco vendors and putting up of promotional boards without the products name but with logo. HPVHA also encountered stiff resistance on gutkha ban from the vendors and the traders

Interventions: HPVHA initiated a strong policy advocacy amongst the political set up, policy formulators, programme implementers. A concept note on

the economics and feasibility of biri rolling unit was worked out and circulated. A bidi roller had to roll only 750 per month or practically 25 bidis a day according to the memorandum of understanding and her income would be meager amount of Rs 30 and HPVHA stated that if other family members too are into bidi rolling, the maximum earning shall be Rs 180 (6 as an average family size). Facilitation was done for formation of Enforcement and flying squads and its officials were trained to issue challans and take action on promotional boards. Community awareness and public education was done along with the rural Panchayat officials on the need for opposing the biri industry and gutkha issue.

Outcomes: Biri industry was closed, an achievement witnessed nowhere in India. Out of 175 tobacco vendors 48 have gone in for product substitution in Shimla town only and has stopped selling tobacco products. Gutkha was banned in Himachal. About 10 000 tobacco promotional boards from shops and restaurants were removed.

Conclusion: HPVHA has witnessed both success and drawbacks during this campaign. Though gutkha ban has been notified, non compliance is seen by some vendors with selling the product at a very high price. Taxes on cigarettes have been raised from 18% to 36% and on biri form 11% to 22%. The shrewed and low tactics of the industry need to be watched carefully.

PC-792-03 Mouth freshener serves as a surrogate for tobacco product advertisements in India

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Background: Article 13 of FCTC and Indian anti-tobacco legislation prohibits advertisement of tobacco products. Tobacco industry is carrying out aggressive advertisement of the non-tobacco products having same brand name and packaging design to tobacco products. Present study was conducted to assess whether advertisements in Indian print media were for the intended products or serve as a surrogate for tobacco products.

Design/methods: Three Indian vernacular newspapers in Himachal Pradesh—an Indian State were observed between 1 January to 31 March 2012, simultaneously a cross-sectional survey using a pre-tested checklist was also done across 720 tobacco shops in 12 district headquarters. These newspapers were screened again between 1 October to 31 December 2012 followed by a survey across 388 shops in one of the district headquarter.

Results: In first phase, total 27 display advertisments (seven brands) of mouth freshener (also called pan masala—a non-tobacco product containing arecanut)

were seen. The advertised brand of mouth freshener was not available in any shop whereas gutkha (processed tobacco with lime) of same brand name and package design was being sold in 446 (72%) shops. In second phase, total 18 advertisements (four brands) of mouth fresheners were noticed. Field survey revealed that total 322 (82%) shops have mouth fresheners which included the advertised products as well. However, total 73 (19%) and 209 (54%) shops were also selling gutkha and zarda (raw tobacco product) of same brand name and package design.

Conclusions: The 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-793-03   Point of sales advertisements in a district of North India: how compliant are they with legislative measures?

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Background: Tobacco companies use various methods of advertising for promotion of their products. In line with Framework Convention for Tobacco Control (FCTC), Section 5 of the Indian tobacco control legislation (COTPA-2003) prohibits direct and indirect advertisements of tobacco products at point of sale (POS). The present study was conducted to ascertain the level of compliance of Section 5 under COTPA 2003 and its subsequent rules.

Design/methods: A cross-sectional study conducted in district Mohali, located in Punjab state of Northern part of India, in month of March–April, 2013. A total 360 point of sale of tobacco products (POS) were randomly selected with equi-proportionate representation from three social strata (Urban, Rural, Slums). Data input was double-checked for accuracy and analyzed using SPSS software for windows version 16. χ^2 test was used to test associations between independent and dependent variables. The level of statistical significance was set at $P < 0.05$. The study was approved by the Institute Ethic Committee PGIMER.

Results: 55.5% tobacco selling in all the covered areas were through permanent shops, while rest through movable kiosks. The compliance was very poor in rural and semi urban areas with 67.7% point of sale without health warning board, although brand promotion was bit less with 26.9% only. There is complete violation of Section-5 in movable kiosks, with showcases easily visible to minors.

Conclusion: It can be concluded that there is less compliance of section 5 in rural and semi-urban areas. Stricter implementation is needed focusing on these areas. Most of moveable kiosks don't comply with Section-5 regulations. They are more harmful and difficult to control by legislative measures as their location varied with time.

PC-794-03   Role of media in policy advocacy on pictorial health warnings: a case from Nepal

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Background: Tobacco use a big public health problem in Nepal. More than 15 000 people die due to tobacco use every year. Overall prevalence of tobacco use 28.5% (males 53.4% and females 19.6%). To address this epidemic, WHO Framework Convention on Tobacco Control (FCTC) was ratified in 2006 and a comprehensive tobacco control act was adopted in 2011. Key features of the act are complete ban of tobacco advertisements, promotion and sponsorship, complete ban of smoking and at least 75% pictorial health warning (PHW).

Objectives: To explain the role of media to make effective policy advocacy and build policy pressure in adoption of PHW directives in 2011.

Approaches: Approaches included one to one meetings and interview with high official of Ministry of Health (MOH) and governments, disclose tobacco industry (TI) delay tactics, and government officials' intention and disclosure of pictorial health directives to the public to build pressure for adoption of the PHW directives.

Results: Due to TI interference at the highest level of policy making at MOH in 2011, issuance of PHW's directives got delayed. Media visit and briefing on PHW were done with then Prime Minister, and Chief Secretary of Government of Nepal. Pressure was put upon health ministers and other officials of MOH to release the directives. In addition, public disclosure of the directives was made. Series of publications were made in different national daily newspapers. As the results, it was issued a day before the date of enforcement of the PHW as per the tobacco control act in 2011. PHW's directive of Nepal includes at least 75% of both the upper front and back of packages of tobacco products. But PHW is yet to be implemented in Nepal due to TI litigation at the Supreme Court of Nepal. Media advocacy are being continued for early settlement of the litigation.

Conclusion: Media is an important partner in policy advocacy and high level pressure for tobacco control. Public support is the key to advance tobacco control which can be built by effective mobilization and partnership with media. Disclosure of TI interferences and government's negligence to media plays a vital role to build policy pressure.

TREATMENT EQUALS PREVENTION FOR TUBERCULOSIS AND HIV

PC-795-03   Drug-resistant tuberculosis and HIV co-infection in Cambodia, 2006–2012

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Background: HIV infection is associated with increased risk of death in people with multidrug-resistant tuberculosis (MDR-TB) worldwide. 6.3% of TB patients in Cambodia are HIV+. Cambodia's drug-resistant treatment (DR-TB) program includes HIV+ persons as a priority group.

Design/methods: A retrospective cohort analysis was conducted of all DR-TB patients (mono, poly, and MDR) initiating second line therapy in Cambodia, 2006–2012. Before 2011, smear-positive (sm+) re-treatment patients were screened for MDR using DST. In 2011, criteria expanded to include all HIV+ sm+ patients. In 2012, guidelines included GeneXpert for screening HIV+ patients with signs or symptoms of TB. MDR-TB patients with HIV receive care coordinated between the MDR-TB and HIV programs.

Results: Between 2006–2012, 281 patients initiated treatment for MDR-TB, of whom 280 had known HIV status, with 56 (20%) of patients HIV+. 74 drug-resistant TB patients initiated second-line treatment for non-MDR drug-resistant TB, including 21 (28%) HIV+ patients. HIV+ MDR-TB patients were on average younger (36 vs. 46 years, $P < 0.001$) but similar in sex (66% male vs. 68% male) and baseline BMI (17.0 vs. 17.2, $P = 0.6$) compared to HIV-uninfected MDR patients. 52 (95%) of HIV-infected persons were receiving or initiated HAART at the time of MDR diagnosis. 11 (20%) HIV-positive patients initiated MDR-TB treatment in the community compared to hospital, similar to HIV-negative patients (25%, $P = 0.4$), and 67% of HIV+ patients initiated in the community had an outcome of cure or completion compared to 52% initiated in the hospital ($P = 0.5$). HIV+ patients had a higher proportion of deaths than uninfected patients (39% vs. 14.1%, $P = 0.002$) before 2011. However, among the 136 patients initiating treatment since 2011, there have been similar proportions of early deaths between HIV+ and negative: 2 (8%) vs. 6 (5%), $P = 0.6$. Treatment outcomes were similar ($P = 0.2$) between HIV+ and HIV-uninfected patients with non-MDR drug-resistant TB, with 0 deaths among 6 HIV+ patients, 5 cures, and 1 default.

Conclusion: HIV was significantly associated with higher risk of death in MDR-TB in Cambodia, but early indicators suggest that this disparity may be decreasing. Community-initiated treatment is as successful as hospital-initiated treatment in HIV+ persons. Early case-finding and diagnosis of TB among HIV+ persons including deployment of GeneXpert and strong community-based treatment support may contribute to improved outcomes in HIV+ persons with DR-TB.

PC-796-03   HIV-TB patients accessing ART in integrated and non-integrated clinical services in primary health clinics in Kinshasa and Kisangani, DRC

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Background and challenges to implementation: Despite the clear benefit of early initiation of antiretroviral therapy (ART) in patients with HIV-associated TB (HIV-TB), only 48% of HIV-TB patients were started on ART in 2011. Access to CD4 count in resource-poor settings constituted a major barrier before WHO's 2010 recommendation of ART for all patients with HIV-TB regardless of CD4 count.

Objective: To report on ART initiation rates in patients with HIV-TB by the end of TB treatment after implementation of WHO's 2010 guidelines.

Intervention or response: Between November 2010 and December 2012 we implemented Provider Initiated HIV testing and counseling (PITC) in 65 and 13 TB clinics in Kinshasa and Kisangani, respectively and asked nurses to verify and record effective linkages of HIV-TB patients to HIV services and initiation of ART. Clinics were supplied with HIV tests and cotrimoxazole.

Results and lessons learnt: In Kinshasa, of the 15 294 TB cases recorded (76% from 30 clinics with integrated HIV services), 385 were known HIV+ before TB diagnosis, 14 394 (96%) were tested. Of the total 1969 HIV-TB patients, 98% were initiated on cotrimoxazole and 65% of the 1546 not on ART at TB diagnosis were initiated on ART by the end of TB treatment. In Kisangani, of the 2120 TB cases recorded (62% from 5 clinics with integrated HIV services), 155 were known HIV+, 1828 (93%) were tested and 96% of the 470 HIV-TB patients were initiated on cotrimoxazole and 51% of the 367 eligible patients were initiated on ART. The proportion of HIV-TB patients initiated on ART varied substantially from month to month but overall increased over time, in Kinshasa from 52% in the last quarter of 2010 to 78% in the last quarter of 2012 and in

Kisangani from 39% in April–May 2011 to 83% in the last quarter in 2012. Patients from integrated clinics were more likely to be initiated on ART compared to those diagnosed in clinics with no onsite HIV service though the gap was smaller in Kinshasa (67% vs. 60%) than in Kisangani (61% vs. 39%).

Conclusions and key recommendations: Despite the removal of CD4 count as barrier, substantial logistical challenges continue to limit initiation of ART in patients with HIV-TB in the severely resource-constrained context of DR Congo.

PC-797-03   Are HIV infected tuberculosis patients under India's National AIDS Control Programme started on ART promptly?

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Background: India has third highest burden of HIV infected tuberculosis (HIV-TB) patients in the world. World Health Organization (WHO) recommends that all HIV-TB patients should be initiated on antiretroviral therapy (ART) irrespective of CD4 count. While this policy has been adopted by India since November 2011, anecdotal evidence suggested gaps in implementation. Hence, we aimed to assess the proportion of HIV-TB patients not initiated on ART in a nationally representative sample of ART centres of India.

Design/methods: We conducted a nation-wide cross-sectional study involving review of routine records (TB-HIV registers) maintained at the ART centres. We calculated sample size of 768 (assuming 50% ART initiation, 5% precision and design effect of 2). Of 287 ART centres in India, 32 were randomly selected and it was decided to enrol all consecutively registered HIV-TB patients from each centre between January–March 2012 or about 24 patients per centre, whichever is later, to achieve the sample size.

Results: Of the 1442 HIV-TB cases registered at the selected ART centres, 314 (22%, 95%CI 20%–24%) were not initiated on ART. Among 1128 on ART, we had valid information on date of TB treatment initiation and ART initiation in 917 cases. The median (inter-quartile range) duration between starting TB treatment and ART initiation was 20 (14–40) days. But in about 15% cases the ART was initiated after 8 weeks of initiating TB treatment. Further out of 241 HIV-TB patients with CD4 count >350/mm^3, 66 (27.4%) were not on ART as compared to 139/1182 (20.2%) patients with CD4 count <350/mm^3 (P = 0.01). Of 400 HIV-infected extra-pulmonary TB (EPTB) patients, 106 (26.5%) were not on ART as compared to 208/1042 (20%) of pulmonary TB patients (P < 0.01). ART initiation did not differ by age or sex of patients.

Conclusion: About 1 in 5 HIV-TB patients who were registered at ART centres were not on ART. This is a missed opportunity to place patients on life saving treatment. Non-initiation of ART was more likely among EPTB patients and those with a CD4 count higher than 350/mm^3, possibly indicating a lack of awareness of latest national guidelines among the health care providers at ART centres. Urgent measures are required to bridge this gap which include training and intensive supervision, monitoring and review.

PC-798-03   Clinical and epidemiological profile of multi-resistant tuberculosis cases reported in the state of Amazonas between 2001 and 2010

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Background: The most prevalent resistance to medicines for tuberculosis, in Brazil, is the acquired type. In this context, the treatment abandonment and inappropriate use of treatment are seen as the main factors associated with this problem. Therefore, it was tried to identify the clinical-epidemiological profile of multi-resistant tuberculosis cases reported in the Amazon, between 2001 and 2010.

Design/methods: This is a descriptive study of multi-resistant tuberculosis cases reported in the Notifiable Diseases Information System and Epidemiological Surveillance System of Multi-resistant Tuberculosis. The analysis was performed by the statistical program Minitab 15.0.

Results: A total of 74 cases were reported between 2001 and 2010. Thus, 47 were male (63.5%) and 27 female (36.4%). The ages ranged from 18 to 60 years and with increased frequency between 20 and 49 years (74.3%). The highest frequency regarding education was identified in patients who had 1 to 3 years of education (47.9%), followed by 4–7 years of education (20.8%). Of the 74 analyzed cases, 43 underwent anti-HIV serology and 5 were positive. This corresponds to 11.6% of the patients co-infected with the virus. It is noteworthy that 50% of the analyzed cases had a background of previous treatment for tuberculosis.

Conclusion: The data suggest that the resistance in the state of Amazonas is affecting individuals in the working age and low educational level. Furthermore, it is important to note that the history of previous treatment was relevant to this study, suggesting the need to discuss possible treatment failures, such as lack of compliance and effectiveness in monitoring the case. Brazil does not present a high rate of resistance to anti-tuberculosis medications. However, it is

necessary to consider the need to monitor the increase in the number of reported cases since the spread of these resistant strains is a problem for TB control in the country.

PC-799-03   MDR-TB treatment outcomes among HIV-infected and non-HIV-infected patients in Swaziland: a review of routinely collected data

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Background: Multidrug-resistant TB is a significant problem in Swaziland in 7.9% of new patients and 33.3% of previously treatment patients. Additionally, HIV co-infection exists in 83% of these patients. The World Health Organization (WHO) reported that in 2010, 350000 people died who had active TB and HIV infection among TB/HIV co infected patients. This paper describes the relationship between HIV and MDR-TB treatment outcomes among patients in Swaziland.

Methods: Analysis of routine data collected in the national TB hospital MDR-TB register for patients enrolled on treatment between January and December 2009 was conducted. The analysis was disaggregated by HIV status.

Results: Ninety-four (94) patients were registered in 2009. Sixty-six (70%) patients were HIV positive, with 35 being females and 30 males. Seventy-two percent (47/66) were on ART (16 males and 31 females).

Among the 66 HIV positive cases, 52 (79%) had a favorable treatment outcomes (that is either cured or completed treatment). When the treatment outcomes were analyzed by status of HIV treatment; among those on ARV, 28/47 (60%) had favorable outcomes while among those who were not on ARVs 6/19 (32%) had favorable outcomes. Among the 31 HIV negative case, 16 (55%) had favorable treatment outcomes.

Overall, the treatment outcomes of HIV positive MDR-TB group on ART were better than the MDR-TB HIV positive group not ART.

Conclusion: The results show a need for strengthened TB and HIV integrated services to ensure early and timely ART initiation to improve the treatment success rate. Integration of HIV and TB programs should be adopted as the 4th 'I' to intensified case finding, infection control, isoniazid preventative therapy (IPT).

PC-800-03   Investigation for tuberculosis delays start of antiretroviral therapy in South African primary care clinics

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Background: Patients with HIV presenting to start antiretroviral therapy (ART) should be screened for TB, but diagnosis may be delayed, particularly if the initial smear or Xpert MTB/RIF test is negative, necessitating a sputum culture, and this may delay ART start. Our aim was to quantify attrition following HIV diagnosis and association TB investigation with time to ART start in 21 primary care clinics delivering nurse-led ART care in South Africa.

Design/methods: We created two retrospective cohorts: 'HIV test to CD4 test', a consecutive sample of adults testing HIV positive after 1 April 2012, measuring days from HIV test date to date blood was taken for CD4; and 'CD4 to ART', consecutive adults attending to collect a CD4 result of $\leqslant$200 cells/μL from July–November 2011, measuring days from date blood taken for CD4 to ART start date. Data, including whether TB symptoms were reported or investigations sent, were collected from routine records from June–Aug 2012, and time to ART start were compared using the Kruskal-Wallis test.

Results: HIV test to CD4 test: 424 adults (69% female, median age [interquartile range, IQR] 32

	Median days from		
	n CD4 test to P ART start (IQR)	n CD4 test to P CD4 result (IQR)	n CD4 result to P ART start (IQR)
All	369 **42** (29–66)	380 **13** (8–22)	363 **25** (14–44)
	—	—	—
Male	126 **37** (26–66)	147 **11** (7–19)	124 **24** (14–50)
	0.13	0.001	0.78
Female	243 **43** (31–65)	244 **14** (8–27)	239 **25** (14–43)
CD4 0–49	97 **35** (25–55)	96 **10** (7–17)	92 **20** (11–42)
CD4 50–99	86 **42** (32–62)	90 **14** (8–25)	85 **22** (14–45)
	<0.001	0.009	0.02
CD4 100–149	89 **39** (28–66)	90 **13** (8–21)	87 **22** (14–42)
CD4 150–200	97 **55** (37–71)	104 **15** (8–30)	99 **33** (19–50)
No TB symptoms	200 **43** (30–66)	206 **14** (8–27)	197 **23** (14–41)
	0.78	0.004	0.17
TB symptoms	169 **40** (28–67)	174 **11** (7–18)	166 **27** (14–49)
No sputum	143 **42** (28–61)	130 **12** (7–18)	144 **26** (14–42)
Smear only	138 **39** (28–67)	118 **14** (8–24)	131 **20** (13–36)
	0.16	0.17	0.003
Smear & culture	88 **49** (31–78)	86 **13** (8–20)	88 **33** (15–60)
No TB treatment	307 **39** (27–57)	317 **13** (8–22)	302 **22** (13–37)
	<0.001	0.99	<0.001
TB treatment	62 **69** (39–106)	63 **13** (7–23)	61 **56** (27–79)

[27–40] years) were included. Only 222/424 (52%) had blood taken for CD4. Among the 83 (37%) who did not have blood taken the day of HIV testing the median time to the blood taken was 2 days (range 1–45). CD4 to ART: 409 adults (64% female, median age 36 [IQR 31–43] years) were included. 377/409 (92%) started ART, a median 42 (IQR 29–66) days after blood taken and a median 25 (IQR 14–44) days after collecting a CD4 result. CD4 test date to ART initiation was longer for people with higher CD4 counts; CD4 result to ART initiation was longer for those with sputum culture sent vs. smear or no TB investigation; and both times were longer for those who started TB treatment vs. those who did not (see Table).

Conclusion: Delay in starting ART among severely immunosuppressed patients remains substantial, particularly among those investigated for TB, and new South African guidelines aiming to reduce this delay for people with CD4<200 are an important advance. However, strategies to ensure adequate TB screening, diagnosis and treatment at this stage remain inadequate; point of care tests for TB, and algorithms identifying those at high risk of TB in order to allow rapid TB treatment start (followed by ART) are urgently needed.

PC-801-03 Implementation of tuberculosis intensified case finding, isoniazid preventative therapy, and infection control in global ART programs

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Background: WHO guidelines for TB prevention and control among HIV-infected populations focus on the 'three I's': Intensive case finding, Isoniazid preventative therapy (IPT), and Infection control (IC). Despite the known benefits to HIV-TB program integration, challenges abound.

Design/methods: WHO guidelines for TB prevention and control among HIV-infected populations focus on the 'three I's': Intensive case finding, Isoniazid preventative therapy (IPT), and Infection control (IC). Despite the known benefits to HIV-TB program integration, challenges abound.

Results: Data collected from 47 sites in 26 countries:

14 (30%) SA, 7 (15%) WA, 8 (17%) EA, 5 (11%) CA, 6 (13%) AP, and 7 (15%) CCASA. 83% sites actively screened all patients for TB at enrollment into care, with 38% using targeted symptom-based screening, and 45% utilizing symptom-based screening plus additional diagnostics, and 17% for clinical suspicion only. TB and HIV services were co-located within the same facility in only 45% of sites; under the same roof in 15%; with capacity for cross-facility referrals in 38% of sites. ART was provided for all HIV-TB patients at most sites (72%), with provision of ART for those with CD4 < 350 cells/mm³ in 26% of sites. Specialized clinics with dedicated staff for TB patients was available onsite (60%), offsite (21%), or not available (19%) of sites. IPT was available at ART initiation in 17% and for TST+ patients in 9% of sites. Separation of sputum smear+ patients from HIV+ patients on inpatient wards, the emergency department (ED), or outpatient clinics was standard practice in 62% of sites, ranging from 43% (WA) to 83% (AP). Separate waiting rooms/EDs for coughing patients were not available in majority (70%) of sites; with 34% reporting that they offered no specific protection to health care workers (HCW). Additional site-specific IC measures included optimized natural

	Implementation of Three I's (n = sites)						
	Asia-Pacific (n = 6) n (%)	CCASA (n = 7) n (%)	Central Africa (n = 5) n (%)	East Africa (n = 8) n (%)	Southern Africa (n = 14) n (%)	West Africa (n = 7) n (%)	Total (N = 47) n (%)
Isoniazid preventive therapy (IPT)							
IPT available*	1 (17)	2 (29)	0	1 (13)	3 (21)	1 (14)	8 (17)
Infection control measures							
Separation of sputum-positive and HIV-positive patients on inpatient wards, ED, and outpatient clinics	5 (83)	4 (57)	3 (60)	5 (63)	9 (64)	3 (43)	29 (62)
Separate waiting room and EDs for coughing patients	2 (33)	2 (29)	1 (20)	4 (50)	4 (29)	1 (14)	14 (30)
Optimized natural ventilation through appropriate windows	3 (50)	3 (43)	2 (40)	4 (50)	8 (57)	1 (14)	21 (45)
Operated and maintained ventilators	3 (50)	5 (71)	2 (40)	1 (13)	4 (29)	2 (29)	17 (36)
TB screening for medical staff working with TB patients	5 (83)	5 (71)	0	3 (38)	3 (21)	1 (14)	17 (36)
Staff wear masks in close contact to TB patients	5 (83)	6 (86)	2 (40)	3 (38)	7 (50)	4 (57)	27 (57)
Turn-around time for TB diagnosis, days							
Smear-positive patients, median [IQR]	7 [5–7]	7 [3–7]	4 [4–7]	2 [1–2]	3 [2–5]	5 [4–7]	4 [2–7]
Smear-negative patients, median [IQR]	6 [2–17]	14 [5–18]	14 [14–15]	5 [2–6]	7 [3–14]	15 [11–15]	7 [4–14]
Intensified case finding							
Specific intensified case finding program	2 (33)	2 (29)	3 (60)	6 (75)	7 (50)	3 (43)	23 (49)
Household intervention with contact tracing	0	1 (14)	1 (20)	3 (38)	6 (43)	1 (14)	12 (26)

* All adults at enrollment or at ART start.

window ventilation (45%) and the provision of ventilators (36%). Specific intensified case finding programs were available in only 49% of sites.

Conclusion: Implementation of TB prevention and infection control measures was low and varied considerably by region. There is an urgent need to scale-up TB infection control and preventative measures at HIV care and treatment sites. Improvements in facility-based infection control measures and practices, the majority of which are not costly, could have significant public health benefits at both the HCW and patient level.

PC-802-03   Achieving good isoniazid preventive therapy uptake and completion rates in rural South Africa

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Background: Isoniazid preventive therapy (IPT) is a core part of the World Health Organization's strategy to reduce tuberculosis (TB) transmission. Since the roll out of IPT in South Africa in 2010, relatively poor uptake has been recorded; by the end of 2011 only 373 000 of 5.6 million people living with HIV in South Africa had received IPT. Few data are currently available about IPT uptake in newly diagnosed HIV patients. Here we report on our experience of the IPT programme at a district level hospital in rural South Africa where we operate a community-based system with a collaborative approach to HIV and TB.

Methods: We used electronic records from our anti-retroviral therapy (ART) database to investigate provision of IPT to ART initiators. Two time periods were studied: November 2010 to April 2011 (soon after introduction), and throughout 2012. Our primary aim was to identify what proportion of patients eligible for IPT were initiated on therapy. Secondary aims were to quantify what proportion of patients completed treatment, and identify whether patients initiated on IPT went on to develop TB.

Results: Over the two time periods studied the proportion of eligible patients prescribed IPT increased from 36.9% to 65.5% ($P < 0.001$). Of those initiating IPT in the first time period, 104/150 (69.3%) completed at least 5 months of therapy and 74/150 (49.3%) completed at least 5.5 months. We only identified one patient receiving IPT that went on to develop TB.

Conclusions: From the initial roll out of IPT in November 2010, there has been a significant increase in the proportion of patients initiating ART prescribed IPT at our hospital. This is encouraging in view of the globally reported figures of poor uptake of IPT. We utilised electronic databases to gather this information, and reflect that such databases appear to be underused at the local level to provide feedback on programme implementation.

PC-803-03   Is TST a barrier to implement the 36-month isoniazid preventive therapy strategy in HIV-infected patients in a resource-constraint setting?

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Background: WHO recommends implementing isoniazid preventive therapy (IPT) in HIV programs. IPT is effective in preventing tuberculosis (TB) in patients with positive tuberculin skin test (TST). However, in resource-limited settings implementation of TST can be challenging. We assessed the feasibility of TST for IPT initiation in Mathare HIV clinic, Kenya.

Design/methods: Prospective cohort study. HIV-infected patients were eligible for inclusion if aged ≥15 years, symptom screen negative for TB, had no previous TST or contraindications to IPT. TST-positive (≥5 mm induration) patients were started on 36 months IPT. TST-negative patients did not receive IPT. For a subgroup of patients, TST reading was repeated to assess reading agreement.

Results: Between June and October 2012, 897 HIV infected patients were assessed and 550 included. Of those assessed, 160 (17.8%) symptom screened positive for TB, 85 (9.5%) had previous TST, 69 (7.7%) had IPT contraindications, 23 (2.6%) were on secondary IPT, 8 (0.8%) did not consent, 2 (0.2%) were <15 years.

Among those included, 372 (67.6%) were female. Median age was 39 years (IQR 33–45). ART had been initiated in 460 (83.6%) patients. Median CD4 count was 564 cells/μL (IQR 427–749) and 6.2% had <200 cells/μL. A total of 188 (34.2%) had received prior anti-TB treatment.

In total, 491 (89.3%) had TST administered. Fifty-nine (10.7%) patients declined TST: 55 unable to come for reading and 4 not willing to perform the test. Among those with TST administered, 414 (75.3%) had an interpretable result: 72 (14.7%) did not come for reading and 5 (1.0) came late. Of the 204 IPT eligible patients, 196 (96.1%) were started on IPT.

TST was positive in 206 (49.8%) patients. The proportion of TST-positive was 29.2% in patients <200 CD4/μL and 51.0% in those ≥200 CD4/μL ($P = 0.038$). Prior anti-TB treatment was not associated to TST-positive result (54.0% vs. 47.6%, $P = 0.224$). In the multivariate analysis being on ART (OR 1.7, 95%CI 1.0–2.7) and CD4 count ≥200 cell/μL (OR 2.8, 95%CI 1.1–6.9) were associated to TST-positive.

TST reading agreement was 99.5% (kappa = 0.99) for positive/negative TST result.

Conclusion: Implementation of TST was feasible in an urban HIV clinic in programmatic conditions. This

strategy avoided treating unnecessarily a high proportion of patients and allowed providing 36 months IPT to the eligible patients. We recommend implementing TST-based IPT in urban settings and to evaluate its feasibility in rural settings.

PC-804-03   Baseline variable differ between HIV-positive and -negative MDR-TB patients in the South African PETTS cohort

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Background: Mortality among MDR TB patients are high, but significantly higher among those with HIV than those without HIV infection.

Objective: To describe baseline demographic, clinical and bacteriological differences between HIV-infected patients and those without HIV and to determine if any is associated with higher mortality among HIV positive patients.

Design/methods: The South African PETTS cohort consisted of 266 patients with known treatment outcome and HIV status. We compared baseline clinical, demographic, socio-economic and bacteriological variables between the two HIV-status groups. Spoligotyping of strains will be available for the final presentation.

Results: In this preliminary analysis, 54.5% of the cohort was infected with HIV, in Mpumalanga province slightly more patients were HIV infected than in the other three provinces. 52.6% of the cohort was male, while 66.7% of females were HIV-infected (significant $P < 0.001$). Slightly more HIV-infected cases were unemployed. Significantly less patients without HIV had primary MDR-TB, more HIV-infected patients were previously treated for TB, and fewer of these were previously treated with second line treatment ($P = 0.041$). 60% of the cohort was resistant to ethambutol while HIV-positive patients had significant lower rates of resistance. 30.8% of all cases were resistant to any one of the three injectables at onset of treatment, 28.2% to all three, 11.3% had XDR-TB. More HIV-positive patients died (64% vs. 35%), while the default and failure rates were higher among those without HIV.

Conclusion: There are distinct differences in baseline characteristics between the two HIV groups and genotyping of baseline isolates may contribute understanding of these differences and treatment outcomes.

PC-805-03   How do TB-HIV patients fare two years after completing treatment for tuberculosis in India?

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Background: The Revised National Control Programme (RNTCP) of Indiahas been implementing the intensified TB-HIV package since 2006 as part of TB-HIV collaborative activities. As a policy, all TB patients with HIV and CD4 count less than 350 cells/mm^{3} received antiretroviral therapy (ART), cotrimoxazole prophylaxis therapy (CPT) and standardized anti-TB treatment as directly observed treatment. On completion of TB treatment, the patients continued ART and CPT and were no longer monitored by the programme. There is no information documented on their well being; there are concerns of long term survival, adherence to ART and relapse of TB among these patients. In order to assess the longevity of these patients we aimed to determine the proportion of TB-HIV patients with successful TB treatment outcomes who were alive and on ART after two years of completing TB treatment.

Methods: All the TB-HIV patients registered in 2009 under RNTCP in two districts (population 7.5 million) having successful TB treatment outcomes were included in the study. The programme staff made individual patients' home visits and ART centres to ascertain living status and adherence to ART.

Results: Among 8381 TB patients registered, 711 were found to be TB-HIV, of which 513 patients had successful TB treatment outcomes. We found 227 (44%) of patients were alive two years after treatment completion with 189 (83%) on ART. Of those alive, 17 (7.5%) of patients had developed tuberculosis.

Conclusion: Our study shows that one third of patients had died two years after successfully completing TB treatment and majority of them were adherent to ART. Concerted efforts by RNTCP to periodically monitor TB/HIV patients after TB treatment completion can enhance long term survival rates.

OPERATIONAL CHALLENGES IN CHILD LUNG HEALTH

PC-806-03   Oxygen and pulse oximetry in childhood pneumonia: a survey of student clinicians in Cambodia

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Background: Pneumonia is the leading cause of death in children younger than five years of age in Cambodia and globally. Hypoxemia, a frequent complication of pneumonia, is a risk factor for death.

Design/methods: To better understand the current training on the use of oxygen and pulse oximetry among student clinicians in Cambodia, and student clinicians' perceptions and practices regarding the role of these tools in the management of childhood pneumonia, we conducted a survey among 332 graduating medical and nursing students in attendance at the University of Medicine and Science and the Medical Care School in Phnom Penh.

Results: Most respondents reported learning about oxygen (96%) and pulse oximetry (72%) during their training; however, while 84% of nursing students and 34% of medical students reported availability of oxygen at their current facility, only 16% overall reported having a pulse oximeter available (Figure). Further, more medical students (88%) than nursing students (66%) reported being trained on the use of pulse oximetry. Forty-nine percent of the medical students and 76% of the nursing students reported having never or infrequently diagnosed or cared for children with pneumonia. Yet, despite their limited contact with childhood pneumonia during their training, 72% of students considered the disease either more important or one of the most important childhood health problems. Most students reported use of oxygen (90%) and of pulse oximetry (81%) as moderately or extremely important in the management of childhood pneumonia. When compared to other tools, pulse oximetry was viewed as equally important as patient history, physical exam, World Health Organization Integrated Management of Childhood Illness criteria, and chest radiographs in the diagnosis of childhood pneumonia. Notably, medical students generally considered pulse oximetry to be more useful than did nursing students.
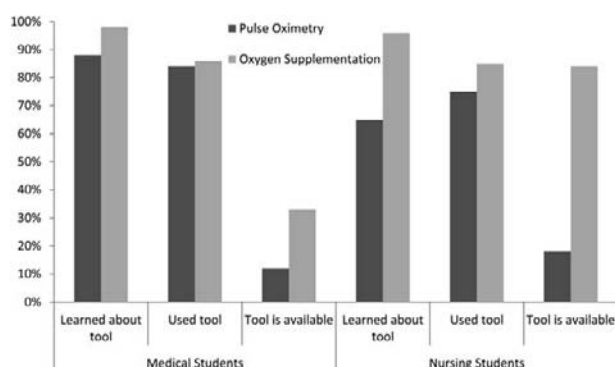
Figure Student exposure to tools.

Conclusion: Despite education during their training and an appreciation by students of the effectiveness of pulse oximetry and oxygen in the management of

childhood pneumonia, our data indicate that pulse oximetry may be underused due to low availability in Cambodia.

PC-807-03   It's hard work, but it's worth it: the task of keeping children adherent to isoniazid preventive therapy

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Background: Isoniazid preventive therapy (IPT) offers children unique protection against TB, but it has been consistently difficult to implement especially in developing country settings. TB levels in South Africa are extremely high especially in poorer communities such as those where this study was conducted, with the current growth of MDR TB being of major concern. This research was done as part of a major initiative over many years to reduce rates of infection.

Design/methods: The study was done in three community primary health care clinics where very high rates of TB have been recorded. In depth interviews were done with two parents who were giving their children IPT treatment and two staff from each clinic. The key issues explored were knowledge and attitudes towards IPT, problems in accessing the treatment and adhering to it, and community responses to the treatment.

Results: For those parents who had already committed themselves to using the treatment it was seen as very good, they had a good sense of the risk of TB to their children often arising out of personal experience, and they had very positive views about the clinic. The nurses acknowledged that this perspective was not shared more broadly and there did remain a lot of resistance to treatment, with parents not wanting to acknowledge the risk, sometimes not wanting to make the effort on the part of their children and there being misinformation about IPT. Some internal problems in the clinic relating to shortages of staff, waiting times and some conflict between staff and a few community members did act as further deterrents. Finally adherence was affected by the levels of social problems in the community, some stigma attached to TB and its link to HIV, and the extended period of treatment required for IPT.

Conclusion: The parents that did adhere to IPT show that the regime is possible to follow even in very difficult circumstances and there is much to be learned from them. At the same time there are lessons in terms of improving some aspects of clinic services, correcting misinformation about IPT, reducing stigma and providing additional support to parents that would be important for extending the use of IPT.

PC-808-03   Improving childhood tuberculosis management in Cambodia: isoniazid preventive therapy

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Background: Cambodia National Center for Tuberculosis and Leprosy Control (CENAT) developed guidelines for the management of childhood TB in 2008 which are aimed at strengthening case finding, diagnosis and treatment of childhood TB. Although the guideline contains provisions for IPT implementation and management, they have seldom been implemented. The objective of IPT is to prevent TB contact children from developing TB.
Intervention: The pilot implementation of childhood TB management focusing on IPT by CENAT and JATA/TB CARE I/USAID started in July 2012 in 3 operational districts of 77. The main activities of the childhood TB IPT initiative are: orientation workshops, clinical trainings for IPT screening and 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 TB contact children to health centers and hospitals for TB screening and diagnosis on the pre-appointed day. We also conduct supervision to provide on the job training for health center staff on screening for IPT for TB contact children aged less than 5 years old.
Results: For the first data collection of 9 months (July 2012–March 2013), 236 TB contact children were screened and eligible for IPT. Among those, 58 children were completed IPT with healthy status, 1 developed TB, 6 defaulted and 171 has been ongoing IPT.
Conclusion: The IPT can be implemented at health center level and the contact tracing and diagnosis at hospitals for childhood TB plays an important role in TB case detection for TB in children. Cambodia NTP should expand this intervention to other districts.

PC-809-03   Assessment of Kabul City's 15 hospitals' performance in childhood tuberculosis case detection and notification

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Background: In early 2010, National TB Control Progam (NTP) started to focus on childhood TB develop Standard Operational Procedures (SOPs) for TB in Children and the health staff was trained on TB in children. Recently, NTP supplied tuberculin skin test (TST) to hospitals in Kabul City and other provinces. Despite of mentioned efforts, childhood TB is still negleted due to health staff's lack of awareness of the magnitude of the problem. This study aimed to assess performances and challenges of childhood TB case detection and notification in Kabul City's hospitals and explored the existing challeges towards TB case dectection and notification among children.
Method/design: In 15 hospitals (9 public and 7 private) where NTP has already expanded TB care services, 2012's registers and reports were reviewed. Findings were recorded in assessment form.
Results: During year 2012, 386 000 children (0–14 years) presented in hospitals' OPDs. TB suspect identification rate found very low as 2300 (0.6%) children were diagnosed as TB suspects while 10% of the suspects, 212 children were diagnosed as confirmed TB which is high. Out of 15 hospitals only 8 hospitals had chest X-ray and TST facilities and child TB household contact investigation was initiated only in 7 hospitals. Furthermore, NTP's existed case notification format was not applicable to notify SS+ re-treatment, extra-pulmonary and other cases among children (0–14) separate from adults.
Conclusion: Study findings indicated that still childhood TB is missing among children present in Kabul City hospitals' OPDs. NTP and NGOs working in TB control need to improve the quality of childhood TB diagnostic services and increase TB suspect identification in Kabul City hospitals. Moreover, in order to explore the magnitude of childhood TB problem in the country NTP needs to revise the case notification form to capture data on all forms of TB among children 0–14 years.

PC-810-03   A review of the standards of care in the diagnosis and management of children with suspected tuberculosis

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Background: Tuberculosis (TB) in children is a significant but poorly described public health problem globally and in Kenya. It is estimated that 11% of TB cases in developing countries occur in children less than 15 years of age. It is likely that the true burden of paediatric TB remains unknown because confirmation of diagnosis in young children is challenging. According to a 2011 WHO global TB control report, there were around 132 000 new TB cases in Kenya. It is one of the 22 high burden countries. We sought to understand how well Kenyan hospitals adhere to the WHO's International Standards for TB Care when managing TB in children.

Design/methods: A retrospective review of case records of patients admitted to six primary and secondary referral hospitals between September 2011 and September 2012 was undertaken to document the clinical assessment, treatment and outcomes of the children admitted. Process of care of children with suspected TB was reviewed amongst these records. We also created a checklist of 30 indicator items necessary for providing TB care in children and assessed their availability at each of the hospitals by direct observation.

Results: We reviewed 10 657 files and identified 4849 diagnoses of lower respiratory tract infections (LRTI). Of these, 146 (3.0%) had a diagnosis of suspected TB. A history of cough lasting more than three weeks was seen in 191 (3.9%) of the LRTI cases with a documented positive report of TB contact in 124 (2.6%). Chest radiographs were done for 59 of those who had a chronic cough. Only 24 sputum tests were done. Availability of the indicator items within hospitals had a median score of 15/30 and a range of 15/30 to 23/30. None of the hospitals did sputum induction, and only one reported doing gastric aspirates. Mantoux reagent was absent in all six hospitals and none had the capacity to do TB cultures, although they all could do Ziehl-Nielsen and Auramine staining. The Figure summarises these 30 indicators.
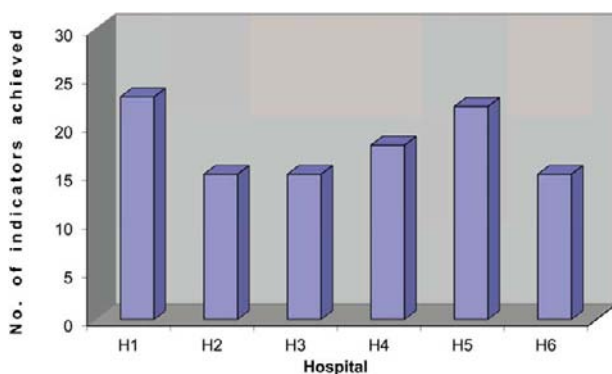
Figure   Counts of key items available to provide TB care.

Conclusion: WHO IST standards of care recommend that patients with at least 2–3 weeks of cough should be fully evaluated for TB including a chest X-ray and good attempts made at sputum collection. The hospitals have great difficulties in diagnosing TB and these are missed opportunities. A high index of suspicion is needed especially among LRTI cases, plus following the available diagnostic guidelines.

PC-811-03   Intensified tuberculosis case finding among malnourished children in nutritional rehabilitation centres, Karnataka, India: missed opportunities

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Background: Childhood TB is under-notified globally as well as in India. National TB programme in India has amended its policy to actively screen all children with high risks for TB, to address this gap. Malnutrition is one of the important risk factors associated with TB. In India, severe acute malnourished (SAM) children identified at the villages by the health workers are referred to nutritional rehabilitation centres (NRC), for effective management. NRCs are the specialised health clinics manned by a paediatrician and established under National Rural Health Mission, thus presenting a unique opportunity for intensified screening and diagnosis of TB. We aimed to assess the processes and results of TB screening conducted in selected NRCs of Karnataka.

Methods: We conducted a cross-sectional study in 6 sub-districts of Karnataka State, India, having established NRCs, covering a total population of ~1.75 million. We reviewed the records (registers maintained by health workers and patient files maintained by NRCs) of all children identified by health workers during January–December 2012.

Results: Of 1927 SAM children identified by the health workers, 1632 (84.7%) reached NRCs for evaluation. Of them, 1173 (71.9%) were evaluated for TB; 460 (36.7%) were adequately evaluated as per the diagnostic algorithm of the National TB programme while the rest 743 (63.3%) were not. Among those not following diagnostic algorithm, tuberculin skin test (TST) alone was conducted in 307 (41.3%), chest X-ray alone in 99 (13.3%) and no investigations were conducted in 337 (45.4%). While 17 (4%) children were diagnosed as TB among those who followed the standard diagnostic algorithm, only 2 (0.3%) TB cases were detected among those who did not follow it. All 19 diagnosed TB children were put on treatment.

Conclusion: Though most SAM children reached NRCs, evaluation for TB among them was suboptimal. While no evaluation was done in one-third of children, standard diagnostic algorithm was not followed in two-thirds of children evaluated and this could have possibly resulted in under diagnosis of TB. Even among those who were evaluated as per the diagnostic algorithm, the TB detection rate was much below expected. The reasons for this missed opportunity and the low case detection rates remain unclear and needs further research.

PC-812-03   Assessment of the screening of children exposed to tuberculosis in Kisii, Kenya

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Background: Kenya is among the 22 highest tuberculosis (TB) burdened countries in the world with 11.5% of its TB cases being children (0–14 years). Given that children have increased risk of progression to active and more severe forms of TB, early detection of *Mycobacterium tuberculosis* is critical. Though current recommendations are that all children exposed to TB should be screened, this is rarely implemented in endemic settings primarily due to resource constraints.

Design/methods: In January and February 2012, we administered questionnaires to TB affected patients at two health facilities in Kisii, a town west of Nairobi, to assess the screening practices of children exposed to TB. Patients were recruited from the TB clinic if they had children younger than 15 years living in their households.

Results: A total of 29 questionnaires were administered. The respondents had a mean age of 36 years wih an average of two children in each household. 90% of respondents had pulmonary TB and 52% had positive sputums. 72% had none of their household members screened, 13.8% had some screened while 10.3% had all members screened. 58.2% gave 'not being informed' as a reason for not having family members screened. Only one out of nine (11.1%) children under five exposed to sputum positive TB had been screened and started on isoniazid.

Conclusion: A majority of the assessed TB affected households remain unscreened, with a need to improve health education about TB screening. Health counseling should include an emphasis on screening those exposed as well as a discussion of the barriers to screening. Implementation of national guidelines to screen and initiate prophylaxis (isoniazid) in children under five remains poor. An assessment of paediatric TB guidelines utilization in Kenya is warranted, specifically screening, diagnosis and treatment of TB.

PC-813-03   Experience of child tuberculosis training in Bangladesh

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Background and challenges to implementation: Childhood tuberculosis remains a neglected issue within National TB Control Programs (NTP) in many high burden countries. In Bangladesh, the case detection rate for childhood TB is only 3.15%, although an estimated 11% of new TB cases occur in children under age 15, due to lack of facilities and inadequate capacities to identify and diagnose childhood cases.

Objective: To increase the number of pediatric TB cases identified and correctly managed.

Method: The USAID supported TB CARE II project assisted the NTP and WHO to organize clinical and programmatic training for doctors to develop their capacity on the management of child TB. Standard training materials were developed following the National Pediatric TB Guidelines and tested. A TOT was conducted involving senior level pediatricians, followed by a series of trainings of pediatricians from peripheral and rural levels. In total, 138 doctors were trained from September to December 2012. The 5-day training covered diagnosis, treatment, and prevention/IPT. The trainees were pediatricians from medical colleges, district level doctors, consultants from chest disease clinics, upazila level health managers and doctors from 15 districts.

Results and lessons learnt: Ensuring active participation of peripheral level pediatricians in the training was a challenge because of their involvement in private practices. Additional efforts were made to involve district NTP staff in encouraging the pediatricians to participate in the training. After the first few batches of training, it was noted that many pediatricians do not report the child TB cases diagnosed by them through the NTP system. In the subsequent training sessions, revised materials incorporated an increased emphasis on describing the NTP reporting and recording systems, the referral mechanisms, and coordination with NTP for case management. An assessment of the intervention will take place in mid-2013.

Conclusions and key recommendations: The NTP took a positive role to ensure participation of the district and sub-district level pediatricians. The NTP nominated a person in the subsequently batches of training to take a session on reporting, recording and referral system. The positive attitude of NTP was the key for successful child TB training.

PC-814-03   Treatment of childhood tuberculosis in selected areas of Bangladesh: BRAC experience

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Background and challenges: National tuberculosis control programme with its NGO partners has made much progress in adult TB patients' diagnosis and treatment, but the access to child TB patients is limited in Bangladesh. Though accurate status of child tuberculosis is unknown, NTP with the partners gave priority for child TB diagnosis and management since 2010 to provide equitable access of high quality TB care.

Intervention: NTP developed child TB guideline in 2010 and took initiative to orient medical doctors in large hospitals including other government health facilities and private medical practitioners specially the pediatricians. These private medical practitioners are brought under referral network. Child TB symptomatic and children who are in close contact of smear positive TB patients are examined. After proper assessment done by clinicians through the simple symptom based approach adopted by NTP, a child is diagnosed as TB cases. Diagnosed child TB patients are referred to NTP centers for treating under NTP. BRAC front line health workers ensured DOT and encourage parents to visit medical doctors if there are any complications. NTP supplied child friendly dispersible drugs to all TB centers. Data from peri-urban areas of Dhaka city was collected and analyzed.

Result and lesson learnt: The proportion of case diagnosis increased from 2% (2009) to 5% in peri urban areas after introducing intervention (at 2010) and remain static. Female cases 260 (59%) were higher than the male 184 (41%). Among them, 214 (48%) were pulmonary TB and 230 (52%) were extra pulmonary TB cases. They were mostly referred from specialized hospital (77%). Few were referred from private sectors (23%). Possible explanations may be availability of specialist and diagnostic facilities in hospitals. Among the cases registered in 2011, 31 were cured and 157 completed. The treatment success rate was 97% which indicates DOTS remained highly efficacious for child TB management.

Conclusion: Pediatricians in large and specialized hospitals and private medical practitioners need to be oriented on child TB and establish network with NTP services. Child TB <5 years, needs special attention since they are at higher risk for mortality. For early diagnosis active contact tracing and screening is strongly recommended.

PC-815-03 Effective specialized training and implementation of national pediatric tuberculosis clinical guidelines in Tanzania

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Background: Tanzania is among only a few countries that have developed specialized national clinical guidelines and a training curriculum for the management of tuberculosis (TB) in children. Countrywide one-week trainings were conducted for 481 healthcare workers in mid-2012. The impact of such trainings is not well understood.

Design/methods: We developed a standardized survey to assess the knowledge and practices of healthcare workers of pediatric TB diagnosis and treatment. We interviewed a convenience sample of physicians and nurses actively working in settings that cared for children in Dar es Salaam and Pwani regions.

Results: Between 26–28 March 2013, 24 physicians and 17 nurses were interviewed in TB clinics, HIV care and treatment centers, reproductive and child health clinics, pediatric outpatient departments and pediatric inpatient wards at three health facilities. 80% had attended a national training. The average scores were 84% on general knowledge questions, 77% on diagnosis, 80% on treatment, 86% on monitoring TB treatment, and 88% on TB and HIV co-management. Reported practices were mostly in accordance with national guidelines, although tuberculin skin testing (TST) and sputum culture were often not routinely obtained (15%, 4/27 and 44%, 12/27 respectively). Lack of TST supplies was reported by 6/19, 32% of healthcare workers. Use of isoniazid preventive therapy (IPT) was high: 10/14 (71%) had ever prescribed IPT. Those who did not prescribe IPT cited a lack of single isoniazid tablets as the reason.

Conclusion: Healthcare worker knowledge of pediatric TB management was high after training. Practices in pediatric TB were in accordance with national guidelines except where access to supplies impeded implementation. Training and provision of essential materials should be coordinated with updated guideline implementation to ensure effectiveness.

PC-816-03 The impact of a referral pathways change regarding respiratory burden of disease in children, Cape Town

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Background: Khayelitsha Sub-District (KSD) is an informal settlement in Cape Town with higher childhood morbidity and mortality rates compared to the other Cape Town Sub-Districts. In April 2012 a change in the Khayelitsha SD referral pathway was implemented with the opening of the Khayelitsha District Hospital; and with children referred to Tygerberg Children's Hospital (TCH) for more specialised paediatric care instead of Red Cross Children's Hospital. The aim of this study was to assess the impact of this change in referral pathway on the respiratory burden of disease for children younger than 13 years of age in the TCH acute admissions ward.

Design/methods: This is a retrospective interrupted time series study of routine health information collected during two 6 month seasonal periods; 1 April 2011 to 31 August 2011 and 1 April 2012 to 31 August 2012. Data was collected from paper admission registers of the TCH acute admissions ward and analysed for age, sex, diagnosis and admissions/discharges

using standard parametric and non-parametric methods with SPSS software. The study was approved by the Stellenbosch University Ethics Committee.

Results: A total of 4916 children were admitted during the two 6 month study periods; 2446 in 2011 and 2470 in 2012. Nearly half of all children were admitted for acute lower respiratory tract infections; similar in both study periods (45% in 2011; 44% in 2012). Referrals from KSD accounted for 10% of the admissions overall, with an increase from 8% in 2011 to 12% in 2012 ($P = 0.009$). The most common diagnosis was bronchiolitis in 2011 (42% vs. 35% in 2012, $P = 0.002$), while it was Pneumonia for 2012 (38% vs. 27% in 2011, $P < 0.0001$). Tuberculosis was similar for both study periods (7% and 6%). Most children were under the age of 5 years for both study periods (95% vs. 96%), of whom two thirds were below the age of 1 year (64% vs. 68%). Associated malnutrition in the overall study population was similar in both study periods (14% vs. 12%), but differed significantly for the KSD (5% in 2011 vs. 16% in 2012, $P = 0.01$). Median length of stay was 1 day (IQR 1–2) for both periods, but more patients required admission to an in-patient ward for on-going care in 2012 (43% in 2012 vs. 36% in 2011, $P < 0.0001$). More children required intensive care, 5% in 2011 to 7% in 2012 ($P = 0.4$), but fortunately the mortality did not increase (0.1% vs. 0.25%).

Conclusion: Acute lower respiratory tract infections account for a high proportion of burden of disease in children. The change in referral pathway did not lead to a significant increase in total patient numbers referred, but there was an associated increase in acuity and co-morbidities, which may necessitate changes in resource allocation.

TRANSMISSION AND TREATMENT OF CHILDHOOD TUBERCULOSIS

PC-817-03   Kidney tuberculosis in children and teenagers in an epidemic region

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Introduction: The level of the child's incidence with tuberculosis (TB) gives an evidence of severity epidemic situation in the region and insufficiency of special medical service.

Material and methods: History cases of 131 patients with urogenital tuberculosis (UGTB) in Siberia and 819 UGTB patients in Kyrgyzstan were picked up. Among them history cases of children and teenagers were selected and analyzed.

Results: In Siberia only two children and one teen-

ager with UGTB were revealed (2.3% among all cohort of UGTB), all had 1st level of kidney TB inflammation—TB of parenchyma. All children were asymptomatic and were diagnosed as they had contact with TB infection. Seventeen-aged girl had a long history of recurrent urinary tract infection (UTI), and as far as antibacterial therapy was insufficiently effective UGTB was suspected and her urine was cultured. All children and teenager had positive culture in urine; *M. tuberculosis* was sensitive to all anti-TB drugs. All had isolated kidney TB. In Kyrgyzstan 38 children and teenagers with UGTB were diagnosed (4.6% among all UGTB patients). Seventeen patients were children and 21—teenager. All had a long history, underwent surgical interventions, 6 had fistula, two teenagers—microcystis (bladder TB grade 4). Kidney TB 1st level was diagnosed in two children only, kidney TB 2nd level—in 4 patients, in 8—kidney TB 3rd level, and in 3—polycavernous kidney TB (4th level). One boy had also genital TB. Thus, 64.5% patients were revealed in late complicate dstage. Only one patient had isolated kidney TB, in others lymphonodal, skeletal, pulmonary TB was diagnosed. Mycobacteriuria was found in 11 children, in 3—with growth in sputum. Among 21 teenagers complicated UGTB was diagnosed in 11 patients (52.4%). Mycobacteriuria was in 9 and in the rest diagnosis was confirmed by histology. Generalized TB was in 17 patients. Surgery was performed 11 children (64.7%) and 16 teenagers (76.2%).

Conclusion: Late diagnostic of UGTB predominated in Kyrgyzstan, nevertheless in Siberia all children and teenager were revealed in-time and cured by chemotherapy, without surgery. Medical service should be improved in the regions with severe TB epidemic.

PC-818-03   Effect of family DOT on treatment success rates among new child tuberculosis patients: a non-inferiority trial under the RNTCP in Gujarat, India

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Background: World Health Organization recommends direct observation of therapy (DOT) to support tuberculosis (TB) patients and ensure treatment completion. As per national programme guidelines in India, a DOT provider can be anybody who is acceptable and accessible to the patient and accountable to the health system, except a family member. This poses challenges among children with TB, who may be

more comfortable taking medicines from their parents/family members than from unfamiliar DOT providers. There is no evidence from India if provision of DOT by a family member is inferior to standard practice. We conducted a non-inferiority trial to assess the effect of family DOT on treatment success rates among children with newly diagnosed TB and registered between June–September 2012.

Methods: All districts ($n = 30$) in Gujarat state were randomly assigned to the intervention ($n = 15$) or control group ($n = 15$). In the intervention districts, adult family members were given the choice to become their child's DOT provider. In the control districts, DOT was provided by a non-family member. We performed intention to treat analysis and compared treatment success rates (cured and treatment completed) between the two groups.

Results: A total of 624 children with newly diagnosed TB were registered during study period (359 in intervention district and 265 in non-intervention district). The two groups were similar with respect to baseline characteristics like age, sex, type of TB and initial body weight. TB treatment success rates among the intervention and control groups were 95.8% and 93.2% respectively ($P = 0.15$).

Conclusion: DOT by a family member is not inferior to that by a non-family member among new TB patients in children and can attain international targets for treatment success under programme conditions. National guidelines in India should be revised to allow the option of having a family member provide DOT for children with TB.

PC-819-03   The effectiveness of the treatment of MDR-TB in children and adolescents depending on its duration

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Target: To study the effectiveness of treatment of tuberculosis with multidrug resistance with anti-TB drugs of the second line depending on duration of intensive and continuation phase of treatment.

Materials and methods: Group 1—50 patients treated by short courses (intensive phase 2–4 months, continuation one 12–16 months), before adoption of standard schemas and terms of treatment during 2001–2006. Group 2—50 children and adolescents treated with drugs of the second line by terms recommended by WHO (intensive phase not shorter than 6 months and continuation phase 18 months) during 2007–2008. The groups of comparison were virtually identical by age and gender. It should be noted that during 2001–2006 incidence of drug resistant TB among children and adolescents constituted 37.5% while in 2007–2008 it was 8.1% only ($P \leqslant 0.05$).

Results: Effectiveness of the treatment constituted

84.0% in the Gr.1, relapse occurred in 10.0% of children and adolescents from this group. Three adolescents with MDR TB died (6.0%). Dynamic observantion of children and adolescents of the Gr.2 showed that treatment was effective in 48 (96.0%). Out of 16 persons with positive smear outcome 'cured' was determined in 11 (22.0%). Outcome 'treatment completed' was determined in 32 (64.0%) of children and adolescents. Failure was confirmed in 2 (4.0%) of patients and they were administrated the treatment with the drugs of the third line.

PC-820-03   Influence of smoking on tuberculosis transmission to children

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Background: Environmental tobacco smoke (ETS) favours progression from latent tuberculosis infection (LTBI) to tuberculosis (TB) in adults and probably LTBI in children exposed to smear-positive smoking cases. We studied the influence of tobacco smoking and other factors in the transmission of TB to household contacts under 15 yr in a European city with moderate TB incidence.

Methods: A population-based retrospective observational study inBarcelona, on all smear positive pulmonary TB cases that started treatment from 2005 to 2011 and their contacts under 15 yr was performed. Sociodemographic, clinical and risk factors of index cases and sociodemographic, intensity of contact and result of study of children contacts were studied. The intensity of contact was defined as close (> 6 hours/day) or occasional contact (< 6 hours/day). Current smokers were defined as those who smoke one or more cigarettes per day. Data were collected through Barcelona TB Control Program. A descriptive analysis of the cohort was performed. Multivariate logistic regression was used and odds ratio (OR) with 95% confidence intervals (CI) were calculated.

Results: Among the 597 smear-positive index cases, 237 (39.7%) had household contacts under 15 yr. There were 122 males (51.5%), 174 (73.4%) were 25–50 yr, 156 (65.8%) foreign-born, 135 (57%) had > 30 days of diagnostic delay and 83 (35%) were smokers. A total of 374 household contacts younger than 15 yr were enrolled. There were 189 males (50%), 223 (59.2%) Spanish-born and 323 (86.3%) close contacts. 10.1% had TB-disease, and 28.1% LTBI. After adjustment, the associated factors to LTBI or TB in contacts were: male sex of index case (OR 1.9, CI 1.2–3), age 15–24 yr of index case (OR 6.4, CI 1.6–25.2) and age of contacts 5–9 yr (OR 1.8, CI 1.1–3.1) and 10–14 yr (OR 2.2, CI 1.3–3.8). Associated factors to LTBI or TB in 223 Spanish-born

contacts were: > 30 days diagnostic delay (OR 2.3, CI 1.2–4.3), cavitation (OR 2.1, CI 1.2–3.8), smoking (OR 2.4, CI 1.3–4.5) and previous TB treatment (OR 5.3, CI 1.4–9). In foreign-born contacts only sex of index case was significant after adjustment (OR 2.9, CI 1.4–6).

Conclusion: To be a smoker index case is associated to LTBI or disease among Spanish born children household contacts. Diagnostic delay, cavitation and previous TB treatment was also associated. The ETS control interventions will contribute to prevent children infection.

PC-821-03   Analysis of *N*-acetyltransferase-2 gene in Venezuelan children with tuberculosis reveals high genotypic diversity related to significant pharmacokinetic variety

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Background: The genetically polymorphic arylamine *N*-acetyltransferase type 2 (NAT2) enzyme is responsible for isoniazid (INH) metabolism. NAT2 genotype-guided dosing stratification of INH has been proposed as a method to minimize adverse reactions in adult tuberculosis (TB) patients. Few studies have investigated the relationship between acetylator genotype and phenotype in children. Phenotypic classification could provide an easily accessible alternative to genotypification.

Design/methods: NAT2 genotyping and phenotyping were performed in 30 Venezuelan TB patients aged 1 to 15 years included between May and October 2011. Genomic DNA was isolated for sequencing of the coding region of the NAT2 gene. Two methods assessing the acetylator status phenotypically were performed: determination of the plasma half-life of INH and calculation of the metabolic ratio of acetyl INH and INH at 2 hours post dose.

Results: Sixteen different NAT2 haplotypes were identified. One new mutation, corresponding to a new haplotype of the NAT2*7 allele, was identified in two children. Most children carried genotypes that result in intermediate or slow acetylating (43% and 40% respectively). Exposure and apparent clearance of INH differed significantly between genotypically slow and fast acetylators (13.3 vs. 4.5, *P* < 0.01 and 6.9 vs. 15.9, *P* = 0.021 respectively). Both the metabolic ratio as well as the half-life of INH significantly
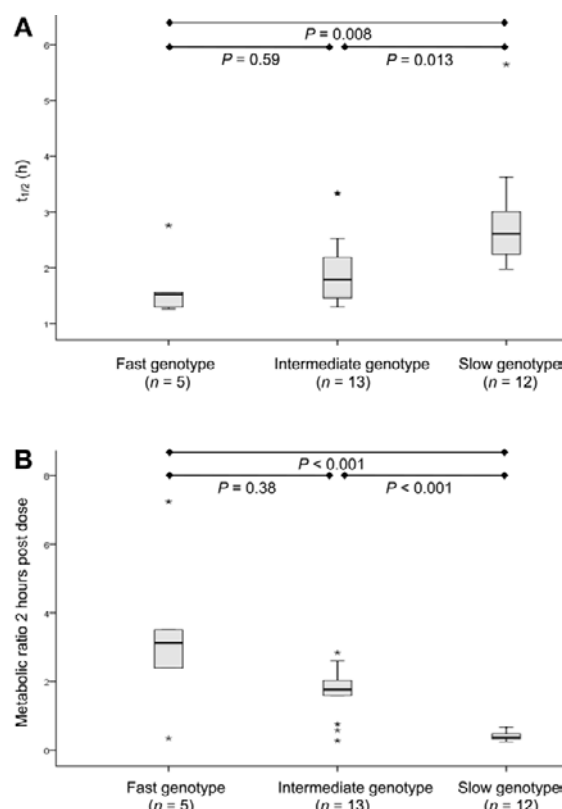
Figure Acetylator phenotype represented as **A**) half-life of isoniazid and NAT2 genotype and **B**) metabolic ratio of isoniazid and NAT2 genotype. The boxplots show the median half-life ($t_{1/2}$)/metabolic ratio values and the interquartile ranges. The whiskers represent the highest and lowest values that are not outliers. Asterisks represent outliers.

distinguished genotypically slow from genotypically fast or intermediate acetylating children (Figure). Genotypically fast acetylating children could not be discriminated from genotypically intermediate acetylating children based on phenotype. Possibly, this is related to the influence of NAT2 enzyme maturation on the acetylator phenotype as a positive correlation of INH clearance with age was observed (Pearson's *r* 0.37, *P* = 0.045).

Conclusion: The large degree of variability in NAT2 haplotypes in Venezuelan children can lead to interindividual differences in exposure to INH when anti-TB drug dosing guidelines are standardized for the whole country. We observed a clear difference in pharmacokinetic parameters between genotypically slow and genotypically intermediate or fast acetylating children. Phenotypic methods provided a distinction between genotypically slow acetylating children and the other two groups. In young children, phenotyping may better reflect INH metabolism than determination of NAT2 genotype due to enzyme maturation.

PC-822-03   Acute PTB and latent tuberculous infection in children with community-acquired pneumonia in the metropolitan area of Medellín, Colombia

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Background: TB must be suspected in all chronic respiratory symptomatic patients. We wanted to describe the incidence of acute pulmonary TB and the prevalence of LTBI in children hospitalized with CAP in 13 health care institutions from Medellín, Itaguí, Bello and Envigado, Colombia.

Design/methods: Cohort study. Children from 1 month to <18 years were included if they had acute respiratory symptoms (≤15 days), a chest X-ray with new pulmonary opacities, and their parents and/or children aged ≥7 years signed the consent and the assent forms. They were excluded in case of any immunosuppression by treatment or illness, neurological disorders, bronchiolitis, hematological cancer, chronic lung diseases, or if they was on antibiotics in the last 72 hours. Induced sputum (for auramine-rhodamine stain and cultures in MGIT and Löwenstein-Jensen medium), blood and urine samples, and a nasopharyngeal swab were taken to study the etiology of CAP. Tuberculin skin test was applied to all children according to CDC guidelines. This study was approved by the University of Antioquia's Ethics Committee and the one of each participant institution. All children were followed for 1, 3, 6 and 12 months. Results are expressed as percentage, median and interquartile range (IQR). Bivariate and multivariate analyses were done.

Results: We screened 1410 children and 525 were included, but 25 of them should be excluded because they did not have studies for TB available. APTB was diagnosed in 2.4% (12/500) of children (6 cultures positive and the other 6 with immunological and epidemiological criteria, pneumonic consolidation and CAP). The median age was 3 years (IQR 2–7). 10 kids received anti-TB treatment with good clinical response; the other two were lost to follow-up. LTBI was detected in 2.6% (13/500). The median age was 3 (IQR 2–4). 5/13 received isoniazid for 6 months; the other 8 did not because of different causes (4 mothers refused the treatment, 1 was in studies to rule out a primary immunodeficiency, 1 was 14 years old and did not have a recent contact, 1 is still waiting for the medication, and 1 was lost to follow-up). There were no differences in clinical variables or laboratory findings among children with APTB, LTBI and those negative for TB.

Conclusions: APTB was found in 2.4% of children with acute CAP. This disease should be considered in the differential diagnoses of all these kids in high-prevalence settings, even if they do not have ≥15 days of respiratory symptoms.

PC-823-03   Clinical spectrum of tuberculosis in HIV-infected children initiating antiretroviral therapy before 2 years of age

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Background: Early initiation of antiretroviral therapy (ART) in HIV-infected infants reduces mortality and opportunistic infections including tuberculosis (TB). However, young HIV-infected children remain at high risk of TB-related morbidity and mortality following exposure. This study documents the manifestations of TB disease in HIV-infected children <2 years of age on ART.

Methods: Retrospective cohort study; records of children <2 years of age who started routine ART at Tygerberg Children's Hospital, Cape Town, 1 January 2003–31 December 2010 were reviewed. Demographic and clinical data at ART initiation (baseline) and TB episodes (including disease spectrum) after ART initiation, to 30 June 2012, were recorded. TB episodes were any TB diagnosis presumed/confirmed to be caused by *Mycobacterium tuberculosis*. TB immune reconstitution syndrome (TB-IRIS) was defined as TB diagnosed within 3 months of ART initiation. TB diagnosed >3 months after ART initiation was incident TB. Children with TB-IRIS, incident TB and those without TB were compared by baseline characteristics. Baseline demographics, immunological, virological and nutritional status, and history of prior TB were variables in a logistic regression model to predict either form of post-ART TB and death.

Results: In 494 included children (Table), median follow-up time on ART was 10.7 months. Fifty-four TB treatment episodes were recorded after ART initiation: 23 (46%) TB-IRIS (incidence 21.8/100 person years-py) and 31 (54%) incident TB (incidence 3.9/100 py). TB was confirmed in 9/46 (20%) TB cases with documented culture results. Children with TB-IRIS and those with incident TB did not differ significantly by baseline characteristics. Extrapulmonary TB (EPTB) occurred in 6/21 (29%) TB IRIS and in 4/31 (13%) incident TB cases: 4 EPTB IRIS and all incident EPTB were clinically severe (5 disseminated, 2 pericardial and 1 spinal TB). Fifty-two (11%) children died (mortality rate 6.54/100 py). Children with TB IRIS had a high mortality (10.36 deaths/100 py). On univariate regression, starting ART at <1 year of

Table Characteristics of HIV-infected children <2 years of age at ART initiation by occurrence and timing of tuberculosis in relation to initiation of ART*

	Never TB	TB prior to ART	TB IRIS	Incident TB
Median age in months [IQR]	5.7 [3.5 to 9.9] (n = 286)	11.2 [7.4 to 15.8] (n = 161)	6.0 [3.5 to 8.7] (n = 23)	6.0 [4.6 to 9.5] (n = 31)
Male (%)	133 (46.5) (n = 286)	78 (48.5) (n = 161)	11 (47.8) (n = 23)	14 (45.2) (n = 31)
Median WAZ [IQR]	−2.32 [−3.81 to −0.91] (n = 265)	−2.80 [−3.84 to −1.10] (n = 141)	−2.73 [−4.32 to −1.69] (n = 21)	−2.29 [−3.25 to −0.42] (n = 27)
Median CD4+ cell count [IQR]	759 [351 to 1491] (n = 252)	681 [431 to 1226] (n = 142)	930 [483 to 1723] (n = 22)	948 [553 to 1394] (n = 30)
Median CD4% [IQR]	19.5 [12.0 to 28.9] (n = 246)	15.0 [10.5 to 20.6] (n = 142)	21.0 [9.0 to 26.0] (n = 21)	17.2 [14.0 to 22.5] (n = 29)
Severe immuno-suppression (%)	155 (63.0) (n = 246)	110 (77.5) (n = 142)	15 (71.4) (n = 21)	21 (72.4) (n = 29)
Median log10(VL) [IQR]	5.82 [5.28 to 6.42] (n = 221)	5.87 [4.99 to 6.45] (n = 119)	6..04 [5.68 to 6.48] (n = 19)	5.95 [5.03 to 6.47] (n = 25)

*Total overall: n = 494; median age: 7.3 (IQR 4.0 to 13.4) months; male: 233 (47.2%); median WAZ: −2.48 (IQR −3.85 to −0.91); median CD4+ cell count: 757 (IQR 385 to 1404); median CD4%: 17.3 (IQR 11.1 to 26.4); severe immune suppression: 295 (68.5%); median log VL: 5.87 (5.20–6.45).
ART = antiretroviral therapy; IRIS = immune reconstitution inflammatory syndrome; IQR = interquartile range; WAZ = weight-for-age Z-score; VL = viral load.

age was associated with TB-IRIS (OR 4.09, P = 0.06), while weight-for-age Z score $<−2$ was significantly associated with death (OR 5.65, $P < 0.001$).
Conclusions: Young HIV infected children remain at high risk of severe TB manifestations after initiation of ART. High mortality was observed in children with TB-IRIS. Severe malnutrition was associated with death.

PC-824-03   Evaluation of the effectiveness of LTBI treatment among child contacts in Taiwan

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Background and challenges to implementation: Child contacts of contagious TB cases with positive smear or cavitation over chest-radiograph are the targets for tuberculin skin test (TST) and subsequent latent TB infection (LTBI) treatment. The study was to evaluate the effectiveness of current strategies of diagnosis and LTBI treatment.
Intervention or response: 9411 contact children aged younger than 13 years who received TST during April

2008 to September 2009 were enrolled for model derivation. TST results of contacts and contagiousness of TB index cases collected in the web-based TB registry were used to generate the scoring system with a Cox proportional hazards model. The projected active TB risk was estimated with the Kaplan-Meier method. Discrimination was assessed with the receiver operating characteristic (ROC) curve, area under ROC (AUROC) curves. Number needed to treat (NNT) was conducted for cost-effectiveness analysis.
Results and lessons learnt: TST result of contacts $\geqslant$ 10 mm and index cases with smear-positivity or cavitary chest radiograph were scored 2 and 1, respectively, based on the value of regression coefficients generated from the Cox proportional hazards model. For evaluation of the current strategies, 1505 contacts with score = 3 were the priority target of receiving TST as LTBI diagnosis currently in Taiwan. The NNT for each risk score to prevent contacts become patients during the follow-up, would be 65, 498, 1182 for contacts with score of 3, 2, 1 respectively. The AUROC was 0.791 (95%CI 0.71–0.87) for our model based on the current policy of LTBI diagnosis and treatment and the AUROC was 0.76 (95%CI 0.68–0.84) for TST result of contacts $\geqslant$ 10 mm and 0.62 (95%CI 0.54–0.70) for index cases with smear-positivity or cavitary chest radiograph, respectively.
Conclusions and key recommendations: Among child contacts of contagious TB cases with positive smear or cavitation over chest-radiograph, providing LTBI treatment to 65 LTBI child contacts by using 10 mm as a cutoff of TST could prevent one active TB case among the contacts.

PC-825-03   Relationship between tuberculosis rates in children and the community-wide epidemic: results from a mathematical model

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Background: High rates of TB in children may indicate on-going transmission and a failure of TB control.[1,2] However, in Europe the correlation between incidence in children and incidence in adults is greater in high incidence countries than low incidence countries,[3] suggesting a variable relationship between childhood TB rates and the community-wide epidemic.

We developed a mathematical model to investigate the dynamic relationship between childhood TB incidence and on-going community transmission. Our aims were to understand when childhood TB incidence is a good predictor of a population-wide epidemic, what causes differences between countries and the effect of high rates of childhood TB on future control.

Design/methods: We modelled the population in four age groups: 0–14 year olds, 15–44, 45–64 and 65+, with age-specific natural history parameters and realistic mixing patterns. The model was fitted to incidence rates from London in 2011 (45 per 100 000 persons) and the age distribution of cases (6%, 60%, 19% and 15% across the four age groups respectively).

We investigated the impact of changing transmission by between 0.5% and 5% per annum by considering the annual percentage change (APC) in incidence by age group.

Results: Increasing transmission affected age groups by different amounts, changing the distribution of cases by age. The youngest age group, with the lowest TB burden, experienced the largest APC in incidence following both increases and decreases in the community-wide epidemic.

However, the relative impact on children depended strongly on model parameters. As incidence increased, the ratio between APC in children and APC in all TB cases decreased, suggesting that APC of childhood incidence is more indicative of on-going transmission in low incidence settings. The ratio also decreased as the probability of primary progression in adults increased. This suggests that in communities with high rates of HIV co-infection this ratio would not be a good indicator of on-going transmission.

Conclusion: Our model suggests that TB rates in children could indicate recent changes in the epidemic. However, in populations with high TB burdens or high rates of primary progression, childhood TB cases no longer provide a marker for underlying epidemic changes.

1 Smith. Curr Probl Pediatr 31, 5–30 (2001).
2 Wood et al. CID 51, 401–408 (2010).
3 Sandgren et al. Euro Surveill 16, 12 (2011).

TUBERCULOSIS CASE FINDING AMONG VULNERABLE POPULATIONS

PC-826-03   Active case finding of tuberculosis using chest radiography in homeless populations: systematic review and meta-analysis

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Background: In low-incidence nations, tuberculosis (TB) predominantly affects vulnerable populations. Major guidelines recommend active case finding in homeless and under-housed populations. There is currently no consensus as to the preferred screening regimen.

Objective: The primary endpoint was to evaluate the utility of chest radiography (CXR) screening in active case finding for tuberculosis in the homeless and under-housed populations. Other endpoints included performing a qualitative systematic review of the literature and estimating the utility of additional screening methods to chest radiography based programs.

Data sources: Articles were identified through data sourcing of EMBASE, Medline, and the Cochrane Library through November 10, 2012.

Study selection: Studies that assessed the utility of symptom screens, CXRs, sputum sweeps, tuberculin skin tests, or interferon gamma release assays to detect TB in homeless and under-housed populations were sought. 346 articles were obtained after removing duplicates. 16 studies addressed the screening potential of chest radiographs for active TB in low incidence nations and were ultimately analysed for this publication. Nine articles were utilized in the final quantitative analysis, providing a combined sample size of 51 312 CXRs.

Data extraction: Data were extracted using a standardized method by 2 independent reviewers, and then were reviewed by a third independent reviewer.

Results: Of the 51 212 screening CXR performed in the representative cohorts, 412 new cases of TB were diagnosed, for a case finding rate of 804 per 100 000 CXRs. The prevalence of TB in the homeless ranged from 8.4–3300 per 100 000. Six of the seven screening programs that ran longitudinally noted a decrease incidence of TB over time.

Conclusions: Our data suggests that chest radiography is a good tool for active case finding and should be incorporated into TB screening programs in homeless and under-housed populations.

PC-827-03   Detection of active tuberculosis among people living with HIV/AIDS and vulnerable population groups (injecting drug users, migrants, and commercial sex workers)

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Background: In 2010, the Foundation 'Tomsk Anti-AIDS' in collaboration with the regional TB and HIV services has launched the project of TB screening for vulnerable groups in the city of Tomsk. These people are at greater risk of developing TB and MDR TB, likely to have worse treatment outcomes, experienced longer delays in seeking care, and at higher risk of community transmission.

Objectives: To strengthen TB screening for vulnerable groups in Tomsk, Russia by enhancing early detection activities and providing social support during TB diagnostics.

Methods: During 2010–2012, a cohort of 2039 persons was identified as a risk group for TB. Screening was conducted twice a year and included basic evaluation of symptoms (chronic cough, weight loss, night sweats and hemoptysis), PPD, and chest fluorography. Outreach workers at the syringe distribution points and a community clinic have provided field counseling, phlebotomy, and PPD with further referral to TB services for medical evaluation. Nutritional support, hygiene packages and accompaniment used as incentives to complete screening.

Results: In 2010, there have been screened 619 persons from vulnerable groups (6 newly diagnosed TB cases, with 3 MDR-TB cases). Incidence of TB among vulnerable groups was 969 per 100 000 vs. 62.4 per 100 000 in the general population in Tomsk. In 2011, there have been screened 576 persons from vulnerable groups (7 newly diagnosed TB cases, with 2 MDR-TB cases). Incidence of TB among vulnerable groups was 1215 per 100 000 vs. 60.4 per 100 000 in the general population in Tomsk. In 2012, there have been screened 844 (6 newly diagnosed TB cases). Incidence of TB among vulnerable groups was 711 per 100 000 vs. 46.2 per 100 000 in the general population in Tomsk. The data suggests that TB screening for this population has improved significantly since the beginning of the program and become routine activities for vulnerable population in Tomsk. In 2012, the reduction in TB incidence of 41.5% among this population has correlated with decreasing the incidence in general population.

Conclusion: Effective collaboration of the Foundation 'Tomsk Anti-AIDS' with government TB and HIV services has lead to strengthening of TB control and early detection. Implementation of such program requires involvement and guidance from governmental and non-governmental sectors. Such client-centered approach to TB prevention is an urgent priority within the anti-TB/AIDS movement in Russia and countries of FSU.

PC-828-03   Tuberculosis in foreigners in Japan: cases who returned to their own country half-way through treatment

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Background: Number of newly registered tuberculosis (TB) patients in Japan in 2011 was 22 682 and this has been declining year by year. However, the proportion of foreign resident with TB to total TB patients keeps on growing in Japan. Regardless it is reported that some of them are interrupted TB treatment due to a return home country, the actual situation of treatment after their return home is unclear. This study reports the actual situation of foreign resident who diagnosed TB and interrupted the treatment due to return home country and suggest how to manage this population as risk group.

Material and method: Structured questionnaire regarding each foreign resident registered in 2008 as new TB case was sent to 530 public health centers (PHC) throughout Japan through the post. The responses were collected and analyzed with Microsoft Access 2003.

Results and lessons learnt: Responses were obtained from 449 PHCs (response rate 84.7%), and out of them, 243 PHCs (54.1%) were experienced the case of foreign TB patients (total 843 cases). Majority of patients were from China (242 cases), Philippines (237 cases), Korea (71 cases) and Indonesia (46 case). Regarding outcome of treatment, 564 cases (68%) were cured or completed, while 116 cases (14%) moved out of Japan. Most of them were supposed to left for own country. The reasons of return home country were as follows; unspecified, legal troubles, own will, financial reason, disemployment and so on. Only less than half of them were recommended the extension of stay until completion of treatment. Regarding continuation of treatment after return, most respondents gave the referral form to patients to bring nearby health facility, gave remaining drugs until completion or just recommended to go to nearby facility. However, almost all of respondents could not confirm the treatment outcome of patients after return any more. Among patient returned to their country, 22 cases had drug resistant to more than one drug and 11 cases had multi-drug resistant TB. These findings highlighted that there are some difficulties of treatment completion among foreign patients.

Conclusions and key recommendations: It needs intelligence sharing between organizations and it should be developed strategy.

PC-829-03   Active tuberculosis case finding among nomadic pastoralists of northern Nigeria

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Background and challenges to implementation: Nomads by their way of life have minimal access to health care delivery because of their migratory nature for greener pasture. With an estimated population of 450 000, Adamawa, one of the 36 states of Nigeria, has the highest population of nomads. Despite being at risk of contracting TB due to low immunization coverage, poor housing, overcrowding, high rates of bovine TB infection and consumption of unpasteurized milk among other factors, the nomadic pastoralists have had minimal access to TB control services.

With support from WHO through its Wave 2 TB Reach grant in 2011, TB control service was launched within Nomadic Communities of Adamawa State. The objective of this paper is to describe active case finding approaches among the Nomadic Communities of Adamawa State

Intervention or response: A one year retrospective review of the process and results of Active TB Case Finding (ACF) among the Nomads was done. The process involved mapping, advocacy, identification of Community Volunteers (CVs), reorientation of General Health Workers (GHWs) and training of the CVs on sputum collection, transportation and documentation. Sputum samples were tested by AFB microscopy and smear negative samples examined by GeneXpert.

Results and lessons learnt: In general 21 LGA TB supervisors, 63 laboratory staff, 180 CVs and 440 GHWs were trained on ACF processes. A total of 20 907 nomads were screened using TB symptomatic checklist. Of these, 4433 TB suspects were identified. All suspects were tested by sputum AFB microscopy. 884 all forms of TB cases were notified of which 608 (68%) were sputum positive. 654 samples of smear negatives were subjected to GeneXpert test; 45 (7%) were MTB+/Rif−, 10 (1%) were MTB+/Rif+, while 535 were MTB−/Rif−. 64 (9%) had invalid/error results. 642 of all TB cases notified were counseled for HIV, 416 were tested of which 40 (9%) were HIV positive. 35 of the co-infected patients were placed on CPT while 13 were placed on ARVs.

Conclusions and key recommendations: TB constitute a serious public health problem among the Nomadic Pastoralists in Adamawa State.

PC-830-03   Tuberculosis screening for deportees from Iran to Afghanistan by rapid molecular diagnosis kit

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Background and challenges: Every year, around 250 000 Afghan populations deports from Iran to Afghanistan. Deportees are entering and staying illegally and without any document in Iran. Almost all of them are young. About 90% of them in the range of 18–30 years old. They don't have access to the health care service in Iran. Due to living and socio economic conditions, they are considered as vulnerable group for contracting TB, resulting in high incidence of undiagnosed TB among them. Therefore, screening them for TB at the border is crucial to prevent the transmission of TB to their families and general population. However, time limitation constrains effective screening. For this purpose, we developed the simple screening system using the rapid molecu-

lar diagnosis kit for TB (Loopamp; LAMP, Eiken Co.Ltd.) which can diagnose TB within 1 hour in the transit camp.

Intervention: Screening was conducted at the transit camp where all deportees stay for almost 24 hours before returning to their final destinations; where they want reside in Afghanistan. All the entered population in this camp has been screened verbally by well-trained health staffs. TB suspects were identified and one sputum sample was collected from them. Samples were carried to the laboratory and examined by LAMP. Then the results were feed backed to TB suspects. It took nearly 3hours to finish all procedures. In the end, diagnosed TB cases were referred to the nearest health facilities of their residence places for treatment management.

Result: From the starting of the project in September, 2012 till March 2013, 9055 deportees were entered and all were screened for TB. Among them 286 identified TB suspect, 266 suspects (93%) received examinations by LAMP. Ultimately, 16 sputum smear positive TB cases were diagnosed and refereed for treatment. The case notification rate is 2 times higher than in general population in Afghanistan.

Conclusions: Although the results are still preliminary, this system seems to be effective in this setting which requires point-of-care.

PC-831-03   Búsqueda activa de tuberculosis en población indígena del municipio de Cochoapa el Grande, Guerrero México

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Objetivo: Detectar casos de tuberculosis en población indígena, mediante un laboratorio móvil de TB en Cochoapa el Grande de la montaña de Guerrero.

Justificación: La falta de cobertura de detección y diagnóstico oportuno de TB, en localidades accidentadas del municipio de Cochoapa, hacen necesario acercar el servicio a población en riesgo de padecer TB; esté aporta 23% de TBP, en la región ponderado por su marginalidad, el más pobre del país.

Metodologia: Se realizó plan de trabajo, previo recorrido del laboratorio móvil, reuniones de coordinación con autoridades comunitarias, la promoción consistió en perifoneos, pláticas y encuestas, al arranque, se realizaron eventos socioculturales, brigadas para recorrido de localidades acompañándose con un interlocutor de lengua mixteco, las muestras fueron procesadas por químicos certificados, los resultados positivos notificados prioritariamente al personal de salud, capacitándose a tutores comunitarios para supervisión del TAES.

Resultados: Del 30 de mayo al 23 junio 2011, se recorrieron 49 localidades, examinando 593 sintomáticos respiratorios, diagnosticando 7 casos de TBP,

incrementando 40% el diagnóstico, con respecto al 2010, la positividad fué 57,1%+, 28,6%++ y 14,3%+++, 85,7% curó y 14,3% falleció antes de concluir el tratamiento; como monitoreo del 26 de mayo al 16 junio 2012, se realizó recorrido a localidades del municipio no encontrando nuevos casos.

Conclusiones: La estrategia a través de la acercabilidad de los servicios de detección con la unidad móvil logró disminuir el riesgo de morir por TB, en población vulnerable y de la importancia de mantener la vigilancia en áreas marginadas.

PC-832-03 Evaluation of tuberculosis screening for immigrants, 2005–2010

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Objective: To evaluate the effectiveness of the entry and follow-up screening for tuberculosis (TB) among new immigrants in the Netherlands by determining the coverage and yield.

Methods: Data of immigrants who started screening in 2005–2010 were analyzed stratified by cohort, age, gender, diagnosis and incidence in country of birth. Entry screening is done by chest X-ray or TST. Follow-up screening is done by chest X-ray every 6 months for a maximum period of 2.5 years after entry screening, for immigrants from countries with WHO estimated incidence of >200/100 000 population in 2008 or those with inactive lesions consistent with TB at entry screening.

Results: The average yield per 100 000 screened immigrants was 22, 60, 148, 166 and 139 respectively for immigrants from countries with incidences of <50, 50–100, 100–200, 200–400 and >400 per 100 000 population. The average coverage of the follow-up screening decreased from 47% at the first follow-up screening to 21% at the last screening. The yield of follow-up screening for immigrants from high incidence countries is 66/100 000 screenings and the incidence 146/100 000 per person year follow-up. Only 8 (24%) of the 33 TB patients were found by screening. For immigrants with an abnormal X-ray at entry screening, suspected of TB, the incidence during

follow-up was 6044/100 000 person years follow-up. Eleven (79%) of the 14 patients in this group were found through the screening program.

Conclusions and recommendations: This evaluation shows that entry screening of immigrants from countries with a TB incidence of <50/100 000 population does not meet the criteria set in the Netherlands for a risk group (>50/100 000). We therefore proposed a change of legislation to base the need for TB screening for immigrants on entry on the incidence of TB in the country of origin rather than on a specified geographic area. Entry screening is useful to identify persons with inactive TB lesions with a high chance of progression to active disease. The yield of the follow-up screening of immigrants from high incidence countries meets the criterion of a risk group and can be continued based on this criterion. However, efforts need to be made to increase the coverage of the follow-up screening. Further studies into the cost-effectiveness of TB screening may yield more data to decide whether follow-up screening of immigrants from high endemic areas needs to be continued.

PC-833-03 Association of chest X-ray abnormalities with tuberculosis disease among US-bound refugees and migrants from East Africa: retrospective cohort study

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Aim: This study described CXR findings in a large cohort of migrants and refugees population as part of a comprehensive TB screening program and correlated findings with TB diagnosis.

Background: Many tuberculosis (TB) low incidence countries have put in place various surveillance and control measures for immigrant-associated tuberculosis. The US Centers for Disease Control and Prevention (CDC) recommends chest radiograph (CXR) as part of the medical screening for tuberculosis among persons overseas applying for US immigration status. Correlating radiographic patterns with active TB disease would provide evidence for on the effectiveness of CXR in screening for TB and possible scale up to other populations.

Methods: We performed a retrospective cohort study based on data extracted from the IOM computer database and treatment files for US bound refugees and migrants from East Africa between 2010 and December 2012. CXRs were done for all migrants and refugees above 15 years and were interpreted by a consultant radiologist with additional review by IOM physicians. Three sputum specimens for microscopy and culture for mycobacteria were obtained from migrant whose CXR findings were suggestive of tuberculosis. We compared demographics, clinical status and

CXR findings between those with positive sputum smear (SS+) or culture (SC+), and those with negative sputum smear and culture (SC− and SS−).

Results: Between January 2010 and December 2012, a total of 7378 refugees and migrants had abnormal CXR. The main CXR findings included other finding of inactive TB (2722, 36.9%), discrete fibrotic scar or linear opacity (1869, 25.3%), Infiltrates or consolidation (534, 7.2%) and discrete nodules with calcification (221, 3.0%). 132 (1.8%) had either sputum culture or sputum smear positive.

The strongest predictors of TB disease include active infiltrate or consolidation (odds ratio [OR] 7.66 [7.14, 8.21]), active cavitary lesion (OR 6.59 [4.51, 9.64]), active hilar/mediastinal adenopathy (OR 4.16 [2.89, 6.00]), and active pleural effusion (OR 3.35 [1.65, 6.80]). Although the most common, findings of discrete linear opacity (fibrotic scar) and other findings of inactive TB were negatively associated with TB disease (OR 0.68 [0.62, 0.76] and OR 0.77 [0.71, 0.82] respectively).

Conclusion: The combination of CXR finding suggested by CDC is useful for screening migrants and refugees for TB. There is need to investigate further the site of the pathology and differentiate the type of pathology lumped as discrete linear opacity or other findings.

PC-834-03   Pour des espaces de vie sans tuberculose, stratégies et résultats d'un partenariat entre agents de santé et associations du réseau BURCASO

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Cadre et défis : Dans le cadre du projet TB REACH 1 obtenu par le PNT et le PAMAC, BURCASO appui et coordonne 15 associations pour la détection précoce de la TB dans 37 sites d'orpaillage de trois régions sanitaire, dans la Maison d'Arrêt et de Correction, les zones à habitats précaires et les marchés de Ouagadougou. L'objectif global de cette intervention a été d'assurer dans ces sites, la recherche active et le traitement des tuberculeux pulmonaires en vue de réduire la propagation du Bacille de Koch.

Intervention au réponse :
- Formation des animateurs TB associatifs par des agents des Centres de Diagnostic et de Traitement (CDT) en technique de prélèvement et de transport des crachats ;
- Dotation par le PNT, de matériels de prélèvement et de transport de crachat aux associations ;
- Sensibilisation porte à porte ou de hangar à hangar par les animateurs, suivi de prélèvement active de crachats de personnes devant faire objet d'une évaluation en TB ;

- Transport par les animateurs, des crachats collectés vers les CDT pour le BAAR ;
- Appui de l'animateur associatif à l'identification du domicile ou du lieu de l'activité du patient dépisté positif à la TB ;
- Participation de l'acteur communautaire à l'appui conseil de mise sous traitement du patient ;
- Suivi du traitement du patient par le communautaire à la demande de l'agent de santé.

Resultats et leçons apprises : L'intervention de BURCASO en 2012 à permis d'engranger les résultats suivants :
- Entretien de recherche des signes de la TB dans 5000 familles des zones à habitats précaires ;
- Administration d'un questionnaire de recherche des signes de TB à 700 nouveaux entrants dans la Maison d'Arrêt et de Correction de Ouagadougou ;
- Recherche des signes de la TB au près de plus de 20 000 orpailleurs ;
- Entretien de recherche de TB dans 300 hangars ou boutiques auprès de 1500 vendeurs des marchés ;
- Détection précoce et appui à la mise sous traitement de 31 Tuberculeux pulmonaires des sites d'intervention.

Conclusions et recommandations : La toux est l'élément déclencheur pour que le communautaire s'introduise dans le site. L'associatif devient d'avantage un collaborateur important de l'agent de santé et participe à l'amélioration du taux de détection et de guérison des malades TB. N'eut été les retards de financement et l'insuffisance de certaines lignes budgétaires du projet TB REACH 1, l'apport du communautaire allait être plus considérable.

PC-835-03   Impact of the changed active tuberculosis screening protocol among US-bound refugees and migrants from East Africa

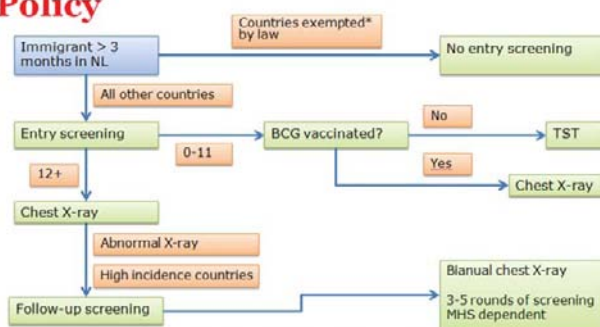A Galev, D Nyachieo, S Elsir, N Thuo, B Opare.
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Aim: This study describes results of TB screening programme for US bound migrants from Eastern Africa, and compares the impact the changed protocol had on detection rates of active pulmonary TB.

Background: All US bound migrants and refugees are required to undergo medical screening for tuberculosis (TB) as part of their overseas application for US immigration status. The TB screening is guided by the US Centers for Disease Control and Prevention (CDC) 'Technical Instructions for TB Screening and Treatment' (TI). The 1991 TI's were revised in 2007 with one of the major changes being the introduction of sputum culture testing.

Methods: We conducted a retrospective review and analysis of data extracted from the IOM computer database and medical bio-data files of US bound

migrants from IOM offices in three East Africa countries (Kenya, Uganda and Tanzania). The review covers the period from January 2004 till December 2012. Old instructions were in implementation in 2004 to 2007, while the new TI's were used in from 2008 to 2012.

Results: Between January 1 2004 to December 31 2012, 94 803 US bound migrants from Kenya, Uganda and Tanzania were screened; of these, 23 616 (25%) were screened between 2004 and 2007. All ethnic, demographic, geographic, social and other characteristics of the screened population remained unchanged between the two periods. Majority (53.3%) were Somali nationals. Refugee constituted 73.3% of all those examined.

Of the 23 616 applicants screened during 2004 and 2007, 21 713 (90%) had CXR, 1028 (4.4%) underwent sputum smears testing. For the period 2008 and 2012, a total of 49 923 (70%) had CXR and 4310 (6.1%) underwent sputum smear and culture testing.

Active TB was detected in 27 between 2004 and 2007, while between 2008 and 2012 a total of 132 cases of active TB were detected. The incidence of active TB among the migrants screened increased by 62% from 114/100 000 during the period 04/07 to 185/100 000 in 08/12.

Conclusion: The 2007 CDC TB screening protocol increased the detection rates of active TB, and increased the percentage of laboratory confirmed TB cases referred to TB treatment.

PC-836-03   Tuberculin skin test, interferon-gamma release assay and incidence of tuberculosis in migrant children

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Background: Incidence rates of tuberculosis (TB) in children who migrate to Stockholm, Sweden vary between 450 and 5 cases per 100 000 person years (in children from Somalia and the former USSR, respectively). We here correlate rates of tuberculin skin test (TST) and interferon-gamma release assay (IGRA) positivity at new entrant screening to these rates.

Design/methods: Children who migrate to Stockholm undergo health screening at school health offices or asylum clinics, and those with a TST of 10 mm or more are referred to one of two paediatric TB clinics. During the school year 2003–2004, 27% of screened Somali and 16% of former USSR children were referred in this way.

During 2006–2012, 808 TST positive children (median age 14.1 years) were referred, and IGRA tests were obtained in 334, based on TST reaction size, presence of BCG scar, incidence of TB and BCG vaccination routines in country of origin, and family history.
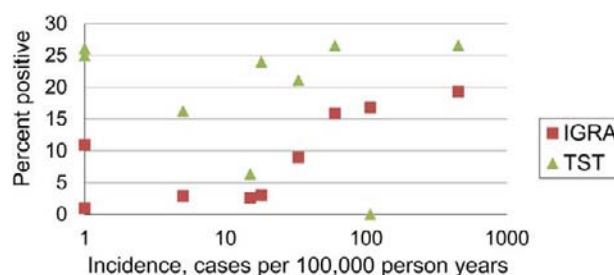
Figure Percentage of positive tests in migrant child populations by incidence of TB.

Results: The rates of IGRA positivity in the TST positive children varied from 63% (Somalia) to 18% (former USSR). Assuming that the rates of TST positivity were unchanged from 2003–2004, the positive IGRA rates in migrant population groups vary between 19% (Somalia), and 3% (former USSR) and correlate more strongly than TST results to our local TB incidence rates.

Conclusion: Our results should inform TB prevention among migrants to Sweden.

TUBERCULOSIS COSTS AND COLLABORATION ISSUES

PC-837-03   Policy options and levers for financing tuberculosis services in Indonesia

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Background: The tuberculosis (TB) control program in Indonesia has made good progress toward reaching the Millennium Development Goals, but needs to continue scaling up services, especially to people who are poor, living in remote areas, or infected with multidrug resistant TB (MDR-TB). At the same time, donor funding is expected to reduce in the coming years and the Ministry of Health (MOH) has recognized the need to increase domestic financing for TB control. The MOH has been debating the best mix of national social health insurance and government budgets that will achieve the TB program goals effectively and efficiently.

Intervention: USAID's TB CARE II project has conducted a series of studies to provide evidence for the policy debate. These include studies on TB control service delivery costs, the economic burden of TB, and insurance coverage and utilization for TB. The MOH also hosted a multi-country workshop to learn from TB financing experiences in other Asian countries.

Results and lessons learnt: The studies indicate that

Indonesia's total recurrent national service delivery costs will increase from US$56 million in 2012 to US$81 million in 2015 but justify this investment based on an estimated national economic burden of TB of US$1.4 billion. The studies also indicated challenges associated with access to accredited service providers, including the high burden of patient transport costs, and the likely under-funding of prevention activities. In addition, current insurance reimbursement rates are less than the cost of services, which means services are being subsidized by government or through patient user fees. The study findings have been discussed by government policy makers and they have developed ministerial guidelines and regulations to ensure that adequate funding will be provided for TB services.

Conclusions and key recommendations: The large investment required for TB control means that it is important to consider all the different options for domestic financing to ensure that sufficient funds are generated and that funding mechanisms optimize performance. It is recommended that a comprehensive financing policy framework be used for all infectious disease programs where donor funding must be replaced with domestic financing.

PC-838-03 The cost of using performance-based incentives for tuberculosis control in the private sector of Karachi, Pakistan

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Background: Over 50% symptomatic tuberculosis (TB) patients seek care in private sector. Indus Hospital engaged private providers using health worker incentives in its catchment area to increase detection and case holding of TB. Patients were notified to NTP and received standard of care at their neighborhood provider. We estimated the cost of this incentive-based program as compared to a TB center with no incentive program.

Methods: Program cost for TB treatment activities were quantified including salaries, diagnostics, equipment, incentives, marketing and supervision. Private providers received non-monetary incentives through marketing and basic clinic supplies. Health workers associated with these providers received monetary incentives for case identification and holding. 45 patients at non-incentive center and 84 patients at incentivized private providers were interviewed between September and November 2012. We measured direct out of pocket household expenditures for consultations, diagnostics, non-TB medicines, meals and transport before and after diagnosis till the end of treatment. Indirect costs from lost earnings were estimated

for the time spent seeking medical care based on the reported earnings by patients. Mobile phones application was used for collecting interview data through electronic data capturing.

Results: Over 2 years 1916 all form TB patients were identified and treated through the incentivized private providers vs. 895 at the non-incentivized TB center. The incentive based program incurred $218 (program $159, patient $59) per patient treated where as, the center based program incurred $177 (program $106, patient $71). Of the private provider costs $22 per patient was for a mobile X-ray unit, which brought services closer to the patient. Almost 50% of the patient costs were spent to seek diagnosis of TB with transport (44%) and non-TB medication (40%) representing the highest proportion. Indirect cost for patients treated at center were higher than those treated at private providers. 78% of the patient successfully completed treatment at the private providers as compared to 70% at the center.

Conclusion: Even though the incentive based program is more expensive, it has less out of pocket expenditure and better outcome for patients. Scale of incentive programs can be undertaken to increase case detection and achieve higher treatment success rates in countries where a substantial proportion of patients seek care in the private sector.

Table The cost of using performance-based incentives for TB control in the private sector of Karachi, Pakistan

	Cost per patient, USD	
	Non-incentive based center	Incentive based private providers
Cost categories	(n = 895)	(n = 1916)
Personnel	72.00	57.00
Incentive	0.00	39.00
Diagnostic test	11.00	11.00
Supervision and monitoring	9.00	16.70
Marketing and communication	6.00	4.00
Training	0.00	0.00
Equipment	7.00	8.00
Mobile X-ray unit	0.00	22.00
Program cost/patient	$106.00	$159.00
Out of pocket patient expenditure	(n = 45)	(n = 84)
Before DOT		
Consultation	3.45	0.36
Test	2.48	1.60
Medication	10.44	4.62
Food and transport	3.19	0.36
Diagnosis		
Consultation	0.00	0.42
Test	0.52	1.55
Medication	1.33	12.72
Food and transport	3.03	2.27
Treatment and follow-up		
Consultation	0.00	0.69
Test	0.00	0.60
Medication	4.21	3.20
Food and transport	11.73	2.79
Subtotal	$40.00	$31.00
Lost earnings	$31.00	$28.00
Total cost	$71.00	$59.00
Total cost per patient	$177.00	$218.00

PC-839-03 Cost and cost-effectiveness analysis of public-private partnership: provision of DOTS for tuberculosis in Bangladesh

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Background and challenges to implementation: Tuberculosis is a reemerging public health problem in Bangladesh. Despite remarkable progress in DOTS coverage, the case detection rate and cure rate yet to be increased to control TB in Bangladesh. Long term therapy and high treatment cost are notable snags responsible for poor accessibility to DOTS and poor TB cure rate among the economically disadvantaged people. Several small and large scale public-private mix (PPM) initiatives have implemented in the country to combat TB. Some of those have demonstrated promising results in provision of DOTS at a lower patient cost. Public private partnership is a challenging initiative to reduce the increasing burden of TB in the country. This cost-effectiveness analysis within comparative analytical design was conducted to find out the most cost-effective DOTS provision model for TB treatment in the country.

Intervention or response: The study was conducted among 252 smear-positive TB patients who were newly diagnosed, successfully treated and cured at three different DOTS provision models; Purely Public (PP), Public-NGO Partnership (PNP) and Public-Workplace Partnership (PWP). TB patients were recruited conveniently by obtaining informed written consent and considering specific selection criteria. Data were collected in terms of treatment costs and treatment outcomes by using a semi-structured questionnaire and checklist. Treatment cost was estimated from patient perspective considering both direct and indirect costs. On the contrary, treatment outcome was obtained by reviewing the medical records of the respective patient provided by the DOTS centre. Data were analyzed by SPSS software. Inferential statistics like χ^2, correlation, multiple regression and ANOVA were done to find any statistical significant association.

Results and lessons learnt: Of all, 34.2% TB patients were recruited in PP, 33.3% in PNP and 32.5% in PWP model. Males were predominant (56.7%) than their counterpart females (43.7%). Average length of absence from work was 11.5 ± 12.74 days and it was significantly higher (16.49 days) in PP model than that of the PNP and PWP models (ANOVA, $P < 0.01$). Average wage loss was significantly higher in the PP model (Tk.2633.36) than that of the PNP and PWP models (ANOVA, $P < 0.01$). Average treatment cost was significantly higher in PP model (Tk.3549.89) than that of PNP (Tk.1246.06) and PWP (Tk.917.58) models (ANOVA, $P < 0.01$) and it was significantly higher in males (Tk.2494.14) than their counterpart

females (Tk.1255.16; χ^2, $P < 0.05$). Both direct (Tk.1507.27) and indirect (Tk.2633.36) treatment costs were significantly higher in the PP model than those of the PNP and PWP models (ANOVA, $P < 0.05$). Businessmen, service holders and farmers incurred significantly higher treatment cost ($>$Tk.1000) than the housewives, students and day laborers ($<$Tk.1000; χ^2, $P < 0.05$). Average treatment cost was linearly related with monthly income of the patients ('t' test, $P < 0.05$).

Conclusions and key recommendations: Public-workplace partnership (PWP) model was emerged by the study as the most cost-effective DOTS provision model for treatment of TB patients. Public-private partnerships with different community based organizations especially PWP model may complement and supplement public health services in provision of DOTS for TB control in developing country like Bangladesh.

PC-840-03 Shifting to private providers, death and migration are the major challenges among missing sputum-positive cases after diagnosis in Punjab, India

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Background: RNTCP has been operational in Punjab, India since 2001 with coverage to entire state in 2004. The state diagnoses about 35 000 TB cases every year among which about 20 000 cases are sputum positive. During 4th Qtr 2012, out of 4945 diagnosed sputum positive cases, 4513 got registered for treatment and 432 cases were missing (initial default) which was about 9% of the diagnosed sputum positive cases. This paper made an attempt to find out the reasons for initial default and/or barriers in bringing those cases into the treatment schedule.

Design/method: Out of 20 districts of Punjab, this analysis was made in 10 districts (50% of the entire state) by following up 257 sputum positive and initial defaulter TB cases of the period October 2012 to March 2013. The analysis was done in two parts, i.e., proportion of sputum positive initial default cases put on treatment with follow up and status of other cases those were missing out of the treatment from the system.

Results: Of 257 initial defaulters, the ratio of male to female was 4:1, i.e., 81% (208) male and 19% (49) female. Among these cases, 45 (36 male and 9 female) cases, i.e., 18% were back into treatment with concurrent follow up and 212 (82%) found missing. Out of the missing, 4 in every 10 cases, i.e., 89 (71 male and 18 female) shifted to further diagnosis and treatment from private service providers. 44 (21%) cases

found to be dead which include 23% (38) male and 15% (6) female. 39 cases (36 male and 3 female) migrated to other places. 26 cases (18 male and 8 female) are untraceable due to wrong address which is one in every 8 missig cases. 7 (4 male and 3 female) cases (3%) were suspected MDR and referred for LPA. 7 cases refused to take DOTS due to lack of faith in the system, drug addiction, self and family stigma.

Conclusion: Failing to spot the diagnosed sputum positive cases is a major barrier in the process of cutting down the chain of transmission. Substantial numbers of cases are shifting to private treatment and the outcome is not known. Retrieval after follow up is higher in female than in male. On the contrary death among initial defaulters is high among male than female. Three pronged approach could mainstream these missing cases into the treatment, (i) adequate counselling on quality treatment being provided and (ii) ensuring proper address proof during diagnosis and (iii) migration information centre for follow up of seasonal migrants.

PC-841-03   The cost of scaling up the tuberculosis control program in Indonesia

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Background: Indonesia's TB control program has made good progress toward its Millennium Development Goals goal but needs to continue scaling up services, especially to the poor, to people in remote areas, and to people infected with Multidrug Resistant TB (MDR-TB). Donor funding is, however, expected to reduce in the coming years and the government has, therefore, committed to increasing domestic financing for TB control through social health insurance and government budgets. It is necessary to understand the cost of scaling up in order to determine the sources of the domestic financing increases.

Intervention: Through USAID's TB CARE I project, Management Sciences for Health developed a costing model for Indonesia using sample data from Central Java Province. The model covers all TB service delivery components, such as active case-finding, diagnosis, and treatment, and is based on epidemiological projections and programmatic targets.

Results and lessons learnt: The model shows that Indonesia's total recurrent national TB service delivery costs would increase from US$56 million in 2012 to US$81 million in 2015 if TB services are significantly scaled-up. These projected costs were then used to envision different financing scenarios—for example, if curative costs are covered under insurance and pre-

ventive costs are covered by the government budget, the average cost per member would be 24 US cents and the average cost for the government budget would be 6 US cents per citizen.

Conclusions and recommendations: These cost projections are being used to decide which service elements can be included in the insurance package and how much should be budgeted at each government level. Additional research is needed on some program elements, such as prevention and defaulter tracing, where data are hard to obtain. It is planned that the costing model will be used in all provinces to inform planning and budgeting and to help analyze cost-effectiveness and efficiency.

PC-842-03   The CBCI CARD GF RCC TB Project: a partnership initiative of India's RNTCP for linking with the Catholic Health Network in the country

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Background: In India, several sectors, besides the government's health department, provide TB control and care services The National TB Programme (RNTCP) has spearheaded many projects to ensure their availability at all points contacted by TB suspects and patients, through various PPM-DOTS initiatives. RNTCP provides 10 different schemes to facilitate linkage of non-government organizations (NGOs) and private providers with RNTCP.

CBCI CARD is a Civil Society Organisation comprising of > 3000 Catholic healthcare facilities (CHFs). CBCI CARD TB Project is GFATM supported Partnership initiative, which endeavors to link CHF network with RNTCP through formal and informal mechanisms; for jointly addressing the needs of TB affected communities.

Intervention: The project is being implemented in 19 states of India, where field consultants visit CHFs, conduct situational analysis of CHF capacity and local needs, liaison with programme managers and CHF personnel and facilitate signing of agreements for suitable NGO schemes. They also conduct sensitizations and trainings to ensure proper implementation of RNTCP guidelines.

Results: 1) During the first phase of the project (April 2010 to March 2013), out of the CHFs listed in the project states, 66% (386/558) hospitals, 51% dispensaries (1028/1998), 66% social service centres (130/197), all (5/5) medical colleges and 65% (57/88) nursing schools and colleges, have been linked to RNTCP. 2) 174 CHFs have signed for 228 RNTCP Schemes. 3) 426 Institutional & 1373 Community DOT Centres offer treatment services to TB patients,

Table State-wise achievements of the CBCI CARD TB Project during Phase-I of implementation (April 2010 to March 2013)

S. no.	State	Total no. of signed schemes	Total no. of CHFs involved under signed schemes	No. of institutional DOT centres	No. of community DOT centres	No. of CHF personnel trained or sensitized	No. of TB suspects referred for sputum examination
1	Andhra Pradesh	12	10	15	90	783	31 818
2	Assam	14	9	41	295	599	6 434
3	Bihar	6	5	19	0	960	5 959
4	Chhatisgarh	8	5	34	96	563	6 261
5	Gujarat	21	14	16	7	744	4 133
6	Goa	1	1	6	0	33	122
7	Jharkhand	10	8	73	20	404	7 268
8	Karnataka	22	18	8	363	999	13 409
9a	Kerala-N	27	14	9	0	875	5 837
9b	Kerala-S	25	18	15	0	1 111	10 985
10	Meghalaya	7	6	23	9	304	2 649
11	Maharashtra	17	13	15	0	776	8 402
12	Manipur	2	2	5	20	108	442
13	Madhya Pradesh	7	5	34	0	446	3 433
14	Nagaland	3	2	6	8	102	413
15	Oddisha	6	6	18	33	386	4 179
16	Rajasthan	1	1	11	5	454	2 943
17a	Tamilnadu-N	11	11	38	122	656	11 474
17b	Tamilnadu-S	10	10	16	6	620	11 745
18	Uttar Pradesh	13	13	24	297	890	19 349
19	West Bengal	5	3	0	2	481	1 577
	Total	228	174	426	1373	12 294	158 832

including 41 DOT centres for drug resistant TB. 4) 12 294 persons were sensitized/trained in RNTCP. 5) 158 832 TB suspects were referred for sputum examination. 6) This has improved the access of RNTCP services because 85% of CHFs are located in rural and hard to reach areas.

Lessons learnt: 1) The process of effective involvement of NGOs under RNTCP Schemes is complex, requiring sustained commitment of several stakeholders. 2) There is provision of funds for services provided under each Scheme, but disbursals are not streamlined.

Conclusions: 1) Civil Society Organisations like CBCI CARD provide a single platform through which a large number of individual healthcare providers, having diverse infrastructures and capacities can be linked through suitable Partnership options. 2) This is a successful and replicable partnership model for recruiting affiliations of health providers associated within pre-existing networks of NGOs.

PC-843-03 Partnership experiences in implementation of tuberculosis control programme in Bangladesh

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Background and challenges to implementation: Tuberculosis is a major public health problem in Bangladesh. WHO ranks Bangladesh 6th among the world's 22 high-burden TB countries. Bangladesh adopted Directly Observed Treatment Short course (DOTS) strategy in 1993 but the tuberculosis has gained its momentum since 2004 by the public-private partnership approach. Before that the progress was slow and coverage of population in hard to reach areas and those with high risk behavior was very low.

Intervention or response: Partnership started with selection of Principal Recipient (PR) among Non Government Organization (NGO) and made agreement with National Tuberculosis Programme (NTP), the government PR. PR-BRAC, in collaboration with NTP, selects the Sub Recipients (SRs) through a competitive bidding process from local, national and international NGOs and corporate sectors considering their geographical location, target population type and coverage, experiences and capabilities. The selected SRs have to go through a thorough capacity assessment process and then sub agreement is made with them. They are implementing activities in their allocated geographic areas and specific target population through assigned activities.

Results and lessons learnt: BRAC as Principal Recipient of Global Fund with other Sub Recipients NGOs played an important role. BRAC itself is implementing national TB programe in 297 sub-districts under 42 districts covering around 93 million population of Bangladesh. BRAC involved 42 Sub Recipients (SRs) including 40 NGOs and 2 big corporate sector organizations in the programme covering about 61 million populations including around 700 000 populations in garments sector. Around 2120 private practitioners were involved in the programme through Public Private Mix activities. Around 2300 People Living with HIV and AIDS (PLHIVs) are brought under the programme through its TB-HIV component. These organizations are operating more than two-thirds of the total microscopy and Directly Observed Treatment (DOT) Centers all over the country and ensuring entire community DOT through about 75 000 providers.

Conclusions and key recommendations: The partnership approach ensures coverage wider area and different unreachable population, increased case detection, high cure rate, effective and efficient use of resources.

PC-844-03   Costs faced by MDR-TB patients during diagnosis and treatment, in Ethiopia, Indonesia, and Kazakhstan

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Background: Patients with multi-drug resistant tuberculosis (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 MDR-TB programs rolling out, it is important to generate patients' costs data and use them to tackle bottlenecks in access to and compliance with MDR-TB treatment.
Design/methods: We adapted the existing TB patient cost tool to include MDR-TB patient costs. The modified tool was used to collect data on direct costs, out-of-pocket costs and indirect costs to patients and their families before and during diagnosis, during the intensive phase, and during the continuation phase of treatment. The tool was used in Ethiopia, Indonesia and Kazakhstan.
Results: Findings on magnitude and key components of costs associated with TB and MDR-TB and potential policy options in the three countries will be presented.

Preliminary results from Kazakhstan ($n = 150$) indicate that the median (IQR) cost for diagnosis of TB was 5.3 (1.2–13.9) USD, with the largest cost share for travel, with no difference between MDR-TB and other TB patients. The median cost for treatment was MDR-TB was 280 (87–469) USD, vs. 195 (67–351) USD for other TB patients, with largest share for loss of income for both groups. Preliminary results from Ethiopia ($n = 194$) indicate that the median cost for diagnosis of MDR-TB is US$44 (5–711), with the largest share for income loss, while the median cost for treatment is US$277 (8–4661), with the largest share of costs for hospital stays. For TB, median cost for diagnosis was US$43 (3–271) with the largest share of costs for food, while median treatment costs were US$125 (14–696), with the largest share of costs for attendant stays at hospitals.

Preliminary data from Indonesia ($n = 261$) indicate a median cost for diagnosis of MDR TB of US$42 (13–98) mainly due to costs for testing and of US$33 (11–64) for diagnosis of TB, mainly due to travel costs.
Conclusion: Our results show the additional economic burden of MDR-TB patients compared to other TB patients. We could only identify the economic burden

for patients who did access (MDR) TB diagnostic and treatment facilities. Still, the data provide important insights for TB control programs. In each country, recommendations and an action plan for the future to decrease the economic burden of (MDR) TB among patients will be developed.

PC-845-03   The economic burden of tuberculosis in Indonesia

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Background: Indonesia's National TB Control Program (NTP) has made good progress toward reaching the Millennium Development Goal for tuberculosis (TB) but needs to continue scaling up services, especially to the poor, to people in remote areas, and to people with multidrug-resistant TB (MDR-TB). At the same time, donor funding, on which the program has built much of its success, is expected to reduce over the next few years. The NTP has agreed on the need to increase domestic financing for TB control but there is a need to convince other government bodies who are involved in resource allocation decisions, such as the Ministry of Finance and local governments. Information on the economic burden of TB can provide important and persuasive evidence on the need to increase financing.
Intervention: Through USAID's TB CARE I project, Management Sciences for Health has developed a model to estimate the economic burden of TB in Indonesia and has populated it with national data. The model covers TB and MDR-TB and includes service delivery costs, household costs, and productivity losses due to temporary disability and premature death. The results are already being used by the NTP to advocate for increasing government budget allocations.
Results and lessons learnt: The model shows that the highest-cost element of economic burden is due to premature death and that the costs of service delivery are relatively small. Using 2012 data, the model shows that if 70% of the total estimated active TB cases are treated, the service delivery costs would be US$68 million but the economic burden of TB would be around US$1.5 billion. If, however, 90% of active cases can be treated the service delivery costs would increase to US$87 million but the economic burden would only be US$850 million. This indicates that the economic burden of TB in Indonesia is high and that investing in TB control is a cost-effective way to improve national health and alleviate this burden.
Conclusions and key recommendations: Indonesia's government should allocate more funds to TB control to alleviate the service delivery costs, household

costs, and productivity losses associated with this disease. The model used in this study is simple, user-friendly, and can be used to estimate the economic burden of TB estimates in other countries. These estimates can then be used to advocate for increased investment in TB control, particularly in settings where donor funding is being reduced.

PC-846-03   Evaluation of Nigeria's tuberculosis strategic plan: can a desk review suffice?

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Background and challenges to implementation: In most countries the implementation of all tuberculosis activities is guided by the national strategic plan (NSP) which is line with the national health plan for the country. All state programmes and partners are supposed to develop annual implementation plans based on the NSP. To assess achievements and challenges during implementation, a mid- and end-term evaluation is usually conducted. With new funding mechanisms, evaluations of plans are also informed.
Objective: Describe, the steps, cost and implications of conducting a mid-term evaluation in comparison to cost of a desk review.
Methodology: A comparative cross-sectional study of the just concluded mid-term evaluation (MTE) of the TB NSP 2010–2015 in a middle-low income country for a period of 2 weeks.

A random selection of 9 states amongst the 36 states plus FCT was carried out. Development Partners and staff of the Federal Ministry of Health were engaged to participate as national reviewers. For the purpose of carrying out an independent evaluation, 26 external reviewers were involved in the evaluation exercise. Country specific evaluation tools were developed to ensure standardization among assessors. Desk reviews of programme data was conducted at national and sub-national levels. Field visits were laso carried out followed by debriefing sessions to all key stakeholders.
Results and lessons learnt: Successful field visits to 9 states planned was achieved. Minimum cost of in-country logistics for conduct of the evalaution was $100 000 (excluding TA cost for 26 external consultants and participation of partners in-country). Data sets presented during debrief sessions were mostly generated from desk reviews. Comparative cost of conducting a desk review for a period of 3 days by 2 persons was approximately $2000, thus, $18 000 required for 9 states. A savings of $82 000 would be made if only desk reviews were conducted. Findings from field visits revealed current practices, knowledge and norms of health care workers, which could not be determined during a desk review only.
Conclusions and key recommendations: While the

MTE will facilitate the emergence of an adjusted/reviewed National TB Strategic Plan suitable for funding from government and Partners, cost of conducting a MTE should be considered thoroughly. Fewer external reviewers should support national consultants in the conduct of reviews. Fewer facilities should be visited.

PC-847-03   Estimating the cost of out-patient tuberculosis treatment: comparison of treatment at polyclinics vs. treatment at home in Tomsk, Russia

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Background: Great resources aimed at combating TB are allocated in Russian Federation, but the cost of the TB case is not clearly estimated for policy makers and service providers. This sector is faced with severe resource constraints. The optimal use of resources requires clear and accurate information on finance flow, and on the impact that resources have on the quality and performance of care.
Objectives: The goal was to calculate cost of the TB services according to the outpatients' sites expenditure and protocol for treating TB patients (polyclinics and treatment at home); also, to compare the cost of different approaches of organizing ambulatory patients' care in Tomsk.
Method: All outpatient facilities situated in one tuberculosis unit (TB dispensary) were assessed in order to evaluate daily practice of TB diagnosis and treatment. We interviewed the organization economists to gather data on modalities for diagnosis, treatment and monitoring of tuberculosis patients. In addition, relevant financial records were scrutinized for data collection. The cost analysis was done for all sensitive and drug-resistant TB outpatients for the years of 2011. Cost incurred on smear microscopy, culture, blood and urine tests, chest X-ray were classified as direct cost. The cost of anti-TB, symptomatic drugs, and food packages were similar for patients at polyclinic and treated at home and not included into calculations. Indirect cost is calculated based on proportion of staff time for TB care delivery and for supervision of TB services. We have incorporated all sources of financing: government budget, income from paid services, Global Fund grant, and funding from PIH. The cost of treatment was determined on the basis of RF regulations with recommendations from the World Bank. The exchange rate was 1$ = 30 RUB.
Results: To calculate the cost of the patient-day treatment, we counted total of 40 603 patient-days for all

analyzed departments in 2011. Of these, 49% of patients were treated at the polyclinics, 51% were treated by the Hospital-at-Home team.

The average cost of treating a patient at the policlinics was $15.4 per day and by the hospital-at-home $16.3.

Discussion: As we have expected, patient oriented approaches are slightly more expensive, but they increase patients' commitment to treatment and improve patients' outcomes. This information is vital for policy makers and planners to allocate adequate budget to the outpatient treatment programs.

PC-848-03 Treatment costs of drug-susceptible and multidrug-resistant tuberculosis: a systematic literature review

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Background: With the increase in prevalence of multidrug resistant-tuberculosis (MDR-TB), treatment costs of TB are expected to increase substantially. A systematic literature review was conducted to summarise the evidence on mean treatment costs per patient for TB and MDR-TB, and to compare methods and results according to country income groups.
Methods: Four databases were searched for cost and cost-effectiveness papers of TB and MDR-TB treatment. The search period was 1990–2013. Study methods were assessed according to pre-defined quality criteria. Cost data were converted to 2012 US$.
Results: The search strategy yielded 3847 articles. Seventy-four TB and 12 MDR-TB treatment cost studies with primary data were included, which provided data for 47 and 12 countries, respectively. There were 46 cost studies (38 TB and 9 MDR-TB) and 39 cost-effectiveness studies (36 TB and 3 MDR-TB).

Cost variation amongst patients within a study was not well captured; in TB studies, 22 (30%) reported some measure of spread [standard deviation ($n = 6$), confidence interval ($n = 6$), or range ($n = 11$)]. Only 4 (33%) MDR-TB studies reported these additional summary statistics [standard deviation ($n = 2$) or range ($n = 2$)].

Patient interviews provided data in 50 out of 74 papers (68%), while 10 (83%) MDR-TB studies obtained patient costs by interviewing patients.

For TB treatment, the greatest proportions of costs were hospitalisation (41%), routine programme management (12%) and drugs (7%). For MDR-TB treatment, the greatest proportions were spent on drugs (26%) and hospitalisation (23%).

Thirty-three (45%) out of the 74 TB studies included a value for loss of income due to illness. When excluding loss of income, the mean cost of TB treatment in high-income countries (HICs) was US$12 980 ($n = 8$), US$3010 ($n = 12$) in upper middle-income countries (UMICs), US$331 ($n = 12$) in lower middle-income countries (LMICs) and US$375 ($n = 14$) in low-income countries (LICs). The mean MDR-TB costs was US$70 791 ($n = 4$) in HICs, US$17 569 ($n = 7$) in UMICs, and US$8094 ($n = 1$) in LMICs.
Conclusion: This is the first review of TB treatment costs that includes studies from all regions of the world. While some of the variation in costs between countries can be explained by real differences, which is partly correlated by country income group, differences in methods used are an important explanation. In the paper we provide recommendations for standardised costing approaches according to setting and health system.

PC-849-03 Involving different groups in different modalities through ACSM for increasing access to tuberculosis services

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Background and challenges to implementation: Tuberculosis is a major public health problem in Bangladesh. TB related stigma is a key challenge particularly among the poor, ethnic minority groups and women, who experience increased barriers to accessing TB services. The USAID supported TB CARE II project has developed a series of targeted communication and social mobilization programs to bring about positive changes in behavior for increasing use of TB services.
Objective: To enhance knowledge and awareness of TB among community decision makers, women and vulnerable communities for increasing early diagnosis and treatment adherence.
Method: The TB CARE II supported local NGOs for conducting community outreach and awareness raising activities. Several target groups including school children and youth, religious leaders and members of local Chambers of Commerce (CoC) were identified for heightened communications and social mobilization efforts. From April to December 2012, the project and its local partners conducted sensitization workshops with these groups in 32 districts. A target messaging platform was designed for each, with consistent themes around basic TB signs and symptoms and where to access TB services. Students are targeted with messages via a sports related program, while presentations with CoC included messages related to impact of TB on the workplace. A unique live talk show was telecast by a private TV channel including an audience Q&A session on TB, which was recorded and aired during outreach sessions in rural areas.
Results and lessons learnt: The project was able to reach 128 schools and approximately 35 000 students with educative messages on TB. The project conducted

2910 group sessions reaching 58 200 people across the country; 300 000 people directly benefited from the video show.

Conclusions and key recommendations: ACSM activities were conducted throughout the country to enhance early access to TB diagnostics and treatment services and to involve them in DOTS services. Targeting ACSM activities are useful when there is policy level involvement and direct participation of religious and opinion leaders, cured TB patients, vulnerable population, journalist of newspapers and media.

PC-850-03   Cost-effectiveness of future tuberculosis vaccines

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Background: Cost-effectiveness studies of future vaccine technologies can be used to inform candidate vaccine decisions and aid clinical trial design. Here, the impact and cost-effectiveness of different tuberculosis (TB) vaccine profiles in all low and middle-income countries was explored.

Design/methods: An age-structured transmission model was used, incorporating TB, HIV, multi-drug resistant (MDR) TB, Directly Observed Treatment Short-course (DOTS), MDR treatment and ART. The countries were modelled individually and the results aggregated by income group. The 'no-vaccine' scenario was calibrated to population size and TB disease incidence and mortality data from the WHO, including assumed future improvements in TB case detection, TB treatment and ART coverage. Mean lifetime DOTS and MDR treatment costs were determined from a systematic literature review. The novel vaccines were assumed to prevent active disease, have 1–20 yrs or lifetime duration of protection and 20–80% efficacy. In the 'vaccine' scenario, two strategies were modelled starting in 2024: a) 'Infant': annually targeting 6 month olds, or b) 'Adolescent/Adult': annually targeting 10 years olds plus mass vaccination of the 11+ year olds every 10 years. Outcomes were TB cases, deaths and discounted Disability Adjusted Life Years (DALYs) averted between 2024 and 2050. Cost-effectiveness was estimated at varying TB vaccine prices and interpreted by comparing costs per DALY averted with GNI per capita for each income group. Plausible ranges for TB vaccine prices at which the vaccine would be considered cost-effective were created based on uncertainty in disease burden, treatment costs and MDR prevalence assumptions.

Results: Preliminary results from the 22 high burden countries suggest that, over 2024–50, 94 (71–115) million cases of TB disease and 13 (8–19) million TB deaths may occur. Even if protection were lifelong, over 2024–50 an 'Infant' vaccine may prevent less

than 8% (3–10) of this burden, whilst an 'Adolescent/ Adult' vaccine may prevent up to 71% (56–72). Over 2024–50, an 'Adolescent/Adult' vaccine would be cost-effective at higher vaccine prices than an 'Infant' vaccine in all scenarios.

Conclusion: In contrast to a novel, infant TB vaccine with limited duration of protection, over 2024–50 the introduction of a TB vaccine in adolescent/adults may be cost-effective even at relatively high vaccine prices and could alleviate a substantial burden of disease in high burden countries.

TUBERCULOSIS CASE FINDING

PC-851-03   Reporting TB-HIV collaborative indicators: experience using ETR.net in Namibia

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Background: Namibia has high rates of TB and HIV. In 2007, the NTLP introduced the electronic TB register (ETR.net), developed in Southern Africa for TB surveillance. Adapted locally, the system allows the capture and reporting of HIV testing by TB patients; HIV results; ART initiation; CPT coverage, and IPT coverage. A web dispatcher was also customized to facilitate automatic reporting to the central level.

Intervention: An analysis of the routine TB-HIV data collected on ETR.net was made to assess the trends for the 5-year period 2008 to 2012. Although nation-wide rollout of ETR.net was complete by 2008, utilization was not consistent. As such, dual recording and reporting (paper and electronic) was maintained while strengthening ETR utilization.

Results: In 2008, 77% (10526/13727) of registered TB patients were entered in the ETR.nt. Of these, HIV testing was documented for 8644 (82%), compared to 67% in the paper register. This increased to 89% in 2012 with over 97% ETR coverage. The proportion initiated on ART also increased significantly over the 5 years from 27% to 71%. Further increases were noted on cotrimoxazole coverage, from 54% to 98%. Interestingly, HIV prevalence has remained
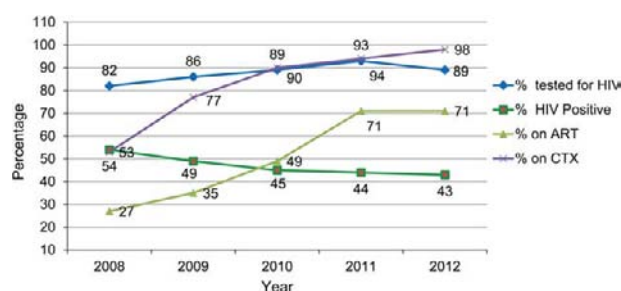

Figure Trends in TB/HIV co-management on ETR.net in Namibia.

lower than that in paper tools, which had reported lower testing rates anyway. This may be closer to the real picture as, over the years, the higher the testing rates, the lower the HIV prevalence. In practice ETR data on TB-HIV was more up to date than in paper registers. However, data in IPT was often inaccurate and difficult to interpret, as the ETR reported IPT provision as a proportion among TB patients with HIV, which is inappropriate.

Conclusion: The ETR provides an opportunity for more sensitive capturing of specific data on TB-HIV prompting the referral and follow-up of co-infected patients. The ETR is unreliable on IPT reporting unless a parallel module is developed to capture this outside of routine patient management. The NTLP can generate TB-HIV collaborative activity reports at the click of a button and use them for resource mobilization and social mobilization purposes. Automatic reporting through the web dispatcher facilitates the timely reporting from district and regions to central level.

PC-852-03   Comparing front-loaded sputum collection with conventional sputum collection for the diagnosis of tuberculosis in Assam and Tripura, India, 2012

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Background: In many high-burden tuberculosis (TB) countries, diagnosis of pulmonary TB relies upon direct sputum microscopy. The standard method requires 2 sputum specimens collected within 2 days as on-the-spot and early morning specimens. Although the morning sputum is likely to contain more bacilli, equal numbers of on-the-spot and early morning specimens have been reported to be positive in areas with a high prevalence of TB. If diagnosis could be completed in a single day by examining two same-day specimens (front-loading technique), this may be more convenient for patients and reduce pre-treatment loss to follow up.

Methods: During October 2012–December 2012, sputum samples were collected for acid fast bacilli smear microscopy according to national policy (on-the-spot collection followed by early morning collection the following day) in seven designated microscopy centres (DMCs) of seven districts in the states of Assam and Tripura, India. In addition, a second sputum sample was collected after an hour of collection of first sample (i.e., front loading) in the same patients.

Those who did not submit the required 3 sputum specimens were excluded from the comparative analysis. The number and proportion of smear-positive TB patients diagnosed with same-day sputum microscopy (spot-spot) was compared with that using the conventional method (spot-morning). McNemar's test was used to compare statistical differences in the proportion smear positive between the two approaches (spot-spot vs. spot-morning) at an alpha of 0.05.

Results: A total of 1758 TB suspects were screened for TB diagnosis. All patients provided the first spot specimen, 1756 (99.9%) provided the second spot specimen, and 1734 (98.6%) provided an early morning specimen. The proportion of smear-positive patients diagnosed by front loading method alone was 18.8%, as compared to the conventional method alone 19.7%. A total of 15 (4.5%) potential cases were missed by front loading method compared to only 1 (0.3%) by the conventional method; however, 24 (1.4%) suspects didn't return next day for the morning sputum sample.

Conclusion: While implementing same-day microscopy increased the number of suspects with at least two specimens, this method missed ~5% of smear-positive cases. In India, this could translate into a large absolute number of missed cases when extrapolated nationwide. These findings call to question the global recommendation of switching to same-day diagnosis over the current policy.

PC-853-03   Tuberculosis screening specificity and sensitivity in models of discretion, protocol adherence and randomness in South Africa

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Background: We explored whether routine TB screening for coughing of two weeks or longer yields greater sensitivity and specificity than relying on the discretion of health workers or a random approach.

Methods: Our analysis is based on a prevalence survey of 31 007 adults in eight high TB prevalence communities in the Western Cape (2010). Culture confirmed pulmonary TB was defined as *M. tuberculosis* isolated from a respiratory sample after inoculation into manual mycobacterial growth indicator (MGIT BD) tubes. Individuals were considered to have culture positive TB if the growth in the MGIT tube was confirmed to be M.tb by 16SrRNA sequencing. Participants were asked about demographic data, typical TB health seeking behaviour.

Sensitivity and specificity of the following TB screening procedures were evaluated using hypothetical

models: (1) the recommended protocol of testing those who report a cough for two weeks or more; (2) three enhanced protocols suggested by the literature; (3) random allocation of coughing clients to testing and (4) screening procedures subject to health worker discretion (as reported by participants). With the three enhanced protocols, screening rules were simulated to include: i) patients with known HIV-positive status, ii) patients with known HIV-positive status who tested after a HIV campaign (uptake 34%), and iii) patients with at least 3 of the 5 TB symptoms. The hypothetical models were based on information about symptoms and health seeking behaviour reported by participants who were currently coughing. We assessed screening procedures based on self-reported information regarding a visit to a clinic for the cough. **Results:** The recommended protocol outperformed current practice in clinics in terms of sensitivity but not specificity. Enhanced protocols tended to have lower specificity but increased sensitivity. The proportion of coughing patients offered a test ranged from 52.6% to 89.5% for the eight facilities.

Table Sensitivity and specificity of six screening procedures for TB tests

	Sensitivity (proportion of those with TB that are tested)	Specificity (proportion of those without TB that are not tested)
Protocol	79.73%	32.63%
Protocol + HIV knowledge	79.73%	28.63%
Protocol + expanded HIV testing	82.43%	27.10%
Protocol + additional symptoms	89.19%	20.99%
Random allocation to test	68.90%	31.10%
Actual screening procedure used in clinics	67.57%	37.21%

Conclusion: Given the benefits associated with an increased sensitivity are likely to be larger than those associated with an increased specificity, the results provide support for adherence to the recommended protocol. The level of variation across clinics for offering a TB test to symptomatic individuals is concerning. These findings should be validated under operational conditions and the different screening algorithms should be further evaluated.

PC-854-03 Periodic active case finding for tuberculosis in Blantyre-Malawi: a follow-on experience from active case finding in Harare, Zimbabwe

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Background: Tuberculosis (TB) remains a major problem in sub-Saharan Africa, responsible for 25% of HIV-associated deaths. Early detection of TB through screening, or 'active case-finding' (ACF) has potential individual and disease control benefits. However, suboptimal TB diagnostics and poor understanding of community engagement limit implementation. Following a landmark trial in Harare, Zimbabwe, we investigated community-wide TB ACF in Blantyre, Malawi.
Methods: Total population size and prevalence of chronic cough were estimated from national and study census data, respectively, adjusted for estimated population growth. Community engagement (leaflet drop, megaphone, mobile camp and household enquiry) was modified until ⩾50% of chronic coughers self-identified to ACF teams, who covered each of 23 catchment areas twice a year from April 2011. Adults volunteering TB symptoms (⩾1 of 4) provided 2 specimens for smear microscopy. Impact evaluation was based on enhanced monitoring of routine case-notifications.
Results: Adult (16+) population was 114450, with 3.2% prevalence of chronic cough. 71 smear-positive participants (HIV prevalence 48.3%) were identified from 3622 ACF participants (2.0% smear-positivity). 40% of participants were men. Median age was 35 years (IQR 27–47). Men had the highest prevalence of chronic cough ($P = 0.022$), night sweats ($P = 0.004$) and smear-positivity ($P = 0.002$). Only 49% of chronic cough had been investigated before. Smear-positive TB case notification rates (CNR) increased from 231 to 421 per 100000 adults, potentially reflecting indirect effects on health seeking as well as direct ACF diagnosis. Reaching target participation required 3 changes to delivery, culminating in door-to-door enquiry for chronic cough.
Conclusions: Periodic ACF based on smear-microscopy and self-reported TB symptoms achieved high participation, with impact beyond direct diagnosis of TB evidenced by a peak in smear positive TB diagnoses. Substantial adaptations needed on transfer to Blantyre were guided by definition of target participation rates for adults with chronic cough. Compared to 'passive' diagnosis, ACF disproportionately identified TB in HIV-negative participants and men: two important

epidemiological resevoirs of undiagnosed TB. Effective ACF has potential to reduce TB transmission and new incident disease, as is currently being investigated through time trends in routine CNRs.

PC-855-03   Gender inequality in the detection of tuberculosis in South Africa

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Background: Gendered roles and stereotypes can lead to unequal access to medical diagnosis and treatment, which can introduce a gender bias in health outcomes. We consider gender inequalities in health seeking behaviour and the subsequent detection of TB by analysing data from a large TB prevalence survey.
Design/methods: Our analysis is based on a population prevalence survey of 31 007 adults in eight high TB prevalence communities in the Western Cape in 2010. Survey participants were asked to report TB symptoms, health seeking behaviour and demographic data. Prevalence of culture confirmed pulmonary TB was defined as *M. tuberculosis* isolated from a respiratory sample. Sputum samples were inoculated into manual mycobacterial growth indicator (MGIT BD) tubes. Individuals were considered to have a culture positive for *M. tuberculosis* if their MGIT tubes had growth confirmed to be *M. tuberculosis* by 16SrRNA sequencing.
Results: 702 culture positive TB cases were identified. 333 were male (47.4%) and 369 (52.56%) were female. Of the males 12 (3.6%) were diagnosed by health services prior to the survey, while 6 (1.6%) of the females were diagnosed by health services ($P = 0.349$).

Females who were symptomatic (coughing for two weeks or longer) reported less often that they have been to the clinic to seek care for the cough prior to the prevalence survey than males (50.7% vs. 36.1%, $P = 0.075$). Symptomatic females visiting clinics were significantly less likely to be asked for a sputum sample than symptomatic males visiting clinics (76.4% for males vs. 63.5% for females, $P = 0.004$). Males who reported coughing and submitted sputum samples at clinics were significantly more likely to have a positive sputum result in the survey (20.6% vs. 11.8%, $P = 0.009$).
Conclusion: Prevalence survey responses about health seeking behaviour showed that a low proportion of cases identified during the survey were diagnosed by the health system. The low likelihood of being asked for a sputum sample amongst symptomatic females with TB is an important contribution to the gender bias in TB detection.

PC-856-03   Higher yield of tuberculosis cases among neighborhood contacts compared to household contacts of smear-positive tuberculosis patients in Cambodia

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Introduction: Cambodia has been conducting active case finding activities on a small scale since 2005. In year 2012, the National Center for Tuberculosis (CENAT), supported by WHO/TBREACH, conducted active case finding for TB nationwide for people who had the worst poverty-access barriers in the country.
Method: TB suspects were identified by village health support groups (VHSG) from household and neighborhood contacts of TB cases registered for treatment during the past two years. VHSG members took all household contacts (with and without TB symptoms) and neighborhood contacts (with TB symptoms) to the active case finding (ACF) camps that were set up at the nearest health centers for TB symptom and chest X-ray screening. After the screening, those who were suspected to have TB were asked to submit one sputum sample each on the spot for Xpert testing. The results were released within 24 hours. In 2012, 8779 household contacts and 23 508 neighborhood contacts underwent symptom and chest X-ray screening at ACF camps.
Results: The project screened 32 287 contacts in 2012. Of them, 3649 contacts submitted samples for Xpert testing. Of them, 792 (89%) bacteriologically positive pulmonary TB patients were diagnosed. 706 were neighborhood contacts and 86 were household contacts. 3% of the symptomatic neighborhood contacts who were screened had bacteriologically positive TB (706/23 508) and 1% of the symptomatic and asymptomatic household contacts had bacteriologically positive TB (86/8779).
Conclusion: The yield of bacteriologically positive TB is far greater among neighborhood contacts compared to household contacts. Hence, national TB programs of at least the high TB burden countries should emphasize screening of neighborhood contacts, and not just household contacts of index TB patients.

PC-857-03   High self-reported HIV positive status among clinic attendees suspected of tuberculosis enrolled in a cluster randomised trial of Xpert® MTB/RIF, South Africa

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Background: In South Africa, a high HIV prevalence setting, the prevalence of HIV among tuberculosis (TB) patients is reasonably well understood. However, little is known about HIV prevalence among clinic attendees suspected of TB ('TB suspects'). The XTEND study is a cluster randomised trial evaluating patient, programme and population level impact of the Xpert MTB/RIF assay roll out in South Africa. As part of this study, TB suspects are being recruited from clinics in four provinces. We describe prevalence of self-reported HIV positive status overall and stratified by factors measured at enrolment, among these clinic attendees.

Methods: Eligible participants are individuals at least 18 years of age, not on TB treatment, attending one of 40 primary health clinics (PHC) part of the XTEND study, who were asked to give sputum by PHC staff. Participants were enrolled on the same day as giving a sputum specimen. Baseline characteristics and prevalence of reporting HIV testing and self-reported HIV positive status are summarised.

Results: 4695 participants have been enrolled. Median age is 36 years, 62% female, and 94% from South Africa. A history of prior TB was reported by 15% of participants. Overall 81% (3802/4695) of participants reported knowing their HIV status and 94% (3574/3802) were willing to share their results; 62% (2239/3574) reported being HIV positive. Among those reporting their HIV positive status: 20% had tested on the same day and 49% had tested positive <3 months prior to enrolment. Median CD4 count (self-report) was 311 cells/μL ($n = 1137$), 33% were currently on antiretroviral therapy. Self-reported HIV positive status differed by gender and age (females: <30 years: 58%; 30–49: 76%; ≥50: 43%), males: <30 years: 40%; 30–49: 73%; ≥50: 40%), province (range 41%–83%), prior TB (70% vs. 61% no prior TB) and Karnofsky score (<80: 73%; 80: 67%; ≥90: 58%). Self-reported HIV positive status was similar by body mass index strata.

Conclusion: Among clinic attendees presenting at clinics for TB investigations, the majority reported having tested for HIV; willingness to share HIV status and prevalence of self-reported HIV positive status was high, and the latter similar to prevalence of HIV among TB cases. Data indicate that individuals with TB symptoms are being offered an HIV test and emphasises the importance of linkage to care for those newly diagnosed with HIV.

PC-858-03   Time to first consultation, diagnosis and treatment of tuberculosis among patients attending a referral hospital in Bahir Dar, Ethiopia

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Background: Early detection and treatment of TB is essential for the success of TB control program performance. Inefficient management of TB may result in serious complications among patients and sustained transmission of TB in the community. The aim of this study was to determine the length and analyze predictors of patients, health systems and total delays among patients attending a referral hospital in Bahir Dar, Ethiopia.

Design/methods: A cross-sectional study was conducted among newly diagnosed TB cases ≥ 15 years of age. Participants were enrolled in the study in a consecutive manner and a semi-structured questionnaire was used to collect sociodemographic and clinical data. Univariate and logistics regression analysis were performed to analyse predictors of patients, health systems and total delays.

Results: The median time of patients delay was 21 days (IQR 7 days, 60 days). The median health systems delay was 27 days (IQR 8 days, 60 days) and the median total delay was 60 days (IQR 30 days, 121 days). Extra-pulmonary TB (EPTB) cases were more likely to experience delay in seeking treatment compared to pulmonary (PTB) cases [AOR 2.59; 95% (CI 1.25, 5.35)]. Patients residing in rural areas had three fold increased patient delay compared to those from urban areas [adjusted odds ratio (AOR) 3.39; 95% (CI 1.29, 8.93)]. Study subjects that first visited hospitals [AOR 0.01; 95% (CI 0.00, 0.08)] and private facilities [AOR 0.03; 95% (CI 0.00, 0.29)] were less likely to have increased health systems delay compared to those that visited health posts. Increased risk of total delay was observed among EPTB cases [AOR 3.08; 95% (CI 1.48, 6.42)].

Conclusion: Majority of the TB patients reported to medical providers within an acceptable time period from the onset of their symptoms. Health systems and total delays were inadmissibly high. Patients with

EPTB and those that first visited health post experienced increased health systems and total delays. Developing a rapid screening test that can be used to refer all TB suspects from health posts to the next level of health care where smear microscopy and other TB diagnostic tests are available is imperative to reduce delay in diagnosis and treatment of TB.

PC-859-03   Contact investigation has greater epidemiological impact than screening on tuberculosis incidence in the Netherlands

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Background: In countries with a low incidence of TB, there are two ways of searching for cases to prevent and treat disease. First, screening of high-risk groups reveals cases among immigrants from endemic regions, drug addicts, homeless, etc. Second, through contact investigation, infections associated with an active TB case are searched by screening its contacts. Both methods are labour-intensive and costly, and it is regularly questioned whether one should drop one or the other. A key difficulty in assessing the epidemiological impact of either control measure, is that it critically depends on the effect of the other. Here, we evaluate the long-term efficacy in the control of TB in the Netherlands in terms of cases averted.
Methods: To this end, we formulated a stochastic model describing the dynamics of the spread of pulmonary TB, as controlled by both screening and contact investigation in a population. Our model catches the interaction between both measures, explicitly tracking whether a case was infected by a diagnosed or undiagnosed case in a high- and low-risk population. We inferred values of model parameters from data on TB cases found by screening, contact investigation or otherwise in the Netherlands (1993–2010). The novelty of our modeling approach lies in the relatively simple mathematical formulation of the contact investigation process, allowing the fit to data on active TB cases; also, it is the first time that data on latent cases are used to calibrate such a model. We thus assessed the epidemiological impact of dropping either screening or contact investigation over a 50-year period (2010–2060), compared to a scenario with the current policy maintained.
Results: We find that average incidence in 2060 is higher when halting contact investigation than when halting screening. This result reflects the impact of contact investigation on the pool of latent and active TB cases, as screening currently is not carried out on latent cases.
Conclusion: We have compared the long-term epidemiological impact, regardless of yield and cost-

effectiveness issues, of stopping screening or contact investigation in a low-incidence country such as the Netherlands. Unless screening is extended to include latent cases, if having to choose between screening and contact investigation, dropping contact investigation is less damaging in terms of cases averted than dropping screening.

PC-860-03   Innovative approach to tuberculosis case finding using recorded radio jingles in Oyo State, south-west Nigeria

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Background: Tuberculosis case finding in Oyo state has been linked to DOTs expansion and community tuberculosis care to contribute to the country seventy-five percent target by World Health Organization. In view of this, different approaches and strategies have been implemented in different states. This is to objectively display quick impact of recorded TB jingle to improve community awareness of TB symptoms, diagnosis, care and support.
Intervention: This is a retrospective comparism of suspects screened and cases notified in Q3 and Q4, 2012 resulting from the use of recorded radio jingles strategy in local languages on memory card, compact disk, cassette, MP3 radio-FM player and collaboration with public music advertisers to improve community awareness of TB in the religious centers, social gatherings and market places also in different service points such outpatient departments and antenatal clinics.
Results: Over five thousand and twenty one suspects were screened in fourth-quarter compared to 3985 screened in third-quarter. Similarly, 19% increase in case notification stratified by sex from 1021 (52% males vs. 58% females) in third-quarter to 1210 (53% males vs. 57% females) in fourth-quarter. 14% of the suspects reported from the hearing of the played TB jingle on MP3 radio players with thirty-two confirmed new smear positive TB case while 5% of the suspects were referred by public music advertisers with twelve confirmed new smear positive TB.
Conclusions and key recommendations: Significant achievement has been documented with the use of this cost effective and cultural acceptable approach in finding more TB cases in Oyo state. Therefore, this innovative method should be scaled up in the zones and nationally in order to reduce missed TB cases in Nigeria.

PC-861-03   Application of NAAT methods on AFB-positive smears for better estimation of definite tuberculosis cases in disease prevalence survey

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Background: In population based prevalence surveys, Culture recovery is often poor as a result of specimen loss during transportation, harsh atmospheric condition coupled with transport delay. In the absence of identification of AFB many TB cases are missed or classified as probable TB cases only if TB suspects have relevant symptoms and/or chest radiograph compatible with TB. Study was conducted effectiveness of WHO endorsed nucleic acid amplification test (NAAT) in identification of MTB and rifampicin resistance on ZN stained AFB positive smears.

Design/methods: A nationwide representative TB disease prevalence survey was conducted in Pakistan 2010–2011 to estimate the prevalence of bacteriologically confirmed pulmonary TB among the adult population ($\geq$15 years). The survey was conducted in 95 clusters to cover sample size of 132 000 populations. All survey participants were screened using interviews and chest X-rays. Two sputum samples were collected from TB suspect and AFB microscopy was done in the field with one sample and the other specimen sent to NTRL for smear and culture. 9285 sputum samples were processed and 283 positive MTB cultures were grown on 162/244 (66%) smear positive specimen and 121 smear negative specimen.

We investigated diagnostic (and RIF resistance detection) effectiveness of WHO endorsed NAAT on 78/82 smear positive cases which either failed to grow on culture (56), or culture contaminated (16) or not applied (10) and therefore failed to meet the case definition 'Definite TB cases'. In 22 cases both line probe assay HAIN MTBDRPlus (LPA) and MTB/Rif assay (GeneXpert) was applied whereas, LPA only was performed in 35 and GX only in 21 cases. Test was

Table   NAAT result on ZN stained AFB positive smears

Smear result	Culture result			LPA		GeneXpert	
	Total	Positive	Failed	Tested *n*	Positive *n* (%)	Tested *n*	Positive *n* (%)
Scanty (<3 AFB)	13	3	10	4	1 (25)	4	4 (100)
Scanty (3–9 AFB)	32	9	23	17	2 (12)	12	9 (75)
1+	92	63	29	23	5 (22)	16	9 (56)
2+	49	41	8	5*	4 (80)	5*	5 (100)
3+	58	46	12	8*	6 (75)	6*	5 (83)
Total	244	162	82	57	18 (32)	43	32 (74)

*Includes one case each positive on LPA and Xpert.

performed on scraped positive smears. MTB/Rif assay was also tested on 52 smear positive culture positive control smears for which Phenotypic DST results were available.

Results: *M. tuberculosis* was detected in 48/78 (61%) cases tested. LPA identified MTB of AFB in 18/57 (32%) smears while Xpert MTB/RIF in 32/43 (74%) cases tested. In 22 cases where both LPA and GX was applied, only 2 cases were detected by LPA in contrast to 15 by Xpert including two detected by LPA as well. MTB was detected in all 56 control smears with 100% agreement with phenotypic Rif resistance (54 sensitive, 4 resistant).

Conclusion: Xpert MTB/Rif assay due to its high sensitivity worked well in detecting MTB in AFB positive smear even with low number of bacilli and improved survey TB case definition in 48 cases.

PC-862-03   Analysis of tuberculosis screening results in six remote villages in Yunnan Province

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Background: In Yunnan province, because of backward economy, traffic inconvenience and ethnic minority population living together, the local health service accessibility is very limited. The finding method of PTB is mainly by passive found. The PTB cases in some remote rural cannot be found due to failure to medical institutions or CDC.

Objective: We carried out PTB active screening in six remote villages in Yunnan Province, in order to know the true epidemic situation and to explore the strategy for controlling and preventing PTB in these places.

Method: The stratified cluster proportional random sampling method was used to select the screening population. People over 15 years old in sampled screening points were administered questionnaire, chest X-ray examination, sputum smear, sputum culture examination and awareness survey in six villages.

Results: 1) The sampling population actually examined was 9305 in six villages, among them 4613 were male, and 4692 were female. 6517 were Han nationality, 2788 were minority. The average age of the sampling population was 43.65 years old. 8606 were asymptomatic, such as cough and expectoration. 699 were symptomatic. Asymptomatic and symptomatic number ratio is 12:1. The average monthly income was 2616 Yuan,101 cases of active pulmonary tuberculosis were detected, among whom 75 cases were male, and 26 cases were female. 56 cases were Han nationality, 45 cases were minority. The average age of the cases was 52.08 years old. 61 were asymptomatic. 40 were symptomatic. Asymptomatic and symptomatic number ratio is 1.5:1. 95 cases were new cases, and 6 cases were known before this survey.

7 cases with pneumoconiosis. 2) The prevalence of active and smear positive was 1085.44/100 000 and 150.46/100 000 respectively among sampling population. The prevalence in male was higher than in female, and gradually increases by age. 3) The risk factors of pulmonary tuberculosis were male, the average monthly income, with TB symptoms, ethnic minority, age, especially the elderly over the age of 60.

Conclusion: The PTB epidemic was heavy in the six remote rural areas in Yunnan province. This means that we should carry out survey actively in remote rural areas, especially in ethnic minority areas, and in focus group, such as the old age group and male group and the pneumoconiosis cases group, so as to find more cases and cure them.

PC-863-03 Intrinsic selection bias using tuberculin skin test conversion as outcome in a household setting

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Background: Studies designed to identify environmental or index-case specific risk factors for tuberculosis infection after a discrete exposure often recruit exposed household or other contacts at the time an index case is diagnosed and then follow this exposed cohort for evidence of tuberculin skin test (TST) conversion. Exposed contacts with a positive TST at baseline are usually not considered in the analysis because it is not known whether their infection occurred after exposure to the identified index case. This design may introduce selection bias if those who remain TST negative at the time of index case diagnosis are more intrinsically resistant to TB infection than the general population.

Design/methods: We enrolled 4125 household contacts of 1085 newly identified drug sensitive adult tuberculosis patients from August 2010 to August 2012 in Lima, Peru. All household members received a tuberculin skin test at baseline. Those who were TST negative at baseline were re-tested 6 months later. We compared risk ratios (RR) of known risk factor for infection using either baseline TST or TST conversion as the outcomes.

Results: We found that RR were reduced or even distorted when TST conversion was used as the outcome; these results are consistent with a strong selection bias. When we constructed an individual-level prediction model to identify the exposed non-converters and used it to exclude those at reduced intrinsic risk for infection, this selection bias was attenuated. We then constructed a simulation designed to sample from a hypothetical cohort that included highly exposed non-converters to better understand the potential magnitude of this bias.

Conclusion: The impact of risk factors for TB infection may be attenuated or distorted when studies only include exposed contacts that remain TST negative at baseline. This bias may also affect studies of other infectious diseases which have long or variable incubation periods, such as HIV. The identification of a group of highly exposed but uninfected contacts may be a useful first step for future studies of genetic or other determinants of protection.

PC-864-03 Higher odds of tuberculosis relapse notification under India's RNTCP as compared to other high burden countries

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Background: India's Revised National Tuberculosis Control Programme achieved full coverage in 2006 and treat all non-MDR TB patients with first line drugs thrice weekly intermittent regimen through out the course. The programme had achieved the 70% case detection and 85% cure rate among new smear positive cases consistently thus achieving the global targets. However, notification of relapse cases under the program was increasing both in absolute numbers and as proportion of all incident smear positive cases. Few studies and a meta-analysis reported higher relapse rates (10–12%) among new smear positive TB cases successfully treated with intermittent regimen. This study compared the proportion of relapse cases among incident smear positive TB cases in India within country and with other high burden countries.

Design/methods: We collected annual data of high burden countries on number of new smear positive and relapse cases notified by countries as per the Global TB Report 2012 and from quarterly reports on case finding from Indian provinces. Proportion of relapse among incident TB cases and odds ratios were calculated for all high burden countries

Results: India alone notified 112 508 relapse cases out of the 226 813 cases notified by all high burden countries. India's notification contribution among all high burden countries for new smear positive TB cases was 30% while for relapse cases it was 50%, odds ratio of 2.32 (2.30–2.34). Most of the provinces in India had high proportion of relapse notification ranging from 27% in Sikkim to 7% in Chhattisgarh. Average proportion of relapses out of incident smear positives in India was 15% second highest after Russian Federation (23%). Odds of proportion of the relapse cases among incident smear positive TB cases in India is higher as compared to all other high burden countries except Russian Federation and highest

Odds of relapse against new smear positive TB cases notified in India in 2011 as compared to other high burden countries

Country	New Smear Positive	Relapse	Odds Ratio
India	642 321	112 508	Reference
Afghanistan	13 789	1 130	2.14 (2.01–2.27)
Bangladesh	98 948	2 701	5.609 (5.40–5.82)
Brazil	40 294	3 555	1.99 (1.93–2.04)
Cambodia	15 812	367	7.55 (6.91–8.24)
China	377 005	34 610	1.91 (1.89–1.93)
DR Congo	71 321	3 761	3.32 (3.21–3.43)
Ethiopia	49 594	2 143	4.05 (3.88–4.24)
Indonesia	197 797	5 348	6.48 (6.30–6.66)
Kenya	37 085	3 356	1.94 (1.87–2.01)
Mozambique	19 537	1 427	2.4 (2.27–2.53)
Myanmar	42 324	4 606	1.61 (1.56–1.66)
Nigeria	47 436	2 515	3.3 (3.17–3.44)
Pakistan	105 733	5 947	3.11 (3.03–3.20)
Philippines	90 876	3 190	4.99 (4.81–5.17)
Russian Federation	29 191	8 590	0.6 (0.58–0.61)
South Africa	129 770	18 394	1.24 (1.22–1.26)
Thailand	33 169	1 915	3.03 (2.90–3.18)
Uganda	25 614	1 302	3.45 (3.26–3.65)
UR Tanzania	24 115	1 079	3.91 (3.68–4.16)
Viet Nam	50 719	6 925	1.28 (1.25–1.32)
Zimbabwe	12 596	1 444	1.53 (1.45–1.61)
High-burden countries excluding India	1 512 725	114 305	2.32 (2.30–2.34)

compared to Cambodia (7.5) as shown in the Table. Odds of relapse in India were 1.91 (1.89–1.93) as compared to China.

Conclusion: Higher proportion of relapse among incident TB cases indicate lower efficacy of the regimens, re-infection and/or of higher proportion of drug resistance. All the high burden countries other than India and some provinces of China use daily regimen and it is plausible that higher TB relapse in India is due to the intermittent regimen. The country programme should consider alleviating major risk factors for relapse including change in regimen and better air-born infection control measures

PC-865-03 Impact of Xpert® MTB/RIF testing on numbers needed to screen to find a case of tuberculosis

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Background: The Xpert MTB/RIF (GXP) assay has been shown to be more sensitive than smear microscopy for tuberculosis (TB) diagnosis and more rapid than DST culture for identifying drug-resistant TB in controlled demonstration studies. However, few studies have described its routine use as a case finding strategy and its impact in a programmatic setting.

Methods: An active case-finding (ACF) intervention was established at 7 private laboratories in Karachi, Pakistan and four in Dhaka, Bangladesh. All individuals visiting the laboratories were verbally screened for symptoms of TB. Those with a positive screen who could produce a sputum specimen received a smear microcopy test and chest X-ray (CXR). Based on a presumptive patient's self-reported history of TB medication or their smear and CXR results, a subset also received a GXP test.

Results: From Oct 2011 to Sep 2012, 429 970 individuals were screened for symptoms of TB, resulting in the detection of 627 smear-positive TB patients (146 patients per 100 000 screened). An additional 562 TB cases were confirmed among those with smear-negative results following CXR and GXP testing, bringing the total bacteriologically confirmed (B+) yield to 1189 (277 per 100 000 screened). GXP testing reduced the number needed to screen (NNS) to find a B+ patient by 47.3% compared with smear microscopy alone (362 [342–383] vs. 686 [634–741]). The impact of GXP testing on NNS was 9% higher among suspects reporting a cough of $\leqslant 3$ weeks compared to those coughing for > 3 weeks. Country-specific differences exist when examining the impact of GXP testing by gender, with females benefiting from testing more than males.

	Karachi, PK	Dhaka, BD	Both sites
All presumptive patients			
SS+ NNS	697 (636–764)	655 (564–760)	686 (634–741)
B+ NNS	389 (363–417)	302 (273–334)	362 (342–383)
Xpert impact on NNS	−44.2%	−53.9%	−47.3%
Presumptive patients with cough $\leqslant 3$ weeks			
SS+ NNS	3557 (2886–4379)	3543 (2496–5022)	3553 (2971–4246)
B+ NNS	1658 (1438–1910)	2099 (1604–2743)	1755 (1548–1989)
Xpert impact on NNS	−53.4%	−40.7%	−50.6%
Presumptive patients with cough > 3 weeks			
SS+ NNS	867 (783–961)	804 (681–948)	850 (779–927)
B+ NNS	508 (470–550)	353 (317–394)	455 (427–485)
Xpert impact on NNS	−41.4%	−56.1%	−46.4%

Discussion: GXP testing significantly reduced the NNS for B+ TB in this intervention. The impact of GXP testing is likely variable across settings depending on the assay's position in the diagnostic algorithm, the quality of adjunct screening/diagnostic tests and rate of error and invalid results. In certain settings, it may be appropriate to consider duration of cough and gender when prioritizing GXP testing. Though we have demonstrated GXP testing leads to significantly higher yields of B+ TB, further research is needed to understand how the assay impacts All Forms TB case detection and its cost effectiveness as a diagnostic tool.

PC-866-03   Quantiferon conversion following TST in HIV-1-infected adults in South Africa is common and relates to baseline Quantiferon response

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Background: HIV infection impairs mycobacteria specific immune responses affecting the diagnosis of latent tuberculosis infection (LTBI). Because Quanti-FERON® Gold In-Tube (QFT) uses the same cut off in HIV infection (TbAg-Nil <0.35 IU/mL), false negatives may occur. The conversion of a negative QFT to positive following TST is well described and is hypothesised to occur in those with pre-existing antigen-specific memory responses where TST results in proliferation of effector T cells. Hence HIV infected persons with falsely negative QFT could potentially be identified with TST boosting (similar in logic to 2-step TST strategy) which in addition may allow consideration of a more appropriate QFT cut off.

Aims:

1 To determine the proportion of HIV-1-infected adults with a negative QFT and TST that convert to QFT positive following TST.
2 To evaluate optimal cut off of baseline QFT that detects converters.

Methods: HIV-1-infected adults being screened for a TB vaccine study in Khayelitsha, Cape Town underwent QFT followed by intradermal injection of 5U PPD. QFT was repeated if randomization was delayed as per protocol.

HIV uninfected adults from the same community had QFT and TST performed in a separate study.

Results: 59.4% (95%CI 55.5–63.3) of 593 HIV-1-infected adults were QFT+ve compared with 75% (95%CI 64.1–85.9) of 64 HIV uninfected ($P = 0.015$).

22 HIV-1-infected, TST−ve (all 0 mm), QFT−ve adults (median CD4 477/mm³ IQR 439–621) had QFT repeated after median 62 days (IQR 49–70), 40.9% (95%CI 18.6%–63.2%) converted. In those who converted, median TbAg-Nil (all units IU/mL) increased from 0.21 (IQR 0.16–0.28) to 0.84 (IQR 0.6–1.89) compared to 0.02 (IQR 0–0.07) to 0.06 (IQR 0–0.1) in non-converters. Both baseline and repeat values were significantly different $P = 0.005$ and $P = 0.0001$ respectively. The groups did not differ by CD4 count or ART status.

ROC analysis showed a baseline cut off of 0.17 IU/ml provided sensitivity of 77.8% and specificity of 92.3% to detect converters. Only 1 QFT−ve, HIV uninfected person had TbAg-Nil >0.17 IU/mL.

Conclusion: QFT positivity is significantly lower in HIV-1-infected adults and considerably higher rates of QFT conversion were observed compared with previously reported rates in HIV uninfected persons in Cape Town (6.25% TST+ve, 0% TST−ve). A cut-off of 0.17 IU/ml gave optimal accuracy to identify converters. The immunological and clinical significance of this needs to be further evaluated.

COMMUNITY ISSUES IN TUBERCULOSIS CONTROL

PC-867-03   Hospitalizations for tuberculosis and social inequity in the state of São Paulo, Brazil

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Background: The studies show that hospitalization for tuberculosis (TB) is a marker of inequity inaccess to the health services. This phenomenon is determined by different aspects, from the social opportunities of the population to the characteristics of health services and systems. The objective of this research is to classify the municipalities of the state of São Paulo about the hospitalizations rates for TB and verify the relation of these occurrences with social inequity variables.

Design/methods: This is an ecological study in which 645 municipalities in the state of São Paulo were selected along with the social inequity variables represented by Gini coefficient (GC) and the Human Development Index (HDI). It was also considered, in the research, the coverage of the Family Health Strategy (FHS) and the number of admissions for TB in the last five years (2008–2012). Since data was arranged in units of different measures, it was performed its standardization, and also, there was a cluster analysis by hierarchical levels through the method of Ward, producing a dendrogram and non-hierarchical ones by the method k-means. Through these techniques, it was possible to identify five groups (clusters) of municipalities according to the social inequity and TB hospitalizations. The groups were analyzed by the variance analysis (ANOVA) and Tukey post-hoc test.

Results: From the results, it is possible to verify the differences among the groups with regard to TB hospitalizations ($P < 0.001$), and group 5 shows values well above the other four groups, with an average of 53.04 TB hospitalizations per municipality. The group 5 also shows higher HDI ($P < 0.0001$); however, with greater inequality on income distribution, considering the CG ($P < 0.0001$). It can be observed (Table) that the HDI is inversely proportional to the FHS coverage. It was found that the groups with

Table Classification of paulistas municipalities according to the variables of social inequity, ESF coverage and hospitalizations for TB, São Paulo, 2008–2012

Variable	Group 1 (n = 137) mean ± SD	Group 2 (n = 67) mean ± SD	Group 3 (n = 178) mean ± SD	Group 4 (n = 134) mean ± SD	Group 5 (n = 129) mean ± SD	P value
Gini	0.37 ± 0.01	0.39 ± 0.01	0.38 ± 0.02	0.42 ± 0.01	0.42 ± 0.02	<0.0001
IDH	0.76 ± 0.01	0.72 ± 0.02	0.77 ± 0.02	0.78 ± 0.01	0.81 ± 0.02	<0.001
ESF	95.25 ± 11.75	86.37 ± 18.44	10.42 ± 16.48	78.65 ± 19.68	24.04 ± 20.17	<0.0001*
Hospital-izations	0.24 ± 1.75	0.05 ± 0.29	1.64 ± 6.65	1.85 ± 7.41	53.04 ± 239.86	<0.0001*

*Violation of normality and variance homoscedasticity criteria required by ANOVA. It was used the non-parametric test of Kruskal-Wallis.
SD = standard deviation.

greater FHS coverage also presented fewer occurrences for TB hospitalizations.

Conclusion: The admissions for TB were not so vigorous in groups with higher social inequity, concluding that the admission is a complex phenomenon, and perhaps, the organization of health services and patients' clinical conditions may explain better its occurrence.

PC-868-03   Tuberculosis and social inequity in health: an ecological analysis using multivariate statistical techniques

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Background: Tuberculosis (TB) as a chronic and social condition represents an important indicator of the relation between health needs and offer, and it may also reflect on social inequity. This study aimed to identify the patterns of São Paulo State municipalities about the relation between TB and indicators of health services and offer, in the social inequity context.
Design/methods: This is an ecological study that considered 645 municipalities in the state of São Paulo and the variables of anti-HIV testing, coverage of Directly Observed Treatment in the Short Term (DOTS), coverage of the Family Health Strategy (FHS), Index of Gini, Human Development Index (HDI), TB incidence rate, percentage of deaths by TB and treatment default. For the classification of municipalities, it was considered the hierarchical level clustering techniques through Ward's method and k-means non hierarchical analysis. The indicators of health services supply and social inequity were constructed by the technique of Principal Component analysis (PC).
Results: It was possible to observe the formation of five groups. Groups 1 and 2 had similar characteristics as the demand for anti-HIV test and TB coefficient of incidence; however, FHS and DOTS coverage varied between them. Group 3 portrayed epidemio-

logical and social contexts equivalent to the first two groups; nevertheless, the coverage of DOTS and FHS reached median values and the abandonment rate was over all groups. Group 4 was characterized by a high coverage of FHS and low coverage of DOTS, despite major social circumstances and incidence coefficient below the observations. Group 5 represented a favorable social status and the coverage of DOTS was higher than the FHS. The groups' structure obtained up to this point was confirmed by the PC analysis, which enabled the construction of two PC which represented 76.96% of the total variance of the standardized original vector. The first PC represented the performance index of the municipalities regarding health services supply, actions for TB control and DOTS coverage. The second PC represented the context and social inequity.
Conclusion: In places with DOTS coverage, there are evidences of better services organization for TB control. The FHS was installed in areas with social problems; however, without DOTS, it does not seem to produce good indicators and DOTS still presents limitations for addressing the social inequity in health.

PC-869-03   Implementing tuberculosis infection control as component of a national hospital licensing program, Guyana

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Background and challenges to implementation: Guyana has one of the highest TB incidences in the Americas (92/100 000 in 2012) and nosocomial transmission of TB in clinical settings is of concern. The Department of Standards and Technical Services, Ministry of Health Guyana has been conducting hospital licensing visits since 1993 and 2004 in the Private and Public Hospitals respectively and is responsible for monitoring performance at facilities nationwide. In 2011, although nine environmental sanitation indicators were included in the site-visit checklist for licensing visits, no indicators addressed TB infection control. In addition, Guyana's emigration rate is among the highest in the world with more than 80% of citizens with tertiary level educations having emigrated. Due to pervasive emigration and the high turnover of healthcare workers, regular infection control training is required and regular TB screening is needed to monitor worker health.
Intervention or response: Infection control (IC) guidelines were developed in 2012 that include TB-specific components. A checklist for TB infection control indicators was developed to supplement the national

licensing tool. In August 2012, the Guyana Ministry of Health provided training for healthcare workers from 8 healthcare facilities to support implementation. The status of key TB infection control interventions was measured at baseline and at 6-month follow-up with the supplemental TB infection control checklist.

Results and lessons learnt: At follow-up, 5 of 8 facilities had formed IC teams and were actively teaching cough etiquette. Five were implementing healthcare worker screening with tuberculin skin test (TST) and offering isoniazid preventive therapy (IPT) to eligible healthcare workers (HCWs). All facilities offered surgical masks to coughers, but only 6 of 8 sites had consistent provision of N-95 respirators for HCWs. At some facilities, a health and safety officer or quality assurance nurse provided leadership in infection control implementation.

Conclusions and key recommendations: There was an improvement in TB infection control practices at facilities 6 months following training. Due to these results, Guyana is permanently incorporating TB IC indicators into its national checklist for hospital licensing. Continuous training will be needed for incoming staff.

PC-870-03   Knowing more about initial default among diagnosed sputum smear-positive pulmonary tuberculosis patients in Gujarat, India

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Background: Under the Indian Revised National TB Control Programme (RNTCP), smear-positive pulmonary tuberculosis (PTB) patients not confirmed as starting treatment are reported as 'initial defaulters'. It is important to know true proportion of initial defaulters and factors associated with initial defaulter for developing better strategy.

Methods: A cross-sectional survey of all reported initial defaulter between October 2010 to September 2011 under RNTCP was carried out in the state of Gujarat, India. Of total 65010 diagnosed smear positive patient, 3159 (4.9%) patients were reported as initial defaulters. These patients were interviewed using semi structured format.

Result: Of reported 3159 initial defaulters, 71 (2.2%) patients had been placed on treatment whose treatment initiation was delayed until the subsequent quarter. 1007 (33%) patient had died before treatment initiation, 627 (20%) patient refused the treatment, 594 (19%) patient initiated treatment outside RNTCP (Private), 525 (17%) having incorrect address or incomplete address and 218 (7%) were migrated.

Conclusion: Nearly 98% of reported initial defaulters were confirmed as not having initiated treatment under RNTCP, which reflects well established reporting system. Improvements in address recording may assist efforts to retrieve patients having incorrect or incomplete address for treatment. Additional evaluations are needed of improved counselling of TB suspects to prevent refusal for treatment, and of reasons for death before treatment initiation. Data also suggest high preference (19%) to treatment from private sector and thus need of greater involvement of private sector in the programme.

PC-871-03   Patent medicine vendors and tuberculosis control: baseline KAP analysis of case detection skills in Osogbo, Nigeria

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Background: In Nigeria, a high proportion of patients affected with tuberculosis seek treatment from patent medicine vendors. This study seeks to assess the knowledge and current practices of PMV in TB control in Nigeria.

Methodology: A cross-sectional descriptive study involving 140 patent medicine vendors within Osogbo metropolis selected by a multistage stratified sampling technique, using self-administered structured questionnaire. Data were analyzed using SPSS version 17.

Result: 140 individuals aged 20–49 years were interviewed. Most respondents (51.4%) were male, married (67.1%) and Moslem (52.9%). The study showed that all the respondents were aware that tuberculosis was caused by bacteria (100%) and more than half (61.4%) knew its mode of transmission and that coughing is the commonest symptom (45.0%). In terms of TB diagnosis, 98.6% mentioned chest X-ray while only 1 (0.7%) mentioned sputum smear. Almost all (93.9%) do not know the duration of treatment as well as names of drugs used for treatment (100%).

Conclusion: PMV have limited knowledge about TB management according to standard guideline. There is need for training among this cadre of individuals.

PC-872-03   Microcredit loan results within the ISIAT project adapting social protection top people living with tuberculosis

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Background and challenges to implementation: Microcredit loans have been used in diverse settings to reduce poverty, which confounds TB control. However, the role of microcredit loans in people affected by tuberculosis (TB) is undefined. We aimed to evaluate microcredit loans for impoverished TB-affected households.

Intervention or response: The study was part of the Innovative Socioeconomic Interventions Against TB (ISIAT) project in Lima, Peru that partnered with an established microcredit organisation. Participating clients were given a schedule for loan repayments and late payments were subject to extra charges. Sociodemographic data including education level and poverty status were recorded during a baseline visit.

Results and lessons learnt: The population was poor, with 22% (64/297) of households living on less than $1 per person per day. For people living with TB, group loans were difficult to implement and were gradually replaced by individual loans. 21% (62/297) of TB-affected households borrowed 117 loans. Access to these loans appeared to be equitable because households that borrowed tended to have lower income, spending, schooling and be more crowded than households that did not borrow. Another 27 households that were not TB-affected also borrowed 34 loans. Of these total 151 loans, 36% (55) defaulted. Factors associated with default are shown in the Figure: the borrower being male (RR = 2.0, $P < 0.02$),

living in a TB-affected household (RR = 1.4, $P < 0.001$), and the loan being larger ($P < 0.001$). Default rates were not associated with schooling completion, income, spending, crowding or loan multiplicity (all $P > 0.1$). Of the total $83 035 loans ($67 326 capital borrowed plus $15 710 scheduled interest and charges), 49% ($40 730) defaulted, including $23 656 in additional charges for late repayments. The ISIAT project facilitated debt cancellation.

Conclusions and key recommendations: Microcredit loans were accessed equitably by TB-affected households. However, microcredit was difficult to adapt to try to help impoverished people living with TB. Stigma hampered the village-banking group loan process necessitating individual, personal loans. Loans to 41% of TB-affected households left them indebted. These results suggest that microcredit loans should be offered to TB-affected households only with caution, careful selection and support. Loan success rates may be improved by targeting specific demographic groups including women, and by providing smaller loans.

Figure   Predictors of microcredit default.

PC-873-03   Perceived quality of health service among tuberculosis patients in Zambia

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Objective: Perception of the quality of health services influence health seeking behaviour and utilization of health services. This study objective was to explore the tuberculosis patient's perceived quality of care of health services in Zambia.

Method: Both quantitative and qualitative methods were used to collect data. Participants were adult tuberculosis patients recruited from six health care facilities from the north-western Province in Zambia. A specially designed questionnaire was translated into local languages and piloted before use. The participants were interviewed using a structured interview schedule, after informed consent was obtained. Another group of participants were invited to take place in focus group discussion facilitated by the researcher. The quantitative data was subject to descriptive analysis and comparisons were made between responses from male and female participants. The data from focus group was subjected to content analysis.

Results: The respondents of the survey included 60 female participants and 51 male participants. The quality of services at the health facility were ranked as good (58%), very good (22%) and bad (5%). Almost half of the respondents (49%) reported that health providers 'listened to their needs and demands' compared to 17% for traditional healers. There were no significant differences between the responses from

male and female participants ($P > 0.05$). Lack of essential resources and long waiting time were common themes emerging from qualitative data. Lack of doctors, ambulance service, beds, wards, toilet and essential equipment seemed to affect the perceived quality of care. In one facility, patients had to wait in a closed corridor before being attended to.

Conclusion: Better training and provision of essential resources to support TB care providers is important to improve the quality of care delivered.

PC-874-03   Effective implementation of smoke-free laws through stakeholders sensitisation of collaborative departments in Himachal Pradesh

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Background and challenges to implementation: The hill state of Himachal Pradesh with a varied geographical terrain has a higher incidence of smoking for men (33.6%) as compared to the national average (32.7%). As per GATS 2010, 21.2% of adults consume tobacco in some form or other. About 40% of the adult male consumes tobacco of which 33% smoke and 3.8% women of adult women consume tobacco with majority smoking. The exposure to second hand smoke at home is 83% in HP and is among the highest in India.

Intervention or response: For creating an environment of safe and fresh air, HPVHA focused on capacity building/empowering of stakeholders for inter sectoral collaborations, creation of effective coalitions. It initiated policy advocacy for formation of Steering Committees at State and District level, creation of flying squads and advocated for notification of courts for compounding the fines and trial for offence on tobacco advertising. It focused on stakeholder sensitization on smoke free laws and conducted about 100 workshop/trainings amongst the authorized personnel. The momentum has now been taken to all district/sub district levels and through rural penetration, panchayat resolutions of smoke free are being passed.

Results and lessons learnt: Micro level networks and collaborations upto the grassroots with cross-sectional stakeholders formed. All district/development blocks are complying with the smoke free provisions, more than 40 000 violators fined in the state in 2 years and about Rs 50 Lakhs amount have been collected as fine by the enforcement officials. About 36 000 stakeholders/enforcement officials sensitized at workshops and meetings. 90% Panchayats have passed smoke free resolutions and compliance of smoke free in the state reached to 83%.

A cadre of sensitized stakeholders from cross section departments, community based institutions has been formed and HPVHA has realized that the social

legislation of smoke free laws has to be initiated from the top focusing on policy advocacy and go down gradually in the hierarchy by strengthening the enforcement mechanism and community awareness.

Conclusions and key recommendations: Unless a resolute effort is made to implement smoke free laws, it will have no concrete consequences. It needs to be efficiently executed and enforced with cross-sectional stakeholders, enforcement agencies, media and policy makers with multi pronged approach from top to bottom or vice verca depending on the situation.

MDR-TB DIAGNOSIS

PC-875-03   La conversión bacteriológica de los casos con TB-MDR: una aproximación a la condición de egreso de la cohorte 2010 en México

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Marco de referencia y desafíos: El PNT de México ha determinado a la conversión bacteriológica de los casos con TB-MDR como aproximación a la condición de egreso de la cohorte 2010 en México, como un un elemento clave para la toma de decisiones en futuras cohortes de tratamiento.

Intervención o respuesta: Se realizó un estudio descriptivo, observacional, longitudinal y retrospectivo, con los siguientes criterios de inclusión: pacientes con diagnóstico de tuberculosis multidrogorresistente (TB-MDR) confirmado por cultivo y pruebas de susceptibilidad y que la localización anatómica fue pulmonar. Todos los pacientes que iniciaron tratamiento con fármacos de segunda línea durante el 2010. Los criterios de exclusión fueron: todos los pacientes con un diagnóstico diferente a TB-MDR. Todos los pacientes que iniciaron tratamiento y que por diversas situaciones suspendieron el mismo antes del los 30 días de haber iniciado, todos los paciente con diagnóstico de TB-MDR con localización extrapulmonar.

Resultados y enseñanza: Se estudiaron longitudinalmente a 222 pacientes con diagnóstico de TB-MDR de la forma pulmonar de los cuales 7.2% (16) de los pacientes fallecieron en los primeros seis meses de tratamiento, 3.6% (8) abandonaron el tratamiento en los primeros seis meses y 89.2% (198) de los casos continuaron su tratamiento. 78% (173) de casos con TB-MDR convirtieron en los primeros 6 meses de tratamiento y 13% (25) no convirtieron en este periodo, todos estos casos tuvieron seguimiento bacteriológico estricto para su valoración durante el esquema de tratamiento.

Conclusiones y recomendaciones: El tratamiento de la TB-MDR es una intervención compleja, que requiere

del seguimiento bacteriológico puntal para el seguimiento y toma de decisiones clínico-programáticas de manera oportuna.

PC-876-03   Comparison of time to MDR-TB diagnosis with the MDR/XDR-TB Colour Test and current algorithm in a resource-poor jungle setting in Peru

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Background: The diagnosis of MDR-TB in resource-poor settings is challenging due to limited capacity for local testing and delays involved in shipping samples to distant reference laboratories. We therefore evaluated the MDR/XDR-TB Colour Test, a thin-layer agar technique in which sputum pot contents are applied directly to a colorimetric culture plate that is then permanently sealed and provides concurrent TB detection and drug-susceptibility testing.

Methods: Sputum samples ($n = 697$) were collected from patients with suspected pulmonary TB and sent to the local laboratory in the Peruvian Amazon. This was equipped with a biosafety cabinet, incubator and microscope but no other TB-related equipment. Sputum was tested immediately by the current standard algorithm using modified-Petroff decontamination and Ogawa culture (without centrifugation). Ogawa positive cultures were then shipped by air to the national reference laboratory for drug-susceptibility testing using (1) rapid molecular testing with the Hain test and/or (2) traditional culture-based testing with the proportions technique. Additionally for this research project, residual sputum was (3) added to disinfectant and immediately applied to the MDR/XDR-TB Colour Test, permanently sealed and incubated locally. All cultures were read weekly. Time to drug-susceptibility testing results were compared between the three diagnostic approaches.

Results: Drug-susceptibility testing results were attempted for 63 samples that were culture-positive by any test. 87% (55/63) were Ogawa culture-positive and all had drug-susceptibility testing results available from the national laboratory. Time from sputum processing to results was median 54 days for Ogawa culture followed by Hain testing and 112 days with the proportions test. Local direct drug-susceptibility testing with the MDR/XDR-TB Colour Test provided results for 94% (59/63) samples and time from sputum processing to drug-susceptibility testing results was median 19 days, significantly faster than the other tests (Figure).
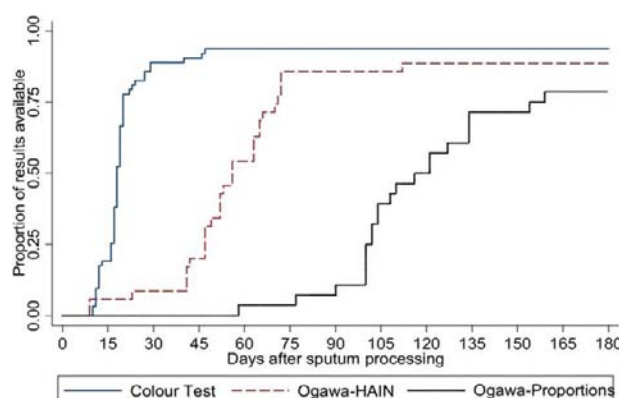
Figure   Drug-susceptibility testing speed.

Conclusions: Local drug-susceptibility testing directly from sputum with the MDR/XDR-TB Colour Test was successfully implemented in a basic jungle laboratory and provided results considerably more rapidly than the current diagnostic algorithm that uses distant testing of positive cultures with a rapid molecular technique.

PC-877-03   The role of Xpert® MTB/RIF test in the effectiveness of treatment of MDR-TB patients

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Introduction: We are observing growth of primary and secondary multi-drug resistance (MDR) in the Russian Federation. In 2011 primary MDR reached 19.4%. Under escalation of MDR TB we need rapid diagnostics of drug resistance and early commencement of adequate treatment of MDR TB patients.

Aim: To evaluate the impact of Xpert MTB/RIF testing on the effectiveness of treatment of MDR-TB patients.

Materials and Methods: The study included 110 patients, newly-detected and ineffectively treated by treatment regimen 1. Along with the standard diagnostic procedures they underwent sputum testing Xpert MTB/RIF. Initially the patients were administered chemotherapy based on Xpert MTB/RIF results: patients susceptible to rifampicin received treatment regimen 1, and patients with rpoB gene mutations associated with rifampicin resistance received treatment regimen 4. Further chemotherapy correction was based on drug susceptibility results obtained by liquid media cultivation using BACTEC MGIT 960. The control group included 50 patients with newly-detected MDR TB determined by liquid media cultivation. These patients initially received treatment regimen 1 before drug susceptibility results, then they received treatment regimen 4. The patients of the both groups matched in forms and extension of TB changes in the lungs.

Results: In the main group resistance to rifampicin using Xpert MTB/RIF was established in 30 patients. Later, MDR TB was confirmed by liquid media cultivation in all the 30 patients. 8 patients had negative Xpert MTB/RIF results. Susceptibility to rifampicin using Xpert MTB/RIF was established in 72 patients (65.5%). These patients included 18 cases (16.3%) with polyresistance to isoniazid and other drugs, but not rifampicin.

The primary evaluation of treatment effectiveness based on Xpert MTB/RIF results was performed during 3-month observation. Sputum conversion confirmed by culture after 2 months of treatment was noted in the group, which initially received treatment regimen 4 (33.3%), while in the control group sputum converted only in 2 cases (4%), $P < 0.05$. After 3 months of treatment sputum conversion was established in 17 out of 30 patients (56.6%) of the main group, and only in 13 out of 50 patients (26%) of the controls, $P < 0.05$.

Conclusion: Xpert MTB/RIF testing allows detecting MDR TB within short time after sputum collection. Initial administration of treatment regimen 4 based on Xpert MTB/RIF results enabled to achieve sputum conversion in 56.6% of patients during the first 3 months of treatment.

PC-878-03   Characteristics of MDR-TB patients in Bangladesh

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Background: Multidrug Resistance Tuberculosis (MDR-TB) is an emerging health problem in Bangladesh and its control is a challenge for national TB control programme. Identified factors could be used for specific control strategy. The characteristics of MDR-TB patients have not been systematically explored in Bangladesh. This study intends to explore the characteristics of MDR-TB patients.

Design/methods: As a part of a case-control study of 250 MDR-TB as cases and 750 non-MDR TB patients as controls we reviewed some characteristics MDR-TB. We included MDR-TB patients from September 2012 to March 2013 from four functional government hospitals of Bangladesh for initiating MDR-TB treatment. Controls are selected based on the site of MDR-TB. Interview and record review were conducted. Data analysis carried out using Stata.

Results: Mean age for MDR-TB patients was 33.8 and 37.9 for non MDR-TB patients. Male patients were 67% and 59% among MDR-TB and non-MDR-TB respectively. A 97% of MDR-TB and 86% non-

MDR TB visited any provider after their first symptom of current TB. Among them, 43% of MDR-TB and 51% for non MDR-TB patients contacted private centers. Patients attending the informal sector were 12% and 45% respectively among MDR and non-MDR. BCG vaccination in childhood was found in 51% MDR and 58% in non-MDR patients. Contacts of TB patients were found among 39% MDR TB patient which is 36% among non-MDR. The total number of contacts was 97 and 273 and MDR-contact was 15 and 4 as reported by MDR and non MDR respectively. It was found that 50% MDR and 46% of the non-MDR TB patients were smoker. Among MDR patients 18% had other co-morbid illness which is 10% among the non-MDR. Total 32 patients were involved in any type of health care occupation which is 4 among the MDR-TB. Previous TB treatment in MDR TB patients for more than once was found in 64% and 34% had at least once. Among the non-MDR patients it was only 6%.

Conclusion: Risk factors related to MDR-TB varies widely among settings. This part of the study provided selected factors, compared to non-MDR TB patients. Association of risk factors will also be conducted. Identified factors could be used for specific control strategy.

PC-879-03   The long term outcomes and impacts of MDR-TB patient in Henan, China

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Background: China has the second largest burden of TB cases in the world and its burden of multidrug resistant TB (MDR-TB: resistant to the two principal chemotherapy agents—isoniazid and rifampicin) is also among the highest in the world. Henan, as one of the most populous provinces in China, bears the highest burdens of TB and MDR-TB cases in the country. Multidrug-resistant tuberculosis in Henan, particularly the impact on clinical and socioeconomic outcomes compared to non-MDR-TB, is poorly documented and requires investigation.

Design/methods: The aim of this paper was to understand the long term outcomes of MDR-TB in Henan, China. To achieve the aim of the study, a prognostic cohort study was conducted. People with TB from 17 counties (150 non-MDR-TB and 100 MDR-TB patients) were sampled from the drug resistance survey dataset that had been generated by Henan TB Control and Prevention Institute in 2001 and long term (9-year) outcomes were ascertained.

Results: Among MDR-TB patients at follow up the proportion who had died was twice that among non-MDR-TB patients (43.0% vs. 21.6%). There was a much lower cure rate among MDR-TB patients (63.8%) than non-MDR-TB patients (92.0%).

Socioeconomic outcomes also differed. The MDR-TB patients were less able to work, and more often changed their future plans and health behaviour. MDR cases had lower household incomes and were less wealthy. MDR-TB cases or relatives reported much higher TB treatment costs (30.2% vs. 9.5% exceeding 10 000 Yuan), and more frequent loans (44.3% vs. 26.1%) with less frequent loan repayment (19.0% vs. 4.5%).

Conclusion: The main limitation of the prognostic cohort study was the difficulty in accurately categorising the social and economic outcomes many years after they occurred. Despite the limitation, this thesis produces original findings revealing and quantifying the adverse long term (9-year) clinical and socioeconomic outcomes of MDR-TB and impacts on patient, family and community in Henan Province, China. These findings will assist TB control policy and service in Henan Province and in the rest of China.

PC-880-03   Impact of Xpert® MTB/RIF test implementation on time to diagnosis of drug-resistant tuberculosis and start of treatment in a Russian region

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Background: Rapid detection of drug resistance in patients with TB is essential for optimal patient management and infection control. Our objective was to determine the impact of the Xpert MTB/RIF test (Cepheid, Inc.) on time-to-diagnosis and time-to-initiating appropriate treatment in patients with suspected tuberculosis in a regional specialized referral TB facility in Russia (Vladimir TB Dispensary).

Methods: This prospective cohort study compared patients before availability of Xpert (baseline period, 02/2012–08/2012) with patients after availability of Xpert (implementation period, 08/2012–12/2012) in terms of clinical examination, chest X-ray, smear microscopy, culture, drug-susceptibility testing, time-to-diagnosis and -appropriate treatment. GeneXpert instrument was placed in regional TB laboratory located at the same facility as TB dispensary.

Results: Of 397 patients being evaluated for TB, 175 (44%) were enrolled in baseline and 222 (56%) in implementation periods. Median age was 41 years, 75% were male. TB was diagnosed in 338/397 (85%) patients (94% in baseline and 78% in implementation period, $P < 0.001$); 288/338 (85%) patients had newly diagnosed TB (91% in baseline and 79% in implementation period, $P = 0.002$). Among patients with TB, median time from presentation to TB dispensary to test result for rifampicin susceptibility was

26 days (mean 29, 95%CI 26–32) before vs. 1 day (mean 8, 95%CI 4–10) after implementing Xpert ($P < 0.001$). All rifampicin-resistant isolates were multidrug-resistant (MDR). After implementing Xpert, the median time to start of appropriate treatment among patients with MDR TB reduced significantly (32 days before vs. 6 days after, $P < 0.001$).

Conclusion: Implementation of Xpert significantly decreased the time to detection of drug resistance and time to start of appropriate treatment among patients with MDR TB, having important implications for control of nosocomial transmission of MDR TB and improving patient treatment outcomes.

PC-881-03   Application of quantitative second-line drug susceptibility testing at a multidrug-resistant tuberculosis hospital in Tanzania

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Introduction: Lack of rapid and reliable susceptibility testing for second-line drugs used in the treatment of multidrug-resistant tuberculosis (MDR-TB) may limit treatment success. This study describes the potential application of quantitative susceptibility testing at KNTH and offer preliminary recommendations for expansion of targeted drug-susceptibility testing for treatment optimization of drug-resistant TB in Tanzania.

Methodology: *Mycobacterium tuberculosis* isolates from patients referred to Kibong'oto National TB Hospital in Tanzania for second-line TB treatment underwent confirmatory speciation and susceptibility testing. Minimum inhibitory concentration (MIC) testing on MYCOTB Sensititre plates was performed for all drugs available in the second-line formulary. Isolates were considered borderline susceptible if the MIC was at or one dilution lower than the critical concentrations established for the MYCOTB Sensititre platform.

Results: Of 22 isolates from patients referred for second-line TB treatment, 14 (64%) were MDR-TB and the remainder had other resistance patterns. MIC testing found 3 (14%) isolates resistant to ethionamide and another 8 (36%) borderline resistant. In contrast, para-aminosalicylic acid was fully susceptible in 18 (82%). No isolate had ofloxacin resistance, but 10 (45%) were of borderline susceptible. Amikacin was fully susceptible in 15 (68%) compared to only 11 (50%) for kanamycin. Ten (71%) of MDR-TB patients had at least one medication that could probable have been modified (median 2; maximum 4).
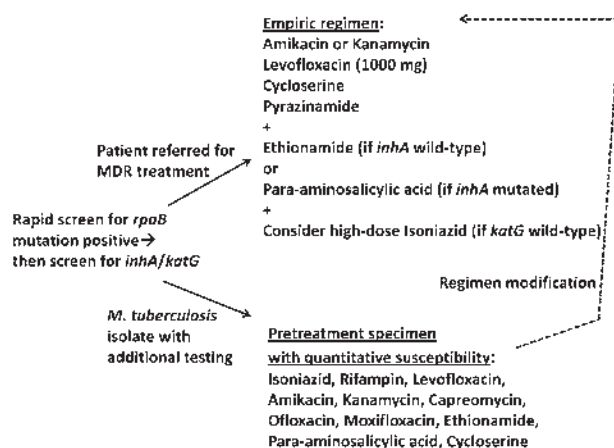
The most common modifications were a change from ethioniamide to para-aminosalicylic acid, and the use of higher dose levofloxacin.

Conclusion: Quantitative second-line susceptibility testing can inform and alter MDR-TB management in Tanzania. Further operational studies are warranted.

PC-882-03   Drug resistance profile of patients with pulmonary tuberculosis in Swaziland

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Background: Swaziland, with a population of 1 million; has an HIV prevalence of 26% among the age group 15–49 years, TB incidence of 1320 cases per 100 000 population and an HIV co-infection rate among TB patients of 80%. In 2009/2010; a population based drug-resistance survey showed that 15.3% of the new TB cases had resistance to one or more first line drugs, 13.4% resistance to isoniazid, 7.7% to isoniazid and rifampicin (multidrug tuberculosis or MDR-TB). Among previously treated TB cases, 45.2% had TB strains resistant to ≥1 first line drug; 45.2% had a strain resistant to isoniazid and 33.8% resistant to at least rifampicin and isoniazid (MDR TB). We reviewed data over 18 months in 2011 and 2012 to determine resistance profiles among new and previously treated TB patients and to inform policy.

Methods: A retrospective study of a national registry of *M. tuberculosis* isolates from 1337 patients referred for isoniazid (INH), rifampin (RIF), ethambutol (EMB), and streptomycin (SM) drug susceptibility testing at the National TB Reference Laboratory in Mbabane between January 2011 and June 2012 was conducted to document the resistance patterns. Drug susceptibility testing was conducted using the MGIT 960 instrument. There were 790 new TB cases and 547 previously treated TB cases. The outcome measures were number and proportion of TB cases with any drug resistance and multidrug resistant TB (isoniazid and rifampin). Data was entered in an excel database and analyzed in Microsoft excel 2010.

Results: Fifty-one percent (674) of the 1337 TB cases were female and 49% (663) male. The mean age was 34 years. Among new TB cases, 312/790 (40%) had TB strains resistant to ≥1 first line drug while among previously treated cases, 70% had TB strains resistant to ≥1 first line drug. Resistance to at least rifampicin and isoniazid (MDR-TB) was observed in 25% (195/790) of the new PTB cases and in 51.2% (280/547) in previously treated patients.

Conclusion: The primary resistance among new TB cases in 2011/2012 is higher than 2009/2010 indicates community or hospital transmission of MDR-TB and the need to strengthen infection control interventions in the country.

PC-884-03   Patients' experiences of accessing MDR-TB diagnosis and treatment in the Xpert® MTB/RIF era in Cape Town

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Background: Xpert MTB/RIF assay (Xpert) is a rapid and sensitive test to diagnose tuberculosis (TB) and rifampicin resistance. Studies have documented the potential benefits in the health system and challenges of using Xpert in resource-constrained health settings, but little is known of patients' experiences.

Methods: A qualitative study was undertaken enrolling adult patients with multidrug resistant (MDR) -TB since a policy change introducing Xpert as a screening test for all TB suspects. Purposive sampling was used to select eleven participants with different MDR risk profiles (previous TB treatment or not), age and gender from 4 clinics for in-depth interviews and folder reviews. Interviews were digitally recorded and transcribed. Thematic analysis was done to identify the main trends of patient's illness pathway.

Findings: Most participants delayed seeking initial care at the clinic, due to inaccurate perception of their symptoms (either dismissing it as bewitchment, fearing the worst or, for those who were HIV-positive ascribing symptoms to their HIV status). For six participants, diagnosis to start of treatment was rapid (3–14 days) and uncomplicated (those with a positive Xpert test). Five participants experienced delays of 1–6 months with MDR-TB diagnosis and initiation of treatment. Patients reported being sent home on antibiotics for a chest infection, often feeling very ill and not being evaluated for TB, being tested repeatedly (with only smears) and negative initial tests. Some patients were diagnosed whilst failing drug sensitive treatment. A final diagnosis brought relief at

knowing, but anxiety about the negative impact of MDR-TB on their personal, social and work lives.

Conclusion: The availability of a rapid diagnostic does not address delays in health seeking behaviour or inappropriate assessment by health services. In the Xpert era, not everyone will benefit from a rapid test due to it not being requested or not being applicable. The Xpert test only forms part of the diagnostic process. All aspects of the process, from early health seeking at the onset of symptoms to appropriate testing to the initiation of treatment, would need to be functioning effectively for the full test benefits to be achieved.

PC-885-03 Interim analysis of programmatic management of drug-resistant tuberculosis implementation in southern Andhra Pradesh, India

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Background and challenges to implementation: Drug resistant tuberculosis is emerging as a major public health problem in India. Revised National Tuberculosis Control Programme (RNTCP) is scaling up diagnostic and treatment services to manage the drug resistant tuberculosis in programme setting.

Intervention or response: In 2012, PMDT was launched in six districts of southern parts of Andhra Pradesh state covering 19 million population. Damien Foundation is supporting diagnostic and treatment initiation services by establishing referral laboratory and hospital for managing drug resistant TB. TB supervisors placed by Damien Foundation in six districts support the follow up of TB patients. The main objective of the study is to do a interim analysis of PMDT implementation. A semi-structured interview schedule was used to interview patients and DOT providers who were initiated treatment between January and October 2012.

Results and lessons learnt: In 2012, out of 761 LPA tests done 227 MDR TB and rifampicin resistant cases were diagnosed and 220 patients were initiated treatment with second-line drugs. We contacted 101 patients or their family members. Majority of the patients are men (76%) hailing from rural (71%) areas with mean age around 36 years. Average time taken for diagnosis and initiation of treatment are six days and 17 days respectively. Nearly 72% of them culture converted and 11% awaiting results. Mean time taken for culture conversion is 148 days. Around 80% of patients are under continuous phase of treatment, 7% have died and 3% defaulted. The number of doses missed ranged from 2 to 88 and mean is 15 doses. Around 47% of patients missed some doses.

Regular follow up sputum examination done by 90% of patients. Around 65% of patients reported adverse events. The most common reasons for missing the dose are delay in the delivery of drugs, adverse effects and outstation travel by patients. Most patients receive injection from Rural Medical Practitioners who are easily accessible. The major challenges faced during implementation are delay in procurement of sputum transport materials, frequent turnover of lab technicians in the referral lab and management of adverse effects in the field are the major challenges faced during implementation of PMDT.

Conclusions and key recommendations: Logistics management and delay in treatment initiation emerged as the major challenge in implementation of PMDT in south Andhra Pradesh districts, India.

PC-886-03 Improvement of laboratory capacity for multidrug-resistant tuberculosis under universal coverage scheme in Thailand

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Background: Thailand was in the list of 22 high TB burden countries. It was approximately notified of 57 641 TB cases in 2011. The prevalence of drug-resistant tuberculosis (DR-TB) has been observed increasingly. National survey in 2011 revealed that MDR-TB was reported 1.7% of new TB cases, and 35% of previously treated ones. Laboratory capacity improvement is important for addressing MDR-TB issue.

Intervention: In 2012, the National Health Security Office (NHSO) and Bureau of TB, Department of Disease control, built up the capacity of TB laboratory services where sputum culture and drug susceptibility testing (DST) could be conducted and supportive to treatment provided to those patients. Eighteen TB laboratory units in the universal health coverage scheme were established as: 1) the units with capacity of mycobacterium culture using solid or liquid media, 2) the units with DST using solid or liquid media. The model and criteria for TB patients who can access the culture and DST have been developed, targeting with 10 000 TB case (each case per one treatment course). The patients were categorized as following: 1) previously treated patients, 2) on-treatment patients (failure of sputum conversion after 2–3 mo.) and 3) pre-treatment (patients with exposure to MDR-TB, TB-HIV or prisoner).

Results: There were 9545 of TB cases enrolled into the service system either the culture or the DST. It was revealed that 48.4% (4617 cases) was pre-treatment patients; 36.6% (3492 cases) was on-treatment patients

and 15.0% (1436 cases) was previously treated patients. Specimens from 5388 TB patients (56.4%) were sent to identify TB strains using culture with liquid media, and 907 samples (9.5%) were examined by solid media. For DST, 4981 cases (52.2%); and 826 cases (8.7%) were tested using solid media and liquid media, respectively. There were 480 cases (8.2%) of MDR-TB that 2.9% (170 cases) were on-treatment patients; 2.7% (159 cases) were pretreatment; and 2.6% (151 cases) were previously treated patients.

Conclusions and key recommendation: The systematic management of MDR-TB can provide TB patients to access the effective laboratory services Laboratory capacity provides the essential role of TB management. In 2013, NHSO has initiated new laboratory techniques with rapid molecular for TB diagnosis and MDR-TB determination including Real Time PCR and Line Probe assays for more effective identification and appropriate treatment of DR-TB patients in Thailand.

PC-887-03 Genetic diversity of clinical *Mycobacterium tuberculosis* strains using a rapid repetitive sequence-based PCR genotyping system in Korea

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Aim: We evaluated the performance of a repetitive sequence-based PCR (rep-PCR) genotyping DiversiLab system (Biomerieux S.A., France) for identifying the genetic diversity of clinical *M. tuberculosis* (*M. tuberculosis*) strains in Korea. The optimal loading concentration of bacilli DNA that possess discriminatory power in this system was assessed additionally.

Methods: Clinical *M. tuberculosis* strains (*n* = 179) isolated from pulmonary TB patients (*n* = 124) and banked in Tuberculosis Specimen BioBank, Masan National Hospital, S. Korea, were employed in this study. After culturing the *M. tuberculosis* strains on solid medium for 3 weeks, the grown colonies were applied for a conventional culture based phenotype drug susceptibility test (DST) for 1st and 2nd line anti-TB drugs. Chromosomal DNA of the *M. tuberculosis* strains were extracted and applied for rep-PCR genotyping analysis by the DiversiLab system according to the manufacturer's recommendations. Results for genetic diversity of the *M. tuberculosis* strains were analyzed using DiversiLab software (version 3.4). In addition, different concentrations (from 1 to 80 ng/ul) of the extracted *M. tuberculosis* DNA were loaded into the DiversiLab system.

Results: Among the 124 patients, 37 patients provided *M. tuberculosis* strains 2 times, and 6 patients 3 times during their hospitalization period. After cul-

turing *M. tuberculosis* strains for 3 weeks, about 8 to 10 hours were required for DNA extraction, genotyping of the *M. tuberculosis* strains and analyzing the data with the DiversiLab system, suggesting the system generated rapid genotyping results of the clinical isolates. Although the manufacture recommends 35 ng/μl as the loading concentration of bacterial DNA for DiversiLab system, a wide range (5 to 80 ng/μl) of DNA was able to discriminate differences in rep-PCR genotyping with 95% similarity level. The 179 clinical *M. tuberculosis* strains employed in this study were allocated into 64 groups when similarity level of 95%. Among the *M. tuberculosis* strains isolated from the 43 patients who provided the *M. tuberculosis* strains more than 2 times, *M. tuberculosis* strains from 27 patients were in the same group with the same DST. *M. tuberculosis* isolates from 15 patients were not in the same group. Interestingly, the *M. tuberculosis* strains of 1 patient were in the same group, but the *M. tuberculosis* strains were evolved from MDR to XDR, suggesting drug resistance acquisition.

Conclusion: This study suggests that rep-PCR based DiversiLab genotyping system is a rapid and simple method to discriminate differences of genetic diversity for *M. tuberculosis*.

PC-883-03 Scaling up MDR-TB in Coast Province, Kenya

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Background: Coast Province had 20 MDR-TB (multidrug-resistant tuberculosis) cases by early 2009. Patients were dying before they could be initiated on treatment. There were no drugs or treatment centre in the province, and only a few who could travel to Nairobi were able to access MDR treatment. Coast Province has a high incidence of TB. Due to good MDR surveillance in place the province is able to suspect and diagnose MDR patients in the province very early. By 2009, Coast had diagnosed 20 MDR patients; none was on treatment, and 10 of the 20 patients died before treatment was started. Health workers were not trained, there were no MDR drugs and no infrastructure for the delivery of services. Treatment of MDR patients in the province started in November 2009 on an out-patient basis in one of the districts, but patients were scattered throughout the province. There was no isolation ward for admission anywhere in the province. Patients in other districts who could not access the treatment centre continued to die.

Intervention or response: All confirmed MDR-TB patients in the province were mapped and their nearest

health institution identified. Teams from health institution with MDR-TB patients, both district and dispensaries, were trained in management and follow-up of MDR-TB patients. Lobbying was done to obtain enough drugs from the central government for all MDR patients in the province. Laboratory follow-up of MDR patients was established and a supervisory team established to oversee MDR-TB patients. Counselling and contact tracing of MDR-TB patients was given high priority through community units.

Results and lessons learnt: All health workers managing MDR-TB patients have been trained and 10 of the 13 districts in coast province have started treatment. Forty-eight MDR-TB cases in the province were started on treatment from November 2009 to August 2012; 11 (23%) completed treatment, 4 (8%) died, and 33 (63%) were currently on treatment. Thirty-four (71%) occurred in males; the mean age was 34 years (SD = 8.8 years, range 9–53). Twenty-eight (58%) cases were from Mombasa County (the capital). Fifteen (30%) reported using illicit drugs. Nineteen (20%) cases were HIV co-infected; the co-infection rate increased from 11% in 2009 to 42% in 2012. 75% of the patients were culture-negative by Month 3 of treatment. Despite decentralization some patients are not able to access the health institution due to long distances. Severely ill patients have no facilities for admission.

Conclusion and recommendations: It is possible to decentralize MDR-TB services to the patients, but it is essential to put proper health systems in place before starting MDR-TB treatment. Health workers must be trained and drugs must be available. Infection prevention control, laboratory, and clinical follow must be established. Community support, especially in counselling and contact tracing, is essential. All diagnosed MDR-TB patients must be put on treatment. Treatment should be as near the patients as possible. Isolation wards are essential for severely sick patients. HIV-positive patients not doing well on standard TB treatment should be screened for MDR-TB.

DRUG RESISTANCE SURVEILLANCE

PC-888-03   Prevalence of tuberculosis and identification of risk factors related to multidrug-resistant tuberculosis in central Nepal

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Background: Limited information is available on the epidemiology of tuberculosis and risk factors of multidrug drug resistance tuberculosis (MDR-TB) in Nepal. This study was designed to explore the epidemiology of tuberculosis and risk factors associated with MDR-TB in Nepal. The objectives of the study were to: (i) to find out the distribution of tuberculosis in central Nepal; ii) to assess the trend of MDR-TB from 1996 till 2008; iii) to study the distribution of XDR-TB; iv) to assess determinants of MDR tuberculosis in terms of socioeconomic, cultural, educational and behavioral factors; environmental factors, biological factors and health service factor in Central Nepal.

Design/methods: The first part of the study was retrospective study done by assembling the secondary information on tuberculosis cases reported in the Central Nepal and trends of MDR-TB and distribution of XDR were calculated by using routine date. To explore the determinants of MDR-TB, matched case control study was conducted.

Results: The case notification, incidence and prevalence rate of Central Nepal were calculated as: 151/100 000; 182/100 000 and 245/100 000 respectively. As per the routine reports, MDR-TB in central Nepal is in increasing trend. The cause of drug resistant in Nepal is the result of complex web of biomedical, sociocultural and behavioral interaction and reporting of individual risk factor is over simplified. However, Injecting drug users are 5.13 times risk of MDR-TB, more likely to suffer from cirrhosis/liver infection, ($P < 0.001$), diabetes ($P = 0.002$) heart disease ($P = 0.044$), gastritis ($P = 0.015$), seizure ($P = 0.045$). As per our study 179 (96.4%) MDR-TB cases had previous history of TB compared to none of the control ($P < 0.001$). As per the finding, history of prior TB, previous smoking habit with OR 4.5 (95%CI 1.24–16.20); social discrimination with OR 5.83 (95%CI 1.77–19.71) remained as the independent predictors of MDR-TB. Out of 7 extensively resistant tuberculosis cases reported in Central Nepal, 3 cases (42.9%) were male and rest of them were female.

Conclusion: The persistence of the stigmatization of MDR-TB and of the people who suffer from it acts as a serious obstacle to the TB control. The present study clearly outlines that the pro-poor approach should augment and enhance the core objectives of national TB control programs to identify and effectively treat more TB patients. The provision of drug therapy in the treatment centres alone cannot address the problem of MDR-TB. Strengthening of DOTS program and to ensure completion of the treatment to avoid future risk of the development of MDR-TB seems crucial endeavour.

PC-889-03 Prevalence of adverse drug reactions among hospitalized MDR-TB patients in the intensive phase in Nigeria

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Background: The adverse reactions of multidrug resistant tuberculosis (MDR-TB) drugs can be fatal in some instances and may require treatment interruptions or change of regimens. We investigated whether these adverse reactions were common among Nigerian patients.

Design/methods: This study was a cross-sectional observational survey of adverse reactions of MDRTB drugs in the first four hospitals (three secondary and one tertiary) to provide large-scale MDRTB treatment through funding from the Global Fund.

Patients on the 8 months intensive phase regimen (weight based dosing) were placed on a standardized regimen consisting of amikacin or kanamycin, levofloxacin, cycloserine, prothionamide and pyrazinamide. The ADRs were clinically determined and recorded on the pharmacovigilance form.

We collected and validated the ADR data of 140 adult patients who had been on the intensive phase regimen (weight based dosing) from January 2012 to March 2013. Descriptive statistics including, frequency, mean, proportion, range and percentage were applied using SPSS Version 16 for Windows. Measures of association were tested by cross-tabulation of variables of interest using χ^2 and odd ratio at P value = 0.05.

Results: More men compared with women (79 vs. 61) constituted the study population. Participants' mean age and body weight were 36.6 ± 11.9 years and 54.20 ± 11.8 Kg respectively. Many ADRs were reported but the most common ones were: hearing loss, 15 (11%); gastrointestinal problems, 13 (9%); psychosis, 11 (8%); tinnitus, 8 (6%); arthralgia, 7 (5%); itching, 6 (4%); peripheral neuropathy, 5 (4%) and diarrhea 5 (4%). Of these, psychosis and hearing loss were serious as the patients were either hospitalized or suffered disability.

Most of the serious adverse drug reactions (SADRs) were observed within the age range, 21–30 years and weight interval, 30–60 kg. Age [age adjusted odd ratio, 4.7 (2.8–8.1); P <0.001)] and weight [weight adjusted odd ratio, 3.3 (1.9–5.7; P < 0.001)] were significantly associated with the SADRs.

Conclusion: MDRTB associated ADRs are common among the participants in Nigeria. Pharmacovigilance services should be strengthened at all the MDRTB centers in Nigeria in order to promote patients' safety.

PC-890-03 Lot quality assurance sampling as a rapid tool for assessing local risk of tuberculosis drug resistance in KwaZulu-Natal, South Africa

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Background: The South African province of KwaZulu-Natal (KZN) has the highest burden of multidrug-resistant tuberculosis (MDR TB) and extensively drug-resistant (XDR) TB in the country. Understanding the spatial distribution of drug-resistance may be useful in identifying root causes of resistance and prioritizing local MDR TB prevention measures. Inconsistencies in drug susceptibility testing (DST) practices and reporting interfere with the ability to rely on routine surveillance data to assess the risk of drug resistance among diagnosed TB cases. Here, we conducted a pilot study to evaluate the utility of Lot Quality Assurance Sampling (LQAS), a sampling strategy to determine whether the burden of disease exceeds a pre-determined threshold, for rapid classification of the risk of drug resistance among incident TB cases in two jurisdictions of KZN.

Methods: Sputum samples were collected from consecutively recruited new smear-positive TB cases identified at each jurisdiction's central laboratory, and tested for the presence of *Mycobacterium tuberculosis* (MTB) and rifampicin (RIF) resistance with Xpert® MTB/RIF, a rapid nucleic acid amplification assay for detection of MTB and resistance to RIF. Microscopy, culture and DST were also performed. We determined a sample size ($n = 82$ isolates for each jurisdiction) and corresponding decision rule (d = 4 isolates with rifampin resistance) to allow us to achieve our desired LQAS performance requirements: smaller than 10% probability of erroneously calling an area 'high risk' if the true risk of RIF resistance was 2%, and smaller than 10% probability of erroneously calling an area 'low risk' if the true risk of RIF resistance was greater than 8%.

Results: LQAS was carried out in the catchment areas of two laboratories in rural KZN, a region in which there has not been systematic surveillance of drug-resistance. Among the 82 isolates collected in one jurisdiction, three (3.7%) were identified as RIF-resistant, classifying this as a low risk area. Five of the 82 isolates (6.1%) in the second area indicated RIF-resistance, deeming it high risk.

Conclusion: In settings where routine surveillance cannot provide reliable estimates of MDR-TB risk at levels of geographic resolution necessary to guide

public health interventions, and where universal access to DST has not yet been achieved, LQAS represents a feasible approach for the rapid assessment of the local risk of MDR TB.

PC-891-03   Need for a nationally representative MDR-TB survey in Indonesia: lesson learnt from sentinel-based surveillance in 2012

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Background: Anti-tuberculosis (TB) drug resistance is an emerging serious public health problem that threatens progress made in TB control in Indonesia. Multidrug-resistant (MDR-TB) cases were notified increasingly in some referral hospitals in the past 5-year, especially among new registered TB patients. NTP has been conducted sentinel-based surveillance in few locations to monitor the trend of TB-MDR occurrence.
Methods: Sentinel-based of 22 health facilities in 4 provinces had been selected. In those selected sites, 527 eligible TB cases had participated. Among them, 491 (93.2%) has information on drug sensitivity testing (DST) results. Out of 491 cases, 437 (89%) were new registered patients, 53 (10.8%) were retreated patients, and 1 (0.2%) was unknown treatment history. Patient and health facility data were analyzed and adjusted for clustering effect.
Results: Among new registered patients, prevalence of any isoniazid, rifampicin, ethambutol, and streptomycin resistance were 9.6% (CI = 6.0–13.2%), 2.5% (CI = 1.0–4.0%), 2.1% (CI = 0.5–3.6%), and 5.7% (CI = 4.0–7.4%), respectively. The prevalence of MDR-TB among new registered and retreated patients were 1.6% (CI = 0.4–2.8%) and 20.8% (CI = 2.5–39.0%), respectively.

Comparing sex, prevalence of MDR-TB among males was higher than females in both new registered and retreated patients. Among new patients, prevalence among males and females were 2.3% (CI = 0.1–4.5%) and 0.6% (CI = 0.1–1.9%), respectively, while among retreated patients, prevalence among males and females were 28.0% (CI = 1.6–54.4%) and 14.8% (CI = 0.1–31.3%), respectively. MDR-TB cases among new registered patients were more likely young adults while among retreated cases were more likely old people.

Comparing to 2009 data in the same location (i.e., East Java province), there was no different of MDR-TB prevalence among new registered patients (2009, 2.0% (CI = 1.0–3.0%); 2012, 2.3% (CI = 0.5–4.0%)). However, among retreated patients, the prevalence was increased from 9.7% (CI = 5.6–13.8%) in 2009 to 30.4% (CI = 4.9–56.0%).

Conclusion: Based on sporadic sites, there is strong evidence that MDR-TB has emerged in Indonesia. We need more accurate information that reflected a real problem in national level. Urgent need to conduct a national representative MDR-TB survey in Indonesia in the near future.

PC-892-03   Drug susceptibility pattern and genotypic diversity of *Mycobacterium tuberculosis* isolate collected from community-based survey in Ethiopia

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Background: The prevalence of multidrug-resistant TB is one of the important indicators to evaluate the effectiveness of the TB control program. Study of TB molecular epidemiology through DNA fingerprinting is an important tool to identify factors that determine disease dissemination and distribution.
Objective: To characterize and evaluate drug susceptibility pattern of *M. tuberculosis* complex isolates collected from different regions of Ethiopia.
Method: The study participants were recruited from 85 kebeles/Gotas which were stratified as urban area, rural area and pastoralist population for prevalence survey. The present study was conducted as a continuation of prevalence survey. The laboratory investigation was carried out on all culture positive samples. The isolates were characterized using RD9-PCR deletion typing and spoligotyping. Drug resistance was tested using indirect proportion method on L-J media.
Result: A total of 92 culture positive *M. tuberculosi-sisolates* were analyzed using RD9-PCR deletion typing. All the isolates were identified as *M. tuberculo-sisspecies*. Among 91 isolates spoligotyping revealed 41 spoligotype patterns with over all diversity of 45%. A total of 64 isolates were grouped into 14 clusters consisting of 2–15 isolates each. The dominate strains of *M. tuberculosis* were SIT53 (15/91) and SIT149 (11/91). Cluster formation within same geographical location was 26.4% for registered spoliotype pattern and 81.8% for newly identified spoliotype pattern. The family assignment showed that majority belongs to T (51%) followed by CAS (15%). Among 90 isolates mono-resistance was found in 27.7% and poly-resistance in 5.5% of cases. MDR were detected in 3.3% of new cases and 1.1% in previously treated cases.
Conclusion: The dominate strains of *M. tuberculosis* were SIT53 and SIT149 which belong to T1 and T3ETH respectively. The strains showed various levels of drug resistance to anti-TB drugs.

PC-893-03   Establishing sentinel surveillance of rifampicin resistant tuberculosis in South Africa

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Background: South Africa (SA) has a high incidence of tuberculosis (TB) and large numbers of drug resistant TB cases. In 2011, SA initiated a phased nationwide implementation of Xpert MTB/RIF (Xpert) rapid diagnostic testing for TB suspects. To date over 1 million tests have been performed, with a national average of 14.55% MTB positivity and 7.14% rifampicin resistance. As per the national algorithm, Xpert rifampicin resistant patients submit a second specimen for confirmation and to test susceptibility to isoniazid and second line drugs. While several time-limited research projects are ongoing to assess the impact of this implementation, this also presented a unique opportunity to introduce a sentinel surveillance system for rifampicin resistant TB in SA to identify prevalent strains, estimate the burden of resistance to other TB drugs, estimate the sensitivity and specificity of rifampicin resistance as a predictor of MDR-TB and determine the impact of implementation over time.

Design/methods: TB surveillance was included into an existing NICD surveillance platform called Group for Enteric, Respiratory and Meningeal disease Surveillance in South Africa (GERMS-SA). Nine enhanced surveillance sites were selected (1 in each province), comprising a hospital and its feeder clinics. Laboratory staff alerts Surveillance Officers (SO) to Xpert MTB positive rifampicin resistant cases. The SO traces the patient to a clinic or hospital and completes a Case Report Form (CRF) including demographic data, predisposing co-morbidities, HIV status and risk factors for TB. Forms are submitted centrally to NICD, checked for quality, captured onto a database and analysed.

Results: Chris Hani Baragwanath Hospital and surrounding clinics in Gauteng were selected as a pilot site. From October 2012 to January 2013, 86 cases of rifampicin resistant TB were diagnosed. Of the completed results thus far, 39/39 Xpert rifampicin resistant cases were confirmed resistant on Hain Line Probe Assay and 23/39 were also isoniazid resistant. Challenges in collecting/following up the second sputum specimen are being addressed and results will be presented at the conference.

Conclusion: Implementation of Xpert testing in SA presented a unique opportunity to establish a sentinel surveillance system for rifampicin resistant TB. Data will be used to monitor trends over time, evaluate aspects of the Xpert implementation and provide information to target resources in the future.

PC-894-03   Implementation of a large anti-tuberculosis drug resistance survey in South Africa

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Introduction: In June 2012, South Africa embarked on a nationwide tuberculosis (TB) drug resistance survey (DRS) to determine the frequency and distribution of drug resistant TB in the country. An earlier survey done in 2001–2002, with sample size 24 896 had suggested that South Africa had high numbers of multi-drug resistant tuberculosis (MDR-TB) but low percentage levels of 'primary' MDR-TB. Considering the size of the country and the diversity of the TB epidemic, the updated survey has a large sample size, 169 125, powered to provide robust estimates at the provincial level. This will inform on the burden of MDR-TB in each of South Africa's nine provinces. In addition, while previous surveys have recruited smear positive cases only, the current DRS, cognisant of the local HIV-TB syndemic, is recruiting TB suspects. Given the continuing high incidence of HIV and the emergence of XDR TB, an updated survey was urgently needed to describe the epidemiology of DR TB in South Africa.

Methods: We describe of the preparation, initiation and implementation of the South African National TB Drug Resistance Survey (DRS) in relation to the study protocol, field experience, training activities, data management, and laboratory and quality assurance processes.

Results: The DRS has been successfully rolled out sequentially to all the 9 provinces of South Africa. This has involved the training of about 1000 health professionals both centrally and on-site in 400 randomly selected clinics. So far, more than 30 000 TB suspects have been successfully recruited. Their sputum samples and questionnaires are all couriered for microscopy, culture and drug susceptibility testing at a central laboratory in Johannesburg. Six hundred first and second line drug susceptibility tests have been performed from 2000 culture positive specimens. HIV testing on sputum has been performed on more than 16 245 specimens.

The survey faces challenges including meeting recruitment targets, higher than expected rejection rates due to leaked specimens, suboptimal laboratory turnaround times which have had to be addressed. Solutions have been sort, tested and implemented without delaying the survey.

Conclusion: As far as we know this is the largest TB DRS that has been undertaken. In addition to providing the National TB Control Programme with a robust estimate of the burden of MDR TB, it has also led to a significant improvement of the laboratory and survey implementation capacity, as well as identifying weakness in routine TB diagnostics and surveillance.

PC-895-03   Utilizing the cohort review process to reinforce standards of care, capacity building, and continuous quality improvement for MDR-TB care in Tanzania

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Background: Cohort review (CR) is a systematic process to monitor and evaluate interim and final outcomes for TB patients. CR is endorsed by the IUATLD and WHO as an integral component of TB control, but there is little published data describing the process, implementation, or impact of CR on the management of MDR-TB. In 2009, the Tanzania National TB and Leprosy Programme (NTLP) initiated MDR-TB care using a standardized regimen and treatment duration in accord with WHO 2008 and national guidelines. In an effort to monitor implementation of new MDR guidelines, track patient/program data, and optimize outcomes, the NTLP began national MDR CR meetings in 2010.

Intervention: Quarterly CR meetings to review clinical indicators and outcomes for each patient in a cohort (based on calendar quarter of enrollment) to include:

- Protocol/tools: Standard Operating Procedures; standardized data collection, case presentation, and outcome summary forms
- Multi-disciplinary participants: NTLP, National MDR-TB hospital and decentralized care clinicians and DOT nurses, District/Regional TB Coordinators, pharmacy/laboratory personnel, specialists (radiology, psychiatry, academia), expert consultants, and program partners
- Cohort reviews at 3 milestones: (allowing 3 mo. after end of enrollment quarter for data review)

6 mo.	Assess early deaths, defaults, culture conversion
12 mo.	Assess transfer to districts, adherence after hospital discharge
24/36 mo.	Assess final outcomes

- Outcome summary: to determine if program objectives met
- Program challenges/action-steps: feedback period to problem-solve active issues.

Results and lessons learnt: 7 CR meetings convened since 2010, programmatic benefits include:

- Data review allowed for accountability and timely intervention
- Cross-discipline reinforcement of training and standardized practice
- Patient/programmatic challenges documented and addressed (ex. laboratory QA and result communication, drug supply, side effects, social, transport, and nutrition issues)
- Strong outcomes for 2009 (36 mo.) and 2010 (24 mo.) cohorts ($n = 35$) reveal low default (5%) and high treatment success rates (74% cured/completed).

Conclusions: Although resource intensive, the CR process has been effective for reinforcement of standards of care, capacity building, and continuous quality improvement for MDR-TB care in Tanzania. This model may be replicated in other low resource settings, however, with larger case numbers, regional rather than national meetings may be more feasible.

PC-896-03   Implementation of e-TB Manager in Viet Nam: early outputs and lessons learned

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Background: Programmatic Management of Drug-resistant TB (PMDT) started in Viet Nam in 2009. In 2011, country ranked as 14th among the 27 countries with highest multidrug-resistant TB (MDR-TB) prevalence rate (WHO 2012). In June 2012, National Tuberculosis Program (NTP) decided to implement a comprehensive web-based tool for PMDT called e-TB Manager (e-TBM). e-TBM was developed by Management Sciences for Health (MSH) through USAID funded program Strengthening Pharmaceutical System (SPS). Since SPS closed in 2012, NTP Viet Nam requested partners to include e-TBM implementation in the USAID-funded program TB CARE I.

Response: NTP Viet Nam established a working group responsible to oversee the e-TBM implementation and consolidate results countrywide. NTP and partners supported key required activities: system customization and translation into Viet Namese, infrastructure assessment and availability at all levels, training for all staff involved in data encoding, data quality monitoring and trouble shouting, and accurate orientation with PMDT annual implementation plan.

Results: About 94% (668/713) of all DR-TB enrolled cases countrywide in 2012 were registered in e-TBM. Currently, over 1000 DR-TB confirmed cases (1045/1153) have been followed-up under treatment using e-TBM within 45 health facilities nationwide (11 DR-TB centers and 35 DOT centers). Since Jun/2012, more

than 200 health professional were trained on e-TBM procedures and approximately 50 000 log transactions were recorded in e-TB. Second-line TB drugs (SLD) management was decentralized and about 81% (9/11) of all DR-TB centers have updated stock levels on e-TBM comparing to physical inventory. Since Jun/2012, SLD forecasting to support procurement processes at the national level have been done using the e-TBM quantification tool. During this same period, no SLD stock-outs were observed in all DR-TB centers.

Conclusions and key recommendations: Due to short time of implementation, it's premature to expect significant changes in cases outcomes, however NTP related increased readiness of real time data for consolidation and analysis at all levels and better monitoring of DOT and stock levels through e-TBM. Previously these data were analyzed through paper-based reports at central level, which led oftenly to missing information and potential errors. Success implementation was possible by: overcoming changing culture process, permanent team effort at all levels and providing regular support/monitor to all units using e-TBM.

PC-897-03   Hepatotoxicity: comparison of RHZ with RHZE

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Background: In Brazil, the tuberculosis (TB) treatment regimen for individuals weighing over 50 kg, recommended by the Brazilian Ministry of Health until 2010, included three drugs; two of them in fixed-dose combined: rifampicin 300 mg/isoniazid 200 mg (2 tablets of RH) and 2 g of pyrazinamide (Z). To prevent the selection of drug-resistant mutants and antituberculosis drug-induced hepatotoxicity (ATDH), the standard regimen today, recommended by the World Health Organization (WHO) and International Union Against Tuberculosis and Lung Disease (IUATLD), is the inclusion of fixed-dose combination (FDC) formulations. The FDC tablets consisting of 4 drugs: rifampicin 150 mg/isoniazid 75 mg/pyrazinamide 400 mg/ethambutol 275 mg—4 tablets of RHZE for 2 months, followed by rifampicin 150 mg/isoniazid 75 mg—4 tablets of RH for a further 4 months. We investigated the incidence of ATDH on RHZ regimen compared with RHZE regimen.

Design/methods: This was a retrospective cohort study with patients who were treated for TB at IPEC/FIOCRUZ-Brazil. The data collection was extracted from standardized medical records. We considered two periods to analyze the different regimen: RHZ—from January 2006 to October 2010; RHZE—from November 2010 to June 2011. The ATDH was defined as an increase in serum alanine aminotransfer-

ase (ALT) levels beyond 2 times the expected normal upper limit (ALT<45 IU/l) while patients were using TB medications, according to criteria adopted by the Council of International Organizations of Medical Sciences (CIOMS).

Results: This study enrolled 260 patients, 170 TB patients and 90 TB-HIV patients. Among TB patients, 98 patients were treated with RHZ regimen and 72 with RHZE. Of the 98 patients treated with RHZ regimen, 23 (23.5%) developed ATDH. In contrast, only 4 (5.5%) patients of 72 under RHZE regimen, developed ATDH ($P = 0.0014$—Fisher's exact test). Between patients co-infected with HIV, of the 79 who were under RHZ regimen, 48 (60.7%) developed ATDH, while 11 patients who were under RHZE, only 1 (9%) developed ATDH ($P = 0.0021$).

Conclusion: In this study, a significant reduction in the incidence of ATDH with 4-drug FDC was observed when compared with separate-drug formulations, even in patients co-infected with HIV.

PC-898-03   Treatment outcomes of persons with multidrug resistant tuberculosis, Kerala, India, 2009–2010

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Background: MDR-TB therapy is less effective, associated with more adverse events and is more costly to treat as compared with standard first line therapy. Inadequate treatment of MDR-TB can lead to unsuccessful treatment outcomes and increases risk for extensively drug resistant TB (XDR-TB). We conducted a retrospective cohort study to describe demographic and clinical characteristics associated with treatment outcomesamong MDR-TB patients.

Design/methods: We included all MDR-TB patients (culture positive *M. tuberculosis* resistant to at least isoniazid and rifampicin) registered in the Revised National Tuberculosis Control Program, Kerala State, India, during 1 January 2009 to 30 June 2010. Adjusted hazards ratios (aHR) were used to assess the association between demographic and clinical factors and treatment outcomes.

Results: Of 179 patients registered, 112 (63%) had successful treatment outcomes (77 cured, 35 treatment completed) and 67 (37%) had unsuccessful treatment outcomes (29 died, 26 defaulted, 9 failed treatment, 2 stopped treatment due to drug-related adverse events, and 1 developed XDR-TB). Eighty-eight percent of those who consumed alcohol during

treatment experienced an unsuccessful outcome as compared to 12% who did not consume alcohol during treatment ($P < 0.001$). Unsuccessful outcome was significantly higher among patients who consumed alcohol during treatment than those who did not (aHR 3.4, 95%CI 1.9–6.3). Sixty-four percent of those who smoked during treatment had unsuccessful outcome as compared to 36% of those who did not smoke ($P < 0.001$). Although many patients were diabetic (33%), ever smokers (39%), or had low body mass index (47%); these factors were not associated with unsuccessful outcomes.

Conclusion: While treatment success of 63% was higher than global (53%) and national (49%) averages, outcomes remained poor overall. Consuming alcohol during treatment and smoking during treatment were significant factors independently associated with unsuccessful MDR-TB treatment outcomes. Tuberculosis control and substance abuse programs need to better integrate co-treatment of TB and addiction.

PC-899-03   MDR-TB surveillance among retreatment cases under program conditions in Cameroon, 2009–2011

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Objectives: Evaluate, after three years' duration, a surveillance and early detection programme of multidrug resistant tuberculosis (MDR-TB), based on systematic drug susceptibility testing (DST) in pulmonary TB cases notified for retreatment (RT), and implemented in two pilot regions of Cameroon under routine program conditions.

Material and methods: Between January 2009 and December 2011, all 53 TB Basic Management Units (BMUs) of the Littoral and the North-West region were asked to send two sputum specimens from all consecutively notified RT cases to any one of the two regional TB reference laboratories for culture and DST. Data from TB notification registers and TB laboratory registers were double entered and validated. Outcome measures were a) the proportion of retreatment cases with DST results, and b) the proportion of MDR cases among the different retreatment sub-categories.

Results: During the period studied, 1892 RT cases were notified; sputum samples of 1127 (59.6%) patients arrived at the laboratories; positive culture results were available for 897 (47.4) of the sampled patients; DST results were available for 770 (41%) of all notified RT cases. Sampling in particular in major BMUs was incomplete, resulting in low coverage. The quality of samples arriving in the laboratories was

regularly of mediocre quality due delay in transport and/or unfavorable storage conditions, resulting in 230 (20.5%) negative culture results. The prevalence of MDR-TB in patients failing Cat. I treatment is very high with 41 in 59 patients (69.5%, 95%CI 56.9–80.2), but it is also significant in patients who relapsed (14%) and in patients resuming treatment after having been lost-to-follow-up (7.9%).

Conclusion: MDR-TB in RT cases in Cameroon, in particular in Failure cases, appears to be high. Systematic culture and DST for RT cases have to become a routine NTP activity. This activity seems feasible; however, organizational constraints for sampling in major BMUs have to be overcome, and logistic arrangements concerning storage and transport of samples need to be made.

PC-900-03   Prescription habits and treatment outcomes for multidrug-resistant tuberculosis patients in Viet Nam

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Aims: To describe, analyze the prescription habit for the MDR-TB patients, and assess the treatment outcomes of the GLC-approved MDR-TB patients and the non-GLC MDR-TB patients in Pham Ngoc Thach TB hospitals in Viet Nam.

Methods: Retrospective cohort study with mixed method: 1) Focus group discussions and in-depth interview with clinical doctors, hospital pharmacists, and the non-GLC MDR-TB patients; 2) review of treatment cards and patients' charts of all the GLC and the non-GLC MDR-TB patients put on MDR-TB treatment during 2010.

Results: Total 282 MDR-TB patients were enrolled in the study (79 GLC and 203 non-GLC MDR-TB patients). The treatment delay is significant higher in the GLC group (12.8 days) than in non-GLC group (2.3 days), $P = 0.004$.

The success rate is significant higher in GLC patients (84.8%) than in non-GLC patients (53.7%). On the contrary, the default rate is significantly higher

Table   DR-TB treatment outcomes by GLC and non-GLC groups, Pham Ngoc Thach hospital, 2010

Treatment outcome	GLC n (%)	Non-GLC n (%)	P value
Total	79 (100.0)	203 (100.0)	<0.001
Cured	62 (78.5)	99 (48.8)	
Completed	5 (6.3)	10 (4.9)	
Failure	2 (2.5)	5 (2.5)	
Default	5 (6.3)	52 (25.6)	
Died	3 (3.8)	0	
Transfer-out	0	2 (1)	
Still on treatment	0	1 (0.5)	
Not evaluated	2 (2.5)	34 (16.8)	

GLC: Patients approved by Green Light Committee program.

in non-GLC patients than in GLC patients (25.6% vs. 6.3%), $P < 0.001$. The risk of the unsuccessful outcome is higher in non-GLC patients (hazard ratio = 4.6, 95%CI 1.8–11.8).

It is an emerging problem that the non-GLC MDR-TB patients do self-administered second-line anti-TB drugs, no DOTS support, follow-up and default tracing.

Conclusions: The MDR-TB treatment management in GLC is better than in non-GLC patients in Pham Ngoc Thach hospital, Viet Nam. Strengthen Programmatic Drug Resistant TB (PMDT) and Public-private mixed expansion should be consider to improve the default rate in non-GLC patients and prevent further amplification of MDR-TB.

PC-901-03 Initial XDR in *Mycobacterium tuberculosis* isolated from Indian MDR-TB patients

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Background: There are a few reports from India on prevalence of XDR-TB (extensively drug-resistant TB) ranging from 1.5–33.3%. XDR-TB is defined as TB that has developed resistance to at least rifampicin and isoniazid (resistance to these first line anti-TB drugs defines multidrug-resistant tuberculosis or MDR-TB), as well as to any member of the quinolone family (ofloxacin) and at least one of the following second-line anti-TB injectable drugs: kanamycin, capreomycin, or amikacin. Andhra Pradesh state in india initiated MDR case detection and treatment services (DOTS Plus) from the year 2008. LEPRA India–Blue Peter Public health and Research center served as C and DST referral laboratory for four districts under PhaseII of DOTS Plus. Present study aims to look at the frequency of initial XDR among the *M. tuberculosis* isolated from MDR TB patients, before treatment with second line drugs, under DOTS Plus.

Methods: Sputum samples were collected from the MDR suspects identified from four coastal districts of Andhra Pradesh, India during the period 2009–2012. The samples were cultured on LJ (Löwenstein-Jensen media). All *M. tuberculosis* isolates were tested for first line drugs, viz. isoniazid, streptomycin, rifampicin and ethanbutol. All isolates that are resistant to at least isoniazid and rifampicin together are further tested for resistance to ofloxacin and kanamycin (SLD), by proportion method on LJ, as per the standard recommendations.

Results and discussion: Among 781 MDR suspects, 74.3% were male and 25.6% were female, 88% are between 15–55 years and 76% had history of previous treatment for TB. Out of 781 suspects 598 (76%)

yielded positive cultures. 328/598 *M. tuberculosis* isolates were found to be MDR. Out of 328 MDR *M. tuberculosis* isolates, 216 (65%) were susceptible to both ofloxacin and kanamycin, 105 (32%) were resistant to ofloxacin alone and 7 (2.14%) isolates showed resistance to both the drugs (XDR).

Conclusion: Present study reports 2.14% initial XDR among MDR TB patients, from coastal Andhra Pradesh, India, which is in the expected range. It is noteworthy to find a higher frequency of ofloxacin mono resistance. The findings from this study may help in assessing the effectiveness of second line anti-TB treatment in this part India.

PC-902-03 Drug resistance patterns and predominant genotypes of *M. tuberculosis* isolated from tuberculosis suspects at a chest disease clinic, Dhaka, Bangladesh

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Background: Bangladesh is a tuberculosis (TB) endemic country. This cross-sectional study was aimed of screening tuberculosis (TB) suspects for smear and culture positivity rate, drug resistance patterns and prevalent genotypes of *Mycobacterium tuberculosis*.

Design/methods: This study was carried out in a chest disease clinic Dhaka, Bangladesh. Acid fast bacilli were detected in the sputum samples by Ziehl-Neelsen staining. *M. tuberculosis* was isolated on Löwenstein-Jensen slant. Isolated strains were tested for susceptibility to first line anti-TB drugs by proportion method and genotyping was performed by standard spoligotyping technique.

Results: From June through October 2010, 152 TB suspected patients were screened. Male female ratio was 2.3:1. Mean age of the TB suspects was 34.1 ± 13.25 years. Positivity rate of smear microscopy and conventional culture were 21.7 and 24.34% respectively. Thirty-seven strains were isolated and identified as *M. tuberculosis*. Of them, 25 (67.8%) were sensitive to all first line anti-TB drugs. Resistance to streptomycin, isonazid, rifampicin and ethambutol was observed in 9 (24.3%), 3 (8.1%), 2 (5.4%) and 2 (5.4%) strains respectively. Spoligo patterns of 37 strains were matched with SpolDB4. Of them, unique spoligo patterns were detected in 5 isolates and the remaining 32 patterns were grouped into Central Asian (CAS) ($n = 11$), East African Indian ($n = 8$), Beijing ($n = 6$) and remaining 7 (18.9%) strains were included under principal genetic group 2 and 3.

Conclusion: More samples were positive in culture than microscopy. CAS was the predominant genotype. There was no MDR in this population.

PC-903-03   Multidrug-resistant tuberculosis acquisition during clinic-based directly observed therapy predisposes to adverse patient outcomes

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Background: Multi-drug resistant tuberculosis (MDR-TB) is increasing globally, including in countries, with strong National TB Programs (NTP). MDR-TB may be explained by (1) healthy people catching TB for the first time that is an MDR-TB strain, or existing patients with non-MDRTB may acquire MDR-TB because (2) suboptimal therapy allows their strain to mutate or (3) exposure to other patients allows super-infection with an MDR-TB strain. We studied the acquisition of MDR-TB during directly-observed therapy (DOTS) and assessed its clinical importance.
Design/methods: Over a 5-year period, we recruited 600 patients who were diagnosed with proven TB by the Peruvian NTP. The patients were enrolled from outpatient clinics in Lima, Peru. All patients initially received first-line anti-TB therapy according to national guidelines at that time. We collected sequential monthly sputum samples that were tested for TB and MDR-TB. TB strains were compared between diagnosis and follow-up by spoligotyping. Patients were followed for an average of 5 years to assess the outcome measures of TB recurrence or death. Information about recurrence of TB disease was confirmed with the NTP. We defined adverse outcome as TB treatment failure, TB recurrence or death caused by TB.
Results: At study enrolment, 106 (18%) patients had MDR-TB and 65 (61%) of these MDR TB cases had not received TB treatment previously. 494 (82%) patients had TB that was not MDR-TB and so were at risk of acquiring MDR-TB during treatment. 40 of 494 (8.1%) patients acquired MDR-TB during DOTS. Acquired MDR was 2.8 times more likely in HIV patients ($P = 0.001$) and 3.2 times more likely in patients with monoresistance to rifampin ($P = 0.001$). 37 of 40 (93%) patients who acquired MDR-TB had spoligotyping data and in 89% (33/37), the acquisition of MDR-TB was associated with a changed spoligotype. Acquired MDR was 34 times more likely to occur in clinics with higher proportions of patients
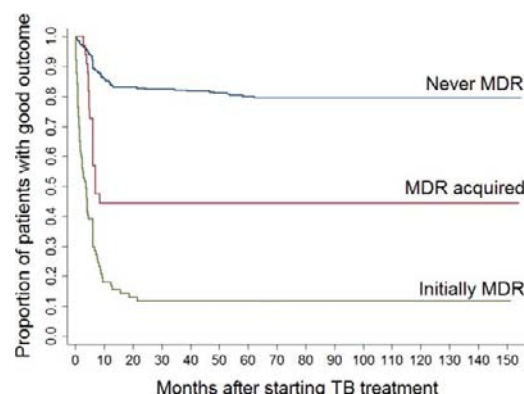
with suspected MDR-TB, suggesting MDR-TB transmission in these clinics. Adverse long-term outcomes were twice as likely in patients who acquired MDR-TB ($P = 0.02$; Figure).
Conclusion: Clustering outpatients receiving DOTS causes patients with MDR-TB and drug-susceptible TB to share the same airspace, risking MDR-TB dissemination. These findings emphasize the need for rapid MDR-TB testing and improved infection control in medical facilities.

REGIONAL AND COUNTRY APPROACHES TO MDR-TB MANAGEMENT

PC-904-03   Cost-effectiveness of mobile phone communication in DOTS-Plus capacity for tuberculosis and MDR-TB case management in upper-north Thailand

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Background: Thailand has implemented of the Directly Observed Treatment Strategy to increase Tuberculosis control program efficacy but could not achieved key TB control program indicators as Indicated by WHO.
Objectives: To compare the effectiveness of DOTS-plus strategy with mobile phone and DOTS-plus without mobile phone in upper north of Thailand.
Design/methods: We conducted two TB control models with DOTS-plus strategy in MDR-TB and non MDR-TB group during April 2008–April 2010 in upper-north Thailand as a control trial study. Model 1 was MDR- and non MDR-TB case management with health volunteer and health facility with DOTS-plus strategy. Model 2 was MDR-TB and non MDR-TB case management with health facility with DOTS-plus strategy plus mobile phone. There were at least

19 patients in each arm of MDR-TB group and 30 patients in each arm of non MDR-TB group. We followed the patients 18 and 6 months for measuring the treatment outcomes of MDR-TB and non MDR-TB group. And cost effectiveness was calculated as the average cost per patient treated successfully.

Results: The treatment outcome of Model 2 was effective than Model 2 with statistically significantly high success rate of 100% while Model 2 had success rate only 73.7% in MDR-TB group and also had high success rate of 100% while Model 1 had success rate in 96.7% in non MDR-TB group ($P = 0.0001$, $P = 0.047$). And the total cost of managing a TB patient to treatment completion of model 2 was lower than Model 1 in both MDR-TB and non MDR-TB group. The higher cost was the cost of laboratory labor, volunteer payment and specimen transportation. It was high about 4.6 time of MDR-TB group and 2 time of non MDR-TB group. The CE ratio reflecting the cost benefits of both MDR-TB and non MDR-TB group in negative territory with CE ratio minus 14.6 in MDR-TB group and minus 5 in non MDR-TB group.

Conclusion: This study describes our experiences with DOTS-Plus by mobile phone and the successful outcome suggests that DOTS-Plus by mobile phone is feasible, affordable and cost effectiveness to extend application of process to area having high MDR-TB rate.

PC-905-03   The prevalence of gaps in the procurement and supply management system of multidrug-resistant tuberculosis drugs in Nigeria

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Background: The existence of gaps (weaknesses) in the procurement and supply management (PSM) system creates drug stock-out, which is a major challenge affecting the control of MDR-TB in Nigeria. We investigated whether there were gaps in the PSM system for the MDR-TB project in Nigeria.

Design/methods: This study was a cross-sectional observational survey of gaps in the procurement, distribution and utilization of MDR-TB drugs between February 2012 and March 2013.

We collected PSM data at the central level and from the first generation hospitals (one tertiary and three secondary) providing MDR-TB treatment in Nigeria. The data was analyzed using the World Health Organization's six early-warning indicators of drug stock-outs and overstock. Five of the indicators have a target of 100% and one (1) has 0% target. Descriptive statistics including sum and percentage distribution was applied in the analysis of the gaps.

Results: Of the 6 drugs quantified, 114% of kana-

mycin, 71% of pyrazinamide, 71% of levofloxacin, 54% of cycloserine and 54% of prothionamide, were received. This suggests that only the quantity of kanamycin received exceeded the quantity expected. In terms of consumption: 100% of kanamycin, 102% of cycloserine and 102% of prothionamide were consumed, suggesting no risk of overstocking. However, only 80% of levofloxacin and 80% of pyrazinamide were consumed, suggesting the likelihood of overstocking. Only 50% of each of the six drugs was received into the country on the date agreed with the supplier, which gives the impression that the supplier was not efficient. In quarter 1 (April–June, 2012) and 2 (July–September, 2012), none of the treatment centers received their orders in full and on time. Also, in the third (October–December, 2012) and fourth quarter (January–March, 2013), 67% and 50% of the treatment centers respectively received their orders in full and on time, suggesting inefficiency in the distribution. No treatment center submitted its report on time in quarter 1 but in quarter 2, 3 and 4; only 50%; 25% and 75% submitted reports on time respectively. No treatment center met the 0% target of placing orders below the minimum stock—in quarter 1, 2, 3 and 4, 33%, 67%, 33% and 33% respectively placed orders below the minimum.

Conclusion: Wide spread gaps were observed in the PSM system. Practical strategies are urgently needed to address the weaknesses and minimize the risk of drug stock-out and overstocking.

PC-906-03   Drug resistance patterns in tuberculosis patients in Germany

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Background: Multidrug-resistant tuberculosis (MDR-TB), defined as resistance to at least isoniazid and rifampicin, poses a threat to the public health, in particular in the WHO Europe Region. While rapid drug susceptibility testing (DST) and standard reporting focus on rifampicin and/or isoniazid resistance, little is known about resistance to other standard anti-TB drugs. Yet, in Germany DST results are systematically captured within the surveillance. This study aims to identify all occurring drug resistance patterns and the affected patient groups in view of further refining diagnostic and treatment strategies.

Design/methods: German case-based TB surveillance data, electronically reported to the Robert Koch Institute from 2002–2011 are used to describe drug resistance patterns for the five standard anti-TB drugs (isoniazid/H, rifampicin/R, pyrazinamide/Z, ethambutol/E, and streptomycin/S) in general and specifically in MDR-TB patients (stratified by sex, age groups, country of birth, and treatment history).

Results: In a pilot analysis covering the years 2002

to 2006, DST information for all five standard drugs (HRZES) was available for 18 628/21 847 notified TB patients. Among 2402 cases with any drug resistance, 28 out of 31 possible different drug resistance patterns were identified. Of those, four patterns were predominant, representing almost three-fourths of drug resistance patterns (S: 22.5%; H: 21.8%; HS: 17.7%; Z: 11.8%). Overall, 402 MDR-TB cases (2.2%) were notified. In 32% of them, resistance to HRZES was reported, 36% were resistant to at least 4 drugs, and only 7.5% of cases showed resistance to HR only.

Conclusion: Drug resistance patterns observed in Germany, particularly in MDR-TB patients, were far more complex than expected. Our findings strengthen the importance of supplementing rapid DST by culture-based conventional DST.

Furthermore, the high proportion of MDR-TB patients with HRZES drug resistance support the WHO recommendation to initiate MDR-TB treatment with four second line anti-TB drugs likely to be effective, and not to rely on any prescribed first-line drug, until detailed DST results are available.

Given the relevance of representative DST data to inform diagnostic and therapeutic in-country strategies, our analyses will be updated and expanded to support the further development of treatment recommendations.

PC-907-03   Auditing drug-resistant tuberculosis case management to determine factors affecting cure rates

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Introduction: The Northern Cape Province of South Africa is reporting an increasing number of multidrug-resistant (MDR) and extremely drug resistant (XDR) *Mycobacterium tuberculosis* (TB) [MC1] patients annually. Outcomes for DR-TB were perceived to be [MC2] poor and therefore an audit to determine patient profiles and evaluate program implementation was done in the two districts Siyanda and Namaqua.
Methodology: All patients diagnosed with MDR or XDR-TB and older than 18 years who had completed treatment in the province from 2007 to 2010 were eligible for review. A retrospective audit of the all the files available in the two linked MDR-TB units [MC3] were done in the fourth quarter of 2012.
Results: There were 164 files, 11 patients were excluded on age. Of the 153 evaluable patients 63 (41%) were female and 90 (59%) male. There were 26 (17%) XDR-TB patients and the remaining 127 (83%) were MDR-TB. Of the XDR: 14 (54%) died, 6 (23%) were cured, 4 (15%) failed therapy, with

1 transfer and 1 defaulter. The MDR group had the same cure rate of 23% (29/127) with 44 deaths (35%), 22 (17%) completed treatment and 21 (17%) defaulted, 8 (6%) failed treatment and 3 (2%) were transferred. Only 38 [MC4] of the 153 (33%) were HIV positive with a male predisposition [MC5] of 68%. [MC6] A history of previous treatment for TB was present for 114 (75%) of those diagnosed with drug resistant organisms [MC7] making it an important risk factor. Compliance in the hospital files with oral as well as injectable therapy was poorly documented and unreliable. There was a trend correlating poorer outcomes with fewer doses.
Conclusions: There are more males than females diagnosed with DR-TB, with males more likely to be HIV positive. A cure rate of 23% is below other reported rates. Previous treatment failure for TB should be further investigated as this is a major risk factor for DR-TB. High death rates of for XDR TB are present and may be related to late diagnosis. Documentation of doses received must be improved to make assessment of compliance reliable.

PC-908-03   Nationwide rapid scale-up of programmatic management of drug-resistant tuberculosis 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 emerging annually among cases notified by the national programme. The programmatic management of MDR-TB (PMDT) in India began in 2007. The programmatic management of MDR-TB (PMDT) in India began in 2007 and nationwide coverage achieved in early 2013. We sought to document the progress and interventions that lead to nationwide scale-up.
Methods: We analysed the effects of systematic participatory scale up planning conducted in 2010, resource mobilization to balance laboratory capacity and second line anti-TB drugs, human resource development, pre-services appraisals, systematic implementation and periodic monitoring to address expansion challenges throughout 2011 and 2012 that have resulted in nationwide access to PMDT services, increased resources, improved laboratory-based rapid molecular diagnosis, better airborne infection control measures at DR TB Centres, and the use of standardized regimens for M/XDR TB and reporting methods.
Results: India achieved nationwide coverage of

PMDT services at a rapid pace. In March 2013, India completed geographical access to PMDT services in all 35 states across 692 districts covering 100% population of 1227 million with 80% access accelerated in 2011 and 2012 compared to early years 2007–2010 (Table). 78 DR TB centres functional with airborne infection control measures. 47 culture DST labs including 36 labs offering LPA and 30 sites offering GeneXpert assay. As on December 2012, a cumulative total of 144688 MDR-TB suspects were offered DST and 21036 lab-confirmed Rif-resistant cases as well as 131 lab-confirmed cases of XDR-TB were initiated on treatment. Programme reviews identified delays in laboratory capacity development, disbursement of funding, and human resources and training as key expansion constraints.

Table Enhancements in PMDT services in 2011–2012 compared to status up to 2010 in India

| Indicator	2007-10	2011-12	Enhancements in 2011-12 (in folds)
Culture-DST Labs (with WRD)	19	47	28 (1.5 folds)
Culture –DST Labs with LPA	4	36	32 (8 folds)
WRD – Xpert-MTB-Rif Sites	0	30	30
States with 100% geographical coverage of PMDT	2	35	33 (16.5 folds)
Districts implementing PMDT services	141	692	551 (4 folds)
Population (in millions) with access to PMDT services	288	1227	939 (3.3 folds)
DR TB Centers functional	20	78	58 (3 folds)
Cumulative MDR TB suspects tested	20965	144688	123723 (6 folds)
Cumulative MDR TB cases diagnoses	6046	27795	21749 (4 folds)
Cumulative MDR TB cases put on treatment	3610	21036	17426 (5 folds)
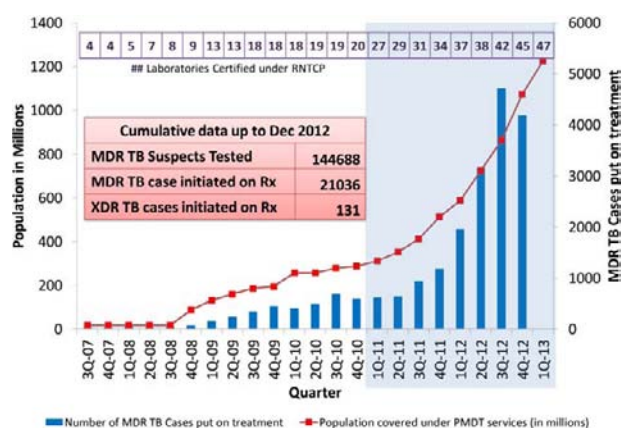
Figure Population in India covered under PMDT services, labs certified and MDR-TB cases put on treatment.

Discussion: Ambitious national PMDT scale-up plans appropriately backed up with financial and technical resources build within the larger TB control initiatives, synergized and executed through a centrally well-coordinated sustained effort in operational planning, implementation and monitoring to promptly address implementation bottlenecks has been the key to successful achievement of nationwide scale up of PMDT services in India and a good lesson to share.

PC-909-03   Is there is an association between delayed MDR-TB initiation and distance to treatment initiation sites in KwaZulu-Natal, South Africa?

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Background: Multidrug-resistant (MDR) tuberculosis (TB) has shown increasing trends in South Africa with an average increase of 16% per annum between 2004 and 2010. Local studies have shown that the mean initiation time at a centralised hospital in KwaZulu-Natal (KZN) was 12.4 weeks, above the accepted rate of 6–8 weeks. The National Department of Health established decentralised MDR-TB treatment initiation centres in 6 hospitals in the province in an effort to reduce treatment delay.
Aim: To evaluate the association between distance of the diagnostic sites from the treatment initiation sites and MDR-TB treatment delay in KZN.
Design/methods: A cross-sectional study was undertaken at decentralised MDR-TB initiation centres in KwaZulu-Natal. MDR-TB patients were identified from registers and an analysis was conducted to determine the distance between the diagnosing facilities and the treatment initiation sites. Treatment delay was measured from the date of the first sputum taken until treatment initiation. Demographic factors like age and gender were assessed.
Results: Data was collected for 365 MDR-TB patients at four treatment initiation facilities in KwaZulu-Natal during a six month period from October 2011 to March 2012. The median distance that patients had to travel to initiate treatment was 50.8 km (IQR 11.2–78.5 km). The median time between the first specimen taken and treatment initiation was 86 days (IQR 58–109 days). There was no association between distance of the diagnosing facility from the initiation centre and treatment delay ($r = 0.0334$, P value 0.5344).

Variable		N (%)	Median distance (IQR)	Median TCT (days) (IQR)
Treatment initiation facility	Hospital A	78 (21.37%)	19.5 (10.2 – 8.7)	86 (55-110)
	Hospital B	99 (27.12%)	50.8 (0 – 88.6)	83.5 (55-106)
	Hospital C	79 (21.64%)	22.9 (13.6 – 49.6)	84 (64-109)
	Hospital D	109 (29.86%)	58.6 (55.3 – 89.2)	91 (50-120)
	Total	365	50.8 (11.2 – 78.5)	86 (58-109)
Gender	Male	165 (45.21%)	49.6 (10.8-71.7)	85 (56-110)
	Female	199 (54.52%)	50.8 (11.2-88.6)	86 (60-108)
Age	0-15 years	4 (1.10%)	0 (0-25.4)	45 (6 - 121.5)
	16-25 years	61 (16.71%)	45.7 (11.2-58.6)	87 (64 - 107)
	26-35 years	144 (39.45%)	50.8 (11.2-88.6)	85 (57 - 110)
	36-45 years	89 (24.38%)	49.6 (6.2-65.5)	91 (50 - 109)
	46-55 years	42 (11.51%)	53.05 (13.6-88.6)	86 (64 - 104)
	>56 years	25 (6.85%)	58.6 (43.4-88.6)	91 (67 - 119.5)
	Mean (SD)	35.66 (12.29)		

Conclusion: Results indicate that there is no significant association between the distance of the diagnostic centres from the initiation centres and treatment delay. A limitation of the study is that the distances from the patient's home to the diagnostic and treatment centres have not been assessed. Other patient related factors influencing delay have also not been assessed.

The median treatment delay of 86 days is unacceptably high. Other health system factors including facility staffing and the presence of TB tracing teams are being evaluated to determine their impact. Health system factors that contribute need to be identified and addressed to maximise the impact of newer, more rapid tests.

PC-910-03   Innovative project of home-based care and support to MDR-TB patients to reduce default rate in three urban areas of New Delhi

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Background: TB Research Centre and National TB Institute reported MDR-TB prevalence levels between 1%–3% in new cases and around 12% in re-treatment cases. PMDT was rolled out in Delhi in 2009 and there were 4 DOTS plus sites in Delhi. PMDT guideline suggests 10 days pre-hospitalisation of all MDR TB patients at DR site in medical college. The goal of new innovative project was reduction in the morbidity and mortality in drug-resistant TB patients with approach of home base care and support. The project started from July 2011 in 3 Chest Clinics with a population of 1.6 million in New Delhi.
Intervention: The two teams, each consisting of a trained counselor, and a nurse after due training in DOTS plus and under guidance of one trained District Medical Advisor provided the home based care and support. Enrolled Patients were visited fortnightly in IP phase and monthly in CP phase. The counseling components included initiation of MDR TB treatment, essentials of MDR treatment, identification of ADRs of treatment and appropriate referral, contact screening, nutrition, promotion of infection control at household-family-community settings and awareness of existing social welfare schemes. The team facilitated coordination between the patient, caregiver, DOT provider, local practitioner, DTO and STO office.
Results: Total 326 MDR-TB patients enrolled in the project during the time span of 21 months (1 July 2011 to 31 March 2013) from 3 selected areas. Interim report of the project suggest that, Out of total 326 patients enrolled, 14 patient has completed the treatment (cured), 7 patient (2.1%) defaulted, 13 patient (3.9%) died, 7 patient (2.1%) failed treatment, 1 transfer out during treatment and 284 (87.1%) are still on treatment till end of March 2013. The PMDT

progress report of Delhi state (TB India 2012 report) suggested that out of total enrolled patients, 13% died, 27% defaulted, 1% failed treatment and 53% had success rate. In comparison to state data, home based intervention has 2.1% defaulter rate and 3.9% death rate which are significantly lower.
Conclusions and key recommendations: Home based care and counseling is one of the vital components in addition to MDR TB treatment. The significant lower defaulter rate and death rate shows positive outlook of the patients in project area. Although project is interim stage at present, home based counseling is useful to reduce the default rate and death rate among MDR TB patients.

PC-911-03   e-SMARTS—electronic surveillance and management of drug-resistant tuberculosis system: an innovative approach to better patient management in India

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Background: The Revised National TB control Programme–India faces large scale, reporting and recording challenges for the estimated 99 000 multidrug resistant TB (MDR-TB) cases. The current recording system is paper based and reporting system, although electronic, is based on aggregated data, reported quarterly, and thus is neither appropriate for patient-based management, nor efficient for real-time action. We describe an innovative web-based electronic surveillance system (Electronic Surveillance and Management of drug Resistant Tuberculosis System [e-SMARTS]) to record, report, and monitor patient-level data of drug resistant tuberculosis cases in Andhra Pradesh, India.
System design: Demographic and clinical information of presumptive MDR-TB patients who submitted sputum samples at microscopy centers were entered via Android TM mobile phones into a centralized online database. Samples were then transported to laboratories for culture and drug susceptibility testing (DST). Real time laboratory results were communicated to the treating physician and other programme staff via system generated emails and SMS (short messaging services). Following this, the MDR-TB patient was referred for treatment initiation to designated Drug Resistant TB Centres (DRTCs). An electronic treatment card was initiated for each patient and was referred back to the periphery for

ambulatory Directly Observed Treatment (DOT). Information on drugs consumed, follow-up culture examinations and other details are updated electronically at all levels of care.

Results: During October–March 2013, 2833 presumptive DR-TB cases (95% of total) were registered via e-SMARTS. Of these, 2702 (95%) were tested for culture and DST. All results were communicated automatically via electronic messaging; including, ~10 802 real-time SMS notifications to 24 programme staff. Of 279 (10%) MDR-TB cases detected, 240 (86%) had treatment initiation details entered at DRTC, and real-time updating of 170 treatment cards of patients on ambulatory DOT is in progress.

Conclusion: e-SMARTS increased data accessibility, promoted data sharing and improved programme efficiency. The main advantage of this electronic web-based system was real-time data sharing at all levels, reduction of paperwork and decreased errors due to data transcription and duplication. Further research is required to assess the impact of programmatic implementation and cost-effectiveness before wider scale-up.

PC-912-03   Implementation of e-TB manager in Indonesia improves national reporting quality and supports informed decision making for tuberculosis control

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Background: In 2011, Indonesia ranked ninth among the world's 27 countries with the highest prevalence rate of multidrug resistant TB (MDR-TB). The National Tuberculosis Program (NTP) began to address this challenge in 2009 by implementing the e-TB manager, a web-based tool developed by Management Sciences for Health (MSH) through the USAID-funded program, Strengthening Pharmaceutical System (SPS). Because e-TBM is used to track MDR-TB cases and manage MDR-TB pharmaceuticals in real-time for improved data quality, the NTP asked its partners to implement this tool as part of their programs. In response, the USAID-funded TB Control Assistance Program (TB CAP) program and the follow-on, TB CARE I, implemented e-TBM at nine TB treatment sites in eight provinces. Since 2009, the staff at these facilities have entered approximately 48 000 transactions into the platform.

Response: To implement e-TBM, the NTP and its partners designed a work plan and established an e-TBM workgroup. This work group customized the e-TBM system to fit Indonesia's needs, hired staff to support the implementation, and equipped the implementing facilities with computers and internet con-

nections. The workgroup then trained over 200 staff involved in health system monitoring and evaluation at the province, district, and health unit levels. Staff learned to use the e-TBM for entering data on MDR-TB suspects screened, patients diagnosed with MDR-TB, and variables linked to MDR-TB treatment (follow-up exams, treatment details and adherence, side effects of medicines, commorbities, etc). Staff at over 30 health units within the nine treatment sites also learned to enter monthly data on their second line TB medicines' stock and usage rate.

Results: According to official reports from 2009 to 2012, the trained staff entered 96% (3976/4150) of all screened MDR-TB suspects and 86% (713/830) of all patients who had been diagnosed with MDR-TB into e-TBM. The NTP used this data to accurately evaluate the growing number of MDR-TB cases and drug supply needs to inform national TB program planning and pharmaceutical procurement.

Conclusion: Implementation of e-TBM in Indonesia has allowed the NTP to effectively monitor health units' MDR-TB data at the province, district, and health unit levels. Real time access to all MDR-TB case data and pharmaceutical supply information has equipped the NTP to develop timely and informed strategic decisions and corresponding interventions.

PC-913-03   Anti-tuberculosis drug resistance among new and previously treated pulmonary tuberculosis patients in Benin

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Background: Drug resistance is an increasing phenomenon generally due to ineffective/suboptimal tuberculosis (TB) -control programs. Therefore, the level of drug resistance is an indicator of the performances of a national TB program. This level is generally assessed by a national drug resistance survey. In Africa, only a few countries have conducted an anti-TB drug resistance survey. In the West African country of Benin, a first drug resistance survey was conducted in 1994–1995. This survey showed a low level of resistance (0.3% multiresistance rate in new cases). However, the survey was conducted in 4 of 6 regions of the country. Furthermore, a six-month-regimen has been adopted in the country since 2007, with now rifampicin during the whole TB treatment for new cases.

Setting: Centers for diagnosis and treatment in all of the six regions of Benin.

Objective: To assess the current level of antituberculosis drug resistance in Benin.

Methods: A prospective study was conducted from 23 February 2009 to 1 January 2010. A total of 450 strains were obtained from smear-positive patients: 405 new cases and 45 previously treated cases.

First-line drug susceptibility testing (DST) was performed for all strains. All MDR (multidrug resistant) strains were tested with second-line DST.

Results: Of the 405 *Mycobacterium tuberculosis* isolates from new cases, 92 (22.8%) were resistant to at least one first-line drug; among them 02 (0.5%) were MDR; all these two patients lived in neighbouring countries of Benin. Of the 45 previously treated cases, 23 (22.2%) were resistant to at least one first-line drug and 6 (13.3%) were MDR. All MDR isolates were susceptible to all second-line drugs tested: no extensively drug resistant (XDR) strain was detected.

Conclusion: In Benin, MDR rate in new cases, as well as in previously treated cases, remained low since 1994–1995.

PC-914-03   Poor use of audiometry screening for hearing loss among drug-resistant tuberculosis patients receiving second-line injectable agents in Khayelitsha, South Africa

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Background: Drug-resistant tuberculosis (DR-TB) treatment includes an injectable agent (aminoglycoside, capreomycin) associated with ototoxicity and potentially permanent hearing loss. Routine screening to detect early onset hearing loss is recommended by WHO and others. Although early detection should enable intervention to prevent progression to permanent deafness, there is scant guidance on protocols and no programmatic evidence from high burden settings. We aim to describe utilization of a hearing screening service and document lessons learned for future programmatic implementation.

Intervention: As part of a decentralized DR-TB programme, a clinic-based audiometry service was established in 2009 to provide baseline and monthly screening to all patients from 10 primary care clinics. A sound-proof booth and a pure tone audiometer were used for air-conduction screening only. Tests were conducted by an audiologist-trained, lay person who recognized abnormal test results necessitating clinician evaluation, and subsequent referral for diagnostic audiology.

Results: Between June 2009 and December 2012, 1816 separate screenings were conducted. However, in 2009–2010 only 54% of required screenings were conducted among 239 patients. Only 24% (58/239) of patients had a baseline screen (<1 week treatment). This increased only slightly to 33% among 317 patients in 2011–2012, after a simplified referral process, improved patient education and financial enablers were implemented. Lack of a baseline screen resulted in difficulty assessing hearing loss as new or pre-existing, while inconsistent screening led to failure to detect early hearing loss and act on this. In addition to poor service utilization, poor access to centralized diagnostic audiology led to difficulties in confirming sensorineural loss.

Conclusions: These data suggest that a local screening service is insufficient in itself to maximize utilization. Greater efforts to train staff and counsel patients on the need for hearing screening and the risk of potential deafness, along with efforts to identify other potential barriers to service access are required. In addition, referrals between health services, including access to diagnostic audiology, require streamlining in order that valid baseline hearing screens can be obtained without delaying treatment initiation.

PC-915-03   Formation of MDR/XDR-TB indicators in the North-West District of Russia

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Background: Region of North-West District (NWD) show highest level of MDR-TB in Russia. Evaluation of the MDR-TB trend and probability of XDR-TB development among MDR-TB in this region is the important TB control challenge in the country.

Design/methods: All drug susceptibility tests (DST) results, provided before treatment, for 3754 new TB cases (NC) registered in 2010–2012 and 320 relapses (R) registered in 2011–2012 from 6 territories of NWD using national routine TB surveillance and laboratory reports were analyzed. Selected territories meet requirements for data representativeness and quality of WHO class A for drug resistance surveillance systems. First line drugs, fluoroquinolone (FqR-TB) and injectable second-line drugs (ISLDR-TB) resistance were analyzed.

Results: After years of gradually growth, MDR-TB trend showed stabilization and decrease ($P > 0.05$) in 2011–2012: from 29.6% to 28.6% for NC, and from 61.9% to 55.0% for R.

NC with MDR-TB contained (2010–2012, 6 territories) 36 cases of XDR-TB—3.4% (95%CI 2.4–4.7) and 24.5% (21.9–27.2) of pre-XDR-TB, which is MDR-TB plus FqR-TB cases—3.1% (2.2–4.3) and MDR-TB plus ISLDR-TB cases—21.4% (19–24). Levels for R (2011–2012, 5 territories) were 7.4% (4.1–12.1), 31.7% (25.2–38.9), 5.3% (2.6–9.5) and 26.5% (20.3–33.4), correspondingly.

ISLDR-TB only component of MDR-TB has growth during the last two years both for NC and R.

FqR-TB for NC was 1.9% (1.5–2.4) including 54.2% (42–66) non MDR-TB cases. Levels for R were 7.5% (4.9–11) and 58.3% (36.6–77.9), correspondingly.

ISLDR-TB for NC was 7.7% (6.9–8.6) including 21.7% (17.1–26.9) non MDR-TB cases. Levels for R

were 20.9% (16.6–25.8) and 25.4% (15.5–37.5), correspondingly.

Only one oblast of NWD (Arkhangelsk) showed relatively low non MDR-TB components both for FqR-TB and ISLDR-TB which can be seen as relatively low: 30.8% (9.1–61.4) and 16.2% (6.2–32) for NC and 14.3% (0.4–57.9) and 6.7% (0.2–32) for R, accordingly.

Conclusion: Growth of MDR-TB level in NWD has stopped last years. However, MDR-TB structure analysis showed the probability of XDR-TB level increase as a result of pre-XDR-TB amplification, on condition of insufficient TB treatment control.

The perceptible portions of non MDR-TB among FqR-TB and ISLDR-TB cases reflect possible using of second line drugs for treatment of not-MDR-TB cases in NWD territories in the past, which can be source of increase of MDR/XDR-TB in the future for separate territories.

PC-916-03 Cost of multidrug-resistant tuberculosis diagnosis and treatment in the Netherlands

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Background: The cost of diagnosis and treatment of tuberculosis (TB), and in particular of multidrug-resistant (MDR) TB, are high. Ten years ago these costs were estimated 9500 euro per TB case and US$60 000 for treatment of a MDR-TB patient in the Netherlands. We studied these costs in 2009.
Methods: Data on TB and MDR-TB cases were obtained from the Netherlands Tuberculosis Register. Hospital admission days for TB cases were available in the Dutch Hospital Data. Admission days and duration of treatment of MDR-TB cases were also retrieved from patient records of the two TB treatment centers in the Netherlands. The costs of hospitalization days and for most TB drugs were available by the Health Care Insurance Board (CVZ). Clinical pharmacologists of the two TB treatment centers provided cost information on second-line TB drugs not available by CVZ.
Results: Twenty MDR-TB patients were diagnosed in the Netherlands in 2009, of which three had extensively drug-resistant (XDR-) TB and 1138 patients were notified with non-MDR-TB. MDR/XDR-TB patients were hospitalized on average for 109 days and treated for 464 days. The average cost for diagnosis and treatment of an MDR/XDR-TB amounted to

€58 568 (hospitalization costs €37 026; medication costs €17 370 and other costs such as follow-up and support €4127). For non-MDR-TB the average cost per patient was €7854 (hospitalization costs €5,848; medication costs €465 and other costs €709). The medication costs forMDR/XDR-TB were 37 times higher than for non-MDR-TB patients.

The average cost per MDR-TB patient was €44 250 and €139 500 for a XDR-TB patient. However, the highest cost for a XDR-TB patient, who was treated for 24 months and admitted for 1 year, amounted to €207 400.
Conclusion: The cost of diagnosis and treatment of a TB case is high and rises sharply with increased drug-resistance of the causative *Mycobacterium tuberculosis*. In the Netherlands, with relatively few MDR/XDR-TB cases (less than 2%) the MDR/XDR-TB diagnosis and treatment costs amounted to 12% of the total costs for TB diagnosis and treatment [Data not shown]. The cost for a MDR-TB patient was 6 times higher than for a non-MDR-TB case; for XDR-TB patients these costs were 18 times higher. To reduce the cost for MDR/XDR-TB treatment, hospitalization should be limited, (expensive) second-line TB drugs should be procured efficiently and when possible (e.g., through therapeutic drug monitoring) used more cost-effectively.

PC-917-03 Drug-resistant tuberculosis treatment costs through Global Drug Facility vs. private market prices: comparison analysis

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Four major second-line drugs account for 80% of a standard regimen and its costs (PAS products combined [sodium and acid formulations], cycloserine, kanamycin and capreomycin). In recent years levofloxacin, the most widely used fluoroquinolone, has also played a driving role in the regimen cost for MDR-TB treatment.

Recent evaluation, based on comparison between GDF and IMS health data, indicates that the cost of quality assured treatments for MDR-TB provided by GDF is consistently lower than the private market retail cost of treatment of unknown quality, supplied globally and in key countries.

While private SLD prices have historically been very high, an interesting convergence in recent years with GDF prices can be observed, possibly due to increasing numbers of patient treatments supplied by GDF.

This analysis was conducted for both high- and low-end MDR-TB treatment regimens. The price dfference for low-end SLDs has been driven largely by cycloserine and, in later years, levofloxacin. For

high-end regimen, capreomycin and PAS also played a significant role in the pricing difference.

Conclusion: GDF in recent years has become a major player in SLD treatment deliveries and is influencing the global trend towards price reduction in the broader market for MDR-TB treatments worldwide, including private markets.

PC-918-03   How to improve ownerships from sub-national level to support nationwide PMDT rapid expansion in Indonesia

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Background: NTP Indonesia had develop national PMDT action plan for 2010–2014 which aim to establish at least one PMDT treatment centers in 33 provinces by end of 2014. Due to several bottlenecks including centralized approach for treatment center selection, the expansion plan was delayed by 2 years, when only 9 treatment centers at 8 provinces has been established until December 2012.

Methods: PMDT treatment centers were selected after a small team from NTP and National PMDT working group visited to the provinces and made assessment for selection. The process was vulnerable to the availability of assessor team. More over the assessment results always consider as central level choice and create a lack of ownership from provincial health office. To speed up the process and to increase ownership, NTP decide to decentralize the approach. Provincial Health Office has role and responsibility to select PMDT treatment center in their owned area, utilize a standard self assessment checklist developed by National PMDT WG. The checklist consists of 9 groups of conditions and requirements that proven very essential to ensure the establishment of new PMDT treatment centers. The data collected by this checklist also utilize to identify gaps that should put under consideration before preparation process started. The summary of this checklist put in a scoring system that could be used if there are several candidates should be selected.

Results: By end March 2013, 19 additional provinces successfully conducted the self assessment and sites selection process which catch up the target for 2013. The progress was allow NTP to continued the preparation process to the next steps such as training, site renovation, etc. NTP also identify the different needs from each provinces and provide assistance to develop provincial specific work plan for PMDT implementation based on basic information and needs. With this improvements, NTP were confident enough to achieve national coverage by end of 2014.

Conclusion: NTP should look after a breakthrough when faced bottlenecks or stalemate conditions. The

national expansion plan need support from sub-national health authorities. Strong leaderships and stewardships from central level are essential in the area where decentralization system are implemented.

PC-919-03   Clinical impact of MTBDR*plus* implementation on MDR-TB treatment initiation and culture conversion in the country of Georgia

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Background: The MTBDR*plus* assay accurately detects the presence of isoniazid and rifampicin resistance and has been endorsed by the World Health Organization for use on AFB positive sputum specimens; however there is limited data on its clinical impact.

The Georgian National Tuberculosis Program (NTP) validated the MTBDR*plus* assay in 2009 and subsequently implemented into clinical practice in late 2010. We sought to determine the impact of MTBDR*plus* implementation on the time to multidrug-resistant-tuberculosis (MDR-TB) treatment initiation and time to culture conversion.

Design/methods: Retrospective analysis of AFB sputum smear positive MDR-TB patients treated at the National Center for Tuberculosis and Lung Disease hospital in Tbilisi, Georgia between 2009–2012. All patients had MDR-TB confirmed by both DST and MTBDR*plus* results. Time to treatment initiation was defined as MDR-TB treatment start date—initial sputum collection date and was compared in the pre (2009–10) and post (2011–12) MTBDR*plus* implementation period.

Results: Among 168 MDR-TB patients, 66 (39%) and 102 (61%) were from the pre-and post implementation period, respectively; 74 (44%) were new TB patients and 94 (56%) had a prior history of TB treatment. The mean time to MTBDR*plus* results was 4.6 days. Among all patients there was no significant difference between the time to MDR-TB treatment initiation in the pre and post implementation periods (29.5 vs. 25.4 days, $P = 0.18$, respectively). Among new TB patients, MDR-TB treatment was initiated significantly earlier in the post vs. pre MTBDR*plus* implementation period (24.5 vs. 38.8 days, $P < 0.01$, respectively). Among 58 patients (34%) with complete culture data there was a non-significant trend towards earlier sputum culture conversion among patients in the post vs. pre MTBDR*plus* implementation period (117 vs. 80 days, $P = 0.12$, respectively).

Conclusion: Implementation of MTBDR*plus* reduces time to MDR-TB treatment initiation among new TB patients and may help decrease time to culture

conversion. Further operational research on increasing clinical uptake and acceptance of MTBDR*plus* assay results is needed.

PC-920-03   Multidrug-resistant tuberculosis in Bulgaria: results of a nationwide survey, 2010

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Background: In 2009, Bulgaria started treating tuberculosis (TB) patients who had in vitro resistance to, at least, rifampicin and isoniazid (multidrug-resistance; MDR-TB) following internationally-recommended norms for second-line anti-TB regimens. To better plan for future needs, the Ministry of Health decided to undertake a first-ever direct measurement of drug-resistance prevalence among a representative sample of TB patients presenting to public health-care facilities and prisoners.

Methods: A nationwide survey based on 100% sampling of pulmonary sputum smear positive TB cases was completed during 2010. Sputum samples were tested for resistance to isoniazid and rifampicin using Geno Type MTBDRplus. MDR-TB cases were tested for added resistance to fluoroquinolones and second-line injectable drugs (extensive drug resistance; XDR-TB).

Results: A total of 563 patients—482 new and 81 previously treated—were enrolled in the survey. The male to female ratio was 3:1 and median age 40 years (IQR 31–52.5 years). MDR-TB was detected in 2.1% of new (95% confidence limits: 1.0–3.8%) and 11.1% of previously treated (95% CLs: 5.2–20.0%) cases. One XDR-TB case was detected. At multivariable analysis, only previous history of anti-TB treatment was associated with MDR-TB (adjusted odds ratio = 6.5; 95% CLs = 2.5–16.8).

Conclusion: The survey showed moderate levels of MDR-TB and documented one XDR-TB case in Bulgaria. At this level of resistance, about 40 MDR-TB cases could be detected each year if all laboratory-confirmed TB cases notified nationally received drug-susceptibility testing (DST). DST should be available for all previously treated TB patients and, if possible, all other TB patients, and coupled with the prompt initiation of treatment of MDR-TB patients.

FINDING, SCREENING AND RECORDING CASES OF DRUG-RESISTANT TUBERCULOSIS

PC-921-03   Do we need to detect isoniazid resistance in addition to rifampicin resistance in the next generation of molecular diagnostics for tuberculosis?

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Background: Multidrug-resistant tuberculosis (MDR-TB) is resistant to both rifampicin (RIF) and isoniazid (INH). Whereas many TB diagnostics detect RIF-resistance, few detect INH-monoresistance, which is common and may increase risk of acquired MDR-TB. An important question is therefore whether 'next-generation' molecular diagnostics should include testing for INH resistance.

Methods: We developed a transmission model to evaluate the incremental impact of INH resistance testing in a population similar to that of India. We allowed for an incremental increase of drug resistance prevalence since the widespread use of anti-tubercular therapy. We considered three tests: a rapid molecular test for TB, the same test plus RIF-resistance detection ('TB+RIF'), and the same plus detection of RIF and INH-resistance ('TB+RIF/INH'). Our primary outcome was the prevalence of INH-resistant and MDR-TB at ten years.

Results: Compared to the TB test alone and assuming treatment of all diagnosed MDR cases, the TB+RIF test reduced the prevalence of MDR-TB among all TB cases from 5.5% to 3.7% (29% reduction, 95% uncertainty range, UR: 17–52%). Despite using liberal assumptions about the impact of INH-monoresistance on treatment outcomes and MDR-TB acquisition, expansion from TB+RIF to TB+RIF/INH lowered this prevalence only from 3.7% to 3.5% further (4% reduction, 95% UR: 3–7%) and INH-monoresistant TB from 15.1% to 15.7% (4% reduction, 95% UR: (−4) −18%). The projected incremental impact of testing for TB+RIF/INH was not qualitatively changed in scenarios that considered INH-monoresistant TB to be equally transmissible to wild-type, under-reporting INH-monoresistant TB by a factor of two, or doubling of MDR-TB prevalence over ten years (e.g., through compensatory mutation).

Conclusion: When added to a rapid test for TB plus RIF-resistance, detection of INH-resistance has minimal impact on transmission of TB, MDR-TB, and INH-monoresistant TB.

PC-922-03 Xpert® MTB/RIF efficaciously shortens airborne infection isolation duration in individuals with presumptive tuberculosis hospitalized in North Carolina

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Background: In the United States the CDC recommends that individuals with presumptive TB are placed in airborne infection isolation (AII) and assessed by 3 respiratory specimens 8–24 hours apart with smear microscopy and culture. Xpert MTB/RIF (Xpert) may be faster and more reliable method than smear microscopy to determine which patients can be discharged from AII.

Design/methods: We prospectively enrolled inpatients with presumptive TB. Smear microscopy was performed daily 5 days/week; Xpert was performed on direct specimen, twice daily 5 days/week. Clinicians were blinded to Xpert results. AII duration was determined based on results of smear microscopy and clinical findings. The observed AII duration was abstracted from electronic order entry, medical records, and laboratory result times. The estimated AII time based on Xpert results was calculated using the actual test time for weekdays and a theoretical test time of once daily on weekends (to reflect future standard protocol).

Results: We collected at least 1 non-bronchoscopy sputum specimen in 177 hospitalized patients. Of these, 23 were not suspected of active TB and were excluded (5 exclusions had non-tuberculous mycobacteria; none were diagnosed with TB). Among the 154 subjects included in the analysis, the median age was 53, 38.1% were female. Five subjects had culture positive TB. One culture positive case was negative for both smear microscopy and Xpert on the first sample. All TB cases were smear and Xpert positive. Xpert also correctly identified 1 case with rifampin-resistance. Median observed AII duration was 68.9 hours (IQR 47.1, 98.3). The median estimated AII duration based on Xpert results was 20.6 (IQR 16.8, 32.0) for the first sample, 39.6 (IQR 25.7, 50.6) for two samples, and 53.7 (IQR 42.7 83.7) hours for 3 samples (Figure). Using liquid culture as the gold standard, the sensitivity was 92.3% (64, 99%) for smear and 100% (74, 100%) for Xpert. The specificity was ≥99.5% (98, 100%) for both smear and Xpert.

Conclusion: In this low TB-burden setting, Xpert testing on 1, 2, or 3 samples dramatically shortened the duration of AII compared to the current recommended smear-based strategy while maintaining diagnostic efficacy. In our population, Xpert with 2 samples captured all TB cases, including one subject with rifampin-resistance later found to be MDR-TB. If validated, these results could impact CDC policy regarding AII for hospitalized patients with presumptive TB.

Figure Duration of airborne isolation for Xpert vs. smear.

PC-923-03 Molecular genetic analysis of primary drug resistance in *Mycobacterium tuberculosis* in patients with disseminated pulmonary tuberculosis

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Aim: To study prevalence of mutations in genes *kat*G, *inh*A, and *ahp*C and *rpo*B, coding drug resistance (DR) to isoniazid (INH) and to rifampicin (Rif) in patients with disseminated tuberculosis.

Materials and methods: Before start of treatment were study 100 patients with newly diagnosed active pulmonary tuberculosis. The patients divided into 2 groups depending on the clinical form. In group 1 included 44 patients with disseminated tuberculosis, in 2, control group—56 patients with infiltrative pulmonary tuberculosis. In all patients, the definition of DR *M. tuberculosis* (MBT) to INH and Rif, and analysis of DNA mutations was carried with biological microchips. Technology research, sets of reagents and equipment were developed of Institute Molecular Biology, Moscow.

Results: DNA of MBT was detected in 32 (72.7%) patients in group 1 and in 46 (82.2%) patients in group 2. Frequency MBT, having a mutation in the genes *rpo*B, *kat*G, *inh*A and *ahp*C, encoding multidrug resistance (MDR) not significantly different in patients with disseminated—10 (31.3%) and infiltrative tuberculosis—13 (28.3%), *P* > 0.05. In both groups, there was approximately equal to the frequency of mutations in gene *kat*G-12 (37.5%) in
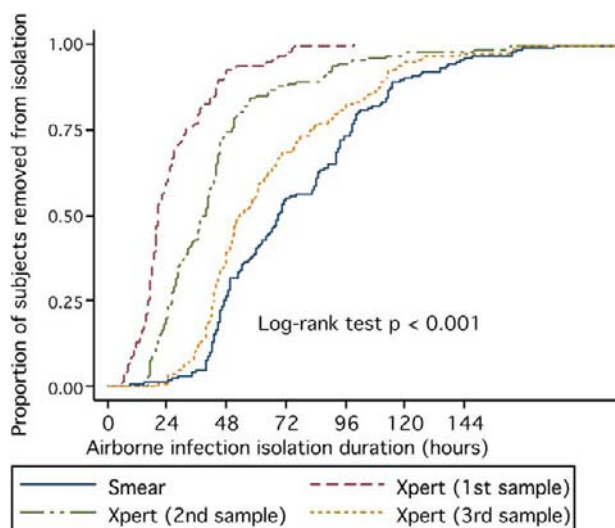
group 1 and 20 (43.5%) in group 2, $P > 0.05$, in the gene *ahp*C—3 (9.4%) and 1 (2.2%), respectively, $P > 0.05$. However, it was found significant excess of mutations in gene inhA, encoding DR to INH in 13 (40.6%) patients in group 1 vs. 7 (15.2%) patients in group 2, $P = 0.0136$. No were significant differences in the frequency and spectrum of genetic mutations in the gene *rpo*B, coding the DR to Rif, frequency of mutations in this gene were 26 (81.3%) in group 1 vs. 33 (77.1%) in group 2, $P > 0.05$.

Conclusions: In patients with disseminated pulmonary tuberculosis is observed a high level of primary MDR—31.3%, which is not significantly different from patients with infiltrative tuberculosis. In patients with disseminated tuberculosis was significantly more frequently observed mutations in gene inhA.

PC-924-03 Pre-entry tuberculosis screening of migrants to low incidence countries: a systematic review

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Background: Pre-entry screening of migrants for tuberculosis (TB) has been taking place for over a decade and participation is a visa requirement in several low incidence countries. The evidence base for pre-entry screening programmes has yet to be established across populations, countries and sites; the aim of this review was to synthesise the published literature on this topic.

Methods: The following sources were searched to identify publications on this topic (1980–2013): Medline, EMBASE, LILACS, Cochrane Infectious Diseases Group Specialized Register, Cochrane Library, Conference Proceedings Index. Inclusion criteria were: experimental study, observational study or systematic review; studies screening migrants, asylum seekers, foreign-born citizens or undocumented migrants; abstracts and full articles published in English; screening for TB by any method, but occurring prior to migration; migration from high to a low incidence country (<40 cases per 100 000 population). The primary outcome for the study was yield of the pre-entry screening programme (independent of method) for TB infection or disease. EPPI Reviewer was used to manage the review. Two reviewers independently screened titles, abstracts, and full text publications against the inclusion criteria.

Results: A total of 1802 publications were identified. After de-duplication and review against inclusion criteria, data were extracted from 19 studies. Two further studies were excluded as they contained dupli-

cate data. 14 studies contained data on screening for active pulmonary disease on a total of 3 758 924 individuals who migrated between the years of 1982–2010. The yield of screening for active TB ranged from 0.0–10.2%. A variety of methods were used for screening, with the majority of included studies using chest radiography. Data were available for migrants to the USA, Australia, Canada and Israel. Three studies published data on screening for latent TB infection, using different screening protocols, with yields varying from 1.6% to 62.4%.

Conclusion: In published studies, pre-entry screening for TB of migrants to low incidence countries has varying yield. Further work should be carried out to identify additional unpublished data and factors associated with yield of screening. International collaboration between countries has the potential to harmonise procedures.

PC-925-03 Pattern of drug resistance in tuberculosis patients treated at a DR-TB unit in a tertiary care public sector hospital in Karachi, Pakistan

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Background and challenges to implementation: Pakistan ranks fourth globally in MDR-TB. Empirical 2nd line treatment is started on the bases of rifampacin resistance diagnosed by GeneXpert. This regimen consists of 4 second line drugs including an injectable and fluoroquinolones (FQ).

Aims and objective: This study was done to observe the drug resistance pattern in DR-TB patients in order to rationalize the present empirical treatment regimen.

Intervention or response: Patients are registered. DST to first and second line drugs is sent before start of DR TB treatment. Results were recorded in DR-TB 01 form and analyzed by Microsoft excel and SPSS 16.

Results and lessons learnt: 795 DR-TB patients were registered in years 2010–2012. Males and female were 406 (51.1%) and 389 (48.9%) respectively. Mean age was 32.17 SD ± 13.46. Treatment failures of CAT1 were 40 (19.6%) and CAT2 were 156 (30.8%). Total treatment failures were 50.4%. After default, first line relapse and others were 5.0% 11.6% and 31.4%. Only 11 (1.4%) were new cases.

Resistance to four first line drugs was present in 80.6% (641) and to 1, 2, 3 and 5 first line drugs was seen in 8 (1%), 25 (3.1%), 79 (9.9) and 39 (4.9%).

Resistance to second line drug was present in 51%. FQ resistance was in 39.6%. Resistance to amikacin, capreomycin, ethionamide, kanamycin, ethionamide + kanamycin and FQ+ ethionamide was seen in 5, 12, 43, 20.11 and 7 percent respectively. FQ

resistance was 40.8% in 'Others' group. In new cases it was present in 36.4%.

Conclusions and key recommendations: Prevalence resistance to second line drugs especially FQ is high in our setting. FQ cannot be counted as effective drug. After stopping injectable we are left with only 3 effective drugs. Therefore in our setting empirical treatment should be started with 5 second line drug.

PC-926-03   Preventing tuberculosis in the foreign-born population of Canada: a mathematical modeling study

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Background: Foreign-born persons contributed 67% of all tuberculosis cases in Canada in 2011 while representing only 20% of the total population. Transmission of tuberculosis among foreign-born persons is relatively infrequent in low TB incidence countries and active cases primarily result from the progression of latent tuberculosis infection acquired prior to immigration. A proposed intervention to prevent this progression from infection to disease is evaluated using a deterministic mathematical model.

Methods: The intervention strategy is based on screening new immigrants for latent tuberculosis within the first year of arrival using the tuberculin skin test and, in those with a positive test, an interferon-gamma release assay. Positive reactors to both tests would be treated with nine months of daily isoniazid (standard treatment). Model validation is conducted retrospectively using data between 1986 and 2002 from Citizenship and Immigration Canada and the Canadian Tuberculosis Reporting System.

Results: Modeling indicates that targeting foreign-born persons who arrive from countries with tuberculosis incidence rates higher than 50 cases per 100 000 population is a cost-effective strategy. Assuming a treatment effectiveness of 75%, this strategy predicts that tuberculosis incidence rates would decrease from 5.4 to 4.6 cases per 100 000 person-years and would save $12 million in active tuberculosis treatment in the year 2002 had such a strategy been implemented in 1986.

Conclusion: Reducing foreign-born tuberculosis will ultimately have a positive impact on the health of immigrants with respect to tuberculosis, the national rate of disease, and can help meet the targets set by the National Tuberculosis Elimination Strategy in Canada and in other high-income immigrant receiving countries. The use of mathematical models combined with epidemiological information can provide useful insights into issues of public health importance such as the one described herein.
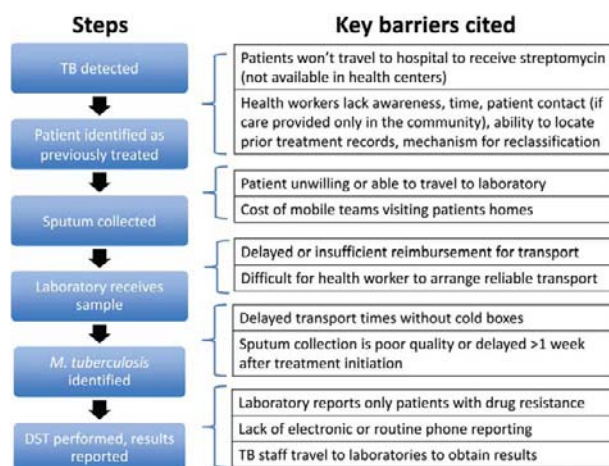
PC-927-03   Finding multidrug resistance in previously treated tuberculosis patients in Cambodia: mixed methods study of health worker and program staff views

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Background: In Cambodia, previously treated tuberculosis (TB) patients are a priority group for multidrug resistance (MDR) testing since their estimated prevalence is 8 times higher than in new patients. One study indicated that two thirds of smear positive previously treated TB patients had no drug susceptibility test results; reasons included sputum was not collected, did not reach the laboratory, or was culture negative. To identify areas for further intervention, this pilot study examines barriers and facilitators for MDR case finding in previously treated TB patients.

Methods: Routine TB case reports from 2010–2012 were analyzed to describe the epidemiology of previously treated patients across the 14 provinces that reported more than 1000 total TB cases annually. Sixteen in depth, qualitative interviews were conducted in April 2013 with staff from the national TB program, partner organizations, and two provinces selected for high and low performance of MDR testing in previously treated patients. The interviews, as well as a special session attended by 22 members of the Cambodia MDR-TB technical working group, aimed to elicit a range of opinions on barriers, facilitators, priorities, and recommended next steps. Interview transcripts and the workshop record were analyzed for common themes as well as those representing unique perspectives. The study was approved by the Cambodian National Ethics Committee for Health Research and the University of California, San Francisco Committee on Human Research.

Results: Previously treated patients as a proportion of all notifications in the 14 provinces ranged from

Steps	Key barriers cited
TB detected	Patients won't travel to hospital to receive streptomycin (not available in health centers)
Patient identified as previously treated	Health workers lack awareness, time, patient contact (if care provided only in the community), ability to locate prior treatment records, mechanism for reclassification
Sputum collected	Patient unwilling or able to travel to laboratory
	Cost of mobile teams visiting patients homes
Laboratory receives sample	Delayed or insufficient reimbursement for transport
	Difficult for health worker to arrange reliable transport
M. tuberculosis identified	Delayed transport times without cold boxes
	Sputum collection is poor quality or delayed >1 week after treatment initiation
DST performed, results reported	Laboratory reports only patients with drug resistance
	Lack of electronic or routine phone reporting
	TB staff travel to laboratories to obtain results

1% to 11%. Preliminary analysis of qualitative data suggests barriers across key steps to MDR detection (Figure). Recording, reporting, and monitoring were specifically cited as barriers contributing to multiple steps. Facilitators included permission to collect sputum without starting a retreatment regimen, eliciting patient history at multiple points during treatment, reporting results by phone, and Xpert MTB/RIF.

Conclusions: Improving identification and testing of previously treated patients would contribute to MDR-TB case finding and permit appropriate treatment. Barriers suggest strategies to build on current interventions to improve MDR-TB case finding. To follow this pilot study, a larger sample and patient interviews could inform a subsequent trial to evaluate phased implementation of a selected intervention package.

PC-928-03   Performance of IGRA among patients with tuberculosis in Denmark, 2005–2011

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Background: Persons with latent tuberculosis infection (LTBI) are at risk of developing active and contagious tuberculosis (TB). Identifying those at risk is a major challenge. In Denmark (DK), the QuantiFERON-test (QFT) has been used to screen for LTBI since 2005. The purpose of this study was to evaluate the performance of the QFT test in a Danish cohort focussing on the influence of age.

Methods: From 2005 through 2011, 16 133 persons were QFT-tested at the International Reference Laboratory of Mycobacteriology and 2347 cases were notified with TB to the Department of Epidemiology at Statens Serum Institut (SSI) in DK. From 12 165 consecutive QFT tests, the phytohaemagglutinin (PHA) values were available.

Results: Among 306 patients with culture positive TB and an available QFT result; 79% had positive, 16% negative, and 5% indeterminate results, resulting in a sensitivity of 83% after excluding indeterminate results. We found that the proportion of positive QFT declined significantly with increasing age (test for trend $P < 0.001$). In order to evaluate the influence of age on the overall test performance, we analyzed the PHA response in 12 165 persons. Individuals were stratified into age groups in relation to high or low PHA response (>10 or <10 IU/ml, respectively) and indeterminate rate (Figure). We found a significant influence of age ($P < 0.0001$); the proportion of patients with a PHA response >10 IU/ml was lowest in the youngest and oldest age groups (49% and 53%, respectively). The rate of indeterminate
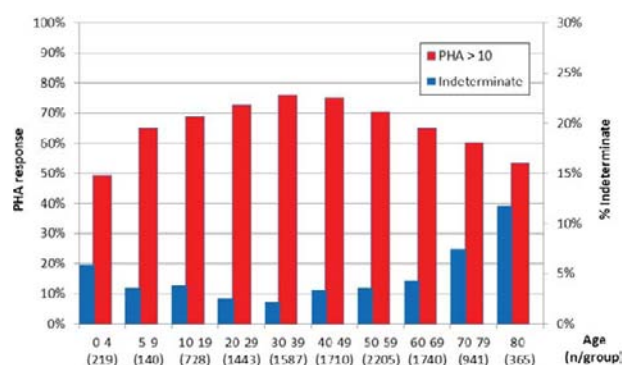
Figure Phytohaemagglutinin (PHA) value and rate of indeterminate QFT test according to age ($n = 12\,165$). Below the age group is stated the number of patients (n) for each age category.

QFT test results was inversely related to the PHA-response and also differed significantly between age groups ($P < 0.0001$), with the largest indeterminate rates found among the young and the elderly (5.9 and 11.8%, respectively).

Conclusion: In DK, an overall TB low incidence setting, the QFT-test sensitivity was 83%. The positivity rate declined with increasing age. Among 12 165 persons tested, there was a significant influence of age on the level of IFN-γ release and on the indeterminate rate. Our data are unique in representing a nationwide dataset from DK from 2005 through 2011 where the vast majority of QFT and all culture-based mycobacterial diagnostic tests were performed at one place in DK at SSI. In this large cohorte we confirmed a sensitivity of the QFT test of 83% and demonstrated significant influence of age.

PC-929-03   Intensified case-finding of MDR-TB cases in Cambodia

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Background: Globally, in 2011, only 19% of MDR-TB patients were diagnosed. Cambodia diagnosed MDR-TB just around 6–10% of the estimated cases from 2007 to 2011. The National Tuberculosis Program (NTP) of Cambodia launched ICF activities for MDR-TB in 2012.

Objective: To increase the number of presumptive MDR-TB patients eligible tested for MDR-TB.

Methods: In Cambodia, presumptive MDR-TB patients eligible for testing include (1) previously treated pulmonary TB cases (2) new smear positive patients who remain positive at month 3 of treatment (3) symptomatic contacts of known MDR-TB cases (4) and smear positive patient living with human immunodeficiency virus. Until 2011, the eligible patients were referred routinely by the peripheral health

systems to the nearest culture laboratories. In 2012, the NTP launched ICF activities to supplement the existing referral system. It was done using two methods; (1) ICF during routine supervision: Supervisory teams reviewed operational district (OD) TB registers proactively to identify the eligible patients. After identifying these patients and confirming that they were not yet tested, the team traced them to collect 3 sputum samples from their nearest health facilities (HF) or their homes and transported them to the nearest culture centers (CC) and (2) ICF using mobile team: The quarterly TB reports were reviewed at the national level to identify the eligible patients. The patients' names were listed from the carbonized papers of OD TB register attached and cross-checked with culture lab registers and OD TB supervisors to identify the eligible who were not yet tested. Then, the team traced them to collect 3 sputum samples at their nearest HF or their homes and transport to the national reference laboratory for testing. All the processes, infection control and cold chain were strictly applied.

Results: There were 1989 eligible patients among notified TB cases in 2012. Of those, 79% ($n = 1578$) were tested, which is almost a two-fold increase compared to 874 in 2011. Of the 1578 who were tested, nearly 50% ($n = 674$) were referred for testing through ICF using mobile teams. As a result, 110 MDR-TB patients were initiated on treatment, which was double compared to the 56 cases diagnosed in 2011.

Conclusion: ICF is an effective intervention for improving access to diagnosis and increasing the number of MDR-TB cases diagnosed, where the routine referral system does not capture all the eligible patients and number of CC is limited.

PC-930-03   Sistema de información macro TB MFR para el reporte y seguimiento de casos de tuberculose con resistencia a fármacos del Programa Nacional de Tuberculosis en México

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Marco de referencia y desafíos: El programa de Tuberculosis en México no disponía de la totalidad de los medicamentos para pacientes con Farmacorresistencia, por lo que se ha apoyado con el Comité Luz Verde para la adquisición de los mismos en aplicaciones previas; una de las grandes debilidades que no permitían el seguimiento adecuado de los casos de tuberculosis MDR era no contar con un sistema de información exclusivo, y que permita el análisis de los datos capturados, realizar cohortes de tratamiento que justifique el uso de los medicamentos como producto de las aplicaciones al GLC.

Intervention or response: En Marzo del 2009 se inició la creación de una base de datos en aplicación Excel-Macros, la cual quedo terminada y lista para su uso en noviembre del mismo año, un equipo técnico del PNT se encargó de seleccionar y determinar las variables consideradas como importantes y se construyó la actual base Macros la cual permite almacenar la información por medio de una máscara de captura dividida en bloques (notificación de caso, seguimiento baciloscópico y cultivos, presentación de reacciones adversas a fármacos RAFA's), el sistema de información creado es interactivo.

Resultados y enseñanza: Se otorgó capacitación sobre el uso de la base de datos a los líderes de los programas de tuberculosis de los estados de la República Mexicana, la capacitación y la asesoría es contínua por parte del PNT. Hasta el momento se tienen 67 personas capacitadas en el uso de la base de datos. Actualmente se utiliza la versión 3.0 en la cual se incluyeron 'campos' tales como peso del paciente, gráficas, tablas dinámicas, cohortes de tratamiento, porcentaje de conversión bacteriológica, reportes nominales entre los más importantes, cabe mencionar que el sistema está protegido y las bases capturadas actualmente no se pueden modificar por los usuarios.

Conclusiones y recomendaciones: Es importante en el seguimiento de los casos con TB MDR contar con un sistema de información específico y exclusivo y brindar asesoría constante a los usuarios desde el PNT. La Macro TB MFR en su versión 3.0 es una herramienta pilar para el desarrollo de la estrategia de TB MFR del PNT en México.

PC-931-03   Prevalence, timing of and risk factors for the appearance of multidrug-resistance during tuberculosis treatment

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Aim: Multidrug-resistant tuberculosis (MDR-TB) can arise during treatment for non-MDR-TB due to a) acquired resistance, b) infection with MDR-TB strain c) unmasking of MDR-TB that was present, but undetected, at the start of therapy ('mixed infection'). We aimed to assess the frequency, timing and risk factors for the appearance of MDR-TB during non-MDR-TB treatment in a high burden country.

Methods: We analyzed data from 2007–2010 from the Moldovan national TB surveillance database. In Moldova, TB is initially treated within hospitals (average length of stay = 92 days) and sputum is routinely obtained and cultured several times during treatment. We calculated the percentage of culture

confirmed non-MDR-TB cases that received a subsequent MDR-TB diagnosis during treatment. We also report the timing of MDR-TB appearance, and utilize a failure-time model to identify individual-level risk factors for MDR-TB appearance during treatment.

Results: Between 7.4% and 9.4% of non-MDR-TB cases were diagnosed with MDR-TB during treatment. Approximately three-quarters of MDR-TB diagnoses were made at the first follow-up test after initial non-MDR-TB diagnosis and around half occurred within three months of initial non-MDR-TB diagnosis (Figure). Among new TB cases, those that had previously been in detention were at a nearly nine-fold increased risk of MDR-TB diagnosis during treatment and those with HIV co-infection were at a six-fold increased risk. Living alone and greater lung pathology were also associated with increased risk of MDR-TB during treatment among new TB cases.
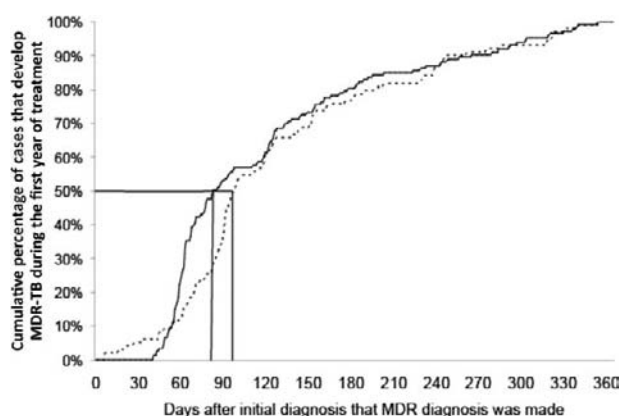

Figure Cumulative percentage of non-MDR-TB cases in whom MDR-TB appeared during the first year of treatment by time that MDR-TB is detected after initial diagnosis. Solid line = new cases, dotted line = previously treated cases. Vertical lines indicate time at which 50% of cases had been diagnosed with MDR-TB (83 days (new cases), 97 days (previously treated)).

Conclusions: That nearly 10% of TB cases were diagnosed with MDR-TB during treatment is striking. The rapid appearance of MDR-TB detection during treatment suggests that in-hospital transmission and mixed strain infections might be driving this phenomenon; this speculation is supported by local studies suggesting high rates of re-infection. Further studies are needed to confirm the mechanisms for the occurrence of MDR-TB during treatment. These studies would have important implications for an expanded role of ambulatory treatment of TB in this setting.

PC-932-03 Resistance to pyrazinamide among patients enrolled in a cohort study of tuberculosis in Lima, Peru

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Background: Drug resistance limits TB treatment success in Peru and globally. Regimens for multidrug-resistant TB (MDR-TB); often rely on pyrazinamide (PZA) as one of the sterilizing components. Yet, resistance testing to PZA is not usually performed. We report the prevalence of resistance to PZA in a cohort study on the transmission of TB in Lima, Peru.

Design/methods: Drug susceptibility testing (DST) was performed on baseline sputum samples from all consenting index patients diagnosed with TB between 2009 and 2012 in 81 health centers in Lima. Testing for isoniazid and rifampin was performed using the proportion method in LJ medium. PZA resistance was assessed with the Wayne method.

Results: Among 4462 baseline isolates from index cases, 3150 were culture positive. Of the 2816 samples with DST results, nearly 32% (899) were resistant to at least one drug; MDR-TB was detected in 11.5% (324). PZA resistance was found in 48.2% (156) of the MDR-TB isolates and in 0.7% (17) of the non-MDR-TB isolates (OR 4.91, 95%CI 4.38–5.43). PZA resistance occurred in 13% (66) of patients who had received prior treatment and only 5% (103) of those without prior treatment (OR 3.05, 95%CI 2.20–4.23).

Conclusion: Resistance to PZA was detected in nearly 50% of MDR-TB strains isolated from patients seen in the public health system in Lima, Peru. Although PZA resistance testing is challenging to perform and interpret, clinical studies have demonstrated that PZA resistance is associated with worse outcomes in the treatment of MDR-TB. To better determine which TB patients may benefit from the unique sterilizing properties of PZA, improved phenotypic testing of PZA and/or inclusion of probes for mutations in the pncA gene in rapid molecular resistance tests will be essential. Susceptibility to PZA cannot be presumed in patients who require treatment for MDR-TB in Peru or in other settings with longstanding use of PZA in repeated first- and second-line TB treatments.

TUBERCULOSIS DIAGNOSTICS: IGRAS

PC-933-03   TST and QFT-GIT for diagnostic workup of childhood tuberculosis: cross-sectional study at Tikur Anbesa Specialised Hospital Pediatric Department, Ethiopia

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Background: Tuberculin skin test (TST) has been used to screen tuberculosis (TB) infection for about ten decades. It has been also recommended as an adjunctive test for the diagnosis of TB in children with sign and symptom where bacteriological conformation is not possible. However, in recent year there are evidences that support the newer interferon-γ assay (IGRAs) has better sensitivity and specificity than TST.
Methods: A cross-sectional study conducted in 310 children suspected of having TB consecutively attending Tikur Anbesa specialized Hospital (TASH) was included in the study. Demographic data and clinical history was collected by research nurse and pediatricians. All children were tested with TST, a commercial ELISA based QFT-GIT (QuantiFERON®-TB Gold In-Tube Assay, Cellestis). The two methods were compared using TB-culture as a gold standard.
Objective: To compare TST and QFT-GIT assay for the diagnostic work up of childhood tuberculosis.
Results: Of 310 enrolled children 281 had full data including clinical history, paired results of QFT-GIT and TST, GA or sputum culture, HIV status, and chest X-ray. The median age of the study participants were 73 months (95%CI 67–79) with a range of 3 months to 14 years. Of the 281 TB suspected children 10.7% ($n = 30$) were found culture confirmed TB cases and 27.8% ($n = 78$) were diagnosed clinically without bacteriological conformation and the remaining 61.7% ($n = 173$) were diagnosed for other diseases. 19.6% ($n = 55$) of the study participants were found HIV positive and 28.5% ($n = 80$) had also contact history with adult TB cases. Majority of the study participants were found BCG vaccinated 92.2% ($n = 259$) and 27.7% ($n = 106$) had low weight for age. The overall TST and QFT-GIT positivity was found 28.1% and 24.6% respectively. However, TST was found positive in 70% ($n = 21$) of those with confirmed TB, 38.5% ($n = 30$) of those diagnosed clinically and 16.8% ($n = 29$) of who had not diagnosed for TB. QFT-GIT was also found positive in 60.3% ($n = 19$) of confirmed TB cases, 47.4% ($n = 37$) of clinically diagnosed TB cases 13.9% ($n = 24$) of who had not diagnosed for TB. In addition 13.9% of QFT-GIT result was found indeterminate. The sensitivity of TST and QFT-GIT was found 70% and 60.3% respectively. Using both TST and QFT-GIT positive result increased the sensitivity to 89.8%. The specificity of TST and QFT-GIT was found 76.9% and 80%. PPV and NPV of TST were found 26.6% and 95.5% respectively, while the PPV and NPV of QFT-GIT was found 26.4% and 94.3%. The concordance of the two tests was found 83.3% (k = 0.56). In both tests patient contact history with known TB cases, low weight for age, and culture or AFB positivity was found highly associated with both TST and QFT-GIT ($P < 0.01$).
Conclusion: TST was found comparable with QFT-GIT for diagnostic work up of childhood tuberculosis.

PC-934-03   Dynamic changes in positive interferon-gamma release assay in a dialysis population: an observational cohort study

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Background: Interferon-gamma release assay (IGRA) is popular for detecting latent tuberculosis infection (LTBI) but its clinical significance is uncertain in high-risk groups other than TB contacts, such as dialysis patients.
Design/methods: Patients under long-term dialysis were prospectively enrolled from March to November 2011 in multi-centers. The QuantiFERON®-TB Gold In-Tube (QFT) was used to detect LTBI. After 6 and 12 months, the QFT was repeated to monitor dynamic changes in QFT results.
Results: Only 204 of 391 enrolled patients completed the study. The initial QFT-positive rate (QFT1) was 22.1%, which decreased to 19.6% after 6 months (QFT2) and 14.2% after 12 months (QFT3). The six-month reversion rate was 45.9% and the conversion rate was 7.7%. Patients with new QFT positivity had a reversion rate of 87.5%, higher than the 20.8% in patients with persistent QFT positivity. The QFT response, difference of interferon-gamma level between TB-antigen tube and negative control, was independent for persistent QFT positivity (odds ratio [OR] 2.41 [1.23–4.72] per 1 IU/ml increment). Using 0.93 IU/ml of QFT1 response as the threshold for QFT positivity, sensitivity was 79% and specificity 76% for persistent QFT positivity. Prior TB had a borderline significance for predicting conversion (OR 6.35 [0.85–47.67]).
Conclusion: In dialysis population with QFT-positive rate of 22.1%, reversion and conversion occur in 45.9% and 7.7%, respectively, within six months. The QFT-positive population is heterogeneous and sub-populations have different reversion rates. Higher QFT positivity threshold can identify patients with persistent QFT positivity to prioritize follow-up and preventive therapy for LTBI.

PC-935-03 Impact of malaria on immunodiagnostic tests for infection with *Mycobacterium tuberculosis*

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Background: Interferon-gamma-release-assays (IGRA) are used for diagnosing tuberculosis (TB) infection, by measuring interferon gamma (IFN-γ) released upon whole-blood stimulation with peptide antigens specific for *Mycobacterium tuberculosis*. The chemokine IP-10 is an alternative immunodiagnostic biomarker for TB infection. IP-10 is released in concert with IFN-γ in 100 fold higher levels. Several conditions are known to compromise the IGRA performance including; young age, glucocorticoid-treatment, HIV, smoking, and helminth infections. Knowledge about the impact of malaria and anti-malaria treatment on these tests is limited.

Aim: To assess the impact of falciparum-malaria on immunodiagnostic tests for *M. tuberculosis* in Tanzanian adults.

Method: In total 242 patients were included for this study; 89 malaria- and HIV-co-infected, 96 malaria-infected, and 57 HIV-infected patients without malaria-infection.

The malaria patients were treated with a standard six-dose regimen of artemether-lumefantrine. All patients were followed for six weeks, 171 patients completed the follow-up (53, 69 and 49 respectively). QuantiFERON®-TB Gold In-Tube Test (QFT-IT) stimulated blood samples were collected on day 0, day 7 and day 42. IFN-γ and IP-10 levels were measured using ELISA. Test-results were obtained using present diagnostic algorithms. Statistics: IFN-γ and IP-10 levels were analysed using Mann-Whitney *U* and Wilcoxon signed rank test, test-results were analysed using McNemar's test.

Results: We found a significant lower IFN-γ and IP-10 response to antigen- and mitogen-stimulation in malaria patients compared to uninfected patients, before anti-malaria treatment was initialized. In the unstimulated samples levels of both IP-10 and IFN-γ were significantly higher among malaria patients. Both observed effects reverted after anti-malaria treatment was completed.

Although IFN-γ levels were affected by concurrent malaria infection, it did not affect the distribution of QFT test results. When using IP-10, we found no difference in positivity rate, but a reduction in the proportion of indeterminate results from day 0 to day 42, from 11% to 2% (*P* = 0.002).

Conclusion: Malaria infection appears to have an impact on immunodiagnostic tests for *M. tuberculosis*, wherefore results from malaria-infected patients should be interpreted with caution. One should consider postponing testing until anti-malaria treatment has been completed. However, studies to confirm these findings are needed.

PC-936-03 Variation over time of response to QuantiFERON®-TB Gold In-Tube test among adults with HIV

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Background: Current evidence suggests that Interferon Gamma Release Assays (IGRA) are at least as accurate as the tuberculin skin test in identifying HIV-infected individuals who could benefit from LTBI treatment.

This study aims to evaluate the variation over time of the response to an IGRA in a cohort of patients with HIV infection, and its possible association with the changes in CD4 cells count.

Design/methods: Patients with HIV who underwent LTBI screening with QuantiFERON-TB Gold In-Tube (QFT-GIT; Cellestis, Carnegie, Australia) in an HIV unit in Rome, Italy in 2006–2011 were enrolled in this study and repeated QFT-GIT after a median of 28.1 months. Patients being investigated or treated for active TB were excluded from the analysis.

Results: 108 patients have been analyzed so far in this ongoing study. At baseline, the mean CD4+ T cell count was 286.2 cell/µl, and QFT-GIT was positive in 8 cases (8.6%) and indeterminate in 7 cases
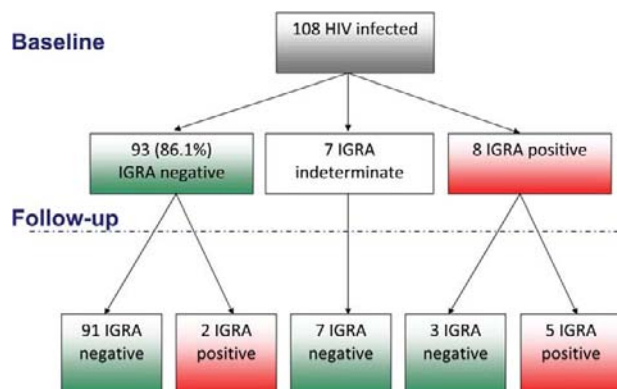

Figure Variation over time of response to QuantiFERON-TB Gold In-Tube test among adults with HIV.

(6.5%). Patients were retested after a median of 28.1, most of them were treated with antiretrovirals and the mean CD4 cell count at the time of retesting increased to 482.6.

At follow-up, of the HIV infected patients who initially had a positive QFT-GIT 3/8 (37.5%) underwent reversion; all those with baseline indeterminate results tested negative and of those initially QFT-GIT negative, 2/93 (2.2%) converted to positive. No association was found between CD4 cells count variation and either QFT-IT conversion or reversion.

Conclusion: In this population, changes in QFT-GIT response seem to reflect test variability and/or new exposure rather than immune reconstitution or deterioration. More data on patients who are severely immunosuppressed when first tested are needed to evaluate the usefulness of IGRA retesting after ART-induced immune reconstitution.

PC-937-03   Use of T-SPOT.TB assay in serial testing of health care staff at the tuberculosis Control Unit of Singapore

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Background: The TB Control Unit (TBCU) of Singapore, a mid-prevalent TB incidence country, treats more than one thousand pulmonary TB cases yearly. Screening of all healthcare staff (HCS), mostly BCG vaccinated, for TB infection is carried out annually. There is limited data on the use of T-SPOT. TB assay in the serial testing of healthcare workers.

Design/methods: From 2007, the T-SPOT. TB assay is used for screening, replacing the tuberculin skin test (TST). All staff, including those with a history of positive TST or treatment of latent TB infection, was tested. The number of staff screened yearly varied from 19 in 2007 to 61 in 2012. T-SPOT.TB assay was interpreted as per manufacturer's guidelines. Borderline results (5–7 spots) were categorised as negative. Conversion is defined as a change from a negative test to positive and vice versa for reversion.

Results: The T-SPOT.TB assay conversion rate was 17.6% in 2008, 11.8% in 2009, 0% in 2010, 8% in 2011 and 14.3% in 2012. Of those with conversion, 4 had increased spot count of <10, while 6 had increased spot count of 10 to 19. Of the 3 converters who were retested after a course of preventive treatment, 2 reverted to negative result (15 spots to 3 spots and 8 spots to 0 spot). 32 staff remained T-SPOT. TB assay negative when tested annually over 1 to 5 years, 27 of whom had within subject variability of ±2 spots. 3 staff had borderline result in at least one of the tests. 2 staff had spontaneous reversion when retested a year later (13 spots to 5 spots and 8 spots to 0 spot).

Conclusion: There is substantial conversion of the T-SPOT.TB assay in serial testing of healthcare staff

at TBCU. Borderline result was seen in only a few staff. HCS who remained assay negative had little variation in the spot counts when tested over 1 to 5 years.

PC-938-03   Screening HIV-positive pregnant women for tuberculosis in India: TST vs. QGIT interferon gamma release assay

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Background: Few studies have addressed the performance of latent TB infection (LTBI) diagnostics during pregnancy. The lack of data has important policy impacts: HIV+ people in Brazil only receive INH preventive therapy (IPT) after testing positive for TB, even though the WHO recommends IPT for all HIV+ adults. South Africa is considering a similar requirement. If LTBI diagnostics malfunction during pregnancy due to immunological changes, HIV+ pregnant patients may miss out on lifesaving therapy. We examined the effect of pregnancy stage on TST and QGIT performance in HIV+ pregnant women in a TB-endemic setting.

Design/methods: Cross-sectional and longitudinal LTBI screening was performed in antepartum ($n = 80$) and at delivery ($n = 54$) at a government hospital in Pune, India. Repeat testing was done at delivery in 43 antepartum women to assess the impact of serial testing. Trained staff administered sociodemographic and medical history questionnaires. Agreement using the kappa statistic and percent positivity with binomial exact confidence intervals was calculated.

Results: Median CD4 was 530 (IQR 358–683) with 47 (35%) of 134 women on HAART. Eighteen (15%) of 119 were TST+. (Fifteen [11%] did not return for TST reading.) For QGIT, 38 (28%) of 134 were positive ($P = 0.02$). Among 119 with both results, QGIT positivity was higher than TST positivity at both antepartum and delivery (Figure). Nine (8%) were concordant positive, 73 (61%) concordant negative, and 37 (31%) discordant. Of discordant women 24 (64%) were TST−/QGIT+. Percent agreement was 66% (κ = 0.14, 95%CI 0.08–0.37) antepartum and 70% (κ = 0.18, 95%CI 0.005–0.37) at delivery. Among 43 antepartum women with repeat LTBI testing at delivery, the conversion rate for TST was 18% vs. 5% for QGIT ($P = 0.04$); reversion rates were 7% and 13% ($P = 0.2$), respectively.

Conclusion: Choice of LTBI test among HIV+ pregnant women affects results. The QGIT returned significantly more positives than the TST overall. Our
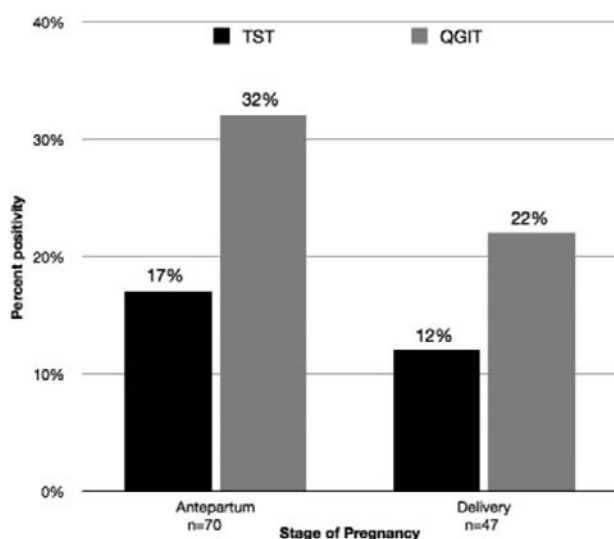
Figure Cross-sectional percent positivity of TST and QGIT in HIV+ women, by stage of pregnancy.

results suggest that 320 HIV+ pregnant women out of 1000 screened by QGIT would receive IPT, while only 170 would receive therapy after TST screening. Timing of the test is also important. Fewer women tested positive for LTBI at delivery than antepartum under both QGIT and TST, suggesting that both tests suffer when immune function reaches its nadir late in pregnancy. Waiting until delivery would reduce the number of women receiving IPT by nearly one-third for both the QGIT and TST tests.

SPATIAL AND TEMPORAL TUBERCULOSIS DISTRIBUTION

PC-939-03   Cigarette smoking and pulmonary tuberculosis in northern California

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Background: A positive association between smoking and increased risk of tuberculosis disease is well-documented for populations outside the United States (US). However, it is unclear whether smoking increases risk of tuberculosis in the US, where both smoking prevalence and disease rates are much lower than in the countries where previous studies have been conducted.
Design/methods: To explore the tuberculosis-smoking association in a general US population, we conducted a nested case-control study among members of Kai-

ser Permanente Northern California (KPNC). We identified all newly diagnosed cases of active pulmonary tuberculosis (PTB) disease between 1996–2010. Each of the 2380 cases were individually matched to two controls by age, gender, and race/ethnicity.
Results: Using adjusted logistic regression, increased PTB risk was observed among ever smokers (odds ratio (OR) = 1.24; 95% confidence interval (CI) 1.10, 1.39), as well as current (OR = 1.31; 95%CI 1.13, 1.52) and past (OR = 1.17; 95%CI 1.00, 1.37) smokers, compared to never smokers. Increased intensity and duration of smoking were also positively associated with PTB risk.
Conclusion: Our findings support the hypothesis that smoking is a risk factor for PTB in a general US population, underscoring the importance of tobacco cessation and prevention programs in eliminating tuberculosis.

PC-940-03   Frequency and seasonal variation of 'TB symptoms' amongst people taking antiretroviral therapy in South Africa

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Background: WHO recommends screening people with HIV for TB at every clinical encounter using a tool comprising any cough, weight loss, fever or night sweats, with further evaluation of those screening positive, and Xpert MTB/RIF as the initial test. In the context of the XPHACTOR study, evaluating a novel algorithm to determine priority for TB investigation, we assessed the prevalence of TB symptoms among adults attending for antiretroviral therapy (ART) in South Africa.
Methods: A systematic sample of adults at two ART clinics were screened for TB using the WHO tool plus questions about other conditions with similar symptomatology, including symptoms of upper respiratory tract infections.

Amongst 304 participants, (63% female, median age 42 years, median CD4 count 388 cells/mm^3, median duration on ART 44 months, 45% reported previous TB treatment and 4% previous isoniazid preventive therapy), 135/304 (44.4%) of participants reported any one of cough, fever, night sweats or weight loss, most commonly cough or weight loss. The prevalence of 'TB symptoms' and upper respiratory tract symptoms was higher in Spring than Summer (Table).
Conclusions: The prevalence of symptoms suggestive of TB was high and varied with season suggesting that viral illnesses influence symptom prevalence. If all those with a 'TB symptom' were tested with

Table Prevalence of 'TB symptoms' by month

Description of criteria	Oct-12 % (n) ($n = 89$)	Nov-12 % (n) ($n = 68$)	Dec-12 % (n) ($n = 31$)	Jan-13 % (n) ($n = 65$)
WHO screening tool positive	53.9 (48)	48.5 (33)	45.2 (14)	27.7 (18)
Current cough	31.5 (28)	17.7 (12)	12.9 (4)	15.4 (10)
Any unintentional weight loss (self-report)	25.8 (23)	26.5 (18)	22.6 (7)	12.3 (8)
Significant unintentional weight loss*	23.6 (21)	23.5 (16)	16.1 (5)	10.8 (7)
Fever	13.5 (12)	7.4 (5)	6.5 (2)	6.2 (4)
Night sweats	12.4 (11)	14.7 (10)	9.7 (3)	10.8 (7)
Cold or flu symptoms in last month	38.2 (34)	27.9 (19)	16.1 (5)	10.8 (7)

Data presented is for $n = 253$ participants enrolled from October 2012 to January 2013.
* ≥10% loss over last 6 months based on clinic or self-reported weight 6 months ago, or self-report of drop of >1 dress/trouser size.

Xpert MTB/RIF, there would be huge resource implications. An algorithm prioritising those who need immediate testing for TB is needed, and will be tested in the XPHACTOR study.

PC-941-03 Spatial variation in testing for tuberculosis and tuberculosis drug resistance in KwaZulu-Natal, South Africa, 2006–2012

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Aim: South Africa is in the midst of a substantial TB-HIV co-epidemic, and rates of drug-resistant TB, including multi-drug resistant TB (MDR-TB) continue to increase. Given the reduced sensitivity of smear microscopy among persons with HIV and the emergence of drug-resistant TB strains, access to and scale-up of more sensitive diagnostic tools, such as culture or newer nucleic acid assays, is urgently needed. Drug-susceptibility testing (DST) using liquid culture has been available in South Africa since 2006, and line-probe assays (LPAs) were introduced in 2010. In 2011, South Africa adopted an initiative to scale-up laboratory capacity for the detection of TB and drug-resistant TB strains, including the implementation of GeneXpert, a new rapid diagnostic technique. Here, we assessed the spatio-temporal patterns of use of available TB diagnostics in KwaZulu-Natal (KZN), South Africa, over a seven-year period.
Methods: We used routinely collected surveillance data from the National Health Laboratory Service in KZN Province, 2006–2012. For each diagnostic method (culture, LPA, GeneXpert), we calculated the percentage of TB suspects (defined as individuals with at least one specimen sent for testing) tested and the

percentage and incidence rate (per 100 000 population) of confirmed TB. We also assessed use of diagnostics for MDR-TB. Each statistic was estimated for each of the 51 sub-districts in KZN. Statistics for culture use were estimated using data from 2006–2012 and those for rapid tests were assessed since their respective time of introduction.
Results: We found substantial geographic heterogeneity in the usage of diagnostic tools within KZN. The percentage of TB suspects tested by culture ranged from 3% to 71% between sub-districts. The average annual incidence of culture-confirmed TB ranged from 0 to 865 per 100 000. The percentage of TB suspects who received testing for MDR-TB by any available method was low and varied geographically (range 0% to 8%). The average annual incidence of confirmed MDR-TB ranged from 0 to 106 per 100 000.
Conclusion: There is marked heterogeneity in use of TB diagnostic tools by sub-district in KZN. In sub-districts where the use of diagnostics more sensitive than smear is worryingly low, there is likely substantial under-diagnosis of TB and MDR-TB. Identification of these areas can inform the scale-up of access to diagnostics; this effort will limit the morbidity and transmission risk associated with undiagnosed TB.

PC-942-03 Effectiveness of performance based management and quality monitoring to improve tuberculosis treatment outcomes in Niger

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Background: Tuberculosis (TB) treatment outcomes were quite poor in Niger. In order to try to improve them, incentives based on performance and close monitoring were introduced in one of the eight regions of the country. We want here to evaluate the impact of that strategy.
Methods: Two regions were selected: Zinder and Maradi. They were comparable according population, socio economic situation and health resources. Before the intervention the two regions had similar poor TB outcomes.

Damien Foundation, a Belgian non-governmental organization supporting the National Tuberculosis Program (NTP), started to provide active quarterly monitoring of 29 health centres treating TB in Zinder in January 2010. A quarterly incentive based on performance of health workers was directly paid according to a monitoring check list. The monitoring was based on careful inspection of patients' data sheets and forms, comparison between forms (laboratory vs. clinical), detailed observation of patients' follow

up, drugs management and review of laboratory procedures with external evaluation of quality. In Maradi the monitoring of 27 TB health centres was provided by the NTP in the same period and the incentives for the health workers was not based on performance.

The study was prospective from 2010 to 2011.

Results: Providing active quality monitoring of facility-level activities and performance based incentives for health workers in Zinder led to better treatment results among the 1218 treated patients in 2011: the rate of successful treatments was higher in 2011 than in 2009 both for new sputum smear positive (ss+) cases (82.9% vs. 76.1%; $P < 0.01$; RR 1.09; CI 1.03–1.15) and for new sputum smear negative (ss−) and extra-pulmonary cases (81.1% vs. 59.6%; $P < 0.001$; RR 1.36; CI 1.24–1.50). We found no significant improvement in the ss+ retreatment group (75.4% vs. 71.9%; $P = 0.66$).

The outcomes among the 1332 patients in Maradi remained poor for new ss+ cases (74.9% vs. 73.3%; $P = 0.5$), for ss+ retreatment (69% vs. 70%; $P = 0.91$) and for new ss− and extra-pulmonary (63.5% vs. 65.7%; $P = 0.45$).

The HIV testing for TB patients was not included in the performance indicators and we found no significant difference after the intervention. In Zinder 54.7% of patients were tested in 2011 and 52.8% in 2009; in Maradi the difference was of 36.9% vs. 34.2%.

Table   Treatment outcomes in the Zinder region, 2009–2011

	Patients (n)	Cured	Treatment completion	Failed	Died	Default	Transfer
Health workers who didn't received incentives and close monitoring in 2009							
New ss+	603	435 (72.1%)	24 (4%)	8 (1.3%)	43 (7.1%)	61 (10.1%)	32 (5.3%)
Retr ss+	64	45 (70.3%)	1 (1.6%)	1 (1.6%)	4 (6.3%)	7 (10.9%)	6 (9.4%)
New ss− and extra-pulmonary	376		224 (59.6%)	0	44 (11.7%)	61 (16.2%)	47 (12.5%)
Health workers who received incentives and close monitoring in 2011							
New ss+	707	550 (77.8%)	36 (5.1%)	21 (3%)	36 (5.1%)	50 (7.1%)	14 (2%)
Retr ss+	57	36 (63.2%)	7 (12.3%)	3 (5.3%)	3 (5.3%)	5 (8.8%)	3 (5.3%)
New ss− and extra-pulmonary	454		368 (81.1%)	3 (0.7%)	53 (11.7%)	17 (3.7%)	13 (2.9%)

Conclusion: Performance-based management based on rigorous monitoring was successful in improving treatment outcomes for new cases of tuberculosis.

PC-943-03   Revised definitions and reporting framework for tuberculosis: 2013 revision

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Introduction: Standardisation of definitions and reporting structures have permitted uniformity in the reporting of indicators of performance of national tuberculosis control programmes for many years. These parameters were last revised by the World Health Organization (WHO) in 2009. Since then, WHO-approved rapid molecular diagnostics have been widely introduced and the treatment of drug-resistant tuberculosis has being scaled-up, necessitating adjustments in the way cases and outcomes are defined and reported.

Methods: WHO held a technical consultation on the revision of definitions and reporting frameworks in May 2011. Several discussions—electronic and physical—with key stakeholders followed since then. Seven national programmes (Belarus, Brazil, Cambodia, Djibouti, Estonia, Pakistan, and Philippines) provided detailed feedback after testing out the revised reporting structures in their settings.

Results: Tuberculosis cases are now classified as bacteriologically confirmed (by smear, culture or WHO-approved rapid diagnostic tests) or clinically diagnosed. For the monitoring of enrolment and outcomes, rifampicin-resistant tuberculosis cases may be enumerated with cases having additional isoniazid resistance (multidrug-resistant tuberculosis; MDR-TB), given that recommended treatment is similar in the two groups. The definitions of cured, treatment completed and treatment failed for patients on second-line MDR-TB treatment have been simplified from those generally used and are applicable also to shorter regimens (e.g., 9–12 months). Register templates can now accommodate the entry of results from molecular testing. Forms for simultaneous outcomes reporting for both first- and second-line treatment cohorts are included.

Conclusion: The revised parameters will apply for WHO global tuberculosis monitoring from 2014. Revisions will be easier to introduce if electronic recording and reporting are already in place.

PC-944-03   Spatial distributions of sputum smear positive pulmonary tuberculosis and socio-economic characteristics of neighbourhoods in Douala, Cameroon

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Objectives: To present the spatial distribution of sputum smear positive pulmonary tuberculosis (PTB+) incidence in Douala, Cameroon, and to evaluate possible links with the socio-economic characteristics of neighbourhoods.

Materials and methods: During one year, all new PTB+ cases in Douala (Cameroon) were spotted with GPS and represented on a map. Spatial clusters of PTB+ incidence were identified. From all patients, demographic and socio-economic characteristics were collected with a semi-open questionnaire.

Their socio-economic status (SES), based on assets and the level of education were measured using principal component analysis and compared with those of the general population of the city of Douala, using DHS data. PTB+ incidence and mean SES of PTB+ patients per Health Area (HA) were computed and the correlation between these two variables was investigated.

Results: During the study period, a total of 2545 permanent residents PTB+ patients were notified. In total, 2132 (84%) of patients were spotted and interviewed. Spatial clusters were identified in sixteen neighbourhoods. Neighbourhoods with PTB+ patient incidence clustering showed on average lower SES values than those of the general population.

Conclusions: There is evidence of significant clustering of PTB+ incidence cases in Douala. Clusters are found in neighbourhoods with an average low socio-economic status. Systematic use of cluster detection techniques for regular TB surveillance in Cameroon could guide the interventions of the National TB Program.

PC-945-03   HIV prevalence among tuberculosis suspects: an added value to the HIV programme in Nigeria

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Background: Despite efforts to increase HCT services in Nigeria, the proportion of the population having access remains sub-optimal. In 2010, the NTP Nigeria expanded access for HCT to include TB suspects. Currently all the 36 states and FCT as part of quality of care provide HCT to all TB suspects and cases.

Objective: To demonstrate the contribution to HIV services through screening of all TB suspects as an entry point.

Methods: The NTP revised its national guideline, training documents, SOPs/algorithms and recording and reporting formats to ensure health care workers provide HCT to all TB suspects. A retrospective study was carried out between 2010 and 2012 in which records of all TB suspects and patients reported to the national programme by facilities were analysed according to HCT uptake and HIV prevalence among TB patients and suspects

Results: With increase in HCT uptake among TB patients to 86% by end of 2012, 82% HCT uptake was achieved among 332 653 TB suspects reported within the same year. A HIV prevalence of 14% (30 119) was recorded among TB suspects (56.5% female: 43.5% male) with a range of 1%–35%, while 23.4% (19 342) was recorded among TB patients. 9 states

out of the 36 states and FCT had HIV prevalence rates >20% among TB suspects; which happen to be same states with high HIV prevalence above national figure of 4.1%. In total, an additional 10 777 HIV patients were detected from routine screening of TB suspects, indicating a 55.7% additional contribution to the HIV patients detected within the TB programme and linked to HIV services.

Conclusions and recommendations: HIV testing among TB suspects increases access to HIV care and provides an opportunity for counselling, education and prevention of further HIV spread. Other disease programmes should endeavour to place HCT as part of quality of care to improve access, especially among states with high HIV prevalence

PC-946-03   Geographic heterogeneity of multidrug-resistant tuberculosis in Georgia

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Aim: In 2011,Georgia, in the former Soviet Union, reported that 11% of new TB cases and 32% of previously treated TB cases had MDR-TB. We aimed to assess if there was geographic variability in the burden of MDR-TB in Georgia and to identify patient-level risk factors for MDR-TB in order to inform the design of targeted interventions against MDR-TB in this setting.

Methods: We used routinely collected surveillance data on notified TB cases and hospitalized MDR-TB cases from 2009 to 2011 to estimate the incidence of MDR-TB per 100 000 people and the percentage of TB cases with MDR-TB for each of 65 municipalities. We also used regression modeling to identify patient-level risk factors for MDR-TB among new and previously treated TB cases.

Results: 1795 MDR-TB cases were reported between January 2009 and June 2011; the average annual incidence of notified MDR-TB was 16.2/100 000 population. However, the notified MDR-TB incidence was much higher in the penitentiary system at 837/100 000. Overall, 10% of newly diagnosed TB cases and one third of previously treated TB cases had MDR-TB. There was substantial variation in MDR-TB burden across Georgia by municipality. The average annual MDR-TB incidence ranged from 0 to 5.0 per 100 000 among new cases and from 0 to 18.9 per 100 000 among previously treated cases. The percentage of TB cases with MDR-TB ranged from 0% to 33.3%

among new cases and from 0% to 75% among previously treated cases. Individuals in the major cities were, on average, at a greater risk of transmitted MDR-TB than those in rural areas [increased odds of 42% (95% confidence interval: 19%–71%)]. Age was also a significant risk factor among newly diagnosed TB cases; those aged 15–25 had the highest risk of MDR-TB while those in older age groups had a decreased risk.

Conclusion: We found substantial geographic heterogeneity in the risk and burden of MDR-TB burden in Georgia. Further studies and interventions should focus on the emergence of MDR-TB within the penitentiary system and in hotspots detected around major cities.

PC-947-03   Geospatial analysis of tuberculosis prevalence and identification of space-time clusters in South Africa, 2004–2012

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Background: The utility of Geographic Information Systems (GIS) as tools for disease surveillance and health service allocation is increasingly recognized within the public health community worldwide. GIS has been used to study geographic distribution of TB and to detect clusters in limited geographical areas in South Africa, but never at a national scale. Historical data on the burden of TB across all the districts and provinces of South Africa has recently become available. We describe the geographical distribution of TB in South Africa and identify hotspots using Geographic Information System software in order to support TB control activities.

Methods: Data on all positive TB test results between 2004 and 2012 were obtained from the corporate data warehouse of the South African National Health Laboratory Service (NHLS). The data were deduplicated and cleaned, and prevalence rates of TB were calculated per 100 000 population. Chloropleth maps of the TB prevalence rates were constructed using ArcGIS version 10.1 (ESRI, Redlands, California). The Moran's I statistic for aggregated data was used to determine whether the pattern of distribution of TB prevalence was random, dispersed or clustered across all 52 districts of South Africa. The Getis-Ord (Gi*) statistic was used to identify and map hotspots.

Results: Preliminary results of the analysis, covering data from 2004 to 2007 and districts in eight out of nine provinces, indicates the presence of statistically significant spatial clustering of TB prevalence in South Africa (Table). Recurring tuberculosis hotspots were identified in districts in the Western Cape and North West province. Hotspots occurred sporadi-

cally in Northern Cape and Free State province. The result of the complete analysis of for all the provinces between 2004 and 2012 will be presented at the conference.

Table Yearly estimates of Moran's I statistic, South Africa, 2004–2007

Year	Moran's I statistic	Z-score	P value
2004	0.56	8.62	<0.0001
2005	0.61	9.43	<0.0001
2006	0.62	9.61	<0.0001
2007	0.63	9.75	<0.0001

Conclusion: Although South Africa has hyperendemic rates of TB disease our analysis demonstrates that there are clusters of areas with exceptionally high prevalence. These clusters occurred primarily in the south western and the north western parts of the country during the study period. Further analysis is needed to identify the drivers of TB prevalence in these areas. These results will support the National TB programme to prioritise interventions in these areas.

PC-948-03   The modeling estimation and projection of tuberculosis prevalence in Indonesia

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Background: In drawing up both the provincial and nationwide plans and policies to control TB in Indonesia, it is important to know the number of people with TB and TB prevalence trend at the both levels. The number is also required in assessing the progress of TB program and it becomes very essential, because it is associated with the target objectives of the MDGs (Millennium Development Goals).

Methods: The models were built based on surveillance data and national survey of TB prevalence in 2004, national basic health survey in 2007 and 2010, and village census in 2008. The methods can be distinguished into two parts: (1) Single Compartment Model (SCM) is used for modeling the surveillance data, for both national and provincial levels, and (2) Poisson Regression Model (PRM) is used to model the results of SCM model for estimating the number of people with TB at district level and 5-year projection of TB prevalence at national level.

Results: The SCM modeling results showed that estimated number of people with TB in Indonesia in 2010 is 497 519 (387 635–607 394). There was a decrease compared to the estimated number of people with TB with the same modeling in 2008 by 3.3% and in 2009 by 1.9% but still 5.7% larger than the

estimates in 2007. The provincial level results showed that estimated number of people with TB is highest in West Java province (79 652 [61 772–97 532]) and the lowest is in Bangka Belitung province (2047 [1622–2471]).

The estimation of TB prevalence per 100 000 population in 2010 is 209 (163–255), about 10 and 15 cases lower than 2009 and 2008 estimates, respectively. We predict that there is no significant different of TB prevalence in 2015 (210 [142–312]). The province of West Papua has the highest TB prevalence estimation per 100 000 population (538 [404–680]) and the province of Yogyakarta has the lowest estimation (136 [110–170]).

One of pertinence of this estimation results is to measure the coverage of TB program. From the results, noted that the nationwide TB program have covered approximately 58% of people with TB in 2007–2009 and slightly decreased to about 51% in the year 2010. **Conclusion:** Since the estimated number of people with TB and TB prevalence in Indonesia varied by province then TB control program should be considered to province specific epidemic of TB. Better reporting and recording system may increase the coverage TB program.
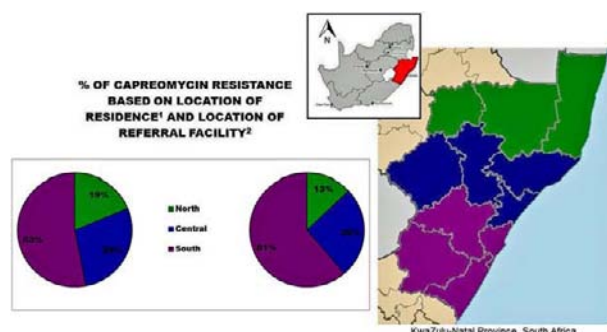
PC-949-03   Geographic distribution of XDR-TB in KwaZulu-Natal, South Africa, and relation to capreomycin resistance

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Background: Drug-resistant tuberculosis (TB) is an important threat to global TB control and comprises an increasing proportion of cases. In South Africa, endemic HIV has led to the spread of extensively resistant TB (XDR-TB) as well as increased mortality and poor treatment outcomes. The aim of this study is to describe the geographic distribution of XDR-TB drug resistance patterns in the KwaZulu-Natal (KZN) Province.
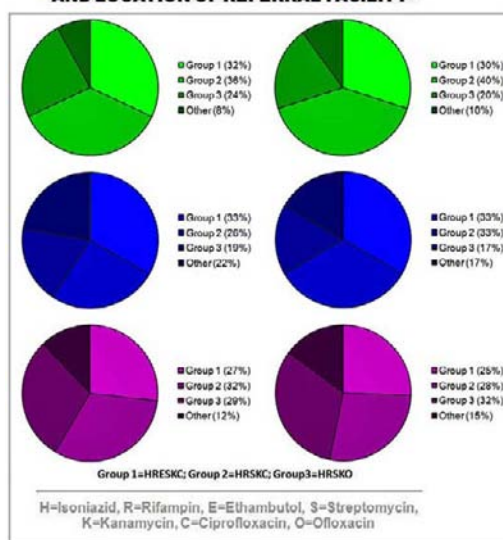**Methods:** Prospective cohort study of XDR-TB patients (PROX Study) at a public TB referral in KZN from August 2009 through July 2011. Written informed consent was obtained. Demographics, routine culture, and initial 6 drug solid-agar drug susceptibility testing (DST) was performed on all isolates. Extended DST (including DST to capreomycin) was performed on a subset of culturable initial and subsequent TB samples.
Results: 104 XDR-TB patients were prospectively enrolled. 100 had admission cultures for XDR-TB

% OF CAPREOMYCIN RESISTANCE BASED ON LOCATION OF RESIDENCE[1] AND LOCATION OF REFERRAL FACILITY[2]

KwaZulu-Natal Province, South Africa

and available residence and referral facility location data. HIV infected patients (78%) were older (mean age 37 vs. 29) and more likely to be female (55% vs. 41%) compared to HIV infected XDR-TB patients. The majority of patients (86%) came from areas other than the Tugela Ferry catchment area. A heterogeneous distribution of DST patterns was observed in the province (Figure). 62.5% (30/48) of isolates tested with extended DST were capreomycin resistant prior to receiving treatment with capreomycin. Acquired capreomycin resistance occurred in 3/6 (50%) of isolates initially susceptible to capreomycin and with serial isolates available for extended DST. Female gender was associated with increased risk of capreomycin resistance (OR 5.38, 95%CI 1.43–20.0, $P = 0.013$). There was no significant relation between capreomycin resistance and home ($P = 0.95$) or referring hospital ($P = 0.24$) location.

% OF OBSERVED STANDARD RESISTANCE PROFILES BASED ON LOCATION OF RESIDENCE[1] AND LOCATION OF REFERRAL FACILITY[2]

Group 1 (32%) Group 2 (36%) Group 3 (24%) Other (8%)
Group 1 (30%) Group 2 (40%) Group 3 (20%) Other (10%)
Group 1 (33%) Group 2 (26%) Group 3 (19%) Other (22%)
Group 1 (33%) Group 2 (33%) Group 3 (17%) Other (17%)
Group 1 (27%) Group 2 (32%) Group 3 (29%) Other (12%)
Group 1 (25%) Group 2 (28%) Group 3 (32%) Other (15%)

Group 1=HRESKC; Group 2=HRSKC; Group3=HRSKO

H=Isoniazid, R=Rifampin, E=Ethambutol, S=Streptomycin, K=Kanamycin, C=Ciprofloxacin, O=Ofloxacin

Conclusions: Resistance patterns associated with capreomycin resistant XDR-TB strains are independent of patient's home location and referral hospital in KZN. The lack of relationship supports earlier data which suggested de novo capreomycin-resistant XDR-TB is widespread in KZN. High rates of acquired capreomycin resistance during treatment are

concerning from clinical and public health perspectives. The apparent association between female gender and capreomycin resistance should be further explored. Further study of the phenotypic and genotypic distribution of drug-resistant TB in KZN is ongoing.

PC-950-03   Introduction of anti-tuberculosis pharmaceutical management guidelines in Madre de Dios, Peru

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Aim: Introduce guidelines to improve the supply of antituberculosis medicines in Madre de Dios (MdD) primary health care facilities.

Methods: A descriptive cross-sectional study was carried out to document the baseline situation for antituberculosis pharmaceutical management in ten health care centers. At the time of the study, these clinics treated 75% of TB cases in MDD. Health care providers at the clinics answered a questionnaire evaluating their knowledge of procedures for requisition (ordering), receipt, storage and use of first line anti tuberculosis medicines. Pharmaceutical management guidelines would be designed based on the findings of the baseline study.

Results: The baseline evaluation showed drug shortages due to the lack of procedures for placing new orders and uniform criteria to define minimum and maximum stock levels. There were also inaccurate inventory control cards which caused filing delays. Treatment was delayed because medicines were ordered only after the positive case diagnosis. There were no procedures to dispose of expired or deteriorated medicines or to reincorporate into the system remaining medicines from patients who had defaulted on their treatments. The storage conditions were poor and lacked proper ventilation. The guideline was specifically oriented to resolve these problems. A four page illustrated pamphlet was validated in a pilot test, adjusted and finally implemented in all the health centers. It's simple, auto instructive design allowed for immediate implementation after its distribution without workshop training. An impact evaluation showed improvement in most of the baseline indicators.

Conclusion: TB medicines management in primary health facilities could improve by designing guidelines tailored to the needs and abilities of the users and targeting solutions to the problems identified in the baseline evaluation.

PC-951-03   Mid-term evaluation of the Nigeria National Tuberculosis and Leprosy 2010–2015 strategic plan: achievements, gaps, limitations: and the way forward

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Background and challenges to implementation: The National Tuberculosis and Leprosy Control Programme (NTBLCP) developed the National Strategic Plan (NSP) 2010–2015. The Strategic Plan is currently in its mid-term of the implementation of activities. Therefore, the NTBLCP carried out a mid-term evaluation of the tuberculosis and leprosy activities in the country. The purpose of this study is to review the progress made so far, identify the gaps and suggest direction for moving the TB programme forward.

Intervention or response: The MTR was carried out in Nigeria from April 8–18, 2013. The reviewers consisted of international and national consultants including civil society and staff of the NTBLCP. Both qualitative and quantitative tools were developed to capture information from the field. Nine states were randomly selected for the exercise. Key informant interview was conducted with programme managers at both the state and local government areas. Also patient interview was conducted as well as direct observation of treatment facilities, laboratories and storage facilities for drugs and other consumables. Data from the field were analyzed and presented.

Results and lessons learnt: There was low proportion of government and private health facilities including prisons provide DOTS services. There is poor follow up of smear-negative, detection of EPTB cases and child diagnosis. There is limited funding for TB and leprosy. The current microscopy expansion target appears inadequate to achieve case notification target. The political commitment for integration TB and HIV programmes at national level is growing. There were no programmatic stock outs of adult first line and second line TB medicines. There was a smooth transition from eight to six months regimen for adults. The Nationally TB clinics outnumber HIV/ART clinics five-fold resulting in suboptimal ART uptake. There were stock-outs of free HIV test-kits in TB facilities. IPT is not happening. About 357 DR-TB cases identified through GeneXpert, while 279 are on treatment. PPM contributed 22% of all TB cases. 8% of TB suspects referred by CVs.

Conclusions and key recommendations: The mid-term review identified the strengths and weakness of the programme and proffered suggestion on the way forward to get the National TB programme on track towards the achievement of the goals of the NSP

2010–2015. There is need for concerted efforts by all stakeholders in order for the country to meet the set goals and targets.

PC-952-03   Determinants of choice of treatment supporter among tuberculosis patients in care in northern Nigeria: the Infectious Disease Hospital, Kano

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Background: Until recently TB treatment in Nigeria was for 8 months but now the country has introduced the rifampicin-isoniazid combination (6 month regimen) which requires observation of treatment throughout the entire duration of treatment. Under a patient centred approach, patients are supported to take anti-TB drugs in the health facility or at home using a treatment supporter (TS). The choice of treatment option is critical to treatment adherence and ensuring a positive treatment outcome.
Objectives: The study is aimed at understanding the role of patient characteristics in their decision to use or not use a treatment supporter.
Methodology: The study is a retrospective review of tuberculosis patients enrolled for treatment from October 2011–September 2012. Study population include both category I and Category II patients in enrolled for treatment at Infectious Disease Hospital, Kano.
Results: A total of 223 patients were enrolled in 2012, higher proportions were male (73.5%); majority fall within the 15–25 year (50.6%) age group. 62.3% of patients opted for a treatment supporter with lower proportion of men (59.8%) than women (69.5%); there was no significant difference among age groups; based on type of disease, 80% EPTB cases compared to 61.1% pulmonary TB cases uses TS; more HIV negative patients with TB (65.2%) used TS than those who are HIV positive (52.8%). Better treatment outcome was associated with used of TS at $P = 0.010$. With 63% among defaulter cases had no TS.
Conclusion: Most TB patients will opt for use of treatment at home with treatment supporter and this is associated with better adherence to treatment.

PC-953-03   Seasonality in transmission of *Mycobacterium tuberculosis* is unlikely to be the only cause of seasonality in tuberculosis disease

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Background: Tuberculosis (TB) notifications show a seasonal pattern in countries across the globe, usually with a peak in spring and a trough in autumn. In the Netherlands, seasonality in TB is driven by periodicity in extrapulmonary TB (EPTB). We examined the hypothesis of increased transmission of TB during wintertime due to crowding, as opposed to increased reactivation or progression to disease due lowered immunity in spring. Key in our studies is the distinction between clustered cases—genotypically identical—and unique cases. The former are usually associated with recent infection, the latter with reactivation disease. Seasonality in clustered cases would reflect enhanced transmission in winter and/or seasonally lowered immunity; seasonality in unique cases would only reflect seasonally lowered immunity.
Methods: First, we fitted (Seasonal) Auto Regressive Moving Average (SARMA) models to clustered and unique culture-positive TB notifications in the Netherlands (1993–2008) to assess seasonality. Deriving the seasonal pattern from STL-decompositions, we compared the heights of the seasonal peaks, to assess the contribution of transmission vs. reactivation as a drive of seasonality. Second, we performed a simulation study assuming most infections occur in winter: notifications were simulated by adding patient delay and incubation period to an infection date randomly taken to be in winter in 80% of cases. The incubation period was imputed from frequency distributions for different TB disease localizations, drawn from the literature. Seasonality was assessed through spectral analysis.
Results: Clustered and unique pulmonary (P) TB notifications showed no seasonal trend, while clustered and unique EPTB notifications were seasonal, with peaks of similar height. Analysis of simulated notifications assuming infection in winter revealed a barely significant seasonality in clustered EPTB cases, and failed to reproduce the observed seasonality in clustered TB notifications.
Conclusions: Our results suggest that increased transmission of TB during wintertime is unlikely to be the (only) cause of the seasonal peak in TB notifications. A factor closer to the notification date likely contributes to the seasonality observed in (EP) TB notifications, such as seasonally altered immunity or reporting bias.

PC-954-03   Social protection for tuberculosis patients: where are we? Experiences of social support for tuberculosis patients in India

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Background: Tuberculosis control over the decades depended on case detection and treatment; neither the DOTS strategy nor the Stop TB strategy addressed the important social support required for TB patients. Most of the TB patients are from low socio-economic status. Social factors are responsible for patients not able to complete their treatment and there is lack of TB specific social protective measures. The Government of India jointly with its provincial governments implements a number of social welfare schemes. India's Revised National TB control Programme (RN-TCP) has taken some important strides in the direction for social protection of TB patients by proactively linking TB patients with social welfare schemes. This case study describes the existing social protection schemes in India and how TB programme has linked the TB patients to the relevant schemes.

Intervention: Central TB Division, Government of India sent out a communication on the need to link all TB patients to the existing social support schemes to all TB programme staff. This was followed up with detailed reviews and discussions in national programme review meetings. Information on the various social protection schemes linked with TB patients were collected and analyzed.

Results: RNTCP was able to facilitate linkage of TB patients to many social protection schemes of Union and State governments. The major TB specific social protection schemes were nutritional support where by TB patients were linked to social protection schemes with monthly supply of free ration of food grains packages. The average cost of such a scheme was less than US$100 per patient per year. Second category of support was through direct financial support in the form of monthly pension to TB patients. This amounts to US$20 per month per patient. A third category of support was linking the MDR-TB patients with Rashtriya Swasthiya Bima Yojna a national health insurance programme. Under this scheme MDR-TB patients pre-treatment evaluations and in hospital expenditure is covered up to US$600. Travel support to TB patients, food supplementation, vocational rehabilitation, soft loans through self help groups for self employment etc were other innovative social protection activities implemented through NGOs.

Conclusions: The post 2015 strategy for TB control should have a strong component to include TB specific social protection and these local experiences could guide national and global policy development.

PC-955-03   Treatment interruptions in new pulmonary tuberculosis patients receiving Regimen I under DOTS in Lima, Peru

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Background: Adherence to tuberculosis (TB) treatment is crucial for bacteriological clearance, interruption of transmission and cure. TB treatment default but also interruptions could lead to acquired or amplified TB drug resistance. We describe the frequency and the duration of treatment interruptions under programmatic DOTS.

Methods: We retrospectively reviewed the treatment charts of patients with new episodes of smear-positive pulmonary TB diagnosed in 2010 and 2011 at 33 health facilities in Lima and treated with regimen I (2HREZ/4H2R2) under DOTS. The dates of receipt of each dose were recorded by the health staff. Regimen I is scheduled 6 days/week in the 2-month intensive phase and 2 days/week in the 4-month continuation phase. Treatment interruption was defined as a dose not taken when scheduled in the intensive phase or within the three days following the last dose in the continuation phase. Treatment outcomes follow WHO definitions.

Results: Due to availability of treatment charts, we included 458 (77.5%) out of a random sample of 591 TB cases. Mean age was 31.6 years (SD 14.6), 277 (60.5%) were men and 6 (1.3%) were HIV positive. Overall, 95.4% had at least one interruption during treatment: 83% in the intensive phase and 88% (365/415) in the continuation phase. More than 10 cumulative days of interruption were observed in 54.8% during overall treatment: 7.9% in the intensive phase, and 41.9% in the continuation phase. More than 5 episodes of consecutive days of interruption were observed in 46.1% during treatment: 7.2% in the intensive phase, and 26.7% in the continuation phase. The median duration of each episode was 2.3 days (IQR 1.8–3.2). In 69.9% there was at least one interruption that implied 7 consecutive days without treatment. Defaults (48, 10.5%) mainly occurred in the continuation phase (33/48, 69%). The proportion of patients with at least one interruption in the first two weeks of treatment was 52.1% (25/48) for defaulters and (102/351) 29.1% for cured patients (Pearson χ^2 10.31, $P = 0.001$).

Conclusions: Even under DOTS, TB treatment interruptions with regimen I are frequent, especially in the continuation phase. The precise impact of specific patterns of interruptions on microbiological and

clinical outcomes should be further studied. It could merit attention of TB programs for the evaluation of strategies to limit their occurrence and effects.

TUBERCULOSIS MOLECULAR EPIDEMIOLOGY AND GENOTYPING

PC-956-03   Predominance of East African Indian strain of *Mycobacterium tuberculosis* among pulmonary tuberculosis patients of the Sahariya Tribe in North Central India

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Background: Tuberculosis is the deadliest infectious disease, caused by *Mycobacterium tuberculosis*. In India, TB has remained in equilibrium with the population and causing high endemicity. In a highly endemic area, strain diversity is expected to be different as compared to epidemic or sporadic incidence where a few specific types predominate. Indian population is composed of people of diverse cultural, linguistic, biological, ethnic and genetic backgrounds, living in different socio-cultural and socio-economic settings. Madhya Pradesh, a state in Central India, is a home to more than 50 tribes, most of which are Primitive Tribal Groups (PTGs). Health status of these tribes is extremely poor due to malnutrition, lack of proper hygiene and illiteracy.

Objective: To identify the predominant *M. tuberculosis* strains which might be responsible for increased burden of tubercular disease among people of Sahariya Tribe of North M. P.

Methods: A total of 111 patients from Sahariya tribe and 115 patients from their non-tribal neighbours were recruited in the study from Sheopur and Gwalior districts, M. P. The recruited individuals were screened for diagnosis by AFB staining, chest X-ray, etc. The sputum samples observed positive for AFB were processed for *M. tuberculosis* culture. Identification of *M. tuberculosis* was done by biochemical assays. Genomic DNA was isolated and PCR for direct repeat region (DR region) was performed using DRa and DRb primers. Reverse blot hybridization was followed by developing the X-ray film. MIRU-VNTR genotyping was performed to discriminate different *M. tuberculosis* isolates (Supply et al., 2000). The data obtained was analyzed by using online tools, SPOLDB4 database and www.miru-vntrplus.org.

Results: Two major spoligotypes, East African Indian (EAI3_IND) (28.7%) and Central Asian strain (CAS1_Delhi) (29.6%), respectively, were observed among tribal and non-tribal populations. The EAI3_IND (41.4%) strain was found to be predominating in patients of Sahariya tribe as a major spoligotype, followed by CAS1_Delhi (25.2%).

Conclusion: The high percentage of EAI3_IND and CAS1_Delhi strains shows that they are predominant in this region. Some other strains are also present but fewer in numbers. Further investigations on these strains and population specific diversity would enable us understand the clinical differences between infections with different strains, treatment response and development of new therapeutic regimens against these mycobacterium strains.

PC-957-03   Molecular epidemiology of multidrug-resistant *Mycobacterium tuberculosis* in Taiwan, 2012

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Background and aim: Approximately 40–50% of multidrug-resistant tuberculosis (MDR-TB), defined as *Mycobacterium tuberculosis* (MTB) isolates resistant to at least isoniazid and rifampicin, confirmed annually were new cases in Taiwan. To investigate the molecular epidemiology of MDR-TB, we conduct a population-based genotyping of MTB isolates from confirmed MDR-TB cases in 2012.

Methods: MTB isolates of 145 (96.0%) confirmed MDR-TB cases were analyzed. Excluding 3 isolates with poor quality of DNA, 142 isolates were genotyped. Genotyping methods, IS6110 restricted fragment length polymorphism (RFLP), spacer oligonucleotide typing (spoligotyping), and 15-loci mycobacterial interspersed repetitive units (MIRU) were used in this study. Genotype data were analyzed using the Bionumerics software. Cluster was defined as at least two isolates harboring the identical RFLP and/or MIRU genotype when the number of IS6110 band in RFLP was equal to or less than 6.

Results: In this study, the medium age of MDR-TB cases was 55 years old and male to female ratio was 3.1:1. The predominant spoligotypes were Beijing (57.2%) and Haarlem (14.5%), while the major MIRU patterns were 424223325173533 (18.3%). There were 43 MDR isolates (30.3%, 43/142) in 16 clusters including 10, 5, and 1 cluster (s) containing 2, 3, and 8 isolates, respectively. Of the 16 clusters, 9, 4 and 3 clusters were Beijing, Haarlem and other non-Beijing genotypes, respectively. The largest cluster containing 8 Beijing genotype isolates including 4, 2, and 2 isolates collected from eastern, northern, and southern Taiwan, respectively. Only one Haarlem

cluster was identified as household transmission, while no epidemiological links were identified among other clusters. In addition, genotypes of isolates obtained from 5 cases notified from a high TB prevalent aboriginal township were distinct. In this investigation, we found the rate of recent transmission was 19.0%.
Conclusions: Even through confirmed MDR-TB transmission was rare, continuous surveillance with more thorough epidemiological investigations is crucial for the preventing dissemination of MDR-TB.

PC-958-03 Laboratory investigation of tuberculosis clusters in Taiwan, 2006–2011

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Background: In 2006–2011, approximately 13 000–15 000 new tuberculosis (TB) cases were notified in Taiwan. TB suspected cluster was defined as two cases notified within one year at the same site. The aim of this study is to conducted laboratory investigations to define true TB clusters/transmission.
Methods: During 2006 to 2011, 369 suspected TB clusters of 1716 *Mycobacterium tuberculosis* strains isolated from 1492 cases were sent to the reference laboratory for genotyping. Exclude 19 suspected TB clusters of 64 cases and one isolate were analyzed for each reported case. Finally, there are 350 suspected TB clusters of 1428 cases in this study. Genotyping methods, spacer oligonucleotide typing and IS6110 restricted fragment length polymorphism (RFLP), were used to identify TB clusters. Epidemiological information was obtained from the Epidemic Report Files Management System (ERFMS) and National TB Registry. A confirmed cluster was defined as having at least two patients' isolates with identical RFLP genotypes and known epidemiologic links.
Results: Of the 350 suspected clusters, 1428 TB cases were notified from northern (49.6%), southern (22.8%), central (19.3%) and eastern (8.3%) Taiwan. Majority of cases were notified from health care facilities (41.8%), hospitals (18.6%) and campus (17.8%). Of the 350 suspected clusters, 130 (37.1%) suspected clusters had identical genotypes. High clustering ratios were in family 75.0% (48/64) and campus 50.9% (29/57). Moreover, of the 38 suspected multidrug-resistant TB clusters genotyped, we confirmed 23 (60.5%) clusters. In this study, predominant genotypes of *M. tuberculosis* in the clustered episodes were Beijing (52.6%), Haarlem (16.3%) and T (7.4%). Concordance was found between laboratory genotyping results and epidemiological links identified in the ERFMS.
Conclusion: Enhanced health management, early diagnosis, implementing latent TB infection treatment and infectious control were effective components for preventing TB clusters.

PC-959-03 Population level genetic, phenotypic and spatial study of tuberculosis in Lima, Peru

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Background: Understanding the association between *M. tuberculosis* strain genotype, tuberculosis transmission, the spatial distribution of incident cases and their association with the drug resistance phenotype helps public health resources to be focused to the highest risk groups and areas.
Design/methods: Between December 2008 and January 2010 in two of the four large suburbs of metropolitan Lima, a total of 14 603 tuberculosis tests were sent from patients with symptoms of tuberculosis both in hospitals and in the community. These generated a total of 5966 positive tuberculosis cultures from 2675 patients. Genotyping with both 15 loci MIRU-VNTR and spoligotyping, together with drug sensitivity testing using the Microscopically Observed Drug Susceptibility assay (MODS) was performed on 2139 (80%) of these culture positive isolates, each from a different patient. Demographic information was collected on a proforma, patient households were mapped using GPS and data on socio-economic status and population density was obtained by combining the dataset with the latest National Peruvian Census.
Results: The Latin American Mediterranean clade was most strongly associated with drug-resistance (OR 2.7, $P < 0.001$, CI 1.98–3.74). The Beijing clade (OR 6.2, $P < 0.001$, CI 3.67–10.57), multidrug-resistant tuberculosis (OR 1.9, $P < 0.001$, CI 1.30–2.72) and isoniazid mono-resistant tuberculosis (OR 2.1, $P < 0.001$, CI 1.34–3.27) were significantly associated with genetic clustering. Within households only 52% (CI 40–64%) of cases were clustered indicating significant transmission outside the home.
Conclusion: This study demonstrates that drug resistance was not distributed evenly across strain genotypes. Instead, strains from the LAM clade were 2.8 times more likely than other strains to be drug resistant and were responsible for 61% of all multidrug-resistance in the region. Genetic clustering suggestive of recent ongoing transmission was significantly associated with multidrug-resistance, isoniazid mono-resistance and strains of the Beijing family.

PC-960-03   Innovative tool to see and share data about patients in a VNTR cluster

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Background: From 1993 onwards, of every positive culture of *M. tuberculosis* the National Tuberculosis Reference Laboratory performs DNA typing. Since 2009 the MIRU VNTR technique is routinely used. Data for 2004–2008 have retrospectively been typed for VNTR. Identical VNTR typing of bacteria found in different patients, will give the same VNTR fingerprint, a so-called VNTR cluster. Results coming from the laboratory are given to the national cluster investigator who shares these results with Municipal Health Services (MHS) in the real-time online registration system of the National Tuberculosis Register (NTR).

Intervention: The NTR, originally meant for the surveillance of tuberculosis in the Netherlands, has been innovated in a way to provide at the level of the Municipal Health Services the possibility to have a look at a specific VNTR cluster. By searching on this specific VNTR cluster an overview of all patients in the cluster—including patient's characteristics as geographical area, social network, risk group, pulmonary TB and infectiousness—can be subtracted from the online database. This gives the public health nurses working at the MHS a direct lead to look if possible epidemiological relationships between patients really exist. These public health nurses of the MHS Services then again add the results of the investigation of epidemiological relations between patients to the NTR.

Results and conclusions: As well as monitoring transmission by observing the number and growth of VNTR clusters, an important role of the national cluster investigator is supporting the MHS doctors and nurses by reporting about these clusters at national and regional level in order to evaluate and improve TB control strategies. In a different way VNTR cluster data is innovatively used to make real time overviews of patients in a specific cluster to find out if there are epidemiological links and get a better insight in transmission of tuberculosis in the Netherlands.

PC-961-03   *M. tuberculosis* genotype distribution in pulmonary tuberculosis patients from Papua and Java, Indonesia: ethnicity, disease phenotype and BCG vaccination status

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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, with certain human populations being more susceptible to particular *M. tuberculosis* genotype families. The degree of evolutionary adaptation might also affect the clinical phenotype of active tuberculosis. We examined these hypotheses in the unique setting of human and pathogen diversity in the Indonesian archipelago.

Design/methods: Between 2011–2013, two cohorts of pulmonary TB patients were established, one from hospitals in Jakarta and Bandung, West Java ($n = 156$ patients), and one from two hospitals in Jayapura, Papua ($n = 185$). Self and parental ethnicity, age, BCG-vaccination status, as well as TB treatment history and TB exposure were recorded, HIV-status was measured, and all *M. tuberculosis* isolates were genotyped using a combination of spoligotyping, MIRU-VNTR and SNP-typing. Genotype distribution was compared between patients in Java and Papua, between ethnicities, and according to age and BCG vaccination status.

Results: Patients in Java were slightly older in Java compared to Papua (median 32 vs. 28 yrs), HIV-prevalence was 1.1% resp 5.4%. Large differences were noted in genotype distribution between Java and Papua. Beijing genotype strains were predominant in Java (32% vs. 16% in Papua), while East-African-Indian (EAI) strains were the most predominant group in Papua (38% vs. 8% in Java). Among patients from Papua, ethnicity correlated with the infecting genotype; Beijing strains were more common among patients with Javanese ancestors, while EAI and LAM/T strains were more common among those with Papuan ethnicity. Patients infected with Beijing genotype strains more often reported a history of previous TB treatment, and less often had a BCG-scar on clinical examination.

Conclusion: These results suggest that evolutionary adaptation is a major factor underlying the differences in *M. tuberculosis* genotype distribution across

Indonesia, and that disease phenotype and protection of BCG-vaccination in Indonesia depend on the infecting genotype.

PC-962-03 A novel approach for automation of MIRU-VNTR genotyping of *Mycobacterium tuberculosis*

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Background: Strain typing is needed to improve control and understanding of tuberculosis (TB) transmission and pathogenicity. Fondation Mérieux is encouraging the implementation of such methods in high-prevalence TB countries in the framework of research, epidemiological and routine purposes. MIRU-VNTR (Mycobacterial Interspersed Repetitive Unit—Variable Number of Tandem Repeat) typing is a well-described molecular method for TB strains genotyping. It is based on mini-satellite allele numbering and requires PCR amplification, electrophoresis and manual allele calling. This process is long, cumbersome and associated with several sources of error. Thus, an alternative method is needed to simplify the protocol and to increase reliability of MIRU-VNTR typing. We describe here a new reliable method using QIAxcel, an automated high-throughput capillary electrophoresis system (Qiagen AG, Switzerland).
Design/methods: Fifteen MIRU loci are investigated according to epidemiological panel described by P. Supply et al., 2006. Tests were performed on TB isolates of different genotypes. They were processed by conventional method and on QIAxcel, for which a specific electrophoresis program was specially designed for this study; allele calling is done automatically by the software.
Results: QIAxcel calculated correct allele calling for more than 555 amplicons from 143 to 1144 bp, providing concordant genotype patterns for various lineages. We observed a sizing accuracy of 1.3% vs. 3.0% for conventional method. The standard deviation obtained for reproducibility tested from 112 to 771 bp, ranged from 0.9% to 0.4% respectively. Mean turnaround time to process 10 MIRU-15 samples from PCR to interpretation is 2.5 working days by QIAxcel vs. 6.5 days by conventional electrophoresis, associated to a lower cost.
Conclusion: QIAxcel system facilitates MIRU-VNTR genotyping. It provides reliable results compared to conventional method through a faster and automated process and would be thus more suited for typing method implementation in high-prevalence TB countries.

PC-963-03 Danish *Mycobacterium tuberculosis* outbreak strain is spreading among Greenlandic Inuit in Denmark and Greenland

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Background: Transmission of *Mycobacterium tuberculosis* continues at high rates among Greenlanders in Greenland (GL) and Denmark (DK), with 203 and 450 notified cases per 10^5 populations year 2010, respectively.
Design/methods: This is a retrospective nationwide case-only register study based on centralized *M. tuberculosis* genotyping through 20 years. The cohort consisted of 7755 genotyped *M. tuberculosis* positive TB cases, 927 cases in GL and 6828 cases in DK, respectively.
Results: We can document, that the predominant Danish *M. tuberculosis* outbreak strain 'C2/1112-15' has been transmitted to Greenlanders in DK, and subsequently to GL, where it is spreading at alarming rates, adding to the already heavy tuberculosis burden in this population group. It is now clear, that 'C2/1112-15' is able to multiply in genetically very different populations. Thus, it might have the ability to spread even further keeping in mind the potential clinical consequences of strain diversity, e.g., the widely spread Beijing genotype.
Conclusion: The introduction of the predominant C2/1112-15 *M. tuberculosis* strain into the Inuit community in the Arctic Circumpolar Region is an alarming tendency which deserves attention. We need to monitor whether this strain already have, or will, spread outside The Danish Kingdom.

TUBERCULOSIS TREATMENT/MEDICAL MANAGEMENT/PROGRAMME

PC-964-03 The necessity of mandatory treatment for tuberculosis: a countrywide observational registry study

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Background: To achieve tuberculosis (TB) control in patients without sufficient treatment adherence, who pose a public health threat, in Estonia, orders for mandatory treatment for TB are issued by a court.

Objectives: To fill the gap in knowledge and evaluate the relative effectiveness of mandatory treatment for TB.

Methods: Data on all treatment cases recorded in Estonia during 2004–2012 were obtained from the Estonian TB Registry. To reduce confounding by potentially unbalanced explanatory covariates, pairwise (1:1) propensity score matching (PSM) was performed using a total of 67 patient demographics- and TB-related parameters, including resistance patterns and treatment duration, at index date (start of treatment). Standard definitions were applied for treatment outcomes. Effectiveness of treatment was assessed using multivariate logistic regression analysis adjusted for matched pairs.

Results: The total sample consisted of 3612 patients, who presented with 3916 treatment cases, out of which 147 cases (3.75%) represented mandatory treatment with duration of 196.0 ± 5.3 days (mean ± SEM). PSM yielded two matched cohorts of 133 patients in both, comprising altogether 3608.1 patient-months. Compared with ordinary treatment, mandatory treatment produced equal rates for cure [odds ratio (OR) 1.24, 95% confidence interval (CI) 0.46–3.70, $P = 0.67$), treatment completedness (OR 0.76, 95%CI 0.12–4.86, $P = 0.77$), ineffective treatment (OR 1.58, 95%CI 0.39–6.47, $P = 0.52$), defaulting (OR 1.39, 95%CI 0.44–4.41, $P = 0.57$), and all-cause deaths (OR 0.73, 95%CI 0.19–2.79, $P = 0.64$). A sub-analysis showed no significance for the rates of either TB-related (OR 0.63, 95%CI 0.15–2.64, $P = 0.52$) or other-cause mortality (OR 1.24, 95%CI 0.14–11.22, $P = 0.85$).

Conclusion: This observational study indicates that mandatory treatment for TB in those cases, where it is justified, yields results that are equal to those achieved in ordinary patients with conventional treatment corroborating the necessity of continuing with mandatory treatment to attain desired outcomes.

PC-965-03   Implementación de la 'plática dinámica' para la búsqueda activa de de casos de tuberculose en sala de espera del centro de salud de Ometepec Guerrero, México

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Objetivo: Detectar casos de tuberculosis entre la población que asiste a la consulta externa a través de la implementación de la plática dinámica de TB en el Centro de Salud de Ometepec del Estado de Guerrero.

Justificación: Dado a la presencia de casos de tuberculosis pulmonar, en el municipio de Ometepec, que cada año en promedio registra 31 casos nuevos de los cuales son de localización pulmonar 93.3%, se hace necesario focalizar la detección en áreas de concentración poblacional entre las personas que acuden a consulta externa en ese centro de salud.

Metodologia: Previo a la consulta, se realizaron platicas breves de tres minutos con la pancarta: ¿Mi TOS es Seca o con flemas?, preguntándoles a las personas en sala de espera, si sabían cómo es la tos seca ó con flemas, invitándoles a levantar la mano los que presentaban tos con flemas por dos semanas, registrándolos en el cuadernillo de Sintomáticos Respiratorios, realizando la toma de baciloscopias de manera inmediata.

Resultados: De marzo-noviembre 2012 a Abril 2013, se examinaron 134 S.R., el rango edad de 15 a 60 y mas años, 52.2% fueron mujeres y el 47.8% hombres, diagnosticándose 7 casos (TBP), la positividad 57% +++, 14.3% ´++ y 28.6% + el tiempo-tos, 9 días/2 meses, ingresaron a TAES, el 28.6% curados y 71.4% continua en tratamiento.

Conclusiones: La estrategia de la plática dinámica que conlleva actividades de información y oferta del servicio de de detección entre usuarios de servicios de salud (consulta externa) demostró utilidad para fortalecer la detección como medida para disminuir la exposición de *Mycobacterium tuberculosis* entre los consultantes.

PC-966-03   A case-control study of factors affecting treatment outcomes for pulmonary tuberculosis in Istanbul

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Background: Tuberculosis is a public health problem and its transmission is a threat to the community. The aim of this study was to determine the factors influencing the treatment outcomes and the effectiveness of NTP in relation to the application of the DOTS program in various sites in Istanbul, Turkey.

Methods: Treatment outcomes of over 18 years old, bacteriologic confirmed 11 186 lung tuberculosis in Turkish Tuberculosis National Database that includes complete data on treatment outcomes for patients recorded in database from January 1, 2006 to December 31, 2009 and had one year follow-up were defined adverse treatment outcome (treatment failure, default, death) and treatment success (cure, treatment completed).

Results: Case group was composed of 464 patients

with adverse outcome, while the control group was composed of 441 patients with cure. Factors associated with adverse treatment outcome were >65 years of age (OR 3.39 [1.99–5.76]); male gender (OR 2.11 [1.49–2.99]); birth outside of Turkey (OR 5.48 [2.13–14.04]); comorbidity (OR 1.85 [1.29–2.65]); bilateral radiologic lesions (OR 2.07 [1.41–3.00]); previous treatment history (OR 3.99 [2.78–5.74]); 3rd month positive microscopy (OR 4.96 [3.04–8.09]) and any H & R +/− others (MDR) resistance (OR 22.64 [6.92–74.08]). There wasn't an association between the adverse treatment outcome and the application site of DOT delivery and the supervisors.

Conclusion: Our findings indicate the similar quality in DOT application and supervision among all patients. However, patients with certain characteristics compatible with being a significant determinant of adverse treatment outcome should be carefully monitored and treated.

PC-967-03   Forecasting the tuberculosis incidence rate in Kazakhstan

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Background: Effective tuberculosis (TB) control requires reliable estimates of current epidemiological situation and future short-term and secular trends. The formation of the incidence rate depends on various factors, including medical, and their effect is not isolated. In Kazakhstan, the TB surveillance includes the registration of several dozen indicators.
Objectives: To evaluate factors having a strongest influence on TB incidence rates in Kazakhstan and to build the mathematical model of short-term trends.
Methods: Three groups of indicators were assessed: indicators of epidemic process; indicators of diagnostics, observation, and treatment; indicators of active case detection and timely diagnostics. Surveillance data from the National TB Program were obtained for the years 1980–2007. Correlation and cross correlation analysis was used to assess the associations and dependency of TB incidence rates from different indicators. Linear and multiple regression analysis and stepwise regression were used to model trends in development of TB incidence rate.
Results: Most of the indicators of quality of diagnosis and patients treatment had high reliable correlations with incidence rate in advance of 3–6 years. The next factors influenced most strongly: the effectiveness of treatment of newly diagnosed pulmonary TB (PTB) by cavity closure ($r = -0.887$; lag 4 years),

measures on patients isolation ($r = -0.801$; lag 5 y), the extent of surgeon's treatment in patients with PTB ($r = -0.945$; lag 6 y), the incidence rate of exposed persons in bacillary TB foci ($r = 0.924$; lag 3 y), lethality from TB of registered patients ($r = 0.971$; lag 4 y). The regression equation was built up, which describes the prediction model with non-standardized coefficients. The best results were obtained in the model that takes into account the influence of three indicators (with negative lag - 4 y.): the percentage of cavity closure in patients with PTB identified in the previous year; coverage ratio of examinations for tuberculosis; the proportion of patients identified during routine inspections of all new cases (or actively identified).
Conclusions: The quality and timeliness of diagnosis, case follow-up, measures to patients isolate, and the effectiveness of treatment, affect on the incidence rate formation maximally after 3–5 years. We have shown that active case-finding and cavity closure in newly diagnosed TB patients should be considered to control TB in endemic zones.

PC-968-03   Diagnostic patterns of tuberculosis peripheral lymphadenitis in Georgia

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Background: Tuberculosis (TB) is serious public health problem in Georgia. The clinical practice of recent years showed increase of TB peripheral lymphadenitis (TBPL) among adult patients registered at the National Center for Tuberculosis and Lung Diseases (NCTBLD), despite the fact that TBPL was always considered the classical manifestation of primary TB in children and adolescents. Given that TBPL has very few symptoms, this atypical age distribution caused considerable differential diagnostic difficulties. The objective of the study was to detect whether the pediatric age group is a stable diagnostic criteria for TB peripheral lymphadenitis.
Design/methods: Retrospective cross-sectional study was conducted. Data abstracted from the NTP data base regarding 7910 extra-pulmonary TB cases were analyzed. Microbiologic and histo-morphologic verification of diagnosis was performed using pathologic specimens obtained by lymph node puncture or lymphadenectomy. Statistical analysis was performed using Epi-Info (version 3.5.4). Odds ratio (OR) and χ^2 P-values reported.
Results: Out of 7910 extra-pulmonary TB patients TBPL was diagnosed in 801 (10.1%); 4734 (59.8%) were males and 3176 (40.2%) females; 6094 (77%) were adults and 1816 (23%) were children and adolescents of '0–17' age group; 7196 (91%) were

newly diagnosed TB cases. Among TBPL group, 592 (73.9%) were adults, 209 (26.1%)—children and adolescents; men 429 (53.6%), women 372 (46.4%); new cases 715 (89.3%), retreated 86 (10.7%). Adults dominated in new cases 513 (71.8%), as well as in retreated 79 (91.9%). There were only single cases of retreated children and adolescents—7 (8.1%). Overall, pediatric age appeared to have nearly equal risk for lymphadenitis compared to adult age group (OR 1.2, $P = 0.02$), as well as among new (OR 1.23, $P = 0.01$) and retreaded (OR 1.23, $P > 0.05$) cases. Also, females showed to have higher risk (OR 1.33; $P = 0.0001$) overall and in new (OR 1.35; $P = 0.0001$) and retreated (OR 1.2, $P > 0.05$) cases.

Conclusion: The study findings showed that age can no longer considered as one of the strong diagnostic criteria of peripheral lymphadenitis in Georgia. Considering that the NTP is effective particularly in children and adolescents, it is advisable to direct essential measures to early and timely detection of TBPL. Specifically 'TB suspect case Protocol' should include palpation of all groups of peripheral lymph nodes as an obligatory procedure.

PC-969-03: Improving tuberculosis treatment success through commitment of the district management team, uMgungundlovu Health District, KwaZulu-Natal

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Background and challenges to implementation: uMgungundlovu District is the second highest TB burdened in KwaZulu-Natal, South Africa from the eleven districts. Between 2009 and 2012 an average of 9115 TB patients were registered. In 2006 this district was declared as a provincial TB crisis district as the treatment success rate was at 38% for new smear positive patients. Over the years 2006 to 2008 the district's performance remained unsatisfactory until improvements were realized from 2009 to date. The provincial TB program and the district management team committed to do the following:

- Created permanent positions and employed dedicated district TB manager and TB supervisors;
- Established tracer teams to follow up patients;
- Worked closely and effectively with TB program partners;
- Provided training of facility and district staff on TB program management using technical support of URC–USAID TB Project.

Intervention or response: Interventions were instituted in 2010 as part of supporting uMgungundlovu District. Baseline assessment was conducted and plans developed to improve the district TB programme. As part of identifying challenges and finding solutions,

the fishbone template as part of the TB-HIV collaborative Quality Improvement model was used. Intervention developed included training, ETR.net support, support supervision with coaching and mentoring and training. Regular TB programme review and feedback to the facilities was jointly conducted by the USAID TB Project and the Department of Health. Quarterly workshops were conducted, followed by identification of challenges and development of iterventions. ETR.net support was conducted to identify the gaps and facilities with most challenges. These facilities were then provided with on site support, training and mentoring.

Results and lessons learnt: Facilites were able to analyze their data, plan accordingly and track their progress. Share best practices were shared among the facilities during the collaborative workshops. Treatment success rate improved for new smear positive TB cases from 78.1% in Q1/2009 to 84.3% in Q4/2011; Cure rates from 74% to 81.1%, and defaulter rates from 8.2% to 4.7% during the same period.

Conclusions and key recommendations: Treatment outcomes for TB programmes in high prevalence settings can be improved by structured interventions based on proven quality improvement models.

PC-970-03   Tuberculosis diagnostic delay in a tuberculosis control dispensary cohort, Denizli, Turkey

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Aim: To study patient and physican delays in tuberculosis diagnosis. This is an essential part of TB control because early case detection is important.

Method: Patient and physician delays in 2012 tuberculosis patient cohort in Denizli Tuberculosis Control Dispensary (TCD), Turkey, were studied prospectively. A standardized form containing demographic data, factors that may influence patient and physician delays was prepared and filled out with a patient interview. Definition of 'patient delay' is days from first symptom to application to the physician, 'physician delay' is time from patient application to doctor and initiation of treatment, 'total delay' is the sum of patient and physican delays. Mann-Whitney U and Kruskal-Wallis tests were used to compare different groups for delays in diagnosis.

Findings: All 104 tuberculosis patients registered to TCD in 2012 were included. Mean age was 50.7 ± 16.9, male/female case numbers were 54/50. Pulmonary and extrapulmonary involvement was detected in 61, and 43 cases, respectively. Bacteriological diagnosis among pulmonary TB was 75.4%. First, second, and third physicians diagnosed 26.0%, 38.5%

and 35.5% of the patients, respectively. Diagnosis was done in government hospitals (36.5%), in a university (34.6%), in private organizations (9.6%), and in TCD (19.2%). Mean patient delay was 37.5 ± 80.2; physician delay was 76.7 ± 125.3 and total delay was 114.3 ± 142.9 days. In males, pulmonary cases, those with cough and with sputum, those who did not have microscopic examination, and smear positives were significantly longer patient delays ($P <$ 0.05). Physician delay was significantly longer in females, those without cavity on chest X-ray, those with sputum, those without chest X-ray and without sputum examination in the first physician visit. Total delay was significantly longer in cases with weight loss, those who were not diagnosed and those without a sputum examination during first physician visit.

Discussion and result: This is the first prospective diagnostic delay study in a tuberculosis control dispensary cohort in Turkey. Getting a chest X-ray and sputum microscopic examinations are important factors related with delays. Mean patient delay is more than 1 month and mean physician delay is more than 2.5 months; there is a significant variation among patients. Mean physican delay is especially long. This indicates that, there may be a need for health personnel education and to improve tuberculosis laboratories.

PC-971-03   Improving the quality of tuberculosis indicators using linkage database

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Backgrounds: Probabilistic linkage database has been used to qualify the information and get answers more reliable to the tuberculosis (TB) epidemiological situation. The aim of this study was to assess the impact of duplication removal and the linkage between Notifiable Diseases Information System (Sinan) and Mortality Information System (SIM) in TB indicators.

Methods: For duplicates removal was performed linkage between 2008 and 2009 Brazil data from Sinan, with the aim of excluding notifications not removed by Sinan routines performed by states and municipalities. The databases used were constructed in accordance with cases outcomes. A database (Sinan-TB1) was formed by cases filled with outcome situation as transferring or unfilled representing (11.8% of the total cases registered in the period). The other database (Sinan-TB2) was composed of records filled with outcome situation as a cure, default, TB death, death from other causes and multidrug-resistant tuberculosis (MDR-TB). After linkage were defined true matches between all pairs found that showed outcome date recorded in Sinan-TB2 greater or up to 30 days

earlier then the outcome data registered in TB1-Sinan. For the linkage between Sinan and SIM was used the database result of duplicates removal and SIM data that TB was mentioned as basic cause or associated with the death between 2008 and 2010 in Brazil. After obtaining the pairs were considered true matches those associated with the notification of Sinan with the most current outcome date, considering that the death was probably related to the last event in Sinan notified and had the time of death up to 270 days after the diagnosis date in Sinan.

Results: Duplicates removal decreased the percentage of new cases with transfer outcome, ranging from 34.8% in 2008 and 35.5% in 2009. After the linkage between Sinan and SIM, the percentage of deaths from TB among new cases varied 16.4% in 2008 and 14.1% in 2009.

Conclusion: The results describe an alert situation in relation to data quality of cases outcome in Sinan, which includes the main outcome indicator of TB, the cure rate indicator. The databases record linkage can be used as an important tool both in epidemiological research in health, as in the service routine health surveillance.

PC-972-03   10 years of tuberculosis control in Cape Town, Western Cape, South Africa

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Background and challenges to implementation: Cape Town has a population of 3.8 million people and is divided into 8 health sub-districts. It has one of the highest TB case notification rates recorded (698/ 100 000 in 2012). The DOTS strategy was first implemented in 1996. Despite a network of approximately 121 TB treatment points and 101 TB reporting units spread across the city and the availability of quality diagnostics and dependable drug supplies, relatively poor TB treatment outcomes were achieved historically. High HIV infection rates (antenatal prevalence 20.9% in 2011) fuels the TB epidemic. Sub-districts with the highest caseloads had the poorest outcomes. This paper reviews 10 years of TB control measures as prescribed by the National TB Control program (following WHO guidelines) and the results achieved. The experiences and lessons learnt in the process of overcoming program barriers may be translatable to TB control programs elsewhere and have relevance to other programs locally.

Intervention or response: Extensive management efforts had to be invested in the TB program to improve treatment outcomes. A series of new initiatives were implemented in the quest to achieve a new smear positive cure rate of 85%. Various capacity

development activities were implemented, new supportive tools developed and partnerships with civil society were put in place to supplement public health resources. A Plan-Do-Review cycle was instituted with a rigorous monitoring system which included individual health facility assessment and prompt feedback to staff. A system of rewards to affirm clinics achieving 85% cure rates or making significant progress towards that was established.

Results: The Figure presents ETR.net reports on total number of cases registered for treatment and the new smear positive cure rates for over the last 10 years. Against a rapid increase in the number of TB cases, the new smear positive cure rate increased from 70% to 85% in this period. There is now a trend towards a decreasing TB incidence.
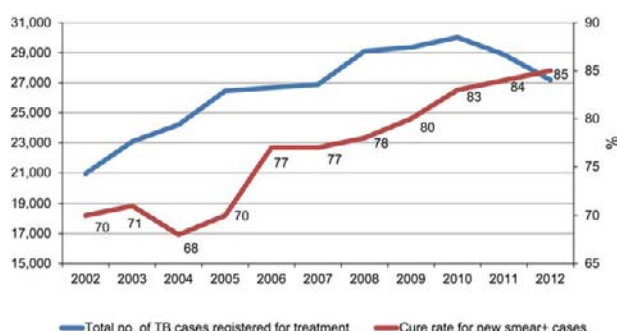

Figure City of Cape Town: TB case finding and new smear positive cure rates.

Conclusions: The elusive 85% cure rate for new smear positive cases has been achieved and the improvements extended to other aspects of the TB program. Sustained buy-in from an increasing large team of managers, nursing staff, doctors, and community health workers helped to achieve this success.

PC-973-03 Digital chest X-ray interpretation for diagnosis of tuberculosis in Zambia: the need for improved standardization

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Background: Reliable chest X-ray (CXR) interpretation, especially in HIV-infected patients, remains a challenge in resource-limited settings. Using digital radiography we evaluated a standardized form, the CXR Reading and Recording System (CRRS) when used by frontline clinicians for diagnosis of pulmonary TB (PTB).

Design/methods: Inmates were screened for TB in 2 Zambian prisons using symptoms, physical exam,

CXR, fluorescence microscopy and sputum culture (Cx). Two Zambian medical officers, CRRS certified readers, by the Lung Institute, University of Cape Town; read all CXRs. Using solid and liquid Cx as the reference standard we evaluated each reader's sensitivity, specificity and inter-rater reliability. CXRs selected for this analysis based on initial evaluation were: (1) all TB patients; (2) all persons with abnormal CXRs; and (3) a random sample of inmates with normal CXRs but not diagnosed with TB.

Results: Between January and July 2011 we screened 3045 inmates, 571 met eligibility criteria and were included in the analysis. 556 (97.4%) were male, mean age 38.6, and 144 (25.2%) had a prior history of TB. Sensitivity and specificity analyses were limited to 503 inmates with valid Cx results, of whom 74 (14.7%) had Cx-confirmed TB. Sensitivity, specificity and inter-rater reliability are shown.

	HIV positive ($n = 200$)		HIV negative ($n = 303$)	
	CXR consistent with TB		CXR consistent with TB	
	Sensitivity (95%CI)	Specificity (95%CI)	Sensitivity (95%CI)	Specificity (95%CI)
Reader 1	0.57 (0.37–0.75)	0.61 (0.53–0.68)	0.62 (0.45–0.76)	0.59 (0.53–0.65)
Reader 2	0.50 (0.31–0.69)	0.60 (0.52–0.67)	0.55 (0.39–0.70)	0.61 (0.55–0.67)

Agreement index	Parenchymal abnormalities	Pleural abnormalities	Central abnormalities	Abnormalities consistent with TB
HIV positive patients ($n = 231$)*				
Kappa (95%CI)	0.35 (0.22–0.42)	0.61 (0.48–0.67)	0.37 (0.25–0.44)	0.49 (0.37–0.56)
Strength of agreement	Poor	Good	Poor	Fair
HIV negative patients ($n = 334$)				
Kappa (95%CI)	0.29 (0.19–0.40)	0.66 (0.55–0.77)	0.35 (0.25–0.46)	0.70 (0.59–0.80)
Strength of agreement	Poor	Good	Poor	Good

Inter-rater reliability appears as a header row above Agreement index.

* 6 CXR unreadable.

Conclusions: Despite similar sensitivities and specificities, CXR interpretation of lung abnormalities consistent with TB showed generally poor agreement between CRRS readers in both HIV-negative and positive patients. Further improvement in inter-rater reliability may be achieved by the modification of the CRRS training system or the implementation of mentoring programs after CRRS training completion.

PC-974-03 Prevalence of pulmonary tuberculosis in persons aged >15 years in Afghanistan: results of a retrospective study, 2010–2012

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Background: Afghanistan is a low income nation with a notably high tuberculosis (TB) burden. The

aim of this study was to determine a nationwide prevalence of pulmonary tuberculosis (PTB) in Afghanistan in the context of patients' gender and treatment history.

Methods: All cases associated with pulmonary tuberculosis recorded between 2010 and 2012 in patients aged >15 years were analyzed. All smear microscopy positive data were analyzed in context of gender and treatment history. Sputum microscopy negative cases, patients inaccessible to smear microscopy and patients with histories of past treatment from private sectors were additionally included in the study. Some of the parameters, namely number of new cases and past cases (due to relapse, or treatment after default, and treatment failure), were included in treatment history.

Results: A total of 59 873 pulmonary TB cases had been recorded during 2010–2012 in patients aged >15 years. Among them, 20 768 (34.7%) were male and 39 105 (65.3%) were female. The highest number of pulmonary TB cases (20 128) was recorded in the year 2011. 4.8% of total patients had no access to microscopic diagnosis, and had been declared as TB patients on the basis of signs and symptoms, whereas those with access showed 79.6% and 20.4% in positive and negative smears respectively. Among the smear positive cases, 91% comprised of new cases, of which 9% received treatment in the past. Among the previously treated cases, 84.9% were relapse cases, 11.4% were failures, and 3.7% comprised of defaults. 3.3% of the total cases had been treated at private sectors with unknown case histories.

Conclusions: This study showed that females were highly susceptible to tuberculosis. Further studies were necessary to investigate the epidemiology of tuberculosis in Afghanistan specially the high prevalence of TB among females. Thus, this is recommended that the control survey should regularly be conducted in order to monitor the situation of TB affliction in Afghanistan.

PC-975-03   Contribution des centres de santé confessionnels à la prise en charge de la tuberculose au Bénin

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Introduction : La prise en charge de la tuberculose au Bénin est faite dans 57 Centres de Dépistage et de Traitement (CDT) répartis sur tout le territoire national. Huit de ces CDT sont des Centres de santé confessionnels qui ont habituellement une grande fréquentation du fait de la qualité des soins qui y sont prodigués.

Objectif : Apprécier le dépistage des cas de tuberculose et l'issue thérapeutique des patients traités dans les centres de santé confessionnels.

Méthode : Etude rétrospective des rapports de dépistage de l'année 2011 et des résultats de traitement de l'année 2010 de chaque CDT du Bénin. Les données des Centres de santé confessionnels ont été appréciées par rapport à l'ensemble des CDT et les objectifs de traitement.

Résultats : Les Centres de santé confessionnels qui abritent des CDT sont présents dans 4 des 6 départements du Bénin. Ce sont : l'hôpital de Tanguiéta dans le département de l'Atacora-Donga, les hôpitaux de Saint Luc, de Bethesda et de So Tchanhoué dans l'Atlantique-Littoral, les hôpitaux de Bembéréké, de Boko et de Papané dans le Borgou-Alibori et l'hopital de Zagnanado dans le Zou-Collines.

En 2011, ils ont eu à leur actif, 10% des 4320 cas de tuberculose toutes formes confondues dépistés au Bénin. Leur part dans le dépistage est élevée dans les départements de l'Atacora Donga (17%), Borgou Alibori (26%) Zou Collines (23%) qui ont soit un accès difficile soit des populations relativement pauvres. Cette part dans le dépistage est plus faible (10%) dans le département de l'Atlantique Littoral où se trouve la capitale économique.

Il s'agit essentiellement des TPM+ dans la majorité des Centres. Mais la fréquence des TEP est particulièrement élevée à Bembéréké (29%) et Zagnanado (41%).

Le taux de succès thérapeutique des TPM+ nouveaux est faible à Bembéréké (72%). Mais il est élevé dans tous les autres centres (87% à 97%) proche du taux de succès enregistré au niveau national (91%).

Conclusion : Huit centres de santé confessionnels ont dépisté 10% des cas de tuberculose enregistrés en 2011 au Bénin. Les TMP+ nouveaux ont connu un bon taux de succès thérapeutique comme l'ensemble des patients pris en charge dans le pays. Mais un effort doit être fait pour améliorer le taux de succès thérapeutique dans un centre et mieux cerner le diagnostic des TEP très fréquents dans deux centres.

TUBERCULOSIS BASIC SCIENCE LABORATORY

PC-976-03 Using TNF-alpha-dependent anti-apoptotic-related gene expression with WBC count to characterize the clinical status of Malagasy subjects with tuberculosis

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Background: Most of *Mycobacterium tuberculosis* (Mtb) infections are contained by the immune host response and remain asymptomatic except for up to 10% of the infected hosts that will progress to clinical tuberculosis (TB). Identifying LTBI with the highest risk to develop disease would be helpful to fightback the pandemy. However, the current tests for latent TB are yet unable to differentiate between persistent and resolved latent infection and biomarkers infection are needed to understand the spectrum of TB disease progression risk. Apoptosis and innate immunity are involved in the control of tuberculosis infection and disease, but their utility as surrogate markers to characterize clinical TB has not yet been investigated. To discriminate the different phases of the clinical TB spectrum, we thus analyzed the blood cell distribution and gene expression of several TNF-alpha dependent apoptotic genes (TNFR1, TNFR2, FLICE, FLIPs) by real-time RT-PCR of peripheral blood cells from cohorts of individuals with active tuberculosis or potential exposure to TB.
Design/methods: 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: Results showed significant elevation of FLIPs expression by infected individuals regardless of clinical status at entry to the study. In the TB contacts, this FLIPs expression was amplified in the household contacts after 3 months of follow up. A higher percentage of lymphocytes were found in the infected household contacts that remained healthy. In contrast, in individuals with active TB, a significant upregulation of TNFR2 expression, a significantly higher percentage of monocytes and a significantly decreased lymphocyte count were seen, compared to subjects that remained healthy. Moreover, the household contacts who subsequently developed signs of TB, also had a significantly high number of monocytes.

Conclusion: These data suggest TB disease may be associated with decreased T-cell survival (perhaps due to apoptosis) while inhibition of apoptosis in monocytes could lead to a relative increase in these cells. The current work paves the way for further investigation on surrogate markers to delineate protective and weak immunity against TB.

PC-977-03 Polymorphism of human genes IFNG, TLR2, TLR4 and host susceptibility to tuberculosis in Russian Slavic population

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Background: Human genetic variation plays its role in host susceptibility to tuberculosis (TB). Furthermore, there may be some correlation between infecting *M. tuberculosis* (MTB) strain/genotype and human allele. Here, we carried out a case-control study of human SNPs (IFNG +874A/T, TLR2 Arg753Gln, TLR4 Asp299Gly) in Russian Slavic population; the results we compared not only for total TB patient group vs. healthy controls but also for special subgroups of TB-patients infected with different MTB genotypes.
Design/methods: A total of 145 *M. tuberculosis* isolates were typed using spoligotyping, IS6110-RFLP and 24-MIRU-VNTR typing. Human SNP genotyping was done for IFNG, TLR4, TLR2 genes in the same TB patients (cases) and 158 HIV-negative unrelated individuals (controls). Both groups included only Russian Slavic individuals defined by self-identification. All persons gave their informed consent prior to their inclusion in the study. All analyses (single-point, genotype, and linkage disequilibrium) were performed with SHEsis software.
Results: Most of the 145 MTB strains belonged to Beijing family ($n = 93$), of them 23 were Beijing B0/W148 variant regarded as Russian successful clone. Analysis of IFNG +874 revealed that in male group: (i) genotypes were in Hardi-Weinberg disequilibrium ($P = 0.01$); (ii) AT heterozygotes prevailed among TB patients vs. controls that, taken together, may indicate a role of this SNP in host susceptibility to TB in Russian Slavic male population. TLR2 minor allele ('TB-susceptible') was identified in higher rate among TB patients than controls: 4.71% vs. 3.16% in total groups and, similarly, when stratified by gender. TLR4 major allele was found in higher rate in female patients compared to controls: 95.1% vs. 90.1% ($P = 0.08$). In females, TLR4-AG heterozygotes were found more frequently in cases than in controls: 19.7% vs. 9.8% ($P = 0.1$).
Conclusion: Comparison of allelic and genotype frequencies in different patient subgroups stratified by

infecting MTB strain genotype, and in healthy controls suggests a trend in difference for INFG +874 alleles between these different groups. Beijing B0/W148 subgroup has rate of 'TB-protective' TT genotype even higher than in healthy controls. On the other hand, patients infected with other Beijing and non-Beijing genotypes indeed had lower rate of TT genotype than controls. This unusual finding should be repeated in the large study and its evolutionary meaning remains to be clarified.

PC-978-03 Novel therapeutic vaccines against tuberculosis and their synergistic efficacy

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Background: Multidrug-resistant (MDR), especially extremely drug resistant (XDR), *Mycobacterium tuberculosis* is a big problem in the world. We have developed novel TB therapeutic vaccines, (HVJ-E/HSP65 +IL-12 DNA vaccine, granulysin vaccine and Ksp37 vaccine), to eliminate XDR-TB.
Design/methods: DNA vaccine expressing *M. tuberculosis* heat shock protein 65 and IL-12 was delivered by the hemagglutinating virus of Japan (HVJ) - envelope. *M. tuberculosis* was intratracheally instilled into cynomolgus monkeys and then treated with the vaccine. Granulysin DNA and Ksp37 (killer specific secretory protein of 37kDa) DNA were 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 also exerted synergistic therapeutic effect by the combination of chemotherapy (INH). This vaccine showed synergistic therapeutic efficacy by the addition of granulysin DNA vaccine in mice. Granulysin vaccine showed synergistic CTL activity against *M. tuberculosis* by the addition of Ksp37 vaccine. 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 these vaccines and chemotherapy (INH+RFP) are now being studied in monkeys.
Conclusion: These data indicate that our novel vaccines might be useful against *M. tuberculosis* including XDR-TB and MDR-TB for human therapeutic clinical applications. Co-worker; Nishida Y, Naka-

tani H, Kano K, Kishigami C, Nakura K, Nagasawa T, McMurray D, Hayashi S, Saunderson P.
State the implications of the results and key recommendations. Present specific findings on how the research addressed the study, question and challenge. Highlight opportunities for future research as well as implications for further research or TB prevention and control programmes.

PC-979-03 TNF-alpha receptors types 1 and 2 on CD14+ cells in peripheral blood mononuclear cell culture in active pulmonary tuberculosis

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Background: Tumor necrosis factor alpha (TNF) is an immunoregulatory cytokine which is critical in control of tuberculosis infection. TNF acts through its membrane receptors types 1 (TNFR1) and 2 (TNFR2). The main target for this mediator in antituberculous immunity are CD14+ cells. It was analyzed whether the percent of TNFR1+ and TNFR2+ CD14+ cells and the number of these receptors on monocytes in spontaneous and lipopolysaccharide (LPS) stimulated cultures of peripheral blood mononuclear cells (PBMCs) differ between patients with active pulmonary tuberculosis (APTB) and healthy individuals.
Design/methods: Peripheral blood was obtained from 25 patients with APTB and 150 healthy individuals. PBMCs were isolated from the whole blood by ficoll density centrifugation method and cultured overnight in 96-well plates with presence and without LPS. The percentage of CD14+ cells expressing TNFR1 and TNFR2 was determined by flow cytometry using phycoerythrin (PE) labelled antibodies to TNFRs (R&D Systems, USA) and FITC labeled antibodies to CD14 (eBioscience, USA) and the number of TNFRs per cell using QuantiBRITE PE calibration beads (BD, USA). Comparisons between groups were performed by Mann-Whitney test.
Results: Percent of TNFR1+ CD14+ cells in unstimulated and LPS stimulated PBMCs culture was higher in healthy individuals than in APTB patients. LPS increased percent of TNFR2+ but not TNFR1+ CD14+ cells in patients with APTB compared with unstimulated PBMCs culture. Number of TNFR1 and TNFR2 on CD14+ cells in unstimulated as well as in LPS stimulated PBMCs culture was higher in APTB patients than in healthy individuals. Culturing with LPS increased number of both TNFR1 and

TNFR2 on CD14+ cells compared with unstimulated PBMCs as in patients with APTB so in healthy individuals. Thus, higher TNF receptors number on CD14+ cells but not percent of cells bearing these receptors in tuberculosis patients compared with healthy individuals is shown what can reflect a greater reactivity of monocytes in response to TNF in lung tuberculosis pathological process.

Conclusion: Data received show that expression of membrane TNF receptors types 1 and 2 on CD14+ cells in spontaneous and LPS stimulated PBMCs differs between patients with active pulmonary tuberculosis and healthy individuals and that these receptors are involved in the pathogenesis of pulmonary tuberculosis.

PC-980-03   Nitrogen oxide features in patients with destructive recurrent pulmonary tuberculosis influenced anti-tuberculosis chemotherapy

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Background and objective: The study of nitrogen oxide (NO) in patients with destructive recurrent pulmonary TB (RPTB) during anti-TB chemotherapy.

Methods: 198 patients were screened for TB: 71 patients with destructive RPTB (1st group), 29 patients with RPTB without degradation (2nd group), 98 patients with newly diagnosed destructive pulmonary TB (NDPTB) (3rd group) and 30 healthy donors (4th group). All patients at admission had infiltrative pulmonary TB. NO status was evaluated by measuring by spectrophotometry the inducible NO synthase in neutrophils (iNOS), nitrite and nitrate levels in samples of venous blood prior treatment and two months later.

Results: At entry, the contents of NO in 1st group iNOS (231.6 ± 7.74) pmol\min\mgB, nitrate (56.35 ± 1.09) mmol/l, nitrite (5.40 ± 0.11) mmol/l; in 2nd group iNOS (307 ± 8.46), nitrate (63.18 ± 1.48), nitrite (6.24 ± 0.17); in 3rd group iNOS (251.7 ± 6.34), nitrate (61.82 ± 1.35), nitrite (5.77 ± 0.11) values were significantly different ($P < 0.05$); compared to 4th group iNOS (81.03 ± 2.36), nitrate (37.98 ± 1.30), nitrite (3.83 ± 0.09). NO levels were significantly higher in 3rd group compared to 1st group, while lowest levels were in 2nd group. After two months of treatment the 1st group had iNOS (104 ± 3.30), nitrate (44.63 ± 1.05), nitrite (4.41 ± 0.10), 2nd group iNOS (85.21 ± 2.98), nitrate (37.17 ± 1.52), nitrite (3.70 ± 0.10), 3rd group iNOS (91.86 ± 1.19), nitrate (41.41 ± 0.90), nitrite (4.14 ± 0.07) meaning that the difference between baseline and post-treatment was significant ($P < 0.05$). After two months of therapy patients in 2nd group had significantly more pronounced decrease in NO than 1st group.

Conclusion: In patients with pulmonary TB had significantly higher output in NO than in healthy controls. Before treatment initiation patients with RPTB had significantly lower rates of NO than in patients with NDPTB. After 2 months on chemotherapy patients with pulmonary TB had significantly lower NO activity. There were significant differences in the indices NO between patients with destructive and without destructive RPTB.

PC-981-03   Quality control of BCG vaccine seed lots by molecular methods

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Background: The use of molecular methods is very important for BCG vaccine manufacturers and control laboratories in performing the quality control assays of this product. A common test is the microscopic examination by Ziehl-Nielsen stain to confirm the presence of AFB in the BCG seed lot and colony's morphology. An absence of virulent mycobacteria is controlled in animals (guinea pigs). This method is costly and time consuming. The multiplex PCR (mPCR) assay was suggested by WHO is proposed as a method for the differentiation BCG sub-strains from each other and from other members of the *Mycobacterium tuberculosis* complex. However this method cannot detect point mutations in the PCR products' sequences and find SNP in the places of primers binding.

The purpose of our study was to determine the genetic stability of Russia BCG vaccine seed lots using currently available mPCR and NGS methods.

Design/methods: We analysed the lyophilized seed lots of BCG Russia sub-strain from the Scientific Center for Expertise of Medical Application Products, Moscow. We have investigated 8 lyophilized seed lots obtained during 50 years: 1948 (44 and 69), 1950 (90), 1954 (150), 1971 (374a), 1982 (367), 1992 (361), 2006 (368). Multiplex PCR was performed as described previously by Bedwell et al. (2001). RD1, RD2, RD8, RD14 and RD16 as well as senX3-regX3 were amplified. The PCR products were then analyzed by horizontal electrophoresis on 3% agarose

gel. We performed a pilot study to determine the feasibility of using NGS for quality control of BCG vaccine seed lots. Investigation was performed by the use of the Illumina MiSeq platform.

Results: All seed lots of BCG Russia sub-strain generated six bands that corresponding to RD8, RD16, RD2, senX3-regX3, RD14 and RD1, respectively. The BCG Russia gave 472, 401, 315, 276, 252 and 196 bp PCR products in the mPCR assay. We have also investigated all these seed lots by next-generation sequencing (NGS). There were no differences between all of seed lots by using these methods.

Conclusion: The present study has illustrated that mPCR assay for BCG identification satisfies the criteria for a routine quality control test. NGS is proposed as a novel test for BCG vaccine control. NGS is a promising method for the rapid assessment of the genetic stability and safety of vaccine BCG. It is expedient to carry out determination of genetic stability when releasing each new series of a vaccine, especially when a new seed lots are applied.

PC-982-03   New insights into accumulation and clearance of clofazimine in the uninfected mouse

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Background: In humans treated with clofazimine (CFZ), the skin discoloration resulting from the accumulation of the drug in tissues takes about 2 years to fade away after treatment cessation. This is consistent with an estimated CFZ half-life of 70 days in leprosy patients. In a recent experiment conducted in mice infected with *Mycobacterium tuberculosis* and treated for 9 months with a CFZ-containing drug regimen, there was also an intense brownish discoloration of tissues, but the discoloration totally faded away by 6 months after treatment cessation, suggesting that the clearance of CFZ is much more rapid in mice than in humans.

Design/methods: An extensive pharmacokinetic study of CFZ given orally to BALB/c mice, 5 days per week at 25 mg/kg was designed to measure the following: (i) the cumulative serum and tissue (lungs, spleen and liver) concentrations of CFZ in these mice and (ii) the rate of CFZ clearance after cessation of drug administration for 4, 8, 12, 16, and 20 weeks. To perform this study, CFZ was extracted from mouse tissues using acetonitrile and measured using liquid chromatography/mass spectrometry (LC/MS). Our LC/MS protocol for CFZ measurement has been optimized to allow multiple reaction monitoring analysis of the compound in the tissues. Calibration curves are linear over the range of 50 ng/ml to 8000 ng/ml.

Results: Data on CFZ accumulation are available up to week 20 of CFZ administration. The main findings are as follows:

- The serum concentrations remained around 1 μg/ml;
- In lung and liver, CFZ concentrations increased progressively to reach 10 μg/g at week 4, and between 50 and 100 μg/g at week 8. Thereafter there was no more increase, indicating saturation at the 75μg/gr of tissue level;
- In spleen, the CFZ concentrations dramatically increased up to ± 7500 μg/g of tissue at week 12 of administration, and then saturated at this level.

Data on CFZ clearance are still at an initial stage, but the lengthier the administration period, the lengthier the clearance of CFZ, i.e., the CFZ concentration decreased at a slower rate in mice administered longer courses of CFZ than in mice that administered shorter courses of CFZ. However, the half-life of CFZ in tissues is much shorter in mice than in humans and may be provisionally estimated at ± 7 days.

Conclusion: Clofazimine accumulates in mouse tissues, but its clearance is much more rapid than in humans

PC-983-03   Increased expression of SOCS1 in extensive caseous lymph node lesions from patients with tuberculous lymphadenitis

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Background: Protection against *M. tuberculosis* infection depends on host interferon-gamma (IFN-γ) responses. However, these responses can be reduced in tuberculosis (TB). The Suppressor of Cytokine Signaling (SOCS) 1 negatively regulates IFN-γ through inhibition of STAT1 activation. SOCS3 controls STAT3 activation through different cytokine receptors. We here compared the expression of SOCS1 and SOCS3 in granulomatous lesions from patients with tuberculous lymphadenitis in situ. We analyzed the expression of SOCS1, SOCS3 and of the chemokine CXCR3 receptor in tuberculous lymph nodes (LN) with extensive (e-LNTB) and focal (f-LNTB) caseous necrosis and in normal reactive lymph nodes.

Methods: SOCS1, SOCS3, CD3, CD68 and CXCR3 (a chemokine receptor and marker of Th1 cells) were stained by immunohistochemistry (IHC) in LN from TB patients ($n = 18$) with extensive (e-LNTB, $n = 8$) and focal (f-LNTB, $n = 10$) necrosis and compared with reactive LNs (r-LN, $n = 8$) from control subjects.

Results: SOCS1 was highly expressed in patients with tuberculous lymphadenitis as compared to r-LN. CXCR3 levels were higher in sections of LNTB with extensive caseous necrosis as compared to those with

focal caseous necrosis and r-LN. SOCS3 expression in sections with focal and extensive necrosis was variable.

Conclusion: Increased SOCS1 expression in granulomas of lymph nodes from TB lymphadenitis patients may be indicative of down-regulated IFN-γ mediated responses and reduced bacterial control at the site of infection.

PC-984-03   Evaluation of pyrazinamide activity in immune-competent and -deficient mouse models of tuberculosis

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Background: Pyrazinamide (PZA) is a key sterilizing drug in the current short-course tuberculosis (TB) drug regimen, and it is becoming increasing clear that PZA is a critical component of promising new drug combinations. How PZA positively contributes to TB drug regimens is somewhat enigmatic, as the mechanism of action of this drug is poorly understood. In addition to its anti-mycobacterial activity, limited studies suggest that PZA may also act in a host-directed manner. Our objective was to investigate this possibility via three sequential experiments

Design/methods: Experiment 1: BALB/c mice, aerosol infected with 3.7 log10 colony forming units (CFUs) M. bovis (which cannot activate PZA), were treated with standard drug regimens with and without PZA to detect host-directed activity of PZA. Experiment 2: BALB/c and athymic nude mice were aerosol infected with H37Rv strain of *M. tuberculosis* (with 3.8 and 3.9 log10 CFUs, respectively) and treated with the rifampicin + ethambutol combination with or without PZA to determine whether the host immune status would influence PZA activity. Experiment 3: *M. tuberculosis*-infected BALB/c (3.16 log10 CFUs) and athymic nude mice (3.35 log10 CFUs) were treated with a rifapentine + ethambutol combination with or without PZA to assess PZA activity when bacterial growth has been totally suppressed in the presence of a rifamycin with a longer half-life than rifampicin.

Results: In experiment 1, PZA did not contribute at all to the killing of *M. bovis*, suggesting that non-activated PZA has neither antimicrobial nor host-directed activities. In experiment 2, the addition of PZA to the rifampicin + ethambutol combination was very beneficial in BALB/c mice but not in nude mice. In the latter, it is possible that the relatively short half-lives of rifampicin and ethambutol did not ensure permanent drug exposure, thus permitting cycles of microbial killing and regrowth which prevented the accumulation of pyrazinoic acid in the bacterial cell. In experiment 3, the antimicrobial activity of PZA was demonstrated in BALB/c and nude

mice, but it was significantly less spectacular in the immune-deficient mice.

Conclusion: Based on these results, host-directed activity of PZA cannot be ruled out in addition to its anti-microbial activity.

PC-985-03   Gene expression analysis of 40 years of hypoxic culture of *Mycobacterium tuberculosis*

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Background: Knowledge of persistent *Mycobacterium tuberculosis* is a key to the control of its disease development but still incomplete. We keep *M. tuberculosis* strains cultured in hypoxic condition for more than forty years. We analysed the gene expression data of these tubercle bacilli in stationary and active phase.

Design/methods: *M. tuberculosis* H37Rv strain was inoculated into Sauton medium in 1964 and incubated at 37°C continuously under presumably hypoxic condition, in which the medium was covered by liquid paraffin in glass bottle and wax-sealed (specimen A). The dormant strain was recovered in 7H9 medium (specimen B) and again kept under 1% O2 for 2 weeks (specimen C). H37Rv stored at −80°C since 1960s was recovered and grown to mid-logarithmic phase (specimen D), and used as comparative reference. RNA was extracted and purified from each culture (specimen A–D) with TRIzol, and was amplified with WTA2 kit (Sigma Aldrich). Whole genome microarray gene expression analysis (NimbleGen) was performed, and the normalised data was analysed using ArrayStar ver.5 software (DNASTAR).

Results: A total of 3988 gene expression data was obtained for each specimen. Two specimens, B and D, showed almost comparative gene expression profile ($r^2 = 0.9208$) and both H37Rv were considered practically same even after 40-years' culture. However, the expression profiles of specimens under hypoxic long culture (specimen A) and 1% O_2 (specimen C) were different. A total of 70 genes were relatively highly up regulated in long culture than in 1% O_2 and others. They were the gene of 3 regulatory proteins, 14 intermediary metabolism and respiration, 26 conserved hypothetical proteins, 5 PE_PPE families, 3 lipid metabolism, 11 cell wall and cell processes, 4 information pathway, and 4 insertion sequences and phages. They included several devR regulons, hupB (MDP-1), rpfC (probable resuscitation factor), and murG/F.

Conclusion: *M. tuberculosis* in decades' hypoxic culture showed a unique gene expression profile, and it was even different from that of short culture in 1% O_2. Hampshire T, et. al. incubated *M. tuberculosis*

under relatively hypoxic (50% dissolved oxygen tension) condition and reported the gene expression changes after 100 days of incubation. Our study also indicated the importance of culture condition for the analysis of latent TB infection model. The gene expression profile in this study would provide a new vision in the understanding of TB persistence.

PC-986-03   Identification of suitable reference genes for qRT-PCR analysis of plasma microRNA in tuberculosis

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Background: Tuberculosis (TB), caused by *Mycobacterium tuberculosis*, is one of the deadliest infectious diseases, with an estimated 8 million new cases per year and 1.5 million deaths per year. MicroRNAs (miRNA) are short, 19–24 nucleotides in length, noncoding RNAs that play an important role in post-transcriptional regulation of gene expression through targeting messenger RNA. Circulating miRNAs exist in a highly stable, cell free form and recent literature has demonstrated their varying expression in diseased states such as malignancy, schizophrenia, diabetes, heart failure and sepsis. Circulating miRNAs have potential as a diagnostic, prognostic and predictive marker. Quantitative polymerase chain reaction is the most common method employed to measure expression profiles of miRNAs. Normalisation is an essential component of a reliable PCR experiment as it is required to differentiate experimentally induced variation to that of real biological differences. This study describes the identification and characterization of an appropriate reference gene for the normalisation of circulating miRNA levels in active tuberculosis, latent tuberculosis infection (LTBI) and healthy people.
Design/methods: Nine miRNAs (let-7, miR-16, mir-22, mir-26, mir-93, mir-103, mir-192, mir-221, mir-451) and RNU6B were chosen as candidate reference genes based on the literature. Expression levels of these candidates were analysed by real time (RT) -qPCR in plasma of 10 newly diagnosed tuberculosis patients, 10 patients with LTBI and 10 healthy volunteers. Normfinder and comparative delta-CT method algorithms were used to select the most suitable reference genes from the ten candidates.
Results: The algorithms revealed miR-192 was the most stably expressed reference gene for circulating miRNA evaluation in LTBI, active tuberculosis and healthy people.
Conclusion: MiRNAs represent a novel class of biological regulators, whose aberrant expression is associated with a range of disorders. Even relatively small changes in miRNA expression profiles may be bio-

logically significant and rigorous normalisation of miRNA expression profiles is critical. We recommend miRNA 192 as a suitable reference gene for plasma miRNA analysis for LTBI, active tuberculosis and healthy persons.

TREATING DRUG-RESISTANT TUBERCULOSIS: CHALLENGES AND SOLUTIONS

PC-987-03   Innovative social protection mechanism for drug-resistant tuberculosis patients

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Background and challenges to implementation: Tuberculosis (TB) is a disease of poverty and in many high burden countries, TB patients incur huge expenditure for diagnosis and treatment of TB. This economic burden imposed by TB disease on individuals and families can be reduced through a well designed and implemented social health insurance schemes, thereby increasing access to healthcare (both in public and private establishment).
Intervention or response: Rashtriya Swasthya Bima Yojna (RSBY), a social health insurance mechanism in India, provides health insurance coverage and protection to people below the poverty line to fund their medical treatment up to US$600 annually for five enrolled members in a household, including US$20 towards transportation expenses (50 Indian rupees = US$1). The State of Chhattisgarh pioneered a multidrug-resistant TB (MDR-TB) package for RBSY beneficiaries. Approved RSBY MDR-TB Package includes— US$61 (for all pre-treatment evaluations), US$66 (MDR-TB follow-up evaluations) and US$112 (Hospital stay @ US$16/day, inclusive of doctors fees, bed charges and medications/ancillary drugs). Beneficiaries need to pay only US$0.50 as registration fee while central and state government pays the premium to the insurer selected by the state government on the basis of a competitive bidding. Every beneficiary family is issued a biometric enabled smart card containing their fingerprints and photographs.
Results and lessons learnt: Within a month of rolling out of this package, four insurance claims were processed, of which three claims were from the RSBY

empanelled private health establishment and one from the Community Health Centre (CHC), indicating huge scope of uptake of standardized services from the private and public establishments, free of cost, which was earlier untapped by the National TB Programme. Since, hospitals empanelled under RSBY are electronically enabled and connected to the server at the district level, this is also ensuring smooth data flow regarding service utilization.

Conclusions and key recommendations: The innovative RSBY MDR-TB package is a step towards attainment of health equity. In order to address the social protection component of post 2015 Stop TB strategy, mechanisms emphasizing collaboration with existing social health insurance schemes needs to find weightage in the national policy framework for TB control.

PC-988-03   The MDR/XDR-TB Colour Test simultaneous culture and drug susceptibility test predicts tuberculosis outcomes in Peru

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Background: Commitment to treating multi-drug resistant (MDR) TB is growing. Many peripheral laboratories lack the facilities to perform drug susceptibility testing (DST), relying on indirect DST performed in reference labs, often with delays of several months. The 'MDR/XDR-TB Colour Test' is a thin layer agar culture method with improved biosafety designed for use in basic laboratories that allows simultaneous TB culture and DST for isoniazid, (H), rifampin, (R), and ciprofloxacin.

Design/methods: DST results for the Colour Test are assigned by growth in drug-containing agar on the first day of TB growth. On occasion there is delayed growth in a drug-containing well in a plate initially read as susceptible. We obtained follow-up of 503 episodes of TB in 492 patients diagnosed between April, 2009 and February, 2011 and used clinical outcomes to assess the clinical significance of different TB growth patterns in the Colour Test. Desirable outcomes were defined as cure or finished treatment. Adverse outcomes were TB recurrence, all-cause mortality, and treatment failure. Hazard ratios (HR) were obtained with Cox regression for H and R separately. We analyzed H-resistance in R-susceptible strains only.

Results: 43 adverse patient outcomes occurred during 521 patient-years of follow-up. Colour Test DST results were available for 79% (399) of the samples. The median time from sample inoculation to results was 20 days (IQR 17–22; maximum 45 days). Among the 351 R-susceptible strains, 16% (57) were H monoresistant and another 28% (97) had delayed growth in H. Overall 11% (43) were MDR strains and 1.3% (5) were R mono-resistant. Another 26% (103) had late growth in R. Figures 1a and 1b show survival

curves for H and R respectively. Initial growth in H had an HR of 6.0 (95%CI 2.2, 17; $P = 0.001$) for adverse outcomes compared to never growth in H. Late growth was similar to never growth (HR 1.0; 95%CI 0.3, 2.1; $P = 1.0$). Early growth in R predicted adverse outcomes with HR = 17 (95%CI 7.4, 40; $P < 0.001$). Late growth was not significantly associated with outcomes (HR 1.5, 95%CI 0.6, 3.9; $P = 0.9$) compared to never growth in R.

Conclusion: The Colour Test provides clinically meaningful drug susceptibility results at the time of first TB growth in an average of 3 weeks and maximum 6 weeks. At this time positive cultures can immediately have a final report sent and the cultures can be discarded or sent for further analysis without prolonging incubation.

PC-989-03   Mise en place d'une cellule nationale de prise en charge de la tuberculose multirésistante : expérience du Burkina Faso

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Contexte et défis : La surveillance épidémiologique de la tuberculose au Burkina Faso est faite à travers le Programme national de lutte contre la tuberculose (PNT), et permet de connaître la situation de la tuberculose multirésistante (TB-MDR). Le suivi et l'évaluation de la prise en charge des cas de TB-MDR sont faits par la cellule nationale de prise en charge de la TB-MDR, mise en place par le comité technique antituberculeux du Burkina Faso. La cellule nationale de prise en charge de la TB-MDR assure ainsi un appui technique au PNT dans la gestion des cas de TB-MDR, l'évaluation des cas suspects, l'appréciation et l'application des directives techniques.

Intervention : La cellule nationale de prise en charge de la TB-MDR est un groupe de travail multidisciplinaire composé de médecins, de pharmaciens, de biologistes, d'infirmiers, d'agents communautaires et d'experts en gestion de la TB-MDR. La cellule peut faire appel, en cas de besoin, à toute autre personne ressource dont la compétence est jugée nécessaire. La cellule nationale de prise en charge de la TB-MDR se réuni une fois par trimestre en session ordinaire et traite de toutes les aspects relatifs à la prise en charge des malades et des suspects TB-MDR, et de la gestion

des médicaments antituberculeux de 2ème ligne. Cette cellule peut aussi se réunir en cas de nécessité en session extraordinaire. Le secrétariat de la cellule nationale de prise en charge de la TB-MDR est assuré par la coordination du PNT. Le secrétariat est chargé de la préparation, la rédaction des rapports et le suivi des recommandations des sessions de la cellule. Il assure aussi au quotidien la liaison entre les membres de la cellule nationale de prise en charge de la TB-MDR.

Résultats et leçons apprises : La mise en œuvre de la cellule nationale de prise en charge de la TB-MDR a permis une meilleure coordination des interventions des acteurs impliqués dans la prise en charge de la TB-MDR au Burkina Faso, une amélioration de la qualité de la gestion des malades et des suspects de TB-MDR et des données épidémiologiques.

Conclusion et recommandations clés : Compte tenue de la complexité de la prise en charge de la TB-MDR, la mise en place de cadre de concertation multidisciplinaire à l'échelle de nos pays est une solution pour améliorer la gestion de ces malades et la prévention de la TB-MDR.

PC-990-03   Suivi de la consommation des médicaments antituberculeux de 2ème ligne par la mise en place d'un outil informatique : expérience du Burkina Faso

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Contexte et défis : Le Fonds mondial et Unitaid font partis des principaux bailleurs de fonds pour l'acquisition des médicaments antituberculeux de 2ème ligne pour les patients atteints de tuberculose multirésistante (TB-MDR). Le PNT reçoit assez régulièrement plusieurs lots de médicaments avec des périodes de validité courte, ce qui entraine des défis pour le suivi des stocks et de la consommation. La nécessité d'un outil informatique pour rationaliser l'utilisation et le suivi du niveau de stock des médicaments est devenue impérative afin d'éviter les ruptures et les surstockages.

Intervention : A l'aide d'un tableur Excel, le PNT a mis en place un outil informatique simple sur Microsoft pour la gestion des médicaments antituberculeux de 2ème ligne et comporte 2 sections. La première section concerne le suivi de la consommation des médicaments de chacune des 2 unités de prise en charge de la TB-MDR à l'aide de feuilles Excel séparées. Chaque feuille Excel comporte les éléments relatifs à l'identité des malades et les quantités de médicaments consommés depuis la mise sous traitement. Ces données sont actualisées tous les mois, de manière à permettre un réel suivi de la consommation, et donc d'évaluer en permanence l'adéquation du stock avec le profil de la consommation. La seconde section concerne la synthèse des consommations des malades du pays et est faite dans une troisième feuille Excel, avec des liens avec les feuilles précédentes. Cette feuille donne la situation des stocks de médicaments nécessaires pour achever les traitements en cours et ceux disponibles pour les nouvelles inclusions. Pour chaque malade, un kit de traitement est virtuellement sécurisé pour toute la durée de son traitement grâce à cet outil de telle manière qu'il ne sera pas en rupture au cours de son traitement.

Résultats et leçons apprises : L'amélioration de la qualité des données sur les quantités consommés et celles disponibles ont permis au PNT de déterminer le profil de consommation des médicaments antituberculeux de 2ème ligne et de prendre les actions propices. Le suivi des consommations des médicaments permet de rationaliser leur utilisation, de réduire les pertes et les risque de détournement, et de rendre compte aux partenaires.

Conclusion et recommandations clés : Les stocks de médicaments antituberculeux de 2ème ligne peuvent être efficacement gérés dans les pays à ressources limités par la mise en place d'outils informatiques simples.

PC-991-03   Out-patient tuberculosis and MDR-TB treatment with community support in Vakhdat district, Tajikistan

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Aim: Outpatient treatment of TB and MDRTB patients in Tajikistan is vital due to lack of human and financial resources as well as relevant infection control measures. The abstract analyzed results of outpatient treatment of TB and MDRTB patients with increased community support.

Background: Quality Health Care project funded by USAID has been implementing the model of outpatient treatment of TB and MDRTB patients with support of community members in the Vakhdat district of Tajikistan since mid-2011 with NTP support. The district has a migrating population of 300 000 people, and the majority of the male adult population are labor migrants; there is challenging geographic and climate conditions in the district and high TB stigma.

Methods: To strengthen knowledge and capacity on TB control (including MDRTB case management) the project conducted trainings for family doctors, nurses and introduced quality improvement approaches to the health facilities. The Vakhdat community religious leaders and volunteers were trained in TB case finding, treatment principles and consequences of

inadequate TB case management. To strengthen the outpatient model, the quality project initiated organization of regular treatment support group meetings which consisted of former and current TB patients, their relatives, DOT nurses, and TB and healthy life style doctors. During the meetings, patients received peer-to-peer education and psychological support.

Results: As results of the conducted activities, TB case finding by community leaders increased from 11.5% in 2011 to 20.6% in 2012. The percent of outpatient TB SS-positive patients treated in PHC facilities increased from 22% in 2011 to 25% in 2012, while the proportion of MDRTB patients who received ambulatory treatment increased from 32% in 2011 to 39% in 2012. Treatment success in the cohort of outpatient TB SS+ patients who were enrolled in TB treatment in 2011 was higher in comparison with the same cohort of TB patients enrolled in 2010. The intermediate result as conversion rate after 12 months of treatment with SLD among cohort of MDRTB patients received course in outpatient conditions was 100% in 2011.

Conclusion: Preliminary analysis showed benefits of outpatient treatment of TB and MDRTB patients in Vakhdat district with increased community members involvement and psychological support.

PC-992-03   Social support: a key factor for adherence to MDR-TB treatment

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Background: Defaulting from treatment remains a challenge for MDR-TB management and care. In 2012, the default rate among MDR-TB patients in Nagpur City, Maharashtra, India was 18%. A qualitative study was conducted to obtain a better understanding of both patient and provider-related barriers to MDR-TB treatment completion.

Methods: In-depth interviews were conducted among a purposeful sample of 20 MDR-TB patients (10 with successful treatment outcome and 10 with unsuccessful treatment outcome), and their respective providers, treated in Nagpur City, India, during August 2012–February 2013. Interviews were designed to capture open-ended responses to identify perceived reasons for treatment non-adherence and default. Providers included both public and private doctors, community volunteers, government, and non-government health workers. Interview transcriptions were analyzed to identify emerging themes.

Results: Among patients with successful outcomes, the majority of patients believed that family and community support was the most important factor that led to treatment adherence. Factors that positively influenced adherence to the MDR-TB treatment were the belief in taking regular treatment was necessary for cure and adults had a responsibility of protecting young children. Among patients with unsuccessful treatment outcomes, barriers to treatment adherence were experiencing drug-related side effects, fear of daily injections and pill burden, unemployment and economic constraints, alcohol addiction, associated illness, treatment from private practitioners and non-licensed providers, restrictive office hours of DOT centers, lack of family support, stigma, and inadequate counseling. Providers related that motivational counseling, nutritional supplementation and strong family and social support encouraged treatment adherence.

Conclusion: To improve MDR-TB treatment adherence, a multifaceted, holistic, and patient-focused approach should be considered at the programmatic level. There is a need to formulate strategies that include linking patients to various government programs, nutritional supplementation, motivational counseling and social support mobilization for treatment adherence.

PC-993-03   Determination of risk factors associated with treatment outcomes of MDR-TB patients in Botswana

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Background: Botswana has been offering second and third line drugs for MDR-TB and XDR-TB treatment and ART, yet it is not documented if this has lead to good treatment outcome and what risk factors determine the treatment outcome. Hence the aim of this study is to determine the risk factors associated with poor treatment outcome on MDR-TB patients in Botswana. We hypothesize that risk factors associated with poor treatment outcome in HIV uninfected and HIV infected patients are similar after accounting for HIV treatment and their immune status.

Methods: This is a retrospective study of MDR-TB cases greater than 14 years old that were initiated on MDR-TB treatment in Botswana from January 2006 to June 2012.

Results: Multivariate analysis (Table) did not show a statistically significant association between HIV infection and poor clinical outcomes (AOR 2.06, 95%CI 0.80–5.31, $P = 0.135$). The multivariate model limited to HIV infected patients, showed an

Table Multivariate analysis of factors associated with poor clinical outcomes among MDR-TB patients co-infected with HIV in Botswana

	AOR	95%CI	$P > z$
Male sex	0.91	0.35–2.37	0.86
Age, years			
30–39	0.50	0.12–2.15	0.35
40–49	0.57	0.18–1.82	0.35
50–59	0.24	0.07–0.88	0.03
>60	1.00		
Baseline CD4 cells (by increases of 100 cells/mm³)	0.82	0.56–1.19	0.29
Culture positivity at baseline	8.42	1.48–48.06	0.02
Culture conversion during treatment	0.07	0.01–0.41	0.00
Culture positivity at 6 months of treatment	3.38	1.90–6.01	0.00
Hypothyroidism	0.88	0.24–3.32	0.86
Hearing loss during treatment	0.42	0.16–1.08	0.07
Hepatitis	2.36	0.40–13.79	0.34
Cavitary disease	0.87	0.32–2.35	0.78
Presence of comorbid diseases	3.70	1.32–10.35	0.01

inverse trend between CD4 T cell counts and poor outcomes, although no category reached statistical significance. Similarly, when HIV infected individuals were stratified by their CD4 T cells and compared against HIV negative patients, the trend suggesting an increased risk of poor outcomes as CD4 cells decrease became more pronounced yet not statistically significant. However, the use of ARTs was consistently protective against poor outcomes on all analysis. Younger age (AOR 0.09, 95%CI 0.01–0.99, $P = 0.049$), culture conversion at some point during treatment (AOR 0.09, 95%CI 0.02–0.36, $P = 0.001$) and hearing loss (AOR 0.40, 95%CI 0.18–0.89, $P = 0.024$) were consistently found to be inversely associated with poor clinical outcomes. Being culture positive at baseline (AOR 9.15 2.21–37.88, $P = 0.002$) and after 6 months of treatment (AOR 4.21, 95%CI 2.49–7.13, $P < 0.001$), and the presence of co-morbid diseases (AOR 3.31, 95%CI 1.43–7.68, $P < 0.01$) were important risk factors for poor clinical outcomes

Conclusion: Risk factors associated with a poor outcome in a high HIV prevalent setting were similar to the HIV negative patients, which included smear positive at initiation of treatment and culture positive at 6 months.

PC-994-03 Notification of MDR-TB, enrolment on treatment and treatment success in countries with the highest global MDR-TB burden

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Background: The global response to detect and successfully treat cases of multidrug-resistant tuberculosis (MDR-TB; resistance to, at least, isoniazid and rifampicin) will influence future prospects for tuber-

culosis control worldwide. The World Health Organisation (WHO) monitors efforts for MDR-TB care by collecting national surveillance data.

Methods: The 32 countries estimated to have >1000 detectable MDR-TB cases in 2010 (representing >90% of the global MDR-TB case-load) were requested to report aggregated data on notification of MDR-TB and enrolments on MDR-TB treatment between January and June 2012 via a dedicated website hosted by WHO. Progress in programme response was considered if the 6-month notification and enrolment figures exceeded 60% of the same indicators for the whole of 2011. Successful outcomes for patients starting treatment in 2009 were also assessed.

Findings: Out of the 32 countries requested, 25 countries located throughout all of the 6 WHO regions reported statistics on notification and 27 countries reported data on enrolments. In 10 countries—including China, India, Indonesia and Pakistan, countries with the highest MDR-TB case-loads—MDR-TB notifications in the first half of 2012 exceeded 60% of those in 2011 (25-country median: 53%; IQR 43–81%). Enrolment on MDR-TB treatment in January–June 2012 was >60% higher than for the whole of 2011 in fifteen countries (27-country median: 62%; IQR 47–77%). Overall, 48% of patients had a successful outcome in twenty-three countries reporting results (median: 62%; IQR 47–73%).

Interpretation: Reported data suggest improvements in several high MDR-TB burden countries in the scale-up of MDR-TB detection and enrolment on treatment in 2012 over 2011. Data from some countries remain incomplete. Countries still need to improve efforts in detection of MDR-TB, enrolment on treatment and treatment success in order to address the global burden adequately.

PC-995-03 Is frontloading an option in community-based active tuberculosis case-finding?

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Background: WHO considers frontloading to be equivalent, in terms of diagnostic accuracy, to existing conventional case-finding approaches by microscopy, irrespective of whether 2 or 3 specimens are used. In active case-finding (ACF), which aims for early TB detection, same-day two-smear sputum collection may prove difficult. Additionally, a front-loaded approach ideally implies same-day reading and reporting of results. We evaluated the feasibility and yield of frontloading in ACF.

Design/methods: Prospective collection of sputum smear results from presumptive TB cases in

community-based ACF between 2–12/2012. Blinded smear reading through LED fluorescence microscopy at a tertiary level laboratory. Spot/spot/morning (SSM) sputum collection, i.e., two spots on day 1 and the morning sample on day 2, was recommended. We calculated the theoretical proportion of TB cases missed if SS and SM approach would have been used in our population and determined the difference between SS and SM using McNemar's test. We also evaluated the time between sputum collection and complete smear microscopy reporting. Any positive result was texted via mobile phone (sms), regardless of number of smears. We followed latest WHO's smear-positivity definition.

Results: Of the 8549 patients providing sputum during ACF, 3770 (44%) were read at SHCH (populations characteristics representative of total community screened). Overall, 1041 of 3770 (27.1%) of cases could not provide same-day 2-spot sputum samples. Of the 2655 (70%) patients submitting 3 specimens, 2331 (64%) were collected following the SSM approach; 142/2331 (6.1%) SSM samples were smear-positive and graded as: scanty in 56 (39%), 1+ in 19 (13%), 2+ in 21 (15%) and 3+ in 46 (32%). Using the SS approach would result in 21/142 smear-positive TB cases missed (14.8%; 95%CI 9.9–21.6) compared to 10/142 TB cases missed (7.0%; 95%CI 3.9–12.5) with the SM approach, implying 7.7%

Figure Flow of smears read at Sihanouk Hospital Center of HOPE laboratory from individuals with presumptive TB in ACF.

(95%CI 0.2–15.3) less smear-positive TB cases with SS detected compared to SM ($P = 0.048$). Although same-day reporting of complete SSM-results was done in 6.9% of the cases, same-day sms was systematically done. The median time between the first sputum collection and reporting of all sputum results was 4 days (IQR 2–7).

Conclusion: Frontloading was feasible although the loss of the morning sample significantly reduced the detection of smear-positive TB cases. Sms-texting also allowed same-day reporting of positive results.

PC-996-03   New definition of MDR-TB treatment failure: change in treatment outcomes

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Background: With the intention of simplifying the monitoring of programs treating multidrug resistant tuberculosis (MDR-TB) patients, the World Health Organization (WHO) revised the definition of treatment outcomes in 2013. The new definition for treatment failure is: treatment terminated or need for permanent treatment change of at least 2 classes of anti-TB drugs because of one or more of the following: lack of culture negativation by the end of the intensive phase, and/or resistance amplification, and/or bacteriological reversion (at least two positive smears or cultures at least 30 days apart) after conversion to negative, and/or if a clinical decision has been made to terminate treatment early due to poor response or adverse events.

Design/methods: We report the proportion of patient meeting the new definition of treatment failure by applying it retrospectively to MDR-TB patients enrolled between 2001 and 2009 in projects supported by Médecins Sans Frontières in Armenia, Abkhazia, Kenya, Swaziland and Uzbekistan. MDR-TB treatment regimens were based on WHO recommendations. As the treatment was individualized and no maximum duration for the intensive phase was defined, we chose a 6 month cut-off for culture negativation. Treatment failures using the revised definition were presented compared to the patients' outcomes using previous WHO outcome definitions.

Results: Among 1455 MDR-TB patients, 551 (37.9%) were retrospectively classified as treatment failures compared to 165 (11.35%) using the previous definition. Among them, 290 (52.6%) had no culture negativation by 6 months, 82 (14.9%) amplified resistance, 126 (22.9%) experienced bacteriological reversion, and 10 (1.8%) never achieved culture conversion. Among MDR-TB patients who were classified as treatment success (808), death (127), and defaulters
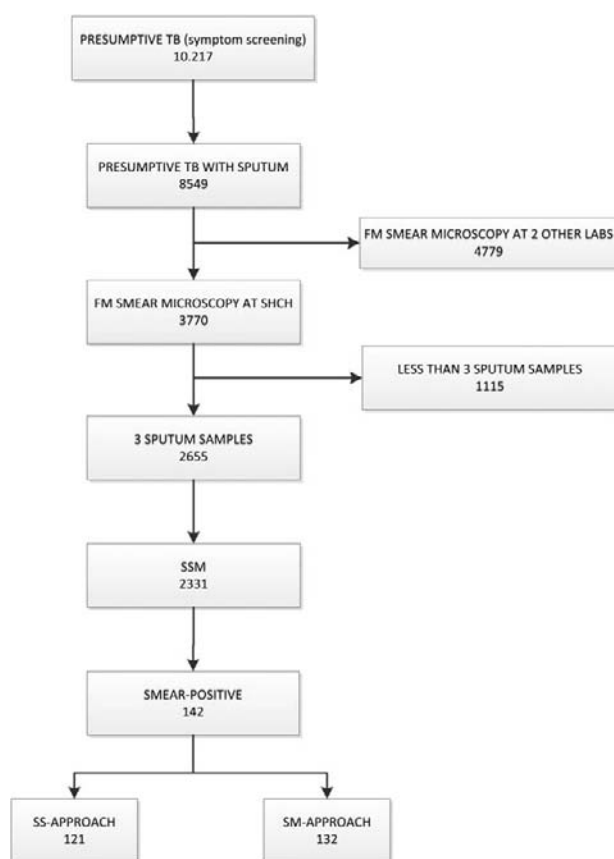
(333) according to the previous definition, 191 (23.6%), 67 (52.8%), and 122 (36.6%) respectively would have been defined as treatment failure with the new definition.

Conclusion: The new definition of treatment failure will have a significant impact on the reporting of MDR-TB treatment outcomes. It may dramatically increase the proportion of failures and decrease the proportion of defaulters, probably better reflecting the reality of the treatment effectiveness.

PC-997-03 Assessment of the socio-economic status and living standards of MDR-TB patients in Archangelsk region of Russia

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Background: Burden of TB disease has a differential impact depending on socio-economic status. Income indicators are used for social status definition in developed countries. In developing world the STOP-TB methodology is based on household assets. We suggest an index of well-being based on the combination of these methods to describe the complex socio-economic situation in Russia. Data collected in the PROVE-IT LPA (Line Probe Assay) project was used to assess the socio-economic status of TB patients.

Objectives: To assess the socioeconomic status and living standards of TB patients with the suggested index of well-being in Archangelsk region.

Design/methods: In April 2011 to March 2012, 112 MDR-TB patients completed a STOP-TB approved questionnaire adapted to Russian socio-economic conditions. The data included cash income, durable household assets and housing conditions (city/countryside; square meters per person; house ownership). The combination of these parameters defined the socio-economic status based on the value of the Integrated Welfare Index (IWI). We produced a distribution of the patients across three socio-economic categories: absolute, relative poverty or relative welfare.

Results: Preliminary results showed that the average age of the patients was 40.4 ± 12.3 years old. 50% patients had primary or secondary education. 28% of them were occupied in service and trade. Mean monthly income of the patients equaled US$249. Median income was US$213. Analysis of the distributions of patients separately by each of the parameters showed that 57% patients were absolutely poor as their income was below the official subsistence income threshold, but according to durable household asset criteria the majority of the patients (44%) were

relatively poor. The observed inconsistencies were addressed in the distribution of patients based on the IWI where 70% were absolutely poor, 23% were relatively poor and 7% were well-off. The burden of TB affected social and private life of the patients: 89% of them lost jobs, 63% experienced a financial burden, 50% had family crises and divorce. Disease resulted in social estrangement and worsening of social well-being.

Conclusions: Socioeconomic status assessed with the IWI presented a more authentic distribution of MDR-TB patients, which reflected the transition economy and legacy from the Soviet system. The results will be used in analysis of clinical and economic outcomes by the socio-economic status of the patients.

PC-998-03 Epidemiología de las reacciones adversas a fármacos antituberculosis de segunda línea en México durante el 2010

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Marco de referencia: El tratamiento de casos con TB MDR y XDR representa un gran desafío en salud pública debido a la frecuencia de reacciones adversas a los fármacos de segunda línea que se usan en ellos, lo que implica un riesgo de abandono del tratamiento.

Intervención o respuesta: Se realizó un estudio descriptivo, observacional y restrospectivo con pacientes en con TB MDR y XDR en tratamiento durante 2010 con fármacos de segunfda línea.

Resultados y enseñanza: Se estudiaron retrospectivamente a 164 pacientes con diagnóstico de TB-MDR (97%) y de TB-XDR (3%), de los cuales el 63% (103) son del género masculino y el 37% (61) son del género femenino; el promedio en edades fue de 43.2 con una DS de 15.4. La localización anatómica de los casos estudiados en el 99% (162) fue pulmonar y el 1% (2) de la forma extrapulmonar. Los 164 pacientes iniciaron con tratamiento estandarizado de segunda línea en un 60% y con tratamiento individualizado en un 40% comorbilidades más frecuentes fueron la diabetes mellitus en un 48.8%, seguida de la desnutrición con 28%, alcoholismo 8.5%, tabaquismo 3.7%, usuario de drogas 3.7, insuficiencia renal crónica 2.4 y SIDA 1.8%. El mayor porcentaje de la presencia de las RAFAs según el mes de tratamiento fue en el los primeros 6 meses de tratamiento de los 24 meses que duró el esquema, las reacciones adversa gástricas se presentaron en el 100% de los casos, seguida de la depresión (31.7%), las artralgias en un 25.6% y la hipoacusia en un 26.6%. El 74% de las reacciones adversas se recuperan y el 26% se recuperan con secuelas, se clasificó a las RAFAs de acuerdo a la intensidad de la manifestación clínica encontrándose que el 7% corresponden a severas, el 59% a leves y el 34% a moderadas; de 164 pacientes incluidos en el estudio

se identificaron un total de 521 RAFAS de las cuales el promedio de la presencia de estas fue de 3.18 RAFAs por paciente.

Conclusiones y recomendaciones: El proceso de atención a las personas afectadas por la tuberculosis MDR/XDR no puede limitarse a indicar sólo un esquema de tratamiento adecuado con fármacos de segunda línea, es aún igual de importante asegurar la prevención y tratamiento de los efectos adversos secundarios que pueden presentarse durante el tratamiento ya que la identificación oportuna de las RAFAs coadyuva a la adherencia terapéutica y su mal manejo pone en riesgo la eficacia terapéutica y hasta la vida de la persona afectada por este padecimiento.

PERFORMANCE OF THE GENEXPERT® MTB/RIF ASSAY

PC-999-03   Experience in the use of molecular-genetic testing with GeneXpert® MTB/RIF for the diagnosis of MDR-TB

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Background: To study the potential use of GeneXpert MTB/RIF as a proxy for MDR-TB.

Design/methods: The study included 97 TB patients. Extraction of MBT DNA and detection of rifampicin (R) resistance was done in the automatic four-module GeneXpert MTB/RIF (USA). All patients had 3 specimens of sputum examined by fluorescent microscopy, as well as cultures on solid media followed by the DST (absolute concentration method).

Results: The GeneXpert method was able to identify MBT DNA in sputum of 52 patients (53.6%). Positive culture results were received for 65 patients (67%). MDR-TB was identified by the method of absolute concentration in 29 patients (44.6%). The results of GeneXpert: resistance to R—24 patients, DNA not isolated—4 patients, susceptibility to R—1 patient. Resistance to R by the absolute concentration method was detected in 36 cases (55.3%). Of them, GeneXpert detected susceptibility to R in 27 patients, in 9 cases MBT DNA was not isolated. All patients with drug resistance confirmed by GeneXpert were switched to treatment regimen IV with the second-line drugs. The sensitivity of GeneXpert MTB/RIF for the diagnosis of MDR-TB was 80%, specificity—100%.

MBT DNA was not identified by GeneXpert in 45 cases (46.4%), of them 6 TB patients (13%) had positive smear results of 3 specimens examination by the fluorescent microscopy, and 13 patients (28%) had positive cultures. Those patients had infiltrative TB without destruction of pulmonary tissues ($n = 39$).

Conclusion: Molecular-genetic method of GeneXpert MTB/RIF has high specificity for a rapid (within 2 hours) detection of TB mycobacteria and DST to rifampicin which allows for a quick replacement of the empiric treatment with the adequate therapy without waiting for the culture results.

PC-1000-03   Xpert® MTB/RIF assay and conventional drug susceptibility testing: a comparative analysis for diagnosis of MDR-TB in Chittagong, Bangladesh

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Background: Tuberculosis is mostly caused by *Mycobacterium tuberculosis* in Bangladesh. Accurate and rapid diagnosis of drug resistant tuberculosis strains is of great urgency at the moment to improve patients' conditions. Xpert MTB/RIF assay involves an automated sample preparation and a real-time PCR instrument, and has previously performed efficiently for diagnosis of *M. tuberculosis* and their respective rifampicin resistant strains. Use of Xpert MTB/RIF accompanied by conventional drug sensitivity test should have better efficacy for diagnosis of MTR-TB strains.

Methods: Sputum samples collected from 425 patients suspected to carry the MDR-TB strains between April 2012 and January 2013 were analyzed by Xpert MTB/RIF and conventional drug sensitivity test as established by the LJ proportion method. The diagnostic performance of Xpert MTB/RIF assay was compared to conventional culture and drug sensitivity tests (L-J proportion method). Presence of *Mycobacterium tuberculosis* confirmed by a positive culture and sensitivity to rifampicin on LJ medium was used as a reference standard for rifampicin resistant TB diagnosis.

Results: Of the 425 samples, 19.8% (84/425) harboured rifampicin resistant *M. tuberculosis* strains, as diagnosed by the conventional DST, where 24 strains displayed sensitivity towards isoniazid. Xpert MTB/RIF detected the presence of rifampicin resistant *M. tuberculosis* strains among the 76 samples, with 85.7% sensitivity and 98.8% specificity. One strain was found to be resistant against rifampicin as determined by Xpert MTB/RIF, which could not be cultured and recovered by the L-J medium. Moreover, Xpert MTB/RIF showed 3 rifampicin resistant tuberculosis strains which were found sensitive by conventional method.

Conclusion: Though Xpert MTB/RIF showed a notably high percentage of specificity, it had few limitations associated with the false negative and false positive results. Hence, use of both Xpert MTB/RIF and conventional DST would be very effective in order to minimize the errors of the diagnosis and ensure appropriate treatment of the patients.

PC-1001-03   Challenges of commodity management for Xpert roll-out at country level; the Nigerian experience

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Background: With the adaption of Xpert machines for screening of DR TB and diagnosis of TB among PLHIV, there is minimal experience to guide commodity management especially the quantification, shipment, storage and distribution of cartridges which needed to be coordinated and supported by a logistics management tool. The initial supply system was based on 'push system' without an actual estimate or consumption data from the peripheral laboratory.

Objectives: To describe challenges with cartridges management in Xpert roll out and possible responsible factors.

Methodology: A retrospective review and assessment of status of cartridges at the central level and among 30 Xpert sites across 22 States in Nigeria by an LMIS tool.

Results: Of 30 Xpert machines installed, 29 are currently functioning in 21 states of the federation and have totally tested 3993 sputum samples, 31% MTB positive of which 27.4% were Rif resistance. Over 4991 cartridges expired within a period of 2 years among 21 functioning sites supported by the different partners. 30% of these occurred at central level and 6 laboratory facilities accounted for 50% of the expired cartridges in the field. Possible reasons were: weak quantification and shipment process; delay between arrival of the machines and cartridges and installation of the machines at the designated sites; delay printing and dissemination of appropriate R&R tools especially LMIS; inadequate budget and system for distribution; challenges with human resource at laboratory level, machines failure and weak capacity for maintenance.

Conclusions: Develop a simple guide on quantification and shipment of cartridges; ensure the use of LMIS tool to match supply based on consumption; integrate cartridges distribution into the routine TB distribution system.

PC-1002-03   A meta-analysis of GeneXpert sensitivity by smear microscopy status for the detection of extra-pulmonary tuberculosis among culture-positive isolates

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Background: In low-income settings with limited access to culture facilities, smear microscopy is often used in combination with clinical suspicion to detect *Mycobacterium tuberculosis* (TB). In 2010, The World Health Organisation (WHO) recommended use of the GeneXpert assay as the initial test for the diagnosis of pulmonary TB in HIV-endemic areas and as a follow-up to microscopy in settings with low HIV prevalence; however, the applicability of GeneXpert for the diagnosis of extra-pulmonary TB (EPTB) has not yet been established.

Design/methods: We searched electronic bibliographic databases (MEDLINE, EMBASE, and Global Health databases) from January 2010 to April 2013 to identify diagnostic accuracy studies comparing GeneXpert to a reference standard of liquid and/or solid culture for the diagnosis of EPTB. We excluded studies that did not report culture positive results by smear microscopy. We extracted information on true positive and false negative results by GeneXpert and microscopy and used DerSimonian and Laird random effects models to determine the pooled sensitivity of the GeneXpert assay for smear positive and negative individuals.

Results: Among 22 studies comparing GeneXpert performance to culture for the diagnosis of EPTB, we identified 14 studies that also reported the smear microscopy results of culture-positive isolates. Among these 14 studies, there were 2359 EPTB samples (median = 89), of which 449 were culture-positive. Smear microscopy identified 186 positives among them (41.4%), while GeneXpert identified 377 of the culture-positive isolates (84.0%). Of the culture and GeneXpert positives, 180 were smear-positive and 197 were smear-negative. GeneXpert's sensitivity for detecting culture-positive EPTB among smear-positive isolates was 97.0% (95%CI 93.5–100.0%) and 78.1% (95%CI 73.4–82.7%) among smear-negative isolates. There was insufficient data reported to determine the specificity of the GeneXpert assay by smear status or to stratify results by HIV status.

Conclusion: Our findings show that GeneXpert performs substantially better than smear microscopy for the rapid identification of cases with EPTB, suggesting that the GeneXpert assay may be useful as an initial test for EPTB. Further research is needed to compare the diagnostic accuracy among individuals with and without HIV and to characterize the specificity of GeneXpert in combination with smear microscopy.

PC-1003-03   Errors associated with Xpert® MTB/RIF testing

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Background: The introduction of the PCR based Xpert MTB/RIF Assay™ (Xpert) has brought a dramatic

change to the diagnostic process with a turnaround time of 2 hours to detection of TB and rifampin resistance. System errors however may reduce the efficiency of the technology due to repeat testing.

Design/methods: 4267 samples were received in the KEMRI/CDC TB laboratory between March 2011 and February 2013 for mycobacterial culture and Xpert including, sputum, gastric aspirate, tissue and tracheal aspirates from post-mortem exam, and fine needle aspirates. Xpert was performed on untreated samples and decontaminated sample pellets and errors were captured and analyzed.

Results: Of 4267 samples received, 179 (4.2%) had errors. The commonest errors were: error codes 5011 (29.6%) detected signal loss; 5007 (19%) and 5006 (4.5%) indicated incorrect amount of reagent, bad reagent, fluid transfer failed, or incorrect sample processing; 2127 (5%) no results; 1018 (5%) valve component failure; 2037 (3.9%) functions called in incorrect sequence, or earlier call was unsuccessful; 2005 (3.4%) a syringe stall detected; 2008 (1.7%) pressure sensor failed or filter clogged and invalid (27.9%). All samples showed a high error rate of 5011. For tissue samples 54.2% of errors were code 5007.

Conclusion: While error rates of <5% are considered within the acceptable range, routine monitoring of Xpert results is critical to ensuring error rates are managed appropriately and these performance indicators are incorporated in the laboratory quality assurance plan. Repeat testing would be minimized using targeted interventions on specific error codes.

PC-1004-03   Performance of GeneXpert® MTB/RIF in tuberculosis patients by smear status in the Arkhangelsk region of the Russian Federation

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Background: Arkhangelsk region has one of the highest rates of primary multidrug-resistance (MDR) in Russian Federation, reaching 30% among new cases in 2012, despite declining incidence of TB. The Arkhangelsk regional antituberculosis dispensary implemented liquid culture, drug susceptibility testing (DST), and the line probe assay Genotype MTB-DRplus (Hain Lifescience GmbH) for rapid detection of MTB and drug resistance. However, diagnosis of MDR TB in smear-negative patients was still delayed. Xpert MTB/RIF (Cepheid, Inc.) can be used in smear-positive and smear-negative specimens. Aim of the study was to evaluate diagnostic accuracy of Xpert in detection of *M. tuberculosis* (MTB) and resistance to rifampicin (RIF), stratified by smear status.

Design/methods: Patients diagnosed with pulmonary tuberculosis using chest X-ray, clinical symptoms and/or microscopy were evaluated with the Xpert system in 2012. Results obtained by the Xpert for MTB detection were compared with results of the Bactec MGIT culture; results for detection of RIF resistance were compared with those of Genotype MTBDRplus. All tests were performed from the same sputum specimen.

Results: Among total of 277 TB patients, 131 (47.3%) had positive smear microscopy result, 165 (59.6%) tested positive in the Xpert, 183 (66.1%) were culture-positive by MGIT. Overall sensitivity and specificity of the Xpert, compared to MGIT, for detection of MTB was 83.6% (95% CI 77.3%–88.5%) and 87.2% (95% CI 78.4%–92.9%), respectively in all TB cases. In smear-negative cases, sensitivity and specificity were 56.3% (95% CI 43.3%–68.4%) and 95.1% (95% CI 87.3%–98.4%), respectively. Xpert detected RIF resistance in 61/165 (36.9%) Xpert-positive patients. Xpert detected MTB 40/146 (27.4%) smear-negative patients, 9/40 (22.5%) of these had RIF resistance. There were no discrepant results in DSTs.

Conclusion: The Xpert system demonstrated high accuracy rates for detection of *M. tuberculosis* and resistance to rifampicin allowing for the earlier diagnosis of MDR. Not all smear-negative/MGIT culture-positive patients were detected by Xpert; thus MDR TB cases could still be missed if Xpert system is used as a stand-alone diagnostic in smear-negative patients.

PC-1005-03   Diagnostic accuracy of the GeneXpert® assay for detection of extra-pulmonary tuberculosis: a systematic review and meta-analysis

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Background: GeneXpert, a nucleic acid amplification test recommended for its rapid and simple diagnosis of pulmonary tuberculosis (PTB), has been implemented in many low-income countries where availability of culture facilities is limited. To date, GeneXpert is infrequently used for diagnosis of extra-pulmonary TB (EPTB), as this form of disease is often pauci-bacillary and therefore difficult to diagnose with conventional microscopy. We sought to determine the diagnostic accuracy of GeneXpert for the diagnosis of EPTB.

Design/methods: We performed a systematic review using the MEDLINE, EMBASE and Global Health databases from January 2010 to April 2013 to identify diagnostic accuracy studies comparing GeneXpert to a reference standard of liquid and/or solid culture for the diagnosis of EPTB. We then performed

a meta-analysis of diagnostic accuracy measures using bivariate random effects models for aggregate and site-specific data.

Results: We identified 21 studies evaluating the diagnostic performance of GeneXpert for detection of EPTB among a total of 5100 isolates (median = 92). Pooled sensitivity was 83% (95%CI 75–90%) and specificity was 98% (95%CI 96–99%) respectively. The positive and negative likelihood ratios were 48.48 (95%CI 18.73–125.50) and 0.16 (95%CI 0.11–0.26), respectively. Significant variation existed between studies (I^2 = 90% sensitivity, 95%CI 87–92%, and 97% specificity, 95%CI 96–98%). Site-specific estimates were available for lymph, pleural fluid, cerebrospinal fluid, gastro-intestinal, and urinary samples. Pooled sensitivities were lower from samples of pleural fluid and urine (75% and 76% respectively). HIV status of patients submitting samples was only reported in one of the 21 studies, and we were therefore unable to stratify by HIV status of patients.

Conclusion: These results suggests that GeneXpert has high specificity but somewhat limited sensitivity for detection of EPTB; thus, although positive GeneXpert test results may be useful to rapidly identify EPTB cases, negative test results provide less certainty for ruling out active EPTB when compared to culture.

PC-1006-03   Rapid diagnosis of MDR-TB using Xpert® MTB/RIF in Vladimir Region, Russia

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Background: Delays in diagnosis of MDR-TB impair patient prognosis and increase the risk of community and nosocomial transmission. Objectives were to compare Xpert MTB/RIF (Cepheid, Inc.) with smear, culture and drug susceptibility tests (DST) for detection of TB and presumptive MDR-TB.

Methods: During August–December 2012, three sputum (Sp) specimens from 128 adults with presumptive TB were tested at the Vladimir Laboratory: (Sp1) Xpert; (Sp2) smear, culture (MGIT) and DST by MGIT (broth) after concentration by NALC/NAOH; (Sp3) smear, culture (Finn II) and DST by absolute concentration (solid) after concentration by Na3PO4. Sensitivity, specificity and 95% confidence intervals (CI) for MTB detection, concordance of results for rifampicin resistance and median times to results were calculated.

Results: A total of 58/128 (45%) patients were culture-positive for *M. tuberculosis*; 41/58 (71%) were smear-positive; 14/58 (24%) were rifampicin-resistant (RIF-R) and 12/14 RIF-R were also isoniazid-resistant

by either DST. Median times to detection were 36 days for Finn II and 27 days for MGIT. DST from date of collection was 64 and 29 days by solid and broth, respectively. For detection of culture-proven TB, sensitivity of Xpert was 86% (95%CI 76–94%) compared to 2 concentrated smears (67%, 95%CI 55–79%) from 2 separate specimens or combined culture results (84%, 95%CI 76–92%) from 2 separate specimens. Xpert specificity was 94% (95%CI 88–100%). Concordance of Xpert for RIF-R was 93% (13/14) and 91% (31/34) for RIF-susceptibility (RIF-S) compared to DST. Xpert results were available within 3 hours of specimen collection.

Conclusion: In this high MDR-TB prevalence setting, 1 Xpert MTB/RIF test was able to detect all (12/12) of the patients with MDR-TB within hours of specimen collection compared to months when conventional methods were used. Rapid detection of MDR-TB may enable earlier initiation of effective therapy and thereby may improve patient outcomes and decrease transmission.

PC-1007-03   Introduction of GeneXpert® MTB/RIF assay for diagnosis of rifampicin-resistant tuberculosis in Bangladesh

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Background and challenges to implementation: According to WHO, Bangladesh ranks tenth among the 27 high MDR-TB burden countries. An estimated 1.4% of new TB cases and 28.5% of retreatment cases are MDR-TB, as well as an estimated of 3800 cases of MDR-TB among notified pulmonary TB cases. The laboratory confirmed MDR-TB cases were only 509 (13%) of the estimates cases in 2011.

Objective: Demonstrate impact of introduction of Gene Xpert to increase early diagnosis and initiation of treatment of MDR TB patients in Bangladesh.

Method: The Gene Xpert MTB/RIF assay was introduced in Bangladesh in 2012, including placement of 12 machines in sites selected based on case load, geographic coverage, condition of facilities, and availability of lab staff at the National and Regional Reference labs, chest disease hospitals and clinics. Supported by the USAID TB CARE II project, 13 master trainers were developed; training on use of GeneXpert was provided for 28 lab technicians. Diagnostic algorithm and SOP have been developed in consultation with NTP and WHO. The performance of the MTB/RIF assay for rapid diagnosis of tuberculosis and detection of rifampicin resistance in specimens obtained from the MDR TB suspects following the MDR TB suspect criteria.

Results and lessons learnt: During March 2012 to February 2013, a total of 2708 MDR TB suspect

cases were tested from GeneXpert units. Of them, 1597 MTB positive cases including 526 cases of RIF resistance TB (19.42% of suspected MDR TB cases) were found.

Conclusions and key recommendations: Introducing GeneXpert MTB/RIF will enhance the national capacity for early detection of MDR TB. NTP and TB CARE II project are now working to develop linkage with sub district health facilities to GeneXpert labs for referral of suspected MDR TB cases for diagnosis.

PC-1008-03 Implementation of Xpert® MTB/RIF as key tool for expansion of programmatic management of drug-resistant tuberculosis in Indonesia

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Background and challenges to implementation: Xpert MTB/RIF (Xpert) was introduced in Indonesia as routine diagnostic test to detect rifampicin (RIF) resistance in individuals at risk of multidrug resistant (MDR-) TB. Xpert is an essential tool to achieve expansion targets for programmatic management of drug-resistant TB (PMDT) in Indonesia, which are to diagnose 2000 MDR-TB cases and start 1800 on second line treatment by 2013.

Intervention or response: With support from USAID through the TB CARE I project, Xpert was implemented in 5 pilot sites since March 2012 and in 12 additional sites from November 2012 to April 2013. To effectively link diagnosis with treatment, Xpert was installed in sites to provide quality examination for PMDT services.

Results and lessons learnt: From March 2012 to March 2013, a total of 1699 Xpert tests were performed for presumptive MDR-TB cases. Results showed that 1283 (75.5%) were positive for TB and among them 555 (43.3%) were RIF resistant. The initial hesitation of clinicians to treat on the basis of Xpert results has diminished with recent changes in national policy to start each Xpert RIF resistant case on second line treatment immediately. Compared to previous testing with culture and DST, the number of registered presumptive MDR-TB cases increased with 32% in the 5 initial Xpert sites. The total number of tests did not increase due to a temporary stock-out of Xpert test supplies. While notification of RIF resistant cases and second line treatment initiation did not increase, the time to treatment reduced greatly by 66 days. Operational challenges that remain are the establishment of national mechanisms for trouble-

shooting, maintenance and quality assurance. Finally, Xpert results needs to be followed up by culture and DST to complete drug-resistance profiles and monitor treatment, thus improving capacity and quality of these facilities is a critical element of scaling up.

Conclusions and key recommendations: Xpert MTB/RIF has been gradually implemented in Indonesia in line with PMDT expansion to routinely detect RIF resistant cases and effectively start MDR-TB treatment. In order to achieve PMDT targets for 2013, the overall number of presumptive MDR-TB cases receiving an Xpert test should be increased by strengthening sample and suspect referral networks and training of clinicians in peripheral clinics on national Xpert guidelines. Capacity for MDR-TB treatment and culture and DST testing should be scaled up simultaneously.

PC-1009-03 Comparison of Xpert® MTB/RIF with BACTEC MGIT 960 for the rapid detection of *Mycobacterium tuberculosis* resistance in Kazakhstan

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Objective: To identify sensitivity and specificity of Xpert MTB/RIF in native and concentrated samples of pathological materials in comparison with other laboratory methods.

Materials and methods: From 8/2012 to 12/2012 the pathological materials from 575 MDRTB suspects have been evaluated through the XpertMTB/RIF at the National Centre for TB Problems. However the results from only 98 patients were available and were obtained from the following samples: 92–sputum, 4–bronchoalveolar lavage, 1–cerebrospinal fluid, 1–the pus. In 67 cases the study was conducted with a native sputum, and in 31 cases it was done after the centrifuging and decontamination of materials from the new and re-treatment cases with a high risk of having MDRTB.

The following tests were conducted in all the native sputum samples: XpertMTB/RIF, BACTEC MGIT and smear microscopy. In the meantime, the Xpert-MTB/RIF and BACTEC MGIT tests were performed on the above-mentioned samples obtained from the process of centrifuging and decontamination.

Results: MTB+Rif resistance was detected in 44.8% (30 out of 67) of samples by the XpertMTB/RIF. According to the Bactec MGIT data the concordance of the MTB + RH resistance for the same samples was 86.7% (26 out of 30), and the concordance of only RIF resistance was 3.3% (1 out of 30). The total concordance onRIF resistance was 90%.

MTB+Rif Sensitive was detected in 55.2% (37 out of 67) of samples by the Xpert MTB/RIF. According to the BACTEC results the alignment with MTB+

RH sensitive for the same samples was 64.9% (24 out of 37), and the alignment with only RIF sensitive was 27% (10 out of 30). The total concordance of MTB+RIFsensitive was 91.9%.

The Sensitivity of smear microscopy in comparison with XpertMTB/RIF was 56.7% (38 out of 67). The analysis of sensitivity of two methods (Xpert-MTB/RIF and BACTEC MGIT) conducted from the same samples showed that XpertMTB/RIF in comparison with BACTEC allowed to detect more TB cases and to observe more RIF resistance due to the high sensitivity. Moreover, the Xpert enabled to find MDR TB additionally in 5 patients from samples with a very low volume of DNA.

Conclusion: The Xpert MTB/RIF has a high sensitivity of 90% and a specificity of 91.8%. In addition, this method allows to diagnose in a short period of time and to use the less amount of samples.

PC-1010-03   Impact of Xpert® MTB/RIF on case notification, treatment initiation and diagnostic delays for individuals at risk of MDR-TB in Indonesia

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Background: With support from USAID/TB CARE I, Xpert MTB/RIF (Xpert) was introduced in Indonesia as routine diagnostic to detect rifampicin (RIF) resistance in individuals at risk of multidrug resistant (MDR-) TB. This study set out to assess the impact of using Xpert on MDR-TB case notification, treatment initiation and diagnostic delays.

Design/methods: Data resulting from diagnosing individuals at risk of MDR-TB was gathered from routine registers of three provincial referral hospitals. A comparative analysis was done between diagnostic performance of culture and drug-susceptibility testing (DST) in 11 months before, and Xpert testing in 11 months after Xpert introduction. Outcomes measured were the proportion of individuals that received a test, that tested RIF resistant, that started second line treatment, and time from registration to treatment.

Results: Before Xpert introduction, a total of 920 presumptive MDR-TB cases were registered from March 2011 to January 2012. Of them, 834 (91%) received culture, 555 of 834 (67%) tested positive for TB, 327 of 517 (63%) with a DST tested RIF resistant, and 125 of 327 (38%) RIF resistant cases started second line treatment within a median of 81 days.

After Xpert introduction, a total of 1213 presumptive MDR-TB cases were registered from March 2012 to January 2013. Of them, 808 (67%) received an Xpert test, 659 of 808 (82%) tested positive for TB, 296 of 808 (45%) tested RIF resistant, and 72 out of 296 (24%) RIF resistant cases started second line treatment within a median of 15 days. Comparing before and after, the number of presumptive MDR-TB cases that registered increased with 32%, but the total number of tests did not increase due to a temporary stock-out of Xpert test supplies. Notification of RIF resistant cases remained equal with 37% (296/808) among all tested with Xpert compared to 39% (327/834) with culture and DST. Treatment initiation among RIF resistant cases decreased with 17%, while time to treatment reduced by 66 days.

Conclusion: The introduction of Xpert to diagnose RIF resistance among presumptive MDR-TB cases in three sites in Indonesia did not increase the proportion of RIF resistance found and cases started on second line treatment. However, Xpert did considerably reduce the time to treatment for new RIF resistant cases. The outcomes of this study catalyzed a national policy change to start all types of presumptive MDR-TB cases with an Xpert RIF resistant result immediately on 2nd line treatment.

ASSESSING KNOWLEDGE, ATTITUDES AND PRACTICE IN THE TREATMENT OF TUBERCULOSIS

PC-1011-03   Assessment of tuberculosis-based knowledge, behaviours and practices of non-medical people surrounding tuberculosis patients in Ouagadougou

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Background and challenges to implementation: TB is a public health problem in the world. The hope of the World Health Organization (WHO) in the fight against this contagious disease rests on the implementation of the DOTS strategy. The success of this strategy passes necessarily by the entourage of patient involvement.

Intervention or response: It was a prospective cross-sectional study with descriptive purpose, which was performed for a period of three (3) months from July 1 to September 30. People closed to 155 tuberculosis patients distributed in all diagnosis and treatment centers of the city of Ouagadougou. A semi-structured individual and anonymous written questionnaire, which was administered by interview, was used for

data collection. Processing and analysis of data collected were performed using SPSS software in its version 17, Word and Excel 2007. The significance level 'P' was 0.05

Results and lessons learnt: The sample consisted of 208 caregivers of patients, sex ratio was 1.05 and the average age was 36 years old. In non-medical patient's entourage, 20% had a good general knowledge about tuberculosis, 69% a partial knowledge and 11% a bad knowledge. 72.3% of those who had a partial knowledge were not educated. If generally, patient's relatives had a good knowledge about symptoms of tuberculosis (98.1% about cough), they however had very limited knowledge about modes of transmission (only 33.7% knew that sexual relations were not a means of transmission) or about the existence of drug resistance, (61.1% were not informed). About attitudes and practices, 7.2% of patient's caregivers would refuse to shake hands with a TB patient, 20.2% would refuse to sit by his side and 60.1% would refuse to eat with him in the same plate. We found that 35.1% of the entourage of TB patients would refuse people to know that their loved one is suffering from tuberculosis and as justification, 87.6% had stated the fear of stigma from others.

Conclusions and key recommendations: Non-medical entourage of TB patients had a very fair knowledge about tuberculosis. To improve this weakness, education for health at the community level and care centers is necessary. It could take place through authority's commitment and active participation of schools and learned societies.

PC-1012-03 Knowledge, attitude and practice survey for tuberculosis among high risk groups and general population in Georgia, 2012

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Background and challenges to implementation: A knowledge, attitude and practice survey on tuberculosis among high risk groups and the general population was carried out in Georgia in 2012. The study aimed to collect information on knowledge, perceptions, and actions taken by TB suspects, patients, and health providers in relation to TB disease and its management in the country.

Interventions or response: In this cross-sectional study, data were collected through face-to-face individual interviews by specially designed questionnaires for each targeted group (health providers, patients, high risk populations especially patients with related co-morbidities, and the general public).

Results and lessons learnt: Totally 1590 subjects participated in the survey. Only half of the respondents

in all groups knew about the availability of free TB treatment and diagnostic services. The main reasons for not seeing a doctor when symptoms potentially related to TB occur was uncertainty regarding where to go. The study design included a survey of university students as a proxy to the general public, which showed lowest level of TB related knowledge (Figure). In addition, close to twenty percent of high risk individuals, including HIV positive patients, did not know how TB is treated. TB self-treatment was reported in 28.2% of prior TB patients. TB related knowledge was insufficient among health care workers, particularly in private settings and among nurses. A high level of TB-related stigma was confirmed by the fact that 50% of the respondents would either hide their illness (11%) or disclose to close people (38%). One third of prior TB patients who disclosed their status experienced a negative change in relationships with friends and community members.
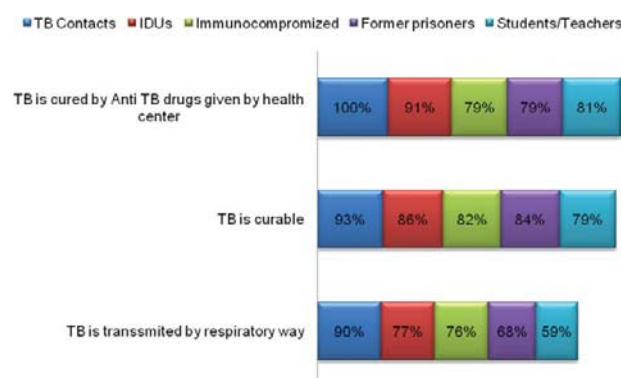

Figure TB knowledge among different target groups.

Conclusions and key recommendations: The findings indicate that strong action should be taken to increase knowledge about the disease including better information on where and how to get TB care. Health care workers in particular require stronger training on TB symptoms and treatment. Intensive advocacy efforts among different target groups are required to reduce a dramatically high level of stigma. TB patients and their families should not suffer from rejection and social isolation.

PC-1013-03 Frontline health care workers' knowledge of tuberculosis in rural Southeast Nigeria

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Background: In low-income countries, healthcare workers are 5.7 times more likely to develop tuberculosis than the general population. The degree of risk is dependent on multiple factors, like healthcare setting,

and the effectiveness of tuberculosis infection control measures. Healthcare workers lack of knowledge may contribute to their risk of developing tuberculosis. With limited tuberculosis infection control activities in health institutions across Africa, there is need to evaluate information challenges in tuberculosis services delivery from the front-line in order to clarify priority areas for intervention. We examined the knowledge of tuberculosis among frontline healthcare workers in rural Nigeria.

Design/methods: A cross-sectional study was conducted in December 2011 during an interactive educational training organized for tuberculosis-focal persons in charge of 45 rural health facilities administering the directly observed treatment short course strategy (DOTS) by the National Tuberculosis and Leprosy Control Programme in Ebonyi State. All the participants completed a self-administered questionnaire assessing knowledge on tuberculosis disease, treatment and infection control. Participants with ≥70% of correct responses were considered to have good knowledge.

Results: Of the 52 healthcare workers surveyed, 48% were professionals (doctors/nurses). The mean age was 36.3 ± 10.6 years. Most of the respondents were female 27 (52%), had tertiary education 43 (83%), and 33 (63%) have worked in TB care for five years or more. Only 14 (27%) of the respondents had a good knowledge score. Mean knowledge scores varied across job categories (F = 6.2, $P < 0.001$) and with duration working in TB care (F = 30.7, $P < 0.001$). Knowledge gaps existed regarding TB disease and treatment, but the most deficits were found in infection control.

Conclusion: Tuberculosis knowledge gaps were found among rural healthcare workers, this may influence their risk of nosocomial tuberculosis infection: therefore they should be re-educated about tuberculosis especially infection control.

PC-1014-03 Role of primary care providers in detection and follow-up treatment of tuberculosis in Georgia

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Background and challenges to implementation: Despite considerable progress towards achieving many critical TB control objectives, TB case detection still remains passive in Georgia indicating limited involvement of primary care providers in early TB diagnosis. Since 2004 the state heavily invested in this sector by remodeling and equipping 163 PHC facilities, retraining 1726 physicians and 1771 nurses into family physicians and nurses. However, utilization of primary care services remained low (0.85 visits per person per annum). USAID Georgia TB Prevention proj-

ect undertook operational studies to assess the degree of involvement of family physicians in TB detection and follow-up, evaluate barriers and contributing factors to effective TB management.

Intervention: The project team conducted key informant interviews, focus group discussions and surveyed 412 family physicians and nurses countrywide utilizing a tailored questionnaire.

Results and lessons learnt: Despite possessing a wide range of TB care-related competencies, family physicians and nurses still play a limited role in TB detection and follow-up. Only 9% of TB suspects were referred from primary care providers to TB services in 2012. Among those 5% were referred within two weeks of onset of symptoms. Currently, poor linkages between the primary and secondary care services do not allow for adequate information flow from and to family physicians and TB specialists. Family physicians do not receive confirmation of TB diagnosis and treatment initiation from TB specialists after referral. DOT during the intensive and continuation phases is largely provided by TB specialist. The share of patients who return to the community and receive DOT from a village primary care nurse varies significantly by regions and provider networks—from as low as 13 to 49%. Additionally, the survey found that family physicians and nurses are positive about updating their skills and knowledge in TB management. They state that training should be aimed at improving their skills of early TB detection, decision making on referral and follow-up.

Conclusions and key recommendations: Although important, training alone cannot substantially change providers' behavior. Adequate regulatory and financing mechanisms should be in place that would encourage early TB detection by primary care providers, strengthen linkages between primary and specialized TB services and support quality treatment in the community.

PC-1015-03 Social determinants of the tuberculosis epidemics in Nigeria: a qualitative study

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Background: The determinants of disease at the population level have long been established by public health professionals to be different from the determinants of disease at the individual level. This principle underscores the practice of public health itself and is reflected in the strategies employed for disease control at the population level. Decades from establishing the importance of social factors as crucial determinants of health indices at the population level, most health interventions still fail to address these factors in their approach to combatting diseases. This is perhaps because of the complexities in addressing

social factors which are rooted in deeper political and cultural contexts that may be difficult to address by unilateral health programs. Interventions like the engagement of communities in the control of TB and partnerships with private health sector to improve access to TB services have been employed in Nigeria, however, marginal success has been recorded towards the elimination of the disease as a public health issue. This study addresses the socioeconomic factors that may be associated to TB control in Nigeria but which are not taken into account in the design and operationalization of TB control activities. The factors being studied in this paper is income level in relation to economic indices.

Method: Qualitative methodology using in-depth interviews, key informants interviews and focus group discussion was employed. This was done as part of a KAP survey conducted in six states namely: Akwa Ibom, Ebonyi, Gombe, Katsina, Benue, Ondo.

Results: It was observed that although TB services are free, hidden costs such as cost of transportation, loss of working hours on farm and other manual jobs and the cost of eating three meals per day because of the medicine intake during the TB treatment are some of the reasons patients seek care outside the orthodox health sector or not at all. These factors were also implicated in treatment default. Patients simply stop coming for DOTS because they have no money for transportation.

Conclusion and recommendations: Interventions designed for the control of TB in the population should address the distal socioeconomic factors such as lack of transportation fare and loss of man-hours as a result of the disease. Future studies should be conducted to explore the implications of addressing socio-economic factors in the design of TB interventions.

PC-1016-03 Evaluation of a hospital referral system in selected hospitals in Manila and Quezon City, Philippines

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Introduction: The Philippines ranked 6th among 22 high burden countries for tuberculosis (TB). Through private-public mix framework and Department of Health Administrative Order engaged hospitals. The objectives are: 1) To evaluate the referral system in hospital TB clinics and DOTS facilities in Manila and Quezon City, 2) To identify factors that influence arrival of TB patients at peripheral DOTS facilities and 3) To recommend measures to address gaps identified in the study.

Methods: The evaluation utilized descriptive and audit design. TB patients were profiled. A case control study identified risk factors. Focus group discussion

was conducted. Cases are TB patients referred from the hospital TB clinic to peripheral DOTS whose referral slip was not returned. Controls are TB patients reffered from the hospital TB clinic to peripheral DOTS whose referral slip was returned successfully.

Results: At the 5 TB clinics, patients were advised to return lower half of the referral slip once seen at the peripheral DOTS facility. At the 79 peripheral DOTS facilities, 20% of TB register were updated. There were 230 TB patients interviewed. All were knowlegeable of TB. 73% were accepted TB patients while 27% were lost TB patients in the external referral system. Lost TB patients who knew TB treatment was daily and supervised at the health center were 3 times more like not follow referral from TB clinic to peripheral DOTS than controls. (OR 2.58, 95%CI 1.21–5.55; $P = 0.01$). On focus group discussion, perceived barrier were conflict of schedule for directly observed treatment (DOT) for TB patient and the absence of communication between the TB clinic and the peripheral DOTS facility for service providers.

Discussion and conclusions: The lack of communication between TB clinic and the peripheral DOTS hindered arrival of patients to peripheral DOTS facilities. Patients' knowledge and attitudes affected the flow of referral. Patients do not want facility-based DOT. In conclusion, the external referral system was simple and easily carried out. Gaps identified hastened or delayed arrival of referral to peripheral DOTS. The external referral system is recommended in the scaling up of hospital TB DOTS and find solutions to address patients refusal to undergo facility-based DOT.

PC-1017-03 Barriers to tuberculosis evaluation: a qualitative study of providers in Uganda

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Background: At routine health centers in Uganda, we found previously that only 54% of patients with chronic (>2 weeks) cough were being referred for sputum AFB examination, 74% were completing examination if referred, and 84% were initiating treatment if smear-positive. To identify barriers to uptake of recommended TB evaluation practices, we conducted a qualitative study of health center staff focusing on

health system behaviors and processes of care that might be modified with targeted interventions.

Methods: The study took place at six government-run district health centers in Uganda which function as the main point of care for patients accessing health care services. We obtained permission from clinic directors to interview health center staff about barriers to TB evaluation. We conducted in-depth interviews with clinic staff, focusing on clinicians most engaged in patient care. Interviews were transcribed, coded using a standardized framework, and analyzed to identify emergent themes.

Results: Twenty-two health care providers, including 14 clinicians, were interviewed regarding their perceptions about barriers to TB care. Contextual barriers to TB evaluation included: 1) economic barriers—general poverty coupled with high costs of seeking TB care; 2) geographic barriers—physical remoteness of patients from health centers; 3) socio-cultural barriers—stigma and health illiteracy surrounding TB; and 4) health status barriers—patients being too sick to access health care services. Contextual barriers interacted with the following health system barriers to inhibit high-quality TB evaluation: 1) limited resources—drug and supply stock-outs, limited space for patient care, and poor ventilation; 2) inadequate human resources—low motivation and high turnover of staff and lack of training; 3) poor service implementation—multi-day TB evaluation and limited capacity for follow-up; and 4) poor coordination of services—within the clinic and between TB and HIV services.

Discussion: Our findings reinforce that TB programs in high burden countries should take steps to enable diagnosis of TB followed by initiation of treatment at a single health center visit. However, health system barriers, if not addressed, are likely to blunt the impact of introducing new diagnostic strategies or tests. These results can help generate much-needed multifaceted interventions targeting modifiable health system factors to improve the quality of TB evaluation services.

PC-1018-03   Assessment of human immunodeficiency virus and tuberculosis knowledge in correctional facility nurses in Alberta

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Background: Human immunodeficiency virus (HIV) and tuberculosis (TB) rates are disproportionately higher in the incarcerated compared to the general population, thereby serving as a prime environment for targeted care. Unfortunately, HIV seropositive inmates report perceived discrimination and missed antiretroviral doses resulting in compromised care. In addition, crowded living conditions, poor ventilation and delayed diagnoses have resulted in TB outbreaks in facilities.

Correctional facility Registered Nurse (RN) competency in HIV and TB management may mitigate some of these concerns. We measured baseline HIV and TB knowledge of correctional facility RNs and quantified changes after a targeted educational workshop with the aim of developing an effective educational tool for this group of health care workers.

Design/methods: A cohort of health care staff was surveyed at 3 provincial correctional facilities (Alberta, Canada) in 2012. Validated knowledge and confidence survey instruments were administered to participants to measure perceived need for further HIV and TB education, HIV and TB knowledge, attitude towards HIV patients, and confidence in providing TB care before and after provision of a targeted HIV and TB workshop. Changes in knowledge were compared using paired t-tests.

Results: Of the 35 study participants, 22 were RNs. At baseline, formal education in HIV and TB was documented in 5 and 4 of the RNs respectively. Whereas nursing attitude towards HIV patients remained unchanged, basic HIV knowledge significantly increased by 1.5 ± 0.5 ($P = 0.007$) from a baseline of 33.6 ± 1.9 post intervention. Although basic TB knowledge remained unchanged, advanced TB knowledge increased by 1.7 ± 0.5 ($P = 0.003$) from a baseline of 5 ± 1.6, and confidence in TB care, originally scored as 24.8 ± 11.1, increased by 10.3 ± 1.9 ($P < 0.001$) post-intervention. Perceived need for further HIV and TB education at baseline was 17.9 ± 2.1 and 17.2 ± 2.0 and significantly decreased by 2.4 ± 0.5 ($P < 0.001$) and 2.2 ± 0.6 ($P = 0.04$) respectively post-intervention.

Conclusion: Our study demonstrates that correctional facility RNs may not always receive HIV and TB training during employment and that directed HIV and TB workshops can significantly increase knowledge and confidence in providing care for affected individuals.

PC-1019-03   Non-government organizations' involvement in tuberculosis care: a community based study conducted in 30 districts of India

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Background: India launched TBC program in 1955. Since then, there have been significant advancements in implementation of tuberculosis (TB) control activities. Usually, the Central TB Division, which formulates

the implementation policy and this policy, percolates down the line, to the State TB Society, to the District TB Society and to the primary health care centres, but the patient is not necessarily involved in the entire exercise. A significant change in this orientation is necessary to make an overall impact on program efficiency with community participation thorough NGOs.

Method: A cross-sectional community based survey was conducted on 'Knowledge, Attitude and Practice (KAP) study of Tuberculosis in India' during the months of January to March 2011. 10 primary sampling units each from 30 districts of the 374 project Axshya Districts were selected by stratified cluster sampling techniques. A semi-structured questionnaire was designed to collect all relevant information on knowledge, attitudes and practices towards TB by various local NGO representatives.

Results: A total of 51 NGO's were found during the baseline KAP survey. Most of them were working at district level. The key areas of their work included rural development, sanitation, education, domestic violence/gender, TB, other health related and some other areas not specified. When assessed for their knowledge on TB as defined in the study, all of them were aware of TB and that it is curable; 80% were aware of the correct duration of treatment; 90% were aware of DOTS and 94% of the correct symptoms. Out of the interviewed, 85% of them have suggested Government DMC for TB diagnosis and 86% of them mentioned government hospital for treatment. However it was observed that 26 (51%) were involved in TB care of which only 14 (27%) were involved in various RNTCP schemes.

Conclusion: National Strategic Plan (NSP) 2012–2017 of India highlights on importance of 'Partnership between the public and private sector is essential for universal access and early detection'. In India, under RNTCP, there is a scope for NGOs to be involved systematically in TB care. NGOs need to realize their full potential in TB control/care and therefore there is a need to orient and involve them in TB Care. NGOs could be the key stakeholders along with other agencies in RNTCP in achieving universal access for TB Care goals by 2017.

PC-1020-03   Patient and providers' perceptions regarding need of nutritional supplement in tuberculosis patients in Gujarat, India

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Background: India has the world's highest burden of TB. Despite high case notification rate and cure rates TB notification rates and incidence is declining very slow. One of the major reasons is rampant prevalence of malnutrition, the known most important population attributable risk factors (PAF). However, Indian National TB Program (NTP) has no policy statement or intervention in overall TB control strategy regarding malnutrition. This made ground for quick need assessment of the patient and provider perspectives regarding role of public health nutrition in TB control.

Objective: To assess the perceptions of TB patients and providers regarding role and need of nutritional supplement in TB control.

Methods: Cross-sectional study. Structured questionnaire was developed and used (in English and translated in local language) for assessment of perceptions of a representative random sample of TB patients and providers from all 30 districts and 136 tuberculosis units across the state of Gujarat, India. The tool comprised of identification information and 10 point ordinal scale for level of agreement with score 1 meaning strongly disagree and score of 10 as strongly agree.

Results: 86% of 2979 TB service providers and 95% of 537 TB patients expressed need of free nutritional supplement to all TB patients under TB control programme and 93% and 98% expressed that at least poor TB patients should receive free nutritional
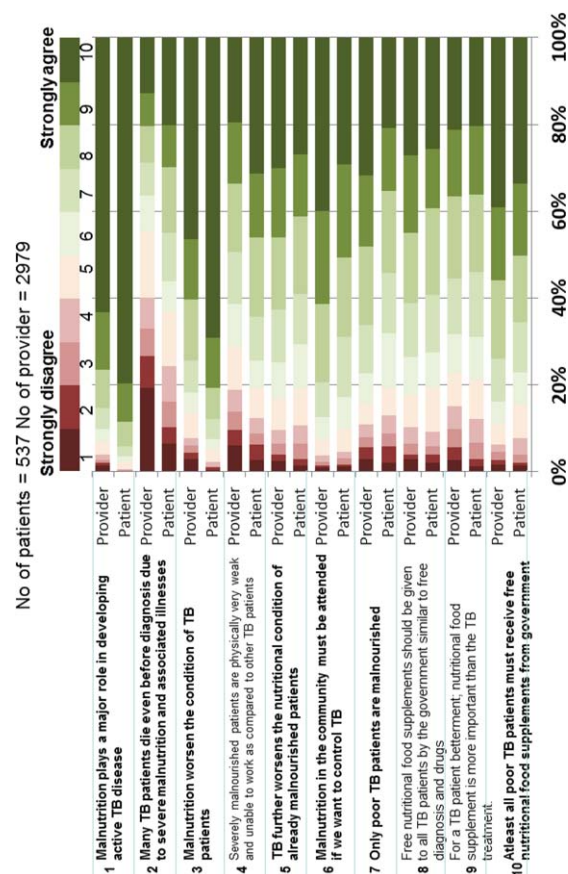

Figure Perceptions of TB providers and patients regarding nutritional supplement to TB patients, Gujarat, India.

supplement. Difference between the perception of males and females was no significant. Educational level did not have significant association with difference in perception in either group of patients and providers. 82% of the respondents felt that malnutrition in the community must be attended if we want to control TB. 38% of the respondents even felt that 'For a TB patient betterment; nutritional food supplement is more important than the TB treatment'.

Conclusion: Very high proportion of patients as well as providers perceives that nutritional supplement to TB patient is important for TB control and strategy is needed to address the issue.

Recommendation: NTP should consider broad strategy for public health nutrition integrated with TB control based on the high level of patients and provider perceptions.

PC-1021-03   Increased susceptibility of smokers to tuberculosis: urgent need for spreading awareness and advocating policy revision

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Introduction: Nearly 17% of smokers of the world live in India. Evidence shows that tobacco smoking increases the probability of contracting tuberculosis. The 2012 WHO report attributes 4% mortality in India due to tuberculosis is attributable to tobacco. Often the symptom of cough which is associated with TB is related to smoking rather than for TB. The study here would throw light on smoker's perception about TB and their awareness about TB. The results direct towards a policy of including TB symptoms along with adverse effects of smoking in the Cigarettes and Other Tobacco Products Act, 2003 (COTPA).

Objective: To review policy documents of tobacco control for TB symptomatic and to analyze KAP among smokers towards TB control.

Method:
1 Policy documents were reviewed to understand whether there has been mentioning about TB symptomatic or cough associated with TB.
2 A cross-sectional sample of 50 smokers within the age group of 19 to 71 were randomly selected from Salem in Tamil Nadu.

Results: The policy documents such as CODPA and NTCP narrates various hazardous effects and intimates warnings to smokers about susceptibility to various NCDs. However, there are no specific instructions on increased susceptibility of TB nor TB related symptoms with smoking. 28% smokers interviewed had basic knowledge about TB symptoms (cough > 2 weeks). Smokers with a frequency of smoking more

Table   Frequency of smoking vs. symptoms of tuberculosis

Frequency of smoking	Symptoms of tuberculosis		RR (CI)	P value
	Yes n (%)	No n (%)		
≤10 Cigarettes/day	11 (69)	5 (31)	2.92 (1.46,5.82)	0.002*
>10 Cigarettes/day	8 (24)	26 (76)	1	

* χ^2 test.

than 10 cigarettes/day were 2.92 times more at risk of contracting TB as compared to those who have less frequency of smoking ($P = 0.002$). 80% of those who were aware about TB were willing to get sputum examined. There are also evidences of histopathological and diseases surveillance of lung damage in smokers which results into increased susceptibility to TB.

Conclusion: Based on the above study, the following recommendations have been arrived at:
• The various institutions governing national tobacco control policies have publicized hazardous indicators about the tobacco use. The policy revisions are needed to include the smoker's susceptibility and attributable risk towards TB.
• As indicated in the study, 72% smokers are not aware that they and their families are susceptible to TB as symptoms portray those related to smoking. Thus, there has to be increased awareness about the link of tobacco and TB.
• There has to be close coordination between TB Control Programme and Tobacco Control Programme.

PC-1022-03   Patients' perception in accessing tuberculosis services in health facilities: a case study of tuberculosis patients in South-West Nigeria

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Background: Even though TB treatment is free in Nigeria, patients are likely to incur costs due to multiple visits during treatment. The economic costs can be an important barrier to TB patients' ability to utilize TB services, access treatment and adhere to TB treatment. The purpose of the study is to determine TB patients' perception of socioeconomic impact of TB disease on TB patients and; to assess the perception of the quality of the delivery of TB health services.

Method: A mixed method approach consisting of a cross-sectional survey of 180 TB patients currently

on treatment in Ogun, Osun and Ekiti states was undertaken. In-depth interviews and focus group discussions were held with TB patients on treatment in selected facilities to explore patient's perception and issues surrounding hidden cost borne by patients.

Results: Majority (74%) indicated travel cost as the main source of expenditure in accessing TB services. Other costs mentioned are food and drink (3.4%); treatment (3.4%) and loss of income generating time (2.8%). Perception of TB patients about social and economic costs of the disease suggests that 79% of patients agreed that TB causes loss of productivity and that the stigma related to TB can make one loose paid job (68%). Additionally, the proportion of respondents who believed that TB could make them lose their jobs, differ significantly between those who attended school and those who did not attend school (87.0% vs. 13.0%). Additionally, most patients 80.6% are of the opinion that quality of health services in general were very good; and 83.1% consider TB services to also be very good. However, only 61.1% of patients were of the opinion that providers listen to patient's needs and demands.

Conclusion: Though TB diagnosis and treatment in Nigeria is provided free of charge patients however bear some expenses which are perceived could cause loss of productivity and jobs. Expansion of TB services could help alleviate cost borne by patients and patients empowerment must be promoted.

MDR SURVEILLANCE

PC-1023-03   Low prevalence of MDR and XDR in strains tested in a Brazilian state. A reality or just lack of testing?

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Background: The surveillance of resistance to drugs utilized in the treatment of tuberculosis (TB) is essential to provide information about the resistance magnitude and trends, an essential knowledge for development of adequate treatment guidelines. In several countries, including Brazil, the resistance profile reality of *Mycobacterium tuberculosis* is unknown; especially for the multidrug-resistant (MDR) and extensively resistant (XDR) strains, which represents a significant menace for this disease effective control.

Objective: To describe *M. tuberculosis* profile of resistance to drugs, as identified in the Center of Laboratory Reference of the State of Minas Gerais.

Design/methods: Cultures in Löwenstein-Jensen medium were developed with 2595 samples that arrived to the Center of Laboratory Reference of the State of Minas Gerais, during the years of 2010 and 2011. Identification and sensitivity tests were (proportion method or Mycobacterial Growth Indicator Tube—MGIT 960) executed on the positive cultures.

Results: 925 (35.6%) out of the 2595 samples exhibited positivity for mycobacteria. From these positive samples, 660 were of *M. tuberculosis* coming from 458 patients. The observed standards were: 390 patients bearing sensitive strains and 68 resistant ones. The MDR frequency was 42/458 (9.2%): rifampicin + isoniazid 35.3% (24/68); rifampicin + isoniazid + streptomycin 17.6% (12/68); rifampicin + isoniazid + ethambutol 2.9% (2/68); rifampicin + isoniazid + streptomycin + ethambutol 5.9% (4/68). The XDR frequency was 2/458 (0.4%): rifampicin + isoniazid + ofloxacin + amikacin + capreomycin + canamycin). For rifampicin alone, the frequency was 8.8% (6/68); for Isoniazid alone 17.6% (12/68); Streptomycin alone 4.4% (3/68); rifampicin + streptomycin 1.5% (1/68).

Conclusion: There was a small amount of patients bearing MDR and XDR during the studied period in Minas Gerais, Brazil. However, such results could not reflect reality, as cultures or sensitivity tests are not part of the routine in that State.

PC-1024-03   Risk factors for multidrug resistance among tuberculosis patients on treatment in Belarus, 2011

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Background: In Belarus (population 9.5 million in 2011) 46% of tuberculosis (TB) cases have strains resistant to at least isoniazid and rifampicin (multidrug-resistance; MDR-TB), the highest levels ever recorded globally. MDR-TB thus presents a key challenge to TB control in this country. We analysed the risk factors for MDR-TB among the TB cases notified to the public health services in Belarus.

Design/methods: We used data registered in an electronic format for all TB cases (new and relapses)

notified in the 7 administrative regions of Belarus in 2011. Multivariable logistic regression was used to identify variables statistically significantly associated with in vitro diagnosis of MDR-TB in the patients ($P < 0.05$).

Results: Of a total 4375 new TB cases and 745 relapses in 2011, drug-susceptibility test (DST) results for both isoniazid and rifampicin were available for 47.1% and 83.8% respectively. Median age was 45 years (IQR 34–53), 78.3% were males, and 5.2% were HIV-infected. MDR-TB was detected in 27.7% of new TB cases and 61.5% of relapses (35.6% overall, 956 cases). Among 2583 TB cases in 2011 with full data on several risk factors, MDR-TB was statistically significantly associated with age <50 (adjusted odds ratios: 1.57; 95% confidence limits: 1.31–1.89), relapse (4.49; 3.68–5.47), and origin from 5 of the 7 regions (range in odds ratios: 1.76–2.44; reference Brest oblast).

Characteristic	Non-MDR ($n = 1646$) %	MDR ($n = 937$) %	P value (relative risk, univariate analysis)	Adjusted odds ratio (95% confidence limits) (multivariable regression)
Age <50	61	69	<0.05	1.57 (1.31–1.89)
Male	77	81	<0.05	1.04 (0.84–1.29)
Relapse	14	40	<0.05	4.49 (3.68–5.47)
Chronic obstructive pulmonary D	3	2	<0.05	0.71 (0.39–1.29)
Diabetes mellitus	2	2	>0.05	1.49 (0.81–2.77)
HIV infection	5	5	>0.05	1.01 (0.67–1.51)
Problem alcohol use	15	17	>0.05	1.02 (0.80–1.29)
Brest Oblast (region)	17	10	<0.05	Reference
Vitebsk Oblast	11	12	>0.05	2.11 (1.49–2.99)
Gomel Oblast	16	14	>0.05	1.39 (0.99–1.96)
Grodno Oblast	9	13	<0.05	2.44 (1.72–3.48)
Minsk area	18	18	>0.05	1.76 (1.28–2.42)
Mogilev Oblast	17	20	>0.05	1.88 (1.37–2.57)
Minsk City	11	12	>0.05	2.00 (1.41–2.83)

Conclusion: The coverage of DST among notified TB patients in Belarus is high enough to permit useful exploration of risk factors for MDR-TB at the national level. In our analysis, the association of MDR-TB with age <50 years reflects the relatively recent emergence of resistance in the country. Differences in frequency by region of the country possibly indicates that risk of transmission and development of MDR-TB also varies by geographical area.

PC-1025-03 Immunoreactivity in patients with generalized MDR tuberculosis

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Background: Increasing prevalence of MDR *Mycobacterium tuberculosis* decreases chemotherapy efficiency and induces studies of pathogenic researches in order to find ways for a patient organism immunity mobilization. The aim of this study is to detect the immunity peculiarities in patients with generalized MDR tuberculosis.

Design/methods: A total number of 92 patients with generalized tuberculosis were observed: 21 produced MDR *Mycobacterium tuberculosis* (MDR TB) culture (group I) and 71—with the sensitive one (group II). Patients' blood samples were tested by serological reactions complex (passive hemolysis reaction (PHR), complement consumption reaction (CCR), lymphocytes blast transformation (RBTL) with PPD; lymphocyte toxicity assay (LTA) with monoclonal antibodies (CD3, CD4, CD8, CD16, CD 20, CD 25, CD 95, HLA-DR); ELISA for TB specific IgG, IgA and IgM.

Results: Specific humoral immunity indicators (PHR, CCR, ELISA IgG) in patients from both groups proved to be high (85.7%–90.0%). T-helpers decreased in 78.9% group I patients and 51.0%—in the group II ($P < 0.05$). The frequency of CD4/CD8 proportion decrease was almost 2 times higher in the group I than in the group II (74.0% vs. 40.0%). Direct correlation between the quantity of CD4+ lymphocytes and CD95+ cells with Fas receptor apoptosis ($r = 0.72$; $P < 0.0001$) in the group I patients was revealed as an indicator of significant T-cells deficit. HLA-DR decreased in 46.1% group I patients and increased in 40.0% of group II patients. The increased specific sensibility (RLBT with PPD) was detected in 95.0% of the group II patients and in 45.5%—of the group I, which implies that lymphocytes of patients with generalized MDR TB tuberculosis did not respond to PPD 2 times more frequently.

Conclusion: 1) The Th2 immune response prevails in patients from the group I which prioritized them for immune therapy on early stages of treatment. 2) Patients with MDR TB demonstrated the decrease in T-helpers, CD4/CD8, HLA-DR and PPD RBTL hyporeactivity.

PC-1026-03 Review of Indonesia's programmatic management of drug resistant tuberculosis, 2009–2012

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Background: With multidrug resistance (MDR) estimated at 1.9% among new and 12% among retreatment notified tuberculosis cases Indonesia is expected to have 6620 MDR TB cases annually and considered among the high burden countries.

Programmatic management of drug-resistant tuberculosis (PMDT) started in mid-2009. National TB Programme follows ambulatory treatment policy with standardized treatment regimen.[1]

Methods: Review of the PMDT supervisory visit report, quarterly and annual report and national guidelines. Review of PMDT and laboratory registers. Medical records; including smear, culture, drug sensitivity test results. Outcomes were defined according to the standard internationally recommended definitions.

Results: By Dec. 2012 eight provinces have nine PMDT treatment centers. Five quality assured laboratories are providing culture and drug susceptibility testing services. A total of 1110 cases were diagnosed with confirmed drug resistance, among these 844 (76%) were registered for treatment. Enrolment of patient increased during 2012, diagnosing 568 drug resistant TB cases and enrolling 434 for treatment which is more than the total number of cases put on treatment during previous three years. A 'borderless approach' to facilitate access was introduced so that patients can receive services from any PMDT implementing site regardless whether they belong to any part of the country. Among 159 cases registered for treatment during 2009 and 2010 period the treatment success rate is over 72%. Conclusion diagnostic capacity is pre-requisite for PMDT expansion. Cure rates (72%) among first two cohort completing treatment is at par with international standards. Initial and during treatment default rates are high; limited programme access, and socio economic support are some of the key limiting factors.

[1] Treatment regimens:

Standard regiment for MDR-TB: Km-Lfx-Cs-Eto-Z- (E)/Lfx-Cs-Eto-Z- (E)

MDR-TB with resistance to kanamycin: Cm-Lfx-Cs-Eto-Z- (E)/Lfx-Cs-Eto-Z- (E)

MDR TB with resistance to quinolone: Km-High dose Lfx/Moxi-Cs-Eto-Z- (E) /Lfx-Cs-Eto-Z- (E)

MDR TB with severe side effect of Cs: Remove Cs with PAS

Standard XDR-TB treatment: Cm-High dose Lfx/Moxi-Cs-Eto-Z- (E) -PAS/Lfx-Cs-Eto-Z- (E) -PAS

PC-1027-03   ExTBCam: an open-source solution for tuberculosis laboratory data management in Cameroon

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Introduction: The management of data for tuberculosis patients tested for drug-resistance is crucial to ensure that the laboratory results are available in a timely manner for decisions on treatment. We describe the creation of an electronic system to service laboratories within the EXPAND-TB project in Cameroon.

Methods: Upon the request of the Centre Pasteur and the National TB Programme of Cameroon, MEDES (www.medes.fr), a publicly-owned not-for-profit institution based in France, developed an electronic application to manage laboratory test results customised to the needs of the country using an open-source software generator (IMOGÈNE; code.google.com/p/imogene/). The system, named 'ExTBCam', can be accessed online via a web browser and permits offline data entry, through a desktop application which runs on Debian/Linux and other operating systems.

Results: Health workers from all the centres managing data for patients with drug-resistant tuberculosis were trained in the use of 'ExTBCam' in December 2012. Data will primarily be entered via laptops provided to the laboratories and health centres. Separate interfaces permit the entry of patient details, indication for testing, type of laboratory analysis and results of testing. The system generates printable tables with test results as well as aggregated reports of testing volumes and stratifications of antibiogramme by patient treatment history. Requesting clinicians can visualise test results online.

Conclusion: 'ExTBCam' is being implemented in four laboratories performing culture, drug-susceptibility testing or molecular tests in Cameroon. The system functions despite infrastructural limitations common to many low-resource settings, and will be evaluated for its impact on programme performance in 2014.

PC-1028-03   Prevalence of anti-tuberculosis drug resistance in Kyrgyzstan, 2011

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Background: Kyrgyzstan, Central Asian Republic, is considered one of the hot spots for multidrug resistant TB (MDR TB) in the world; however these data were based on a small study, conducted in the capital city, Bishkek in 2007.

Objective: To reliably estimate the national MDR TB prevalence and describe the most common drug resistance patterns in Kyrgyzstan.

Methodology: A cross-sectional survey of randomly selected *M. tuberculosis* isolates collected from newly diagnosed sputum smear-positive TB patients, as well as all previously treated patients registered in Kyrgyzstan during January–December 2011. Drug susceptibility testing (DST) was conducted for isoniazid, rifampin, ethambutol, streptomycin, kanamycin, amikacin, capreomycin, moxifloxacin, and cycloserine. MDR TB was defined as resistance to at least isonazid

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: Among 752 enrolled cases with complete treatment history and DST results, 504 (67.0%) were newly diagnosed and 248 (33.0%) were previously treated. Drug resistance to any first-line drug was found in 499 (66.3%) of the TB cases; 304 (60.3%) among new and 195 (78.6%) among previously treated cases. Highest resistance rates were found for isoniazid (46.4%: new cases; 67.3%: previously treated) and for streptomycin (39.5%: new; 58.8%: previously treated). The overall MDR TB rate was 34.4% (26.4% and 51.6% among new and previously treated cases respectively). Among the MDR isolates, 259 (52.1%) were resistant to all first-line drugs. This study revealed 19 XDR TB cases, 9 women and 10 men, previous treatment history was available only for 7 of them.

Conclusions: Kyrgyzstan has one of the highest overall MDR TB prevalence ever reported globally. High MDR rates remain a serious problem for TB control in Kyrgyzstan, therefore timely diagnosis and treatment of drug resistance should be one of the priorities of the TB program. The national TB program should consider the development of an electronic surveillance drug resistance system to accurately assess and monitor MDR and XDR trends over time, to evaluate TB control interventions, rationalize standardized regimens for new and retreatment cases, and assist in proper planning of the programme for managing drug-resistant TB.

PC-1029-03   Novel mycobacterial proteasome inhibitors as potential drugs

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Background: The only known bacterial pathogens with proteasomes are mycobacteria. The *M. tuberculosis* proteasome is an essential component for degradation of certain proteins, for it to survive nitroxidative stress in vitro and for it to remain non-replication state in vivo. Recently some study revealed the *M. tuberculosis* proteasome is a drug target. In this study the *M. tuberculosis* proteasome inhibitor screening model was established. The proteasome inhibitory activity of plant-derived natural products was analyzed. We are looking forward to find novel proteasome inhibitor from them.

Design/methods: Fluorescent substrate Suc-Leu-Leu-Val-AMC can be hydrolyzed by proteasome, and AMC was released. Fluorescence of AMC was recorded at excitation 360 nm, emission 460 nm. The fluorescence values were proportional to the proteasome activity, so we establish the proteasome inhibitors

screening model in vitro. Using this model the inhibition activity of 300 plant-derived natural products was detected, and to calculate the inhibition concentration 50 value (IC 50) of each product.

Results: The IC 50 of the 12 natural products was less than 100 µM. Of which 10 natural products belong to flavonoid products. The best one IC 50 was 36 µM.

Conclusion: The inhibition effect of the plant derived flavonoid products was better than the other chemical classification. We expected to find better inhibitors on *M. tuberculosis* proteasome through structural transformation or modification of flavonoid products.

PC-1030-03   Treatment outcomes among previously treated smear-positive isoniazid-resistant tuberculosis patients in Andhra Pradesh, India

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Background: Multidrug-resistant and rifampicin resistant TB patients in India are treated with World Health Organization (WHO) recommended standardized treatment regimens but no guidelines are available for management of isoniazid (INH) resistant TB patients. There have been concerns that the retreatment regimen recommended by Revised National TB Control Programme (RNTCP) may be inadequate to treat INH resistant TB cases leading to poor treatment outcomes among them. We therefore evaluated treatment outcomes of INH resistant previously treated (PT) smear positive TB patients registered under RNTCP in four districts of Andhra Pradesh, India (population 15 934 572).

Design/methods: All smear positive PT cases were offered drug susceptibility test to rifampicin and INH by Line Probe Assay (LPA). Patients with rifampicin resistance were treated with 24-month standardized regimen for drug resistant TB and INH resistant patients with the 8 month retreatment regimen for TB. A retrospective record review was conducted of all registered PT smear positive TB patients without rifampicin resistance in the districts from April to December 2011. Demographic characteristics of PT smear positive TB cases with and without INH resistance and factors associated with unfavorable treatment outcomes (death, default, failure and transferred out) were evaluated.

Results: Of 1987 TB patients, 771 (38.8%) were tested by LPA—60 (7.8%) were rifampicin resistant, 598 (77.6%) INH sensitive and 113 (14.7%) INH resistant. The groups with and without INH resistance were similar with respect to baseline characteristics like age, sex, type of TB and HIV status. Of INH resistant cases, 49 (43.4%) had unfavorable treatment outcomes (22 [19.5%] defaults, 16 [14.2%]

deaths, 9 [8%] failures and 2 transfers) as compared to 213 [35.6%] among INH sensitive cases (relative risk 1.22, 95%CI 0.96–1.54).

Conclusion: Our study suggests that INH resistance is associated with unfavorable outcomes among PT smear positive TB cases. These results, however, must be interpreted with caution as the association was not statistically significant due to small sample size. Further research with adequate sample must be conducted to substantiate these findings.

PC-1031-03   Survival and predictors of mortality among patients under MDR-TB treatment at St Peter's specialized tuberculosis hospital, 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. The objective of the study is to assess survival and predictors of mortality among patients under MDR-TB treatment in Ethiopia.

Design/methods: A cross-sectional study was conducted from October 2011–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. Risk was estimated to each event occurrence using Kaplan-Meier method and the covariates are fitted to Cox proportional hazard regression model.

Results: Majority 101 (53.72%) of them 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. Factors independently associated with survival time 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, $P < 0.001$) but a one Kg increase in weight have 3% lower hazard of death.

Conclusion: Higher hazard of death was noted in patients who started treatment after a month of period diagnosed as MDR-TB, smoker, 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-1032-03   Mutation frequency in strains of *Mycobacterium tuberculosis* in civilian and penitentiary systems

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Objective: To compare the frequency of diagnosing the multidrug-resistant tuberculosis (MDR-TB) in the strains of TB-infected patients of two groups: the prisoners (group A) and the civilian population (group B).

Methods and materials: The study was conducted on the 90 strain samples obtained from 35 patients of group A and 55 patients of group B. Only one case (2.9%) of a newly detected TB and 34 cases (97.1%) of recurrent disease were found in group A. 15 (27.3%) new TB cases and 40 (72.7%) cases of recurrent TB were found in group B. The following methods have been used in this study: MGIT 960, MTBDR plus and MIRU-VNTR.

Results: The MDR TB has been detected in 100% of cases by using BACTEC and in 94.3% by MDBDR within group A. The resistance to rifampicin was observed in gene *rpo*B WT8 (S531L) in 9.41% of cases and in gene *rpo*B WT7 (H526Y) in 2.9% of cases. Moreover, the gene *kat*G WT1 (S315T1) experienced mutation in 100% of cases. In the meantime, the same methodology was applied to group B. The MDR-TB was found in 96.4% of cases by BACTEC, while the MDRTB*plus* could detect it in 90.9% of cases. The resistance to rifampicin in gene *rpo*B WT8 (S531L) was observed in 87.2% of cases, and in *rpo*B WT3,4—just in 4 cases. When investigating the resistance to isoniazid, the mutation in gene *kat*G WT1 (S315T1) was found in 90.9% of cases. A simultaneous mutation in genes *kat*G and *inh*A WT1 (S315T1 C15T) was detected in 3.6% of cases in this group. According to the MIRU-VNTR, the Beijing-type strain was dominating in prisons (88.6%), while the dominance of this strain type in the civilian sector was not that significant (65.5%).

Conclusion: Based on the data obtained from BACTEC and MTBDR plus, no reliable/significant difference in results could be found in the studied groups. As per MIRU-VNTR, the Beijing-type strains dominated more in the prisons rather than in the civilian sector.

PC-1033-03   Treatment adherence of 138 MDR-TB patients in the first six months in four cities in China

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Background: Successful MDR-TB treatment depends on better patient treatment adherence. Chinese national TB control center is piloting a comprehensive intervention in four cities to improve the effects of MDR-TB control. One of the objectives of the intervention is to improve the patients' treatment adherence through strengthening the cooperation between designated hospital and CDC. This paper aims to analyze the MDR-TB patients' treatment adherence in the first six months and explore the influential factors.

Methods: 138 MDR-TB patients diagnosed by gene chip test were investigated to know their treatment behavior within the first six months in the four pilot cities (Kaifeng, Lian Yungang, Chongqing and Hohhot). The default rate within six months is used to measure the treatment adherence. The default time and the reasons were also analyzed to get the influencing factors.

Results: 22.46% (31/138) of the patients dropped out within six months. In 4 sites, Hohhot had the highest default rate in six months (30.00%); the males (22.64%) had more quit than the females (21.88%); but the area and sex were not significantly associated with the default rate. The average treatment period was 71 days (25–130) when the patients dropped out. The time trend that patients dropped out the project looks like a U-shaped curve, most patients (14) dropped out the treatment in the first two months, the default number will increase gradually after short time drop when treatment goes to the fifth month. 32.26% (10/31) of the patients who dropped out the project because of side effect; and 19.35% (6/31) patients died in six months treatment, 9.68% (3/31) of the patients dropped out due to the economic difficulty.

Conclusion: MDR-TB patients did not get better treatment adherence through the comprehensive intervention. The first two months is the best time to intervention. Side effect, death and economic difficulty are the main reasons for default.

PC-1034-03   The spectrum of drug resistance of *M. tuberculosis* as a predictor of treatment failure for patients who suffer from MDR-TB

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Introduction: In recent years, the number of patients with both a primary and a secondary multi-drug resistance *M. tuberculosis* is rapidly increasing not only in Russia, but throughout the world. In this situation the most relevant is quantitative and qualitative analysis of the spectrum of resistance of *M. tuberculosis*, as well as the identification of resistance combinations to anti-TB drugs associated with failure in the treatment of patients with MDR-TB.

Material and methods: We conducted a retrospective cohort study using the 'case-control' method, 200 MDR-TB patients who completed the treatment according the program DOTS-PLUS had been included in study. Patients were divided into two groups: 100 patients were registered with failure in treatment (main group), and 100 persons who finished course of chemotherapy effectively (control group).

Results: Positive bacteriology in main group characterized by greater massiveness at all stages of treatment ($P < 0.001$). With increasing of numbers of bacilli in the sputum (by microscopy) the possibility of negative outcome also increased (OR 17.33; 95%CI 3.87–77.72). Patients with treatment failure in the beginning of course more often had drug resistance *M. tuberculosis* to pyrazinamide (14% and 2%, respectively, $P = 0.003$), ofloxacin (20% and 6%, respectively, $P = 0.005$), ethionamide (40% and 7%, respectively, $P < 0.001$), ethambutol (56% and 35% respectively, $P = 0.004$) and kanamycin (70% and 43% respectively, $P < 0.001$). During the treatment before the program DOTS-PLUS resistance of *M. tuberculosis* to drugs had been increased: to capreomycin in 2.1 times ($P = 0.005$), to ethionamide—3.6 times ($P < 0.001$), to ofloxacin—3.33 times ($P = 0.003$), to pyrazinamide—4.7 times ($P = 0.005$) and to PAS—2.6 ($P = 0.037$). Resistance to combinations of first-line anti-TB drugs in combination with kanamycin and ethionamide (OR 4.2, 95%CI 1.71–10.27), registration of drug resistance to the first and second line drugs, with the obligatory resistance to capreomycin except fluoroquinolone antibiotics (OR 3.92, 95%CI 1.50–10.23) and the XDR TB (OR 3.92, 95%CI 1.50–10.23) and had prognostic value of a negative outcome for the therapy.

Conclusion: As results of study the main bacteriological predictors of the formation failures in the treatment of patients with MDR-TB were identified. They allow in the initial phase of TB treatment to forecast a poor outcome and apply corrective measures therapeutic action to prevent its.

PC-1035-03   Decentralising DOTS-plus services: Kozhikode model

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Background and challenges: Kerala being a linear strip of land along the Arabian coast with 14 districts and estimated 32 million population, DOTS plus services were instituted for the southern 7 districts with the DOTS plus site at Thiruvananthapuram in December 2008 and the northern 7 districts with DOTS

plus site at Kozhikode in February 2009 with the intention of easy accessibility and management of cases right from treatment initiation till outcome is declared as per the programmatic management of drug resistance (PMDT) guidelines. During our 4 years of experience in managing about 373 MDR-TB cases, we felt that in areas where specialist services are available, decentralising DOTS plus programme will improve patient acceptance and is resource rewarding as the patient who is not sick enough to be admitted need not travel around 300 km (farthest patient) for the sake of fulfilling the guidelines.

Intervention and response: Operational modifications in PMDT instituted in terms of decentralising and revising indications for admitting patients to DOTS plus site.

Results and lessons learnt: The study was a descriptive analysis conducted in the Kozhikode DOTS Plus site, Department of Pulmonary Medicine, in 373 MDR-TB patients enrolled under DOTS Plus programme for CAT-IV regime during the period between February 2009 and April 2013 with the intention for identifying MDR-TB patients who really required admission to a DOTS plus site as against the blanket protocol of admitting all diagnosed MDR-TB cases for evaluation and any adverse effect management. 195 patients were managed as per the PMDT admission guidelines while 149 patients during the last one and a half years out of a total 178 during the same period were managed from the periphery in consultation with the site after initiating the decentralising protocol utilising the internet service and all the medical records were evaluated at the site well in advance and only those who required addressing of any special issues were only admitted to the site. It was noted that all the patients preferred pre treatment evaluation at a centre near to their residence without admission. Only 29/178 (16.3%) patients required visit to the site during pre-treatment evaluation. 54/178 (30.3%) patient required visit to the DOTS plus site for management of adverse effects during the course of their treatment.

Conclusion and key recommendations: Decentralising DOTS plus services can be a cost effective operational modification and can be adopted as a second step in a well functioning DOTS plus programme in resource limited nations, provided there are facilities and well defined referral protocol in the periphery during pre-treatment evaluation and timely reference strategy in the event of occurrence of adverse effects requiring admission to a DOTS plus site.

TOBACCO CESSATION

PC-1037-03 High nicotine dependence among youth who are daily smokeless tobacco users: a cross-sectional study from Chandigarh, India

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Background: Dependency on nicotine is the main obstacle that smokeless tobacco users have to overcome while in the process of quitting the habit. Although India has more number of smokeless tobacco users than smokers, negligible efforts have been made for assessing nicotine dependency among youths. The objective of the study was to describe prevalence and extent of nicotine dependence among daily smokeless tobacco users (15–25 yrs).

Methods: An ethically reviewed, cross-sectional study was done using pre-tested FTND based questionnaire study among school and college going students using stratified random sampling. 12 schools and 6 colleges were selected randomly and 1320 students selected randomly using proportionate population sampling (1032 students from urban area, 162 students who reside in slum area and 132 students rural area). Data entry and analysis was done using SPSS (Version 16).

Results: Out of 1320 students, 57.6% were males and 42.4% were females. Majority ($n = 557, 42.01\%$) of respondents belonged to upper middle class of O.P. Agarwal scale followed by lower middle ($n = 340$, 25.64%)], high ($n = 326, 24.59\%$), poor ($n = 80$, 6.03%) and upper high ($n = 23, 1.73\%$)]. Out of the total study population, 11.36% ($n = 150$) were daily smokeless tobacco users. Out of 150 daily smokeless tobacco users, 7.33% had mild dependence, 29.3% had moderate dependence and 63.3% had severe dependence according to FTND scale. Nicotine dependence was significantly associated with age group ($P < 0.001$), locality ($P < 0.001$), alcohol use ($P < 0.001$) and duration of tobacco use ($P = 0.046$)

Conclusion: Majority (92.6%) of daily smokeless tobacco users have mild to severe dependence and therefore should be offered cessation services at the earliest. Targeted cessation programs should be designed for youth consuming smokeless tobacco so as to reduce future burden of morbidity and mortality.

PC-1038-03 Comparison of the efficacy of varenicline and nortriptyline: short-term treating smoking cessation in an in-patient setting

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Background and rationale: Varenicline is a partial agonist at the α-4 β-2 subunit of the nicotinic acetylcholine receptor that appears to aid smoking cessation by alleviates nicotinic dependent symptoms. Both of psychosocial counseling and pharmacotherapy are effective to quit smoking. The hospital admission also provides the chance to help the patient to abstinence smoking. In this study, we determine the efficacy and safety of Varenicline with Nortriptyline for smoking cessation in hospitalized smokers.
Material and methods: A double blind randomized controlled trial was conducted. We recruited active smoking hospitalized patients, smoked 10 cigarettes/d or more and aged 18–75 years. Participants were randomly assigned (1:1) to receive brief counseling and Varenicline titrated to 1 mg twice per day, Nortriptyline 12.5–50 mg per day orally for 12 weeks. Smoking status was established by self-report and confirmed at clinic visits by exhaled CO measurement. The primary end point was compared the efficacy of Varenicline and Nortriptyline for short-term treating smoking cessation in the inpatient setting. The secondary end point includes the adverse events and Point prevalence Abstinence Rate (PAR) at weeks 2, 4, 8 and 12 of treatment.
Results: A total of 51 participants were enrolled in the study, 25 and 26 to Varenicline and Nortriptyline respectively. Subjects were aged 22–72 years, mean of previous attempts 3.52 and 2.88, and had a mean Fagerstrom score 6.41 and 6.07, respectively. The 12-week PARs were 60% with Varenicline vs. 65% with Nortriptyline. PARs tended to be no statistical significant between Varenicline and Nortriptyline over 12 weeks follow up. The PARs of Varenicline at week 2, 4 and 8 were 48%, 56% and 60%, respectively. The PARs of Nortriptyline at week 2, 4, and 8 were 42%, 57% and 65%, respectively, The patients who were on Varenicline had the nausea symptoms (2/25), headache (3/25), but no complaint of the sleep disturbance symptoms on this study. The patients who were on Nortriptyline had the dry mouth (2/26). Cost of Varenicline and Nortriptyline medication is 10 800 and 135 bahts/12 wks, respectively.
Conclusion: Nortriptyline is as effective as Varenicline for smoking cessation in the inpatient setting with minor adverse effect. Therefore, Nortriptyline is a cost-effective option for smoking cessation treatment in a resource–limited country.

PC-1039-03 Developing a tobacco cessation behaviour change intervention within the Practical Approach to Lung Health in primary care in Nepal

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Background: WHO recommends integrating tobacco cessation within existing public health programmes. WHO's Practical Approach to Lung Health is one such programme. Supported by the Ministry of Health and Population (MoHP) and the National TB Programme (NTP) in Nepal, since 2011, 14 districts have implemented PAL in their primary health care centres (PHCCs). PAL recommends smoking cessation, but does not provide adequate guidance and materials. Furthermore, smokeless tobacco, common place in southern Nepal, is not addressed. In partnership with MoHP and NTP, we developed a behavioural support intervention, embedded within PAL, to help people to quit tobacco. The intervention was implemented in three PHCCs (1 in Kathmandu, 2 in Terai) to develop this intervention.
Intervention: Action research was used with patients and health workers and included: qualitative interviews using photographs taken by patients of tobacco use in their communities; focus groups with health workers; evidence and theory review of tobacco behaviour change interventions. Key challenges in designing the intervention were: health worker's limited time, knowledge of tobacco-related harms and lack of familiarity with behaviour change techniques; low literacy levels among patients as perceived by health workers. The evidence base and 'Stages of Change' theory point to the effectiveness of focusing interventions on those motivated to quit. This allowed more prudent use of health worker time as brief advice alone was given to those not motivated to set a quit date. Health workers were trained on behaviour change techniques and these were integrated within patient education materials, which were assessed during action research cycles and redeveloped with minimal text and clear pictures. A supporting short video was also developed. MoHP staff were involved throughout to enable scale up.
Lessons: Using research evidence and qualitative work allowed the development of an appropriate intervention integrated within routine care. Behaviour change theory and techniques provided health workers with techniques to use with their patients. Working through PAL and with MoHP has maximised potential for sustainability and scale up.
Conclusions: Using evidence and theory, behaviour change techniques and involving patients and health

workers in the design of a tobacco cessation intervention increases appropriateness and potential sustainability. Further research is required to assess the impact on quit rates.

PC-1040-03   Integration of tobacco cessation into DOTS programme in primary care: WHO recommendations and country experience

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Smoking has causal associations with TB incidence and outcome, accounting for more than 20% of global TB incidence. Therefore, the National TB programme and the National Tobacco Control Programme should strengthen their collaboration to achieve mutual benefits. In collaboration with The Union and the WHO Stop TB! Department, WHO's Tobacco Free Initiative developed policy recommendations and identified models on how to integrate TB and tobacco control measures in primary care through the publication of the WHO/The Union Monograph on TB and Tobacco Control in 2008. WHO recommends that TB patients who are smokers should be specifically identified and offered advice and other assistance on quitting. TB care providers are typically in regular contact with TB patients under the DOTS for a minimum of six months. Although this represents a unique opportunity to deliver smoking cessation interventions to more than 1 million tobacco users in a single year, TB care providers' provision of tobacco dependence treatment is low as there are no supportive systems in place in the vast majority of countries. In this vein, WHO has been developing technical resources and providing technical support to assist countries in implementing these policy recommendations. A capacity building training package entitled, Strengthening health systems for treating tobacco dependence in primary care was developed. Technical support has been provided to several countries with both high-burden TB and high-burden tobacco use for integration of brief tobacco interventions into DOTS programme in primary care settings. Country experiences show that integration of brief tobacco interventions into DOTS programme in primary care is feasible and effective. 20–40% of smokers successfully quit at 6 month follow up as a result of advice from TB care providers. There are some lessons learnt from country experiences as well. For example, a smoking status should be included on TB treatment card; an effective incentive system needs to be created; fear of contamination makes tobacco cessation specialists refuse to help TB patients quit smoking. The author will first introduce the WHO recommendations, the potential impact of brief tobacco interventions in TB programs, an overview of WHO technical resources/tools. The author will then present some country experiences, lessons learnt and next steps in advancing this TB and tobacco joint work at country level.

PC-1041-03   Implementation of tobacco cessation strategy among tuberculosis patients in the municipalities of Guarulhos and Barueri, São Paulo State, Brazil, 2012

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Background: The tobacco/tuberculosis (TB) association already has evidence to approach TB patients who use tobacco. In 2011, the National TB Control Program made a proposition on implementing activities against tobacco in the municipalities of Guarulhos and Barueri in Sao Paulo State with the purpose to consolidate and evaluate epidemiological and operational indicators of TB patients under treatment.
Method: Each TB patient under treatment on basic healthcare units (BHUs) linked to the Project was interviewed about tobacco status where was offered treatment and incentives for tobacco cessation. A follow-up recording about outcomes of these patients was created.
Results and discussion: Guarulhos counted with nine (13.8%)/65 BHUs in the project with 57 (14.6%)/390 TB cases diagnosed and Barueri counted with 10 (71.4%)/14 BHUs in the project with 63 (70.0%)/90 TB cases diagnosed. Respectively, 24/57 and 12/63 TB patients were tobacco user and the pulmonary clinical presentation with smear positive represented 18 and three cases in the group responding for 31.6% and 25.0% from all TB cases diagnosed in the BHUs. Also, 58.3% from all 24 and 12 tobacco consumers had high level of addiction. From 19 and eight tobacco users who concluded the six-month follow-up, 15.8% and 12.5% ceased the use of tobacco, 31.6% and 25.0% continued smoking, 10.5% and 12.5% have died, 10.5% and 0.0% were transferred and 31.6% and 50.0% did not express willing in smoking cessation.
Conclusion: Most of pulmonary TB patients in the municipalities involved were tobacco consumers with high level of addiction. The smoking cessation did not depend only on drug support/adequate orientations, but mainly on self-willing, initiative and predisposition to change. Thus, the Project was effective on identification of smoking-TB patient profile, and on driving necessary modifications in the monitoring system in a way to become functional and feasible and showing to the healthcare worker new perspectives and challenges toward comprehensive treatment of TB patients.

PC-1042-03   Opinion regarding tobacco control of 6052 people in 8 districts and 52 blocks of Indore Division of Madhya Pradesh

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Background and challenges to implementation: In order to discourage tobacco consumption, protect non-smokers from second hand smoke, the Cigarette and other Tobacco Products Act, (COTPA) was enacted in 2003 by Indian government. Section 4 of the act prohibits smoking at Public Places. To carry out successful tobacco control intervention it is very important to understand the opinion of general public. In order to assess the level of public awareness of harmful effects of second hand smoke and smokefree laws, public support and opinion regarding smokefree jurisdiction policies the study was conducted.

Intervention or response: The target population for this survey were the residents of 8 districts of Indore Division of Madhya Pradesh, India who access public places frequently. A sampling size of 6052 people (above 18 years) has been arrived at from approximately 12.5 million population for opinion survey. To achieve this sample simple random sampling was done to collect information from all the 52 blocks of 8 districts of Indore Division. The interviews were conducted face to face at the individual level at public places. The interviewers randomly visited the public places of the concerned area and taken the interview. The simple random sampling ensured probability of selection of all the individuals. The data collection was done through semi structured schedule/questionnaire. As the survey area includes rural area and data was collected from villages also.

Results and lessons learnt: 28 percent were smokers. 46 percent of the respondents agree that passive smoking is as dangerous as active smoking. 20 percent did not know that passive smoking is as dangerous as active smoking. 92 percent of the respondents said that government should take strong step to stop smoking. Only 24 percent respondents knew about Indian Tobacco Control Act. Only 19 percent of respondents knew about maximum amount of fine for smoking at public places. 46 percent smokers knew that smoking is prohibited in public places. 93 percent of respondents supported for Smokefree Public Places. 91 percent respondents demanded for display of signages at public places.

Conclusions and key recommendations: Understanding the opinion of general public about various issues related to tobacco control is very helpful in implementation of tobacco control efforts.

PC-1043-03   Smoking habits and degree of nicotine addictions among tuberculosis patients

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Background: Numerous studies evaluate the influence of tobacco smoking on the tuberculosis (TB) development. The aim of our research was to show the smoking habits and the degree of nicotine addiction between patients with pulmonary tuberculosis in the Republic of Macedonia within the period of 2007–2012.

Design/methods: We analyzed data regarding the smoking habits of TB patients from the National TB registry. Also we conducted a survey with reference to nicotine addiction using the Fagestrom questionnaire among the smokers with pulmonary TB hospitalized at the PHI Institute for lung diseases and tuberculosis in Skopje Republic of Macedonia within the period of 2007–2012.

Results: Among all registered TB patients it was shown that 48, 2% are smokers and 51, 8% are non-smokers out of which 69, 8% were of male gender and 30, 2% of female gender. The majority of the smokers (53, 8%) belonged to the middle age group (35–54 years), out of which 38, 5% were at the age below >54 and 7, 7% at the age over <34 years. According Fagenstrom questionnaire the percentage of nicotine addiction was low among 30, 7% of the smokers, on average level between 38, 6% of the smokers and high among 30, 7% of them. The vast majority of smokers (68.9%) smoked more than 20 cigarettes per a day. The pack year's index was higher than 20 among 45, 6% of the smokers.

Conclusion: The percentage of nicotine addiction and pack/years index are bigger among TB patients who smoke. The success of the treatment in these patients depends from both: the TB treatment and the smoking cessation treatment

PC-1044-03   Assessing failure to quit smoking among Pakistani urban population

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Background: Tobacco dependence is a chronic relapsing disease which is potentially treatable. It kills a third to half of its users and most die on average 10–15 years prematurely. At present 5 million tobacco-related deaths occur annually worldwide and the toll is projected to reach up to 1 billion throughout the 21st century. A vast majority of smokers would like to quit but are unable to because variety of reasons.

Objective: To assess factors associated with having ever attempted to quit smoking among current smokers/tobacco users, and the reasons cited for failure.

Design/methods: Free health camps supervised by a physician and manned by trained staff were held across major cities of Pakistan. All consenting participants were administered a self-reporting questionnaire and had there exhaled carbon monoxide level measured.

Results: 12 969 participants were interviewed. 99.3% (12 872) were men. Mean age ± SD was 31.4 ± 10 years (range 13–85). 66.1% smoked tobacco where as 12.6% used smokeless tobacco and 20.5% both. Average duration of smoking ± SD was 8.8 ± 6.5 years (range 0.25–40). Measured exhaled carbon monoxide (ppm) was 12 ± 8 (range 0–215). 12633 (97.4%) participants wanted to quit. 12 708 (98%) had received some form of advice to quit. 81.6% had tried smoking cessation pharmacotherapy. Reasons cited for failing to quit were dependence 1965 (15.2%), unknown reason 1622 (12.5%), friends/peer pressures 1554 (12%), family-related anxiety 771 (5.9%), work-related anxiety 681 (5.3%), changes in mood 390 (3%) and weight gain 82 (0.6%).

Conclusion: A vast majority of participants wanted to quit tobacco use regardless of age, gender or years of usage. Nearly everyone had received advice about quitting, and more than three quarter had tried smoking cessation pharmacotherapy. Three commonest reasons cited for failing to quit were dependence, unknown reason and friend/peer pressure.

PC-1045-03 Outcome of tobacco cessation training among health professionals: experience from Tamil Nadu, India

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Background: Currently there are 274.9 million tobacco users in India. As recommended by Article 14 of Framework Convention on Tobacco Control, tobacco cessation (TC) is one of the key strategies in demand reduction for tobacco control. TC activities were initiated about a decade ago in India by World Health Organization and it recommends integration of TC services in routine health practices. However awareness among health professionals on TC and its methodologies is poor. Training is the key for integration. Current study aims to understand the outcome of training health professionals on TC in Tamil Nadu.

Methods: From 2008 to 2012, professionals from 148 Government and Private healthcare institutions from all 32 districts of Tamil Nadu were trained on TC methodologies and guidance on setting up clinics, in one-day workshops. Telephonic follow up was conducted in March 2013 to find out status of tobacco cessation services such as establishment of TC clinics, integration into their practice, treatment methodologies, challenges experienced and support

required. Of the professionals trained, 65.4% were available. Descriptive statistics was used to analyze data.

Results: Of the participants, 50.2% incorporated TC services in their routine practice; 14.2% set up TC clinics under Community Health, Dental, General or Pulmonary departments. Few (27.1%) took initiatives to set up clinics and 35.2% showed interest to start TC services in future. Challenges reported were administrative setbacks, infrastructure, financial constraints, lack of management/self interest, attrition of trained staff, lack of confidence and time. Counseling was predominantly used by all as TC methodology; one reported using nicotine replacement therapy. follow-up by some institutions (15.5%) was included in routine medical treatment. One fourth reported that they were approached by users for TC services. Expected support to start services was intensive training, funds, IEC materials, free medication. WNTD was observed by 27.7%, of which 7.1% was by rural institutions.

Conclusions: Cessation services should be offered along with other healthcare services and not in isolation. Brief training has been helpful, however further intensive training on methodology in particular, evidence based pharmacological methods is required. It is not a priority for many as yet. Government policies on role of healthcare professionals in TC and governance may bring in a change in attitude and implementation.

PC-1046-03 Correlates of tobacco quit attempts and cessation in the adult population of India: secondary analysis of the Global Adult Tobacco Survey, 2009–2010

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Background: Nearly 275 million adults (15 years and above) use tobacco in India, which contributes substantially to potentially preventable morbidity and mortality. There is good evidence from developed country settings that use of tobacco cessation services influences intention to quit, with a higher proportion of attempts being successful in fully quitting. There is little evidence about cessation and quitting behaviour in the Indian context. This study assesses the socio-demographic characteristics and cessation services used by adults i) who attempted to quit smoked and smokeless tobacco and ii) who were successful in quitting.

Design/methods: The study was a cross-sectional secondary data analysis of the Global Adult Tobacco Survey, India, 2009–10. There were 25 175 ever tobacco users aged 21 years and above included in the study. Bivariate and multivariate logistic regression analysis was done to determine associations between socio-demographic variables and cessation services utilized with attempts to quit tobacco and successful quitting.

Results: Of the ever tobacco users, 10 513 (42%) made an attempt to quit tobacco, and of these 4395 (39%) were successful. Significant associations were demonstrated between male gender, increasing educational attainment and higher asset quintiles for both those who attempted to quit and those who were successful. Younger age groups had higher odds of quit attempts than all except the oldest age group, but also had the lowest odds of successful quitting. Heath care provider advice was positively associated with attempts to quit, but both advice and use of cessation aids were not associated with successful quitting.

Conclusion: This study provides the first national evidence on the relationships between quitting attempts and successful quitting with socio-demographic characteristics, health care provider advice and use of cessation services. The findings of the study have important implications for scaling up tobacco cessation services in India, and indicate a need to re-examine in greater detail the effects of socio-demographic factors, type of tobacco product used and levels of dependency on quitting. Health system factors such as coverage and accessibility of cessation services, type of service, and its duration and follow up also have to be examined in detail to ascertain effects on quitting behavior.

PC-1047-03 Collaborative approach to increase demand and counseling for tobacco cessation in Chennai, Tamil Nadu, South India

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Background: India has more than 240 million tobacco users. Population Services International (PSI) operates a telephone-based tobacco cessation service that serves a catchment area of 37 million tobacco users. Since its inception in 2011, the primary challenge of the Quitline is enrollment of clients. To address this challenge, PSI collaborated with the Cancer Institute and with the dental and nursing colleges to screen patients for tobacco use and refer tobacco users to the Quitline.

Intervention: Professionals from both institutions received an intensive training on tobacco cessation strategies, administration of nicotine replacement therapy (NRT), and were informed of the Quitline services available. Trained faculty members at the Den-

tal and Nursing colleges screen clients for tobacco use. Once identified, these faculty members spend 5–10 minutes with each tobacco user, informing them about the Quitline services and motivating them to avail the free services. If the client consents, his/her contact information is mailed to a PSI coordinator, who in turn assigns the client to a Quitline counselor who will call the client. PSI received free samples of NRT from a pharmaceutical company, which were distributed to clients on a case-by-case basis, as assessed during counseling sessions.

Methods: The Dental and Nursing colleges mailed client names and phone numbers to PSI. PSI counselors called 180 clients and provided counseling, which included pre and after quit counseling sessions. The clients who have quit will be contacted at the end of months 3, 6 and 12 to understand the quit sustenance. Simple descriptive data analysis was used.

Results: Programmatic monitoring data demonstrate that the intervention generated demand for Quitline services. Of the 180 clients who enrolled in the program, most of whom were smokers, 44 quit using tobacco products (24% quite rate) by the end of the third month.

Conclusions: Collaboration between non-profit organizations and healthcare facilities can increase the demand for tobacco cessation services. Counseling through telephone seems feasible. We will conduct further analysis as the program continues to assess long-term successful rates as well as barriers and facilitators or barriers to smoking cessation. We will involve additional dental colleges to increase client referrals and help dental colleges establish their own tobacco cessation services.

DRUG-RESISTANT TUBERCULOSIS: CLINICAL AND PROGRAMMATIC ASPECTS

PC-1048-03 Application of mobile videophone in the DOTS-Plus program of northern Taiwan

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Background: To minimize the distance between the patients and health care-providers, mobile videophones were used to watch selected multidrug-resistant TB (MDR-TB) patients take their medication in DOTS-plus program of northern Taiwan since 2007. The aim of this study was to evaluate the effectiveness of this care model with mixing supporters (S-DOT) and videophones (V-DOT) in DOTS-plus program.

Design/methods: From August 2007 through March 2011, 180 MDR-TB patients were enrolled in this

government-organized and hospital-initiated DOTS-plus program. Thirty-one patients, including 27 patients receiving second-line anti-TB treatment for more than 1 month before enrollment in DOTS-plus program and 4 patients transferred out, were excluded from this study. The remaining 149 patients were allotted to S-DOT group and V-DOT group based on the patients' history of previous anti-TB treatment, cognition of disease, disease severity and sputum status, family support and patient's willingness. In S-DOT group, supporters would visit the patients at prearranged time. In V-DOT group, every patient could call the nurse at prearranged time at anyplace and all pills would be swallowed in view of the mobile videophone. The treatment success rate at 24 months was evaluated.

Results: Among the 149 patients enrolled in this study, the mean age was 48.6 (16 to 93) years with a male to female ratio of 6.5. Ninety-nine patients (66.4%) with mean age of 49.5 years were allotted as S-DOT group, 39 patients (26.2%) with the mean age of 37.8 years in V-DOT group, 1 patient (0.7%) aged 54 years in mixed V-DOT/S-DOT group and 10 patients (6.7%) with the mean age of 72.5 years in hospital/nursing home group. The overall treatment success rate at 24 months was 90.6%. This treatment success rate of S-DOT group (95%) and V-DOT group (97%) was similar, but this rate (20%) was much lower in hospital/nursing home group due to old age and co-morbidity.

Conclusion: Mobile videophones could be used as an effective modality to watch patients take medication in selected cooperative MDR-TB patients.

PC-1049-03   Development of *M. tuberculosis* resistance to second-line anti-tuberculosis drugs during MDR-TB treatment

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Background: Treatment of multidrug-resistant tuberculosis (MDR-TB) requires of long-term use of second-line antituberculosis drugs (SLD). Resistance of *M. tuberculosis* to these drugs can result in poor treatment outcomes.

Objectives: To define the features and risk factors of secondary drug resistance development to SLD during MDR-TB treatment.

Methods: Retrospective cohort study. The analysis of drug susceptibility testing results, socio-demographic and clinical data and treatment history of patients with newly diagnosed MDR-TB registered in Novosibirsk Oblast (Russian Federation) in 2003–2010 was performed. The sample included 308 patients (68.8% male, 31.2% female, middle age 35.8 years, 57.8% urban and 39.3% rural residents) treated by SLD. Initial drug resistance patterns were HRS (92.9%), HRSE (6.8%), HRE (0.3%). For risk assessment two

groups of patients: with acquired SLD-resistance of MTB (71 of 308) and without one (237 of 308) were compared; odds ratio (OR) was calculated.

Results: Development of secondary drug resistance of MBT to SLD was observed in 23.1% (95%CI 18.7–28.1%) of patients. Patterns of secondary drug resistance are presented on the figure. Risk factors associated with SLD-resistance of MBT were rural residence (OR 3.0, 95%CI 1.7–5.3, $P = 0.0001$), presence of destructive lesions of the lung (OR 7.9, 95%CI 1.1–59.7, $P = 0.04$), presence of dissemination (OR 3.9, 95%CI 2.2–7.2, $P < 0.0001$), smear positive MDR-TB (OR 3.5, 95%CI 1.9–6.4, $P < 0.0001$), alcoholism (OR 3,7, 95%CI 2,1–6,7, $P < 0.0001$), treatment interruptions (OR 7.7, 95%CI 4.2–14.1, $P < 0.0001$), noncompliance of national standards of anti-TB chemotherapy (OR 2.7, 95%CI 1.5–5.2, $P = 0.002$). The cure rates for patients with SLD-resistance of MBT and without one respectively were: 16.9% (95%CI 9.5–28.5%) and 93.2% (95%CI 89.3–95.8%), χ^2 $P < 0.0001$; treatment failures were 67.8% (95%CI 55.1–78.3%) and 5.5% (95%CI 3.2–9.2%), χ^2 $P < 0.0001$; death rates were 15.3% (95%CI 8.2–26.5%) and 1.3% (95%CI 0.4–3.7%), χ^2 $P < 0.0001$.
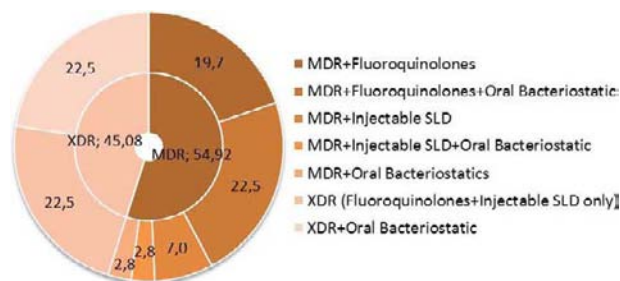

Figure   Patterns of acquired resistance of *M. tuberculosis* to second-line anti-tuberculosis drugs, % ($n = 71$).

Conclusions: The risk of SLD-resistance of MBT is increased in patients with severe forms of tuberculosis and with disadvantages of clinical management in the MDR-TB treatment. Acquired resistance of MBT to SLD may be one of reasons of MDR-TB treatment failures.

PC-1050-03   Serial testing using interferon-gamma release assays in a cohort of young Indian nursing students

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Objectives: To estimate rates of conversions and reversions using the Interferon gamma release assay: QuantiFERON®-TB Gold In-Tube (QFT) among

young nursing trainees and to assess a relationship between exposure and change in continuous interferon-gamma (IFN-g) levels over time.

Methods: Nursing students at a referral hospital in Southern India were approached to participate in a serial testing study using the QFT test. Students underwent testing annually for three years. Detailed data was also collected on exposure to TB in the hospital and in the community during the intervals between testing.

Results: 281 students had complete data for at least 2 test points, 669 data points were included in the final analysis. Among the 281 nurses, 92% (258/281) were female, median age was 17.5 years old. Among the 281 students, 12% (34/281) had worked in health care before starting their nursing program. Upon initial testing 19.3% (54/280) of nursing students were QFT positive. 20/207 (9.6%) of nursing students experienced a QFT conversion upon the first annual testing, 13/51 (25%) experienced a reversion at year one. 11/97 (11.3%) of students experienced QFT conversions at year 2, and 10 students experienced reversions in year 2: 8/11 (72.7%) among students with initial negative QFT and 2/19 (10.5%) students who were positive at both QFT1 and QFT2. Despite collecting detailed exposure data, none of the time-dependent exposure variables investigated were associated with change in continuous IFN-gamma over time using a longitudinal Tobit regression model.

QFT1	QFT2	QFT3
225 negative	187/207 negative	85/97 negative 11/97 converters 1/97 indeterminate
	20/207 converters	8/11 reverters 3/11 positive
54 positive	13/51 reverters	3/3 negative 0/3 converters
	38/51 positive	2/19 reverters 16/19 positive 1 indeterminate
1 indeterminate	1 negative	1 negative

Total: $n = 280$*; $n = 259$; $n = 130$.
* One student did not complete QFT1 but did complete testing at QFT2 and QFT3, this student was included in the longitudinal tobit regression model but not in the above table.

Conclusions: Serial testing using the QFT in this population of young nursing trainees results in high rates of conversions and reversions. Conversions could not be explained through exposure to TB. The QFT test may not be an appropriate tool for LTBI surveillance in this population.

PC-1051-03 Sustained indigenous tuberculosis reduction in Taiwan: an operational research controlled study

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Background: Can the benefit from a brief tuberculosis (TB) elimination program in a high burden indigenous area targeting both active and latent TB infection (LTBI) be sustained once the intervention ends?

Design/methods: This was an operational research study measuring TB incidence over time out to 10 years post-intervention using the McNemar test for both intervention and control populations. The study area involved five contiguous villages overlapping two adjacent aboriginal townships with a total population of 2308 assessed by household survey with the subsequent intervention ending mid-year 1999. This novel intensive TB elimination program was designed to diagnose and treat as many active and LTBI patients as quickly as possible using both standard diagnostic technology and drug regimes as well as enhanced compliance measures. The intervention occurred in four of the five villages. The non-intervention village was the control population.

Results: During the 26 month intervention period, 7.5% of the intervention population was treated for either active or LTBI with compliance rates of 98% and 89% respectively. For the 15 year period 1994–2009, a total of 295 active TB cases were reported in the study area. TB cases from Village A and B were reduced post-intervention at 10 years from 43 to 27 ($P = 0.056$) and from 17 to 7 ($P = 0.041$) respectively. Combined, these two villages reported a 43% drop ($P = 0.007$) in cases. There was no reduction ($P = 0.86$) in the control population. Village C, with an extremely high TB incidence rate (1348/100 000), similar to that of Village B, had no sustained decline

Table Study demographics with tuberculosis (TB) treatment intensity

Village	Population	Indigenous %*	Male/female %†	% Population treated‡		
				LTBI	Active TB	Total
A	1065	81.4	53/47	2.4	2.7	5.2
B	320	87.5	51/49	7.5	5	12.5
C	371	73.3	55/45	5.7	4.3	10
D	29	53.6	44/56	—	—	—
Intervention	1785	80.4	53/47	4	3.5	7.5
Control	523	92.4	54/46	—	—	—
Study total	2308	83.3	53/47	—	—	—

* Self-identified percentage based on 1995 ethnic responses.
† Percentages based on 1978 gender responses rounded to whole number.
‡ Based on 61 active and 80 LTBI (latent TB infection) patients, "total" may not add up as percentages rounded off.

in TB cases despite the intervention although with a reduced treatment intensity. Overall, TB incidence in the four-village intervention population was reduced by 31% ($P = 0.033$).

Conclusion: The significant sustained reduction in TB incidence in the four-village area at 10 years post-intervention in this high TB burden indigenous population can reasonably be attributed to the brief comprehensive TB elimination program. Each village reduction may be related to treatment intensity and baseline incidence rate. A re-analysis at some later date might answer the question of whether the present TB reduction will persist beyond 10 years. By varying intervention time, a future study might elucidate what amount of TB reduction, even to the point of elimination, might be expected for each intervention length.

PC-1052-03   Use of linezolid for drug-resistant tuberculosis treatment in a sub-district hospital in India

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Background: A number of studies have shown that linezolid is efficacious in the treatment of multidrug-resistant tuberculosis (MDR-TB). However, its use is limited by its serious toxicities and the need for strict monitoring. Very few experiences have been described on the long-term use of linezolid for MDR-TB in a resource constrained setting. We studied the treatment outcomes and drug toxicities from linezolid therapy in a cohort of difficult-to-treat MDR-TB patients in a sub-district hospital in India.

Design/methods: From 2010 to date, we prospectively followed 43 drug resistant TB patients treated with a 600 mg once-daily linezolid based treatment regimen at Tibetan Delek Hospital, a sub-district hospital in north of India. Complete blood count was done monthly to check for myelosuppression. Development of peripheral neuropathy was assessed by the treating physician using a set of questions and by clinical examination. Development of optic neuropathy was assessed by an opthalmologist.

Results: Of the 43 patients, 7 had extensively drug resistant TB (XDR-TB) and 35 had pre-XDR TB with resistance to a fluoroquinolone and one had culture-negative drug resistant abdominal TB detected by Xpert MTB/Rif assay. Twenty-five of 43 patients developed peripheral neuropathy of which 20 (79%) developed peripheral neuropathy in the first six months. Fourteen developed myelosuppression with four developing severe anemia (Hb < 5 gm/dL) requiring blood transfusion. Linezolid was stopped in four patients: 2 due to optic-neuropathy and 2 due to recur-

rent myelosuppression (2 patients). Fourteen of 15 patients simultaneously receiving high-dose isoniazid (16–18 mg/kg) developed severe peripheral neuropathy requiring therapy modification, while only 11 of 28 not receiving high-dose isoniazid developed peripheral neuropathy ($P < 0.001$). Thirty-six (85.7%) patients culture-converted within the first 6 months of therapy of which 28 culture-converted within the first 3 months. All the 36 patients had maintained the culture-converted state to date. Three of five patients failing to culture-convert have XDR-TB. One patient had died. To date, 12 patients had been declared cured, 27 patients are presently on therapy, 3 XDR-TB patients have failed to culture convert and one patient with fluoroquinolone resistance had died.

Conclusion: In a cohort of 43 difficult to treat chronic MDR or XDR-TB patients, we found that 85.7% of the patients were able to achieve culture conversion in the first 6 months of therapy. Using linezolid at the pre-XDR stage may prevent the progression to XDR-TB. Linezolid may be more effective in treating chronic drug-resistant TB when combined with other susceptible core drugs like fluoroquinolones. However, its use in resource-limited countries may be limited by frequent side effects needing very close monitoring.

PC-1053-03   Routine supportive supervision guided by standard of care indicators improved tuberculosis service quality in Ethiopia

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Background and challenges to implementation: Help Ethiopia Address Low performance in TB (HEAL TB) is a USAID-funded project implemented by MSH and partners that aims to improve tuberculosis (TB) case findings and the quality of TB services in 187 districts in the five zones of the Amhara and Oromia regions of Ethiopia. In the project zones.

Intervention or response: To assess and improve quality of TB care in Ethiopia, HEAL TB developed 28 standard quality TB care indicators, based on international standards of TB care. Tuberculosis detection, diagnosis, treatment outcome, TB-HIV collaboration, uninterrupted drugs supply and availability, data quality and laboratory quality indicators were focus areas of these indicators. For one year the team mentored and provided supportive supervision to TB services in 691 health facilities including 23 hospitals. This support was undertaken with regional, zonal and district officers. All facilities were visited quarterly by a team that is composed of clinical, community and

laboratory officers. A total of 15 teams were assigned for this support. HEAL TB developed a composite scale using the 28 indicators. Once per quarter the team assessed, categorized and took action based on the level of category for each quality indicator. For each indicator the highest possible score was 2 points. Zero point was assigned for low values. The highest possible score was 56 when computing the total for the 28 indicators. Finally the total score was converted into a percentage. One way analysis for variance was done to assess statistical significance among mean scores of the reporting periods at 95% confidence level.

Results and lessons learnt: Composite scores for health facilities improved steadily and significantly over five quarters (see Figure). The median value increased from 28 to 51.7 over the five quarters. Improved by 84%. There was statistically significant difference of mean scores of the composite scale for the consecutive quarters. (F = 141.82, and $P = 0.000$).
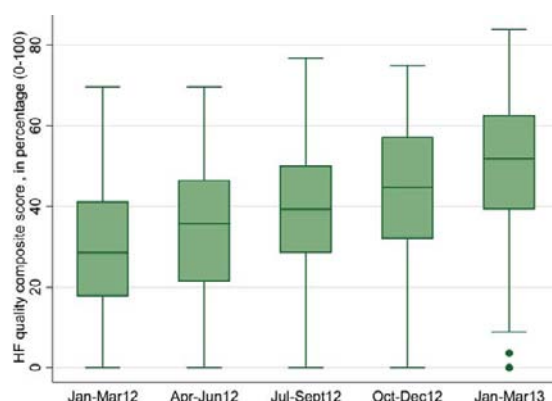

Figure   Trend in median score of composite quality TB score HEAL TB project zone.

Conclusions and key recommendations: Regular supervision using tailored standard of care indicators contributed improved TB service quality. This supervision strategy can be expanded in Ethiopia to maintain and further improve TB service quality. Use of appropriate standard of care indicators also contribute to improved quality of service by helping the mentoring team focus on key areas.

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