

# Xpert MTB/RIF Implementers Global Forum

1-2 May 2014, WHO Headquarters, Geneva

## MEETING REPORT

This year's Xpert MTB/RIF Implementers Global Forum was organized by the WHO Global TB Programme as part of the 6th Global Laboratory Initiative (GLI) Partners Meeting. The Global Forum brought together representatives from high TB, TB/HIV and MDR-TB burden countries, non-governmental organizations, international institutions and initiatives, research institutes from developed and developing countries, industry and funding agencies.

The Forum provided an opportunity to share lessons learned and challenges for wide-scale implementation of Xpert MTB/RIF in different epidemiological and resource settings, with a focus on evidence of impact and linking scaled-up diagnosis with scaled-up access to treatment.

This year's Global Forum was made possible by financial support from USAID, PEPFAR and the Fondation Mérieux.

All presentations can be found on the [GLI website](#).

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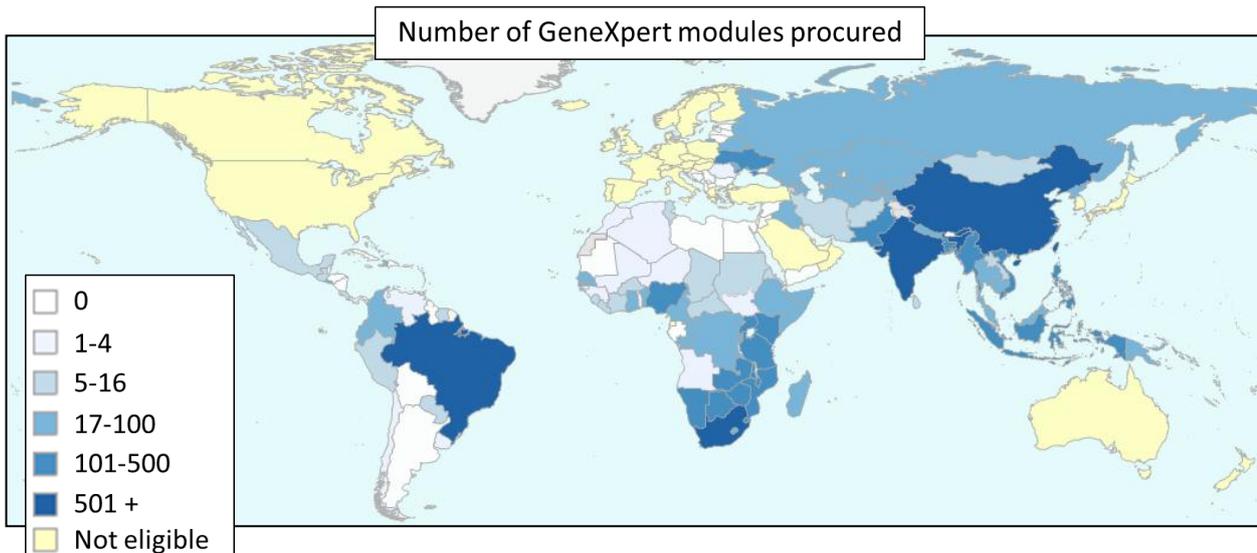
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## SESSION I: Advancements in the use of Xpert MTB/RIF (Chair: Karin Weyer)

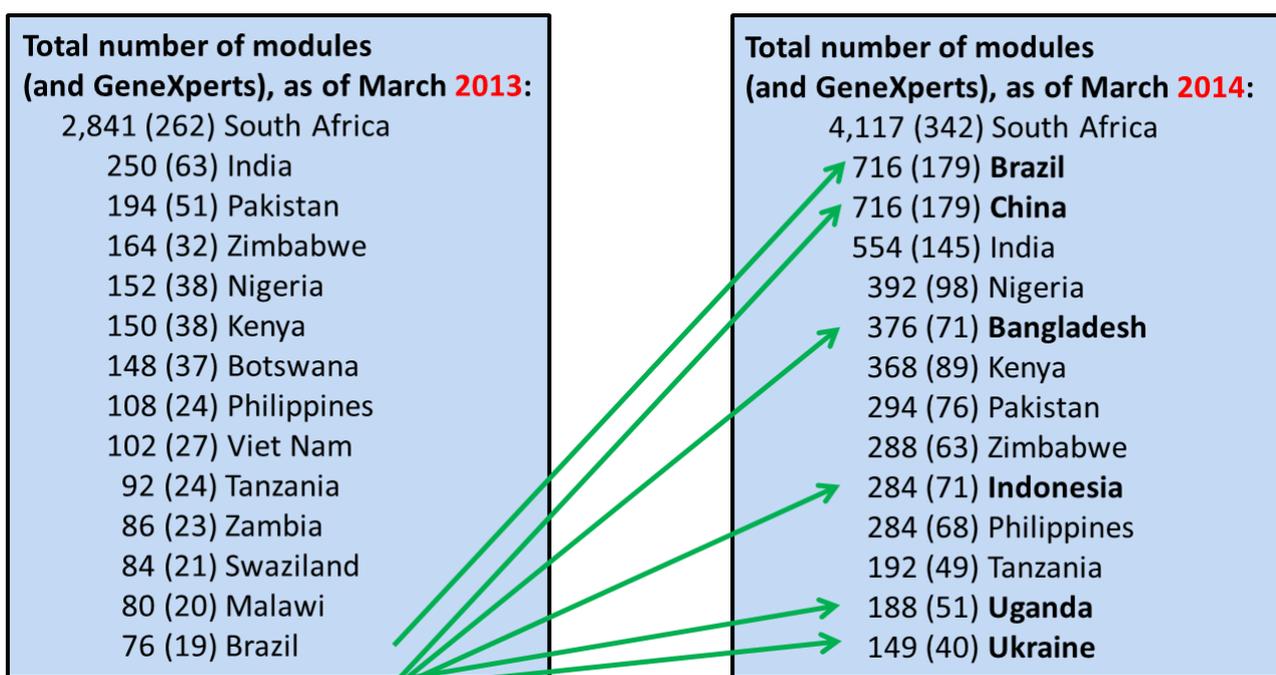
### [Status of the global roll-out of Xpert MTB/RIF: latest progress and tools](#) (presented by Wayne van Gemert)

#### Global landscape of Xpert MTB/RIF use

2,343 GeneXperts (12,103 modules) and 6.3 million Xpert MTB/RIF cartridges have been procured in the public sector in 104 of the 145 countries eligible for concessional prices, as of March 2014. Approximately 1 million cartridges have been procured over each of the previous three quarters.



Over the past year, many countries have significantly scaled up the numbers of modules procured. The ranking of countries in terms of capacity for testing (cumulative numbers of modules procured) has changed significantly in the past year, though South Africa continues to have the largest capacity for testing, with 4,117 modules and 342 GeneXperts.

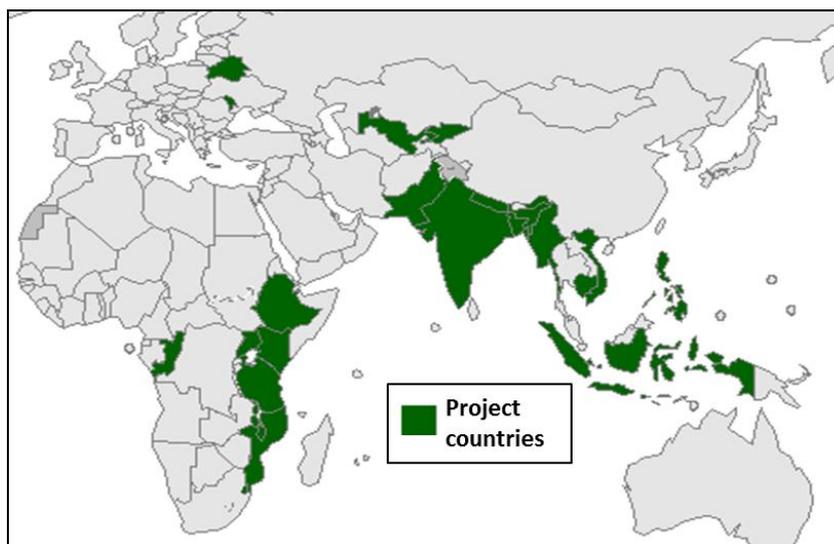




## TBXpert Project

The TBXpert Project is a \$25.9 million UNITAID-funded project for establishment of 234 GeneXperts and 1.4 million Xpert MTB/RIF cartridges in 21 countries. The three-year project (2013-2015) is managed by the WHO Global TB Programme and Stop TB Partnership, with partners including TB REACH, GLI, GDF, EXPAND-TB, African Society for Laboratory Medicine (ASLM), Interactive Research and Development (IRD).

Placement of machines has been aimed at decentralized health centres for the rapid detection of TB, HIV-associated TB, and rifampicin-resistant TB at or close to point-of-care. The project also emphasizes innovative use of machines, including in social business models (see presentation under Session 5: Expanded Access). By the end of 2013, 222 GeneXperts had already been procured.

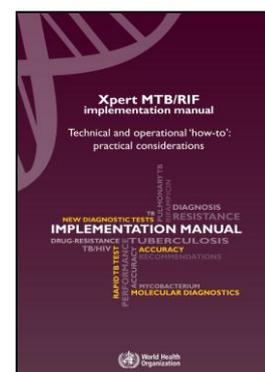


### [WHO Xpert MTB/RIF Implementation manual: selection of patients to test and interpretation of results](#)

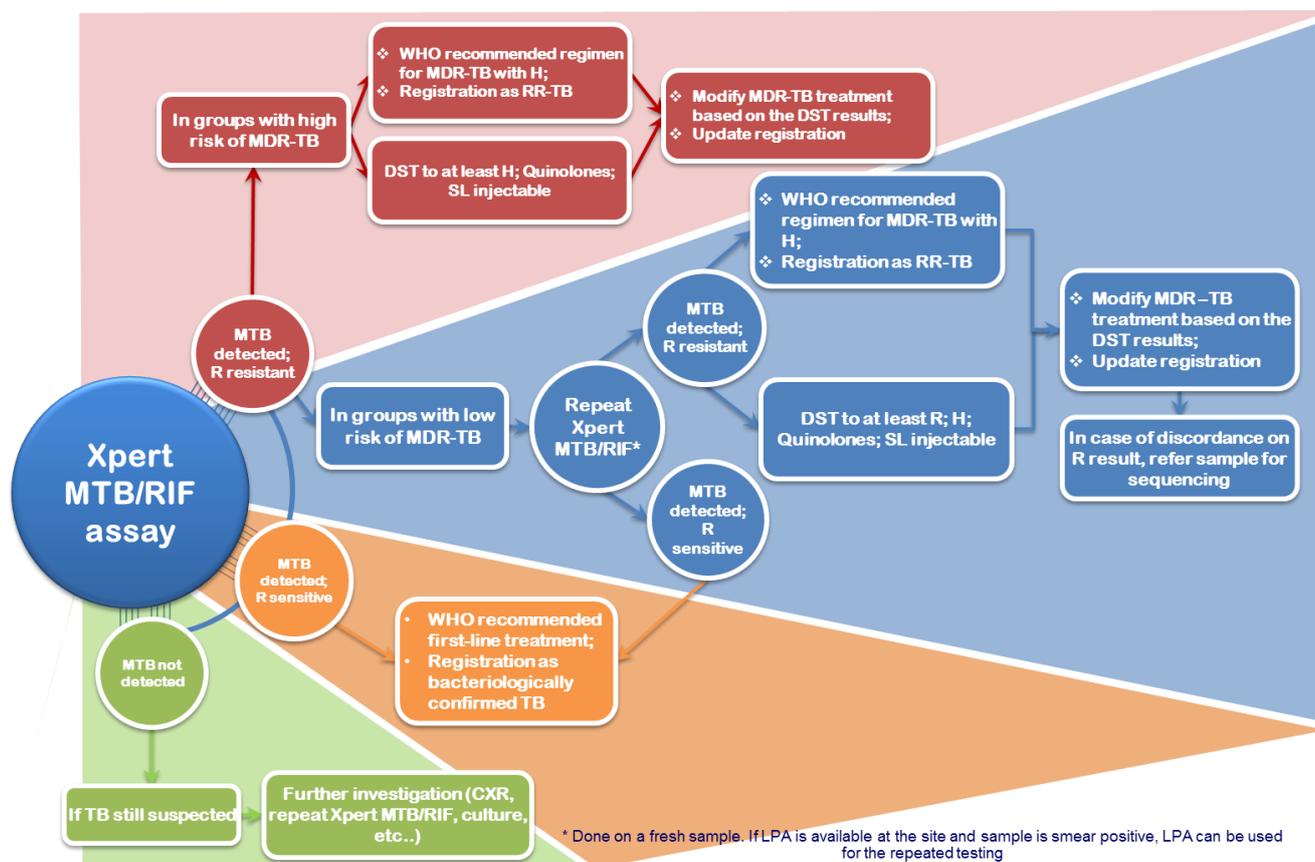
(presented by Fuad Mirzayev)

An updated version of the [Xpert MTB/RIF Implementation manual](#) has been issued by WHO to accompany the Xpert MTB/RIF Policy update. The manual describes:

- Evidence base for the Policy update
- Recommended positioning of the technology
- Testing and managing patients, including the selection of individuals to be tested and how to interpret results (see figure below)
- Case definitions and patient registration
- Practical considerations, including key prerequisites and actions, testing capacity, operation and storage conditions, biosafety, calibration and maintenance, quality assurance, and budgeting guidance
- Monitoring and evaluation
- SOPs for processing extrapulmonary specimens



The implementation manual provides a flow chart describing how Xpert MTB/RIF test results should be interpreted, including the detection of rifampicin resistance in patients for whom this result was unexpected. A full description can be found in the Implementation Manual's chapter [5.3 Interpreting results from Xpert MTB/RIF](#).



Country-specific algorithms should be decided by Ministries of Health within the context of national plans for appropriate management of TB, MDR-TB and HIV-associated TB, including development of screening strategies, timely access to quality-assured first- and second-line anti-TB drugs, and appropriate care delivery mechanisms. The settings and algorithms for using Xpert MTB/RIF should be guided by country- or region-specific epidemiology, available resources, diagnostic tools available in the country, and anticipated cost-effectiveness. Adoption of Xpert MTB/RIF does not eliminate the need for conventional TB microscopy, culture and DST capacity. Microscopy and/or culture remain necessary for monitoring of treatment.

### [Use of Xpert MTB/RIF for diagnosing extrapulmonary TB \(presented by Stephen Lawn\)](#)

The burden of extrapulmonary TB is significant: the 2013 WHO Global TB Report found that 14.8% of notified new TB cases in 2012 were extrapulmonary, and the ECDC Eurosurveillance report found that 22% of notified TB cases in the EU in 2011 were extrapulmonary. Extrapulmonary TB is also frequently found among people with TB/HIV coinfection.

Extrapulmonary TB is difficult to diagnose, given its reliance on invasive procedures and need for expertise when sampling. It is frequently paucibacillary, so clinicians rely on histology and imaging, and patients are frequently treated without bacteriological confirmation.

The 2013 WHO recommendation for use of Xpert MTB/RIF for the detection of extrapulmonary TB on selected specimens (cerebrospinal fluid, lymph nodes and other tissues) was based on the assessment of a commissioned systematic review, an updated version of which has recently been published in the European Respiratory Journal ([Denkinger CM et al. Xpert MTB/RIF assay for the diagnosis of extrapulmonary tuberculosis: a systematic review and meta-analysis. April 2, 2014: erj00078-2014](#)). The evidence base and potential biases in the studies are described in the presentation and in detail in the systematic review.

**WHO recommendations: Xpert MTB/RIF for diagnosis of extrapulmonary TB and rifampicin resistance**

**Cerebrospinal Fluid (CSF):** Xpert MTB/RIF should be used in preference to conventional microscopy, culture and DST as the initial diagnostic test in testing CSF specimens from patients presumed to have TB meningitis (strong recommendation given the urgency of rapid diagnosis, very low quality of evidence);

**Lymph node and other tissues:** Xpert MTB/RIF may be used as a replacement test for usual practice (including conventional microscopy, culture, and/or histopathology) for testing of specific non-respiratory specimens (lymph nodes or other tissue) from patients presumed to have extrapulmonary TB (conditional recommendation, very low quality of evidence).

**Remarks:**

- Individuals presumed to have extrapulmonary TB but with a single Xpert MTB/RIF-negative result should undergo further diagnostic testing, and those with high clinical suspicion for TB (especially children) should be treated even if an Xpert MTB/RIF result is negative;
- For CSF specimens, Xpert MTB/RIF should be preferentially used over culture if the sample volume is low or additional specimens cannot be obtained, in order to reach quick diagnosis. If sufficient volume of material is available, concentration methods should be used to increase yield;
- Pleural fluid is a suboptimal sample for the bacterial confirmation of pleural TB, using any method. A pleural biopsy is the preferred sample. The sensitivity of Xpert MTB/RIF in pleural fluid is very low. Nevertheless, any positive Xpert MTB/RIF result on pleural fluid should be treated for pleural TB, while those with a negative Xpert MTB/RIF result should be followed by other tests;
- Conventional microscopy and culture remains essential for monitoring of therapy and for DST other than rifampicin (including second-line anti-TB drugs);
- Emerging data show that Xpert MTB/RIF detects some rifampicin-resistant strains that are susceptible on phenotypic DST. Sequencing of these discordant results usually resolves in favour of Xpert MTB/RIF, and patients with these strains missed by phenotypic DST and on first-line treatment have poor treatment outcomes;
- These recommendations do not apply to stool, urine or blood, given the lack of data on the utility of Xpert MTB/RIF on these specimens.

Emerging evidence was also shared on the diagnostic yield from screening urine samples from HIV-infected patients with advanced immunodeficiency using Xpert MTB/RIF and lipoarabinomannan (LAM) antigen testing (see [Lawn et al. JAIDS 2012](#))

**Outcomes and follow-up of the GDF GeneXpert procurement stakeholders meeting, Paris, October 2013**  
**(presented by Thomas Vergès)**

The Stop TB Partnership's Global Drug Facility (GDF) aims to expand access to quality-assured first- and second-line TB drugs and diagnostics, and contribute to the development of sustainable procurement and supply management for countries in need. In its diagnostics portfolio, GDF procures technologies for performing liquid culture, line probe assays, and Xpert MTB/RIF (1.3 million cartridges as of April 2014).

Following up on the GeneXpert procurement stakeholders meeting in Paris in October 2013, the following items were presented:

- The Xpert MTB/RIF cartridges will now be packaged in 50-test packs instead of 10-test packs. This improved packaging reduces the gross weight and volume of shipments, with an associated cost savings estimated to be 15-20%. About twice as many tests can now be stored in a given storage space.
- The package insert of the 50-test pack stipulates that the cartridges should be stored at 2 to 28°C, and the cartridges are stable up to 2 weeks at 2 to 48°C after opening the pouch. Variations of temperature to simulate shipments, including the last 5 days at 50°C (summer protocol) or minus 18°C (winter protocol) showed stability.
- In response to a request to have a white paper that documents what is and is not included in an extended warranty, a Warranty Extension agreement has been drafted, which covers preventative maintenance (calibration), module swaps when required, exchange or repair of any defective parts, and shipping charges CIP local airport. GDF can be contacted for more information ([vergest@who.int](mailto:vergest@who.int)).

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**Cepheid: Module Issue Investigation (presented by Martin Colla)**

Cepheid described the occurrence of sites that have observed rising trends in probe-check errors (5007), which Cepheid has determined is due to dust incursion into the instrument and modules. The dust reduces the sensitivity of the modules' optics; however this has been found to be preventable and reversible.

As preventative actions, Cepheid will provide tools to users to allow periodic cleaning of the optical block lenses from outside the module. Users will also be sensitized to the cleanliness of the work area.

As corrective actions, Cepheid will prevent dust from entering GeneXperts by retrofitting the machines with replacement rear panels. The filter holder will be relocated to the outside of the rear panel for easy access, the filter will be changed for one with a finer pore size, and spare filters will be provided for periodic replacement. Remote Xpert (see Panel on *Advancements in electronic recording and reporting systems for Xpert MTB/RIF* in session 4) will enable the early detection of issues and their early resolution.

## SESSION 2: Xpert MTB/RIF for people living with HIV (Chairs: Haileyesus Getahun and Heather Alexander)

### [Xpert for PLHIV: scaling-up through a joint TB and HIV services platform](#) (presented by Lisa Nelson and Nathan Ford)

People living with HIV (PLHIV) have a 30-fold increased risk of TB compared to HIV-uninfected people. Diagnosing TB is challenging among PLHIV, causing delays in detection and treatment of TB, and HIV-associated TB carries a high mortality.

**WHO recommendation: Xpert MTB/RIF should be used rather than conventional microscopy, culture and DST as the initial diagnostic test for pulmonary and extrapulmonary TB in both adults and children living with HIV.**

Studies have found the following benefits of Xpert MTB/RIF for PLHIV:

- Xpert MTB/RIF increases detection of HIV-associated TB (Lawn 2011; Taye 2014)
- Xpert MTB/RIF improves the quality of TB diagnosis (Scott 2011; Theron 2011; O'Grady 2012; Yoon 2012)
- Xpert MTB/RIF facilitates earlier diagnosis and reduces time-to-initiation of TB treatment (Yoon 2012; Bygrave 2012)
- Modelling shows Xpert MTB/RIF to be cost-effective in reducing early mortality among PLHIV (Abimbola 2012; Andrews 2012)
- Xpert MTB/RIF reduces the indirect cost of TB diagnosis (Antunes 2014)
- Xpert MTB/RIF is projected to reduce TB prevalence and mortality in HIV prevalence settings (Menzies 2012)

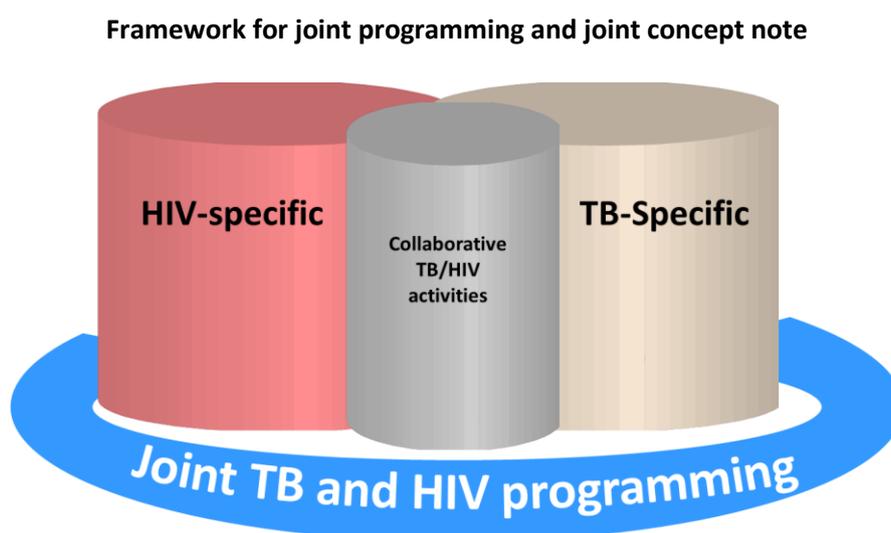
Given this evidence, countries with high HIV prevalence should **include PLHIV as a target patient group for initial diagnostic testing using Xpert MTB/RIF.**

The [WHO 2013 Consolidated ARV Guidelines](#) were described. The scale up of HIV services requires a scale up of lab systems, including for HIV diagnosis (antibody testing and molecular methods), patient monitoring, toxicity monitoring, diagnosis of opportunistic infections, and HIV drug resistance surveillance. Operational challenges include low coverage and poor laboratory infrastructure, the role of point-of-care testing vs. conventional testing, poor linkage to treatment services and unclear data on patient outcomes, specimen transport and results return, quality and reliability of test results, and how to maximize investments and achieve efficiency gains. All programmes (TB, HIV, lab) must work together, and the dynamic development of new platforms (possibility of a single molecular platform for testing in the near future) and strategies offers many new opportunities.

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## **Global Fund Board Decision: submissions of single concept notes for HIV and TB (presented by Annette Reinisch)**

Recognizing the importance of core TB-HIV collaboration services and the need for TB and HIV programs to work jointly, the Global Fund Board's Strategy, Investment and Impact Committee decided that countries with high burdens of TB and HIV shall submit a single concept note that presents integrated and joint programming for the two diseases. This approach will align critical components of the health system, including health information systems, the health workforce, financing, procurement and supply chain management and laboratory and diagnostic services.



Tools and guidelines for the new funding model:

<http://www.theglobalfund.org/en/about/grantmanagement/fundingmodel/>

Information notes: <http://www.theglobalfund.org/en/fundingmodel/support/infonotes>

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## **Making Xpert MTB/RIF change the game for PLHIV: Perspective of the HIV programme manager (presented by Tekalign Megos, Ethiopia)**

Ethiopia has completed an evaluation study of Xpert MTB/RIF to assess the implementation challenges that may arise during implementation, and now recommends the use of the Xpert MTB/RIF as the initial diagnostic test for detection of TB among people living with HIV, among people suspected of having MDR-TB, and among children, and for selected specimens for detection of extrapulmonary TB. Challenges faced include:

- Initial focus was for detection of rifampicin resistance among people suspected of having MDR-TB, instead of as a tool for the rapid detection of TB among people living with HIV;
- Lack of awareness among health professionals;
- Insufficient TB and HIV integration at programme and service levels; and
- Poor networks of Xpert MTB/RIF sites with nearby health facilities

As a way forward, actions will be taken to sensitize clinicians from HIV clinics, build referral linkages to Xpert MTB/RIF sites, and strengthen joint programming.

## **[Making Xpert MTB/RIF change the game for PLHIV: Perspective of the TB programme manager \(presented by Frank Mugabe, Uganda\)](#)**

Uganda estimates that 25% of incident cases are missed each year. Most of the missed cases are believed to be among people living with HIV, children, and people with extrapulmonary TB. Xpert MTB/RIF is seen as a point-of-care test that should be in every high case load HIV care setting, to improve diagnosis of TB, reduce turn-around times, and strengthen access to TB patient management. Uganda has rolled out 55 GeneXperts with support from partners, including FIND, UNITAID, TB REACH and CDC. Xpert is currently used as the initial diagnostic test for PLHIV in TB REACH supported sites, and follows smear microscopy for PLHIV in other sites.

Challenges in Uganda include limited active TB screening in HIV care clinics, recording & reporting weaknesses, referral network issues within and between facilities, inadequate trained personnel, poor communication between clinician and lab personnel and between HIV clinic and TB clinic personnel, lack of patient awareness of the role of Xpert MTB/RIF (especially PLHIV), ownership issues and support of partners in utilization of Xpert MTB/RIF in catchment areas, distant locations of GeneXperts in TB laboratories from HIV clinics, underutilization and short shelf life of cartridges, lack of stable electricity, logistics problems, equipment breakdown with no local capacity to maintain the machines, restrictive algorithms that do not provide access for other non-priority groups, resource constraints for mentorships, supervision, advocacy and training, and possible loss of skill and motivation for smear microscopy.

As solutions, Uganda has developed an implementation plan (over 100 more GeneXperts needed), established a forum of partners to promote ownership, developed and disseminated Xpert MTB/RIF algorithms, increased advocacy and sensitization efforts on Xpert MTB/RIF, incorporated Xpert MTB/RIF into national recording and reporting tools, strengthened specimen referral networks, and identified under-screening for TB among PLHIV as a critical cause of underuse of GeneXperts. The country will aim to strengthen TB/HIV service integration and promote revised TB/HIV guidelines, deploy more GeneXperts to distant facilities, sensitize health workers, train more lab technicians, engage more donors to increase sustainability, urge partners to support utilization of Xpert MTB/RIF in their catchment areas, overcome the fear of the costs of cartridges, back-up equipment in case of breakdowns, and prioritize children (up to 14 years old) for Xpert MTB/RIF as an initial diagnostic test.

## **Xpert MTB/RIF impact data- Evidence from XTEND and TB-NEAT studies**

### **[Findings and implications from the XTEND study \(presented by Gavin Churchyard\)](#)**

**Synopsis of XTEND study:** The XTEND study is a cluster-randomized trial evaluating the impact of Xpert MTB/RIF in South Africa, involving 20 laboratories and 2 primary care clinics per laboratory. Laboratories and the clinics associated with the laboratory were randomized to either the Xpert MTB/RIF arm or microscopy arm, in which implementation of Xpert MTB/RIF was delayed until enrolment of the cohort was completed. The study found a 50% increase in bacteriologically confirmed cases using Xpert MTB/RIF, but this did not result in a decrease in mortality among adults with presumptive TB who were enrolled in the study, measured six months after enrolment. Furthermore, the study found no significant reduction in initial loss to follow-up within 28 days of enrolment, and no significant increase in the proportion of the overall cohort starting TB treatment by six months from enrolment (though the proportion of bacteriologically-confirmed TB cases among those starting treatment increased by 20%). As the detection of more bacteriologically

positive TB cases did not have a significant impact on overall mortality, on initial loss to follow-up and on enrolment into TB treatment in the study setting, the authors conclude that adoption of Xpert MTB/RIF needs to be supported by strengthened health systems linked to the rapid initiation of appropriate care. Furthermore, people must know their HIV status and those eligible should start anti-retroviral treatment promptly. An analysis of costing data is in progress, and population-level impact (eg., incidence, prevalence and mortality) will be determined through mathematical modelling.

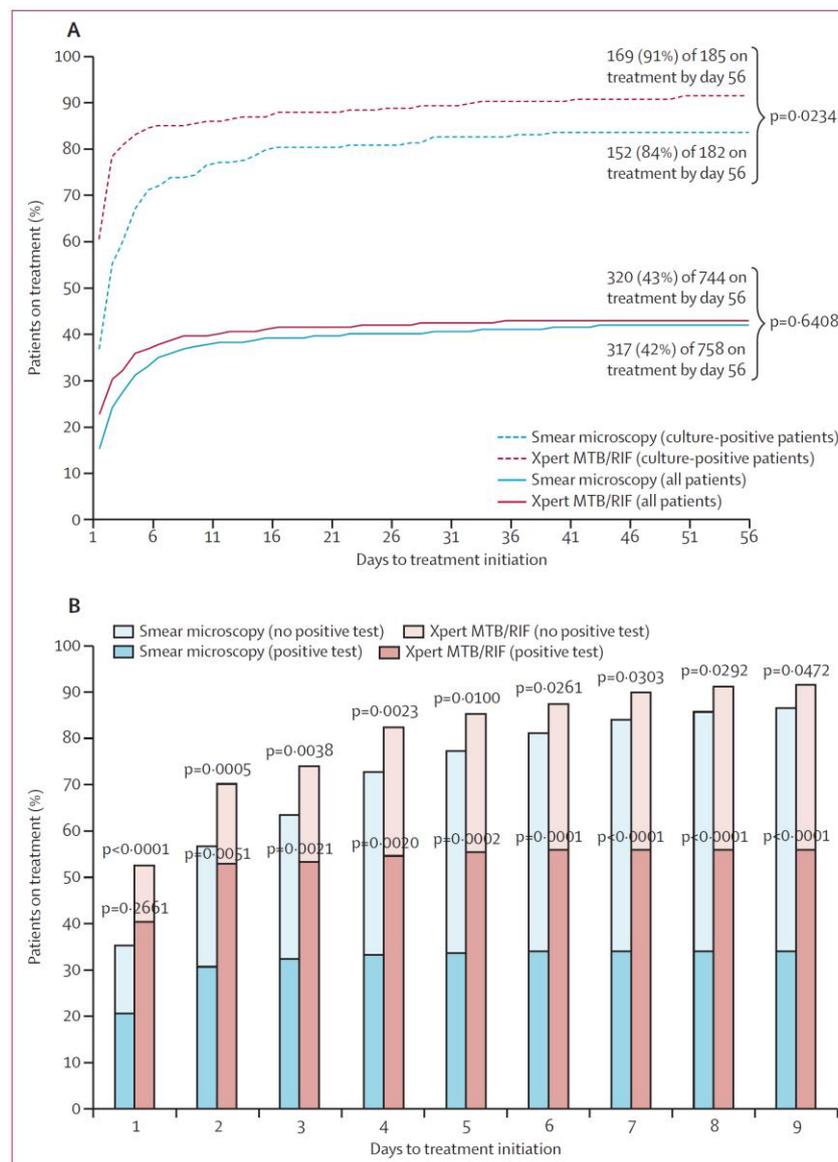
<b>Summary of XTEND results</b>				
<b>Primary outcome</b>	<b>n</b>	<b>Xpert %</b>	<b>Microscopy %</b>	<b>Adjusted Risk ratio (95% CI)</b>
<b>Mortality risk over 6 months</b>	<b>4656</b>	<b>3.9%</b>	<b>5.0%</b>	<b>1.10 (0.75-1.62)</b>
<b>Secondary outcomes</b>				
<b>Secondary outcomes</b>	<b>n</b>	<b>Xpert %</b>	<b>Microscopy %</b>	<b>Adjusted Effect measure (95% CI)</b>
<b>Index test positive</b>	<b>4412</b>	<b>9.2%</b>	<b>7.8%</b>	<b>1.49 (1.00, 2.23)</b>
<b>Initial loss to follow-up, over 28 days</b>	<b>374</b>	<b>17.0%</b>	<b>14.9%</b>	<b>0.96 (0.48-1.93)</b>
<b>% treated for TB over 6 months</b>	<b>4656</b>	<b>10.8%</b>	<b>12.5%</b>	<b>1.04 (0.76-1.43)</b>
<b>% with microbiological confirmation, among those treated for TB</b>	<b>541</b>	<b>78.5%</b>	<b>65.0%</b>	<b>1.20 (0.98- 1.47)</b>

#### **Findings and implications from the TB-NEAT study (presented by Grant Theron)**

**Synopsis of TB-NEAT study:** The TB-NEAT study is a randomized parallel-group multicentre trial evaluating the impact of Xpert MTB/RIF in five primary-care health facilities in four African countries (South Africa, Zimbabwe, Zambia and Tanzania). Eligible patients were randomly assigned to nurse-performed Xpert MTB/RIF at the point-of-care or same-day smear microscopy. The study found that point-of-care Xpert MTB/RIF had a higher sensitivity than microscopy (83% vs 50%), and those tested by Xpert MTB/RIF were more likely to have same-day treatment initiation. Furthermore, Xpert MTB/RIF in peri-urban clinics was feasible when performed by non-technical staff, and had a similar accuracy and failure rate to a laboratory-based Xpert done by technical personnel on the same patients. More patients that were later confirmed to be culture-positive were started on treatment when detected by Xpert MTB/RIF. However no impact was observed on TB-related morbidity among culture-positive patients, as an indicator of clinically important outcomes. The proportions of all patients on treatment in both arms were similar by day 56 of the study, due to high levels of treatment of patients diagnosed with TB on clinical grounds. Of the patients in the microscopy arm who tested negative by smear but who were detected by Xpert MTB/RIF performed at the end of the study using a sputum collected at recruitment, over 90% were treated on empirical grounds anyway.

Treatment based on clinical symptoms alone is postulated to diminish the incremental benefit of Xpert MTB/RIF in these settings, and the presenter suggested that the role of this effect may be underestimated when projecting the impact of any new diagnostic. It must be investigated how the clinical handling of test-

negative patients changes with the long-term implementation of Xpert MTB/RIF, and clinical decision-making and training may need to improve and be given as big a priority as new diagnostics.



**Figure 3: Initiation of anti-tuberculosis treatment in all patients and culture-positive patients, per allocation group**  
 (A) Proportion of all patients in each group or of culture-positive patients only in each group given anti-tuberculosis treatment over the 56 days of the study. After day 9, the proportion of patients on anti-tuberculosis treatment in each group did not differ significantly. (B) Proportion of patients in the first 9 days after recruitment who began anti-tuberculosis treatment as a result of empirical evidence (ie, in the absence of positive smear microscopy, Xpert MTB/RIF, or culture result) and those who began anti-tuberculosis treatment as a result of a positive smear microscopy, Xpert MTB/RIF, or culture result. p values just above each pair of bars are a result of comparisons between groups of the overall number of patients on treatment, whereas the p values across each pair of bars are a result of comparisons between groups of the proportions of patients with no positive test who began treatment on empirical grounds.

More on the findings of the TB-NEAT study and an interpretation of its findings can be found in the following publications:

- Theron G et al. [“Feasibility, accuracy, and clinical effect of point-of-care Xpert MTB/RIF testing for tuberculosis in primary-care settings in Africa: a multicentre, randomised, controlled trial”](#) Lancet 383 (9915), 1–7 February 2014: 424–435.
- Theron G et al. [“Do high rates of empirical treatment undermine the potential effect of new diagnostic tests for tuberculosis in high-burden settings?”](#) Lancet Infect Dis, January 14 2014: pii: S1473-3099(13)70360-8.

## [WHO commentary on the studies \(presented by Wayne van Gemert\)](#) and discussion

Regarding the XTEND study, the findings should be interpreted in the specific context of South Africa, considering its high TB and HIV burden, the diagnostic and treatment algorithms employed in the country, as well as the limitations of the study:

1. Initiation of TB treatment based only on clinical symptoms, particularly for smear-negative pulmonary TB and extrapulmonary TB cases, is common practice in South Africa and other high HIV prevalence settings. As 35% of those treated in the microscopy arm of the study were bacteriologically-negative, the frequent clinical diagnosis of TB likely played a role in reducing the potential impact of Xpert MTB/RIF on increasing the overall number of patients diagnosed and treated, on reducing delay to treatment initiation and consequently on reducing mortality.
2. Unlike most other high TB burden countries, the South African diagnostic algorithm routinely includes culture for people living with HIV presumed to have TB. Including culture in the algorithm increases both the number of smear-negative cases and Xpert-negative cases that would later be bacteriologically-confirmed by culture, effectively reducing the difference between the two study arms in numbers of people who would be started on treatment.
3. The structure of the study and of TB services in general in South Africa uses sputum transport from primary care clinics to laboratories performing microscopy or Xpert MTB/RIF. This referral system prevents Xpert MTB/RIF from being used as a rapid tool for same-visit detection to prevent initial loss to follow-up, which is a frequent problem in South Africa.
4. The study captured only 8 RR-TB cases detected using Xpert MTB/RIF, not providing the power needed to evaluate whether Xpert MTB/RIF had an impact on improving treatment outcomes of RR-TB and reducing transmission of RR-TB as a result of early initiation of appropriate treatment. Additionally a longer time frame would have been needed to assess the impact of Xpert MTB/RIF on mortality of patients with RR-TB.

It was noted from the audience that the study shows that getting HIV+ patients onto anti-retroviral treatment is critical.

Regarding the TB-NEAT study, these findings should be interpreted in the specific context of the study settings, considering the frequent initiation of treatment based on clinical symptoms alone. The study population consisted of ambulatory patients, so the impact of Xpert MTB/RIF on seriously ill patients or on those with extrapulmonary TB was not investigated, however, treatment initiation based on clinical symptoms alone is frequently highest amongst these patient types. The finding that Xpert MTB/RIF is feasible at the POC when performed by non-technical personnel in well-resourced clinics has implications for its potential placement in TB hotspots, such as prisons or high burden communities with high drop-out rates, where it can rapidly inform same day clinical decision making. It was noted from the audience that same-day testing and return of results requires intensive human resources. Similar to the XTEND study, the TB-NEAT study also did not investigate the impact of Xpert MTB/RIF on RR-TB, and on transmission of TB and RR-TB. It should be noted that the lower rates of patient dropout observed among culture-positive patients detected with Xpert MTB/RIF may have an impact on reduction of transmission of TB.

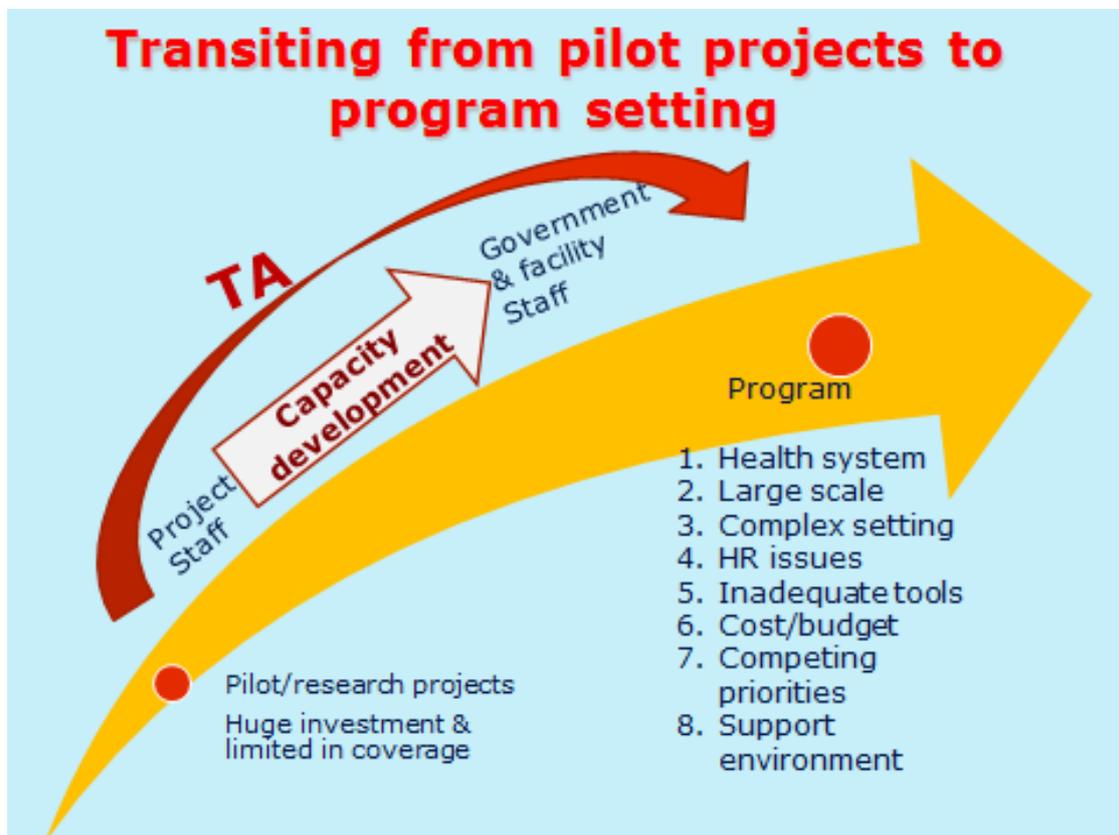
In summary, the two studies confirm that Xpert MTB/RIF can significantly increase the number of bacteriologically positive TB cases. However, to show significant impact on clinically important outcomes for drug-sensitive TB patients, adoption of Xpert MTB/RIF needs to be complemented with the rapid initiation of appropriate treatment and a reduction in the use of treatment based on clinical symptoms without bacteriological confirmation. More research is still needed to evaluate the potential impact of adopting Xpert MTB/RIF on:

- TB case detection and treatment outcomes in other resource-constrained settings with differing health systems;
- detection of RR-TB and subsequent treatment outcomes; it was noted from the audience that the preliminary results from the EXIT-RIF study has shown a significant decrease in delay to start of treatment of rifampicin-resistant patients;
- detection of paediatric TB and subsequent treatment outcomes;
- detection of extrapulmonary TB and subsequent treatment outcomes;
- cost-effectiveness and patient costs;
- reduction of false-positive TB diagnosis, and related adverse effects and costs; and
- reduction of transmission of TB and DR-TB, and reduction of population-level TB burden (incidence, prevalence and mortality).

## SESSION 3: Experiences and lessons learned in the roll-out of Xpert MTB/RIF (Chair: Amy Piatek)

### [TB & HIV programme coordinated roll-out of Xpert MTB/RIF in Nigeria](#) (presented by Mustapha Gidado / Joshua Obasanya)

The roll-out of Xpert MTB/RIF in Nigeria has been coordinated by a group of stakeholders with representation from all partners; the group is responsible for site assessment and selection, development of training manuals, SOP's and recording and reporting tools, monitoring and evaluation including supervision, and technical assistance needs assessment and implementation. As of March 2014, there were 54 GeneXpert sites in 32 states; 80% of machines are within TB/HIV care sites. The roll-out has transitioned from a pilot/research-based use of GeneXpert to a larger-scale programmatic use. Diagnostic algorithms have changed over time, and the specimen examination request form and reporting tools have also been modified.



Of the KNCV/TB CARE I sites, the average utilization per machine has been less than 450 tests per year, with 6% rifampicin resistance among all tested, and 7.4% of tests resulting in errors, invalids, or no results. Among all partners in 2013, 3,345 MTB positive cases were detected, including 573 with rifampicin resistance; however, only 335 were enrolled onto second-line treatment.

Challenges include maintenance, with 14 sites (45%) experiences one episode of fault, and 4 sites (13%) experiencing 2-4 faults. Faults in order of frequency were: modules failure or stuck door, inverter/battery, CPU, barcode scanner unit, and complete equipment failure; the average service interruption was 2-4 weeks.

Less than 25% of tests were for PLHIV, reflecting low symptomatic screening of PLHIV for HIV and non-documentation & referral. Other challenges included, frequent review of algorithms and guidelines, dealing with a paper-based R&R system, programmatic turnaround time in weeks, delayed replacement of failed modules after calibration (no buffer stock), capacity for enrolment of DR-TB, coordination of procurement and distribution of cartridges among all partners, adherence to Xpert MTB/RIF roll-out plan by partners, alignment of the Xpert MTB/RIF roll-out plan with culture and DST labs, and sample transport.

Opportunities include an electronic R&R system (eg. GXAlert), the technical assistance plan funded by the US government, decentralization of PMDT services, the combined concept note for the Global Fund New Funding Model, TB technical assistance to the HIV programme (multi-sectorial), establishment of basic Xpert MTB/RIF local service provision including installation and troubleshooting, and revision of all TB and TB/HIV training manuals.

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### **[Integrating Xpert MTB/RIF into PMDT & PPM activities in India \(presented by RS Gupta\)](#)**

India has implemented the world's largest PMDT service expansion, which started in 2007, and dramatically accelerated from 2011 to achieve nationwide rapid scale-up in March 2013. There are now 37 solid culture labs, 14 liquid culture labs, 45 labs using line probe assay, and 89 centers using Xpert MTB/RIF. National guidelines call for use of Xpert MTB/RIF in programmatic settings for diagnosis of rifampicin resistance among presumptive MDR-TB cases, and to prioritize TB detection among PLHIV and children.

An Xpert MTB/RIF feasibility study found an overall positivity rate for TB detection of 21.8% and a yield of 32.7% over smear microscopy.

The RNTCP TBxpert project supported by WHO, Stop TB Partnership, UNITAID and USAID has established Xpert MTB/RIF technology in 43 sites to scale up rapid molecular diagnosis of TB and rifampicin resistance. The project aims to engage the private sector through innovative PPM initiatives to improve access to rapid testing of patients who attend both the public and private sector. The approaches will send a clear message to private providers that access to tests and treatment are free of cost, what are the clinical indications to tests, that results should be notified progress monitored, and all medium of communications will be used. The approaches will be based on the Standards for TB Care in India, and ICT solutions will be used to bridge the information gap.

Accelerating access to quality diagnosis for paediatric TB cases is the goal of a project establishing 4 Xpert MTB/RIF labs in Delhi, Chennai, Kolkata and Hyderabad. A referral network will be established linking key hospitals and private clinics catering to paediatric populations, a large number of paediatricians will be engaged, and key personnel will be sensitized. Another project will be a PEPFAR-supported initiative that will provide 30 GeneXperts to 4 high HIV burden states, aiming to intensify TB case finding at high burden ART centres in India.

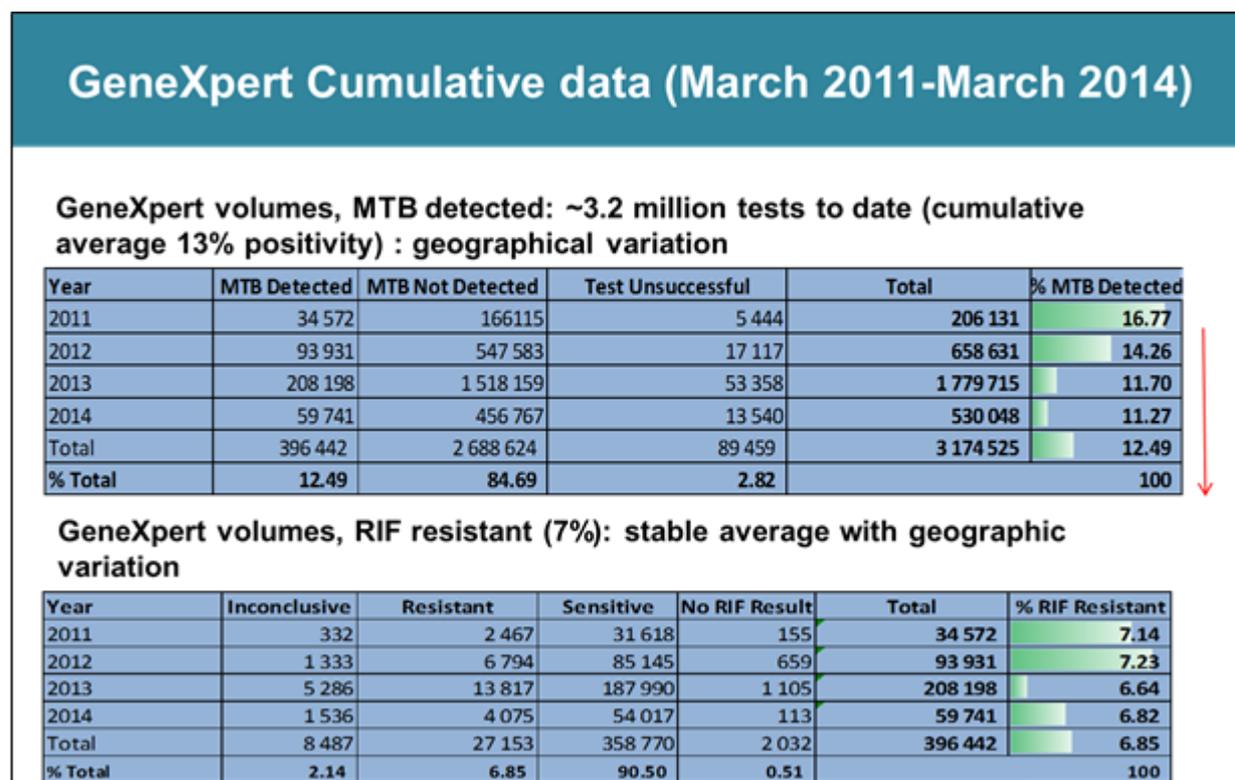
The vision of the National Strategic Plan for India calls for an additional 300 GeneXperts from the Global Fund and 100 GeneXperts from the Government of India in 2014-2015, and another 300 GeneXperts from the Global Fund and 200 GeneXperts from the Government of India in 2015-2016. Priority areas for deployment of the technology will be medical colleges with DR-TB centers, ART centers, urban TB districts, and high workload districts.

**Beyond implementation: health systems strengthening and focus on high risk populations (2011-2014) in South Africa (presented by Wendy Stevens)**

The South African experience in rolling out Xpert MTB/RIF highlighted areas for programme strengthening, including changing from vertical management, improving linkages to care, focusing on high risk populations (including MDR, correctional services, mines), improving testing of extrapulmonary and paediatric specimens, and conducting R&D on other assays. Operational challenges have included improving technical and clinical training and ensuring adherence, strengthening laboratory information systems, and implementing quality management systems (verification, remote monitoring, external quality assessment, and remote calibration).

South Africa has reached 100% coverage in the public sector as per the NDoH plan. There are now 207 centers in all 9 provinces, in all original smear microscopy centers. Over 3.2 million tests had been procured to date, as well as 289 GeneXperts of different capacities. 7 GeneXperts with 80 module capacity (Infinities) have been purchased, and 5 installed to assist with increased numbers expected for high risk populations. In the next phase of roll-out, Xpert MTB/RIF will be used with correctional services, mines and peri-mining communities, and for MDR/XDR.

MTB positivity rates have been falling since 2011 with the larger roll-out, and overall 12.49% of tests have been MTB positive. 6.85% have been rifampicin resistant.



The diagnostic algorithm requires significant simplification, particularly for HIV-positive patients found to be Xpert MTB/RIF negative. The EXIT-RIF study has shown that laboratory results do not equate to patients receiving treatment.

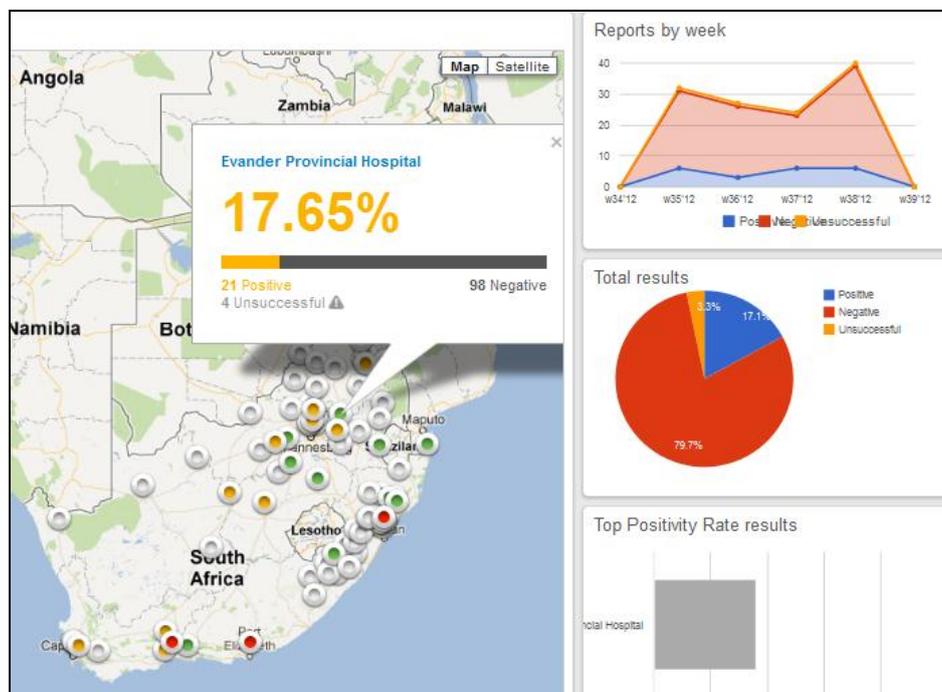
The number of notified cases of MDR-TB has increased from 9,070 in 2009 to 15,419 in 2012. The number of cases enrolled on MDR-TB treatment has also increased, from 4,143 in 2009 to 6,494 in 2012, but the gap between diagnosed and treated is widening. A large linkage to care project has been launched which includes a comprehensive real-time m-Health solution for linking patients to care using electronic records and accessing the NHLS central data warehouse and laboratory information system, as well as other systems.

The EXIT-RIF study was described, which aimed to assess whether rapid diagnosis of rifampicin resistance leads to improved TB treatment outcomes, to determine phenotypic and genotypic drug resistance profile in patients diagnosed with Xpert-rifampicin resistance, and to document management decisions and patient actions in the first 6 months following diagnosis of Xpert-rifampicin resistance. Results are embargoed until the Union meeting.

Regarding module failure errors, 32% of errors have been attributed to instrument malfunction and 32% from temperature related issues. It was noted that the history of modules prior to replacement is not known. A costing and modelling analysis revealed that purchasing extended warranties would cost 25% more than replacing modules.

NHLS has launched a machine verification and external quality assessment programme (3 panels per year) using a panel of 4 dried culture spots (DCS). The DCS are also used to verify performance of machines after transport in mobile vans.

Current recommendations on use of Xpert MTB/RIF for detection of extrapulmonary TB were described, and benefits of Xpert MTB/RIF for diagnosis of HIV-associated peripheral lymph node TB will be described in a forthcoming paper.

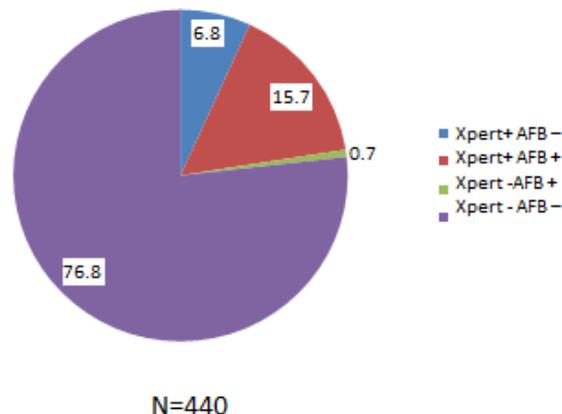


The Cepheid/NHLS remote connectivity project has provided an operational dashboard for real-time monitoring of results, errors, resistance and positivity rates. It is pre-configured on all newly installed GeneXperts.

**Clinical utility of Xpert MTB/RIF in guiding treatment of TB and MDR-TB: experience from Belarus**  
**(presented by Alena Skrahina)**

Belarus has experienced a gradual decline in overall new TB cases in the past 10 years, but the proportion of new and previously treated TB cases with MDR-TB continues to grow. According to national statistics, 34.6% of new TB cases and 70.8% of previously treated TB cases had MDR-TB in 2013. Belarus has approved clinical guidelines for TB and MDR-TB, including a diagnostic algorithm with rapid methods. There are currently 13 GeneXperts, with another 16 planned; the country is in an early phase of its roll-out. The MoH guidelines call for use of Xpert for patients who have failed treatment, relapses, MDR-TB contacts, children and PLHIV with suspected TB. However, Xpert MTB/RIF is not yet performed for all patients indicated in the order. There are plans to use Xpert MTB/RIF as the initial diagnostic test for all patients suspected of TB.

**Xpert and smear microscopy for TB detection**



Clinical practice has changed with introduction of Xpert MTB/RIF. Upon receiving an Xpert-detected rifampicin-resistant result, the doctor should present the case to the MDR-TB consilium, which puts the patient MDR-TB treatment immediately, and further testing is performed using MGIT. The introduction of Xpert MTB/RIF has shown to reduce the delay in start of treatment of patients with MDR-TB from 69 to 9.3 days. While 15.7% of Xpert MTB/RIF results are MTB+ and smear positive, a further 6.8% of Xpert MTB/RIF results are MTB+ and smear negative, reflecting a significant increase in bacteriologically confirmed cases.

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**Experience with the Xpert MTB/RIF assay in routine program conditions with different HIV prevalence and risk of MDR-TB : Epicentre’s feasibility study of MSF sites** (presented by Anne-Laure Page)

MSF programmes have introduced Xpert MTB/RIF in 18 countries (33 programmes), with different prevalences of HIV and MDR-TB. Varying algorithms are used depending on the prevalences (see presentation). The objectives of the study were to use reinforced monitoring data in 4 programmes (Georgia, Kenya, Cambodia, Swaziland) with different HIV and MDR-TB prevalences using Xpert MTB/RIF in routine conditions to describe per-patient diagnostic results, treatment decisions and time to treatment and feasibility (number of tests per day, turn around time).

The study confirmed the added value of Xpert MTB/RIF compared to microscopy, but the relative gains differed, depending on the HIV prevalence, quality of microscopy and possibly the healthcare level. Many inconclusive test results (errors, invalids, no results) were found, which increases costs and complicates operations, including retrieval of a second specimen.

It was observed that diagnostic algorithms were not strictly followed. In high HIV settings, very few tests were repeated after broad spectrum ATB treatment, due to poor adherence by clinicians and/or patients not returning. In low HIV settings, many requests were made for Xpert MTB/RIF prior to broad spectrum ATB treatment, leading to a high number of tests. There was little information gained on the added value of

using/repeating Xpert MTB/RIF after broad spectrum ATB treatment. There were also limitations of routine data collection, and simplified algorithms and trainings are needed.

Patient/specimen flow was found to be crucial for reducing delay to treatment. Avoidable delays were identified in the laboratory, due to workload, organization and processing for culture. Xpert MTB/RIF in replacement or as an add-on to microscopy were found to have similar costs. Workload and complexity were reduced if Xpert MTB/RIF replaced microscopy, however there were some missed cases due to inconclusive Xpert MTB/RIF results. There was a clear added-value for rifampicin detection, with most patients starting on empiric MDR-TB treatment in a reasonable time.

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### **Xpert MTB/RIF Implementation: Results, Impact and Lessons Learned: TB REACH (presented by Jacob Creswell)**

TB REACH promotes early and increased TB case detection using innovative approaches. Grants are provided to projects on a competitive basis. 51 projects are currently reporting Xpert MTB/RIF testing data, and placement of GeneXperts are in mobile vans, chest camps, private laboratories, health centers and district hospitals. Testing algorithms vary, and include Xpert MTB/RIF on all smear negative presumptive TB cases, smear negative presumptive TB cases with suggestive chest X-ray, smear negative and HIV positive presumptive TB cases, all symptomatic presumptive TB cases, all HIV+ presumptive TB cases, all presumptive TB cases with abnormal/suggestive chest X-ray, all seriously ill presumptive TB cases.

295,342 tests have been performed, and 38,668 MTB+ cases and 4,621 rifampicin resistant cases have been detected, with an overall test failure rate of 7.9%. It was noted that the cost per test should consider the running costs for the equipment, including port clearance, infrastructure, warranty, training, maintenance, reporting and transport networks.

Initial analysis of a few projects' data suggested Xpert MTB/RIF may increase numbers of bacteriologically positive cases, but the total number of notified TB cases sometimes decreases or remains stable, due to other factors including treatment based on clinical symptoms alone.



## Xpert Test Results

- Detected 38,668 MTB+ individuals
- Overall Crude Positivity 11%
- Effective Positivity (% among individuals tested - not including failed tests) 14.2%
  - Range per quarter (6.4 - 41.0%) - Median 12.5%
- Rif Resistant 4,621 (1.7% of individuals tested)
  - Range per quarter (0-14.2%) - Median 0.9%
- Failure Rate 7.9%
  - Slowly decreasing but widely variable
  - Range per quarter (1.2-28.4%) - Median 6.9%



Transforming the Fight  
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Uptake of WHO reporting guidelines has been observed to be improving, though differing systems within countries inhibit proper monitoring of impact. Automated reporting systems are seen as being critical.

The largest problem so far is expiration of cartridges, due to restrictive algorithms and poor planning, lengthy customs clearance and storage. Given that failed tests have a large cost, monitoring of user statistics and error codes is critical. Calibration compliance has improved but still is not 100%. There have been large variations in rates of module failure, possibly depending on infrastructure, location and electric supply.

In conclusion, laboratory interventions alone are unlikely to increase the number of people put on TB treatment, and other strategies are needed to test more people to increase case detection. People not being detected may be either in or outside of the healthcare system. Training, reporting and sound algorithms are critical.

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### **GeneXpert roll-out: Achievements and lessons learned: TB CARE I (presented by Kathleen England and Sanne van Kampen)**

TB CARE I works to establish country-specific programmes using a rational systematic approach to intensify GeneXpert implementation. Program strategy includes various activities such as: capacity building, onsite and national level trainings, health systems strengthening, monitoring/supervision, devising a maintenance plan, establishing cartridge logistics programmes and reporting impact indicators. Using experience-directed scale-up, countries are able to expand testing and increase case detection. TB CARE I advocates for Xpert MTB/RIF strategic planning to be incorporated into a larger National Laboratory Development Plan in order to build capacity for all necessary diagnostic testing to identify and follow patients with sensitive and drug-resistant TB.

TB CARE I has developed several tools to assist and guide implementation activities which include: a stepwise roadmap to implementation, a training package (now a part of the GLI training package), guides for supervision and monitoring Xpert MTB/RIF testing and linkage to clinical activities, as well as onsite mentoring and follow-on country implementation reviews. 104 GeneXperts are now in use with TB CARE I support, and 68,547 tests have been performed. 25,964 TB cases and 7,202 rifampicin-resistant TB cases have been detected.

TB CARE I aims to integrate TB/HIV services with Xpert MTB/RIF testing by helping to establish a functional national Xpert MTB/RIF working group with key representatives from the NTP and the National AIDS programme (NAP). Experience demonstrates the importance of initial involvement of the NAP to facilitate trainings of HIV physicians and staff. Other important developments include: onsite testing or direct specimen referral, “one stop shop” treatment programs, infection control in HIV clinic waiting areas, linking HIV and TB data systems, and inclusive M&E mechanisms.

The primary challenge encountered by TB CARE I is establishing complete buy-in by the NTP and getting all stakeholders on the same page. Additionally, it is important to involve all sectors of the health care system. Further challenges are associated with human resource capacity, cartridge logistics and forecasting, poor specimen referral, inadequate recording and reporting, limited computer literacy, lack of maintenance services, under utilization, establishing necessary M&E indicators, and minimizing treatment delays.

Lessons learned from TB CARE I activities:

- 1) It is important to ensure a systematic approach that is in alignment with the National Strategic Plan;
- 2) It is important to form strong leadership through an all-inclusive Xpert MTB/RIF advisory committee;
- 3) It is necessary to ensure capacity for treatment and care;
- 4) Implementation is best directed and coordinated by the NTP;
- 5) There must be effective partner collaborations;
- 6) Clear understanding of the technology leads to optimal utilization, which leads to improved case detection;
- 7) Impact can be assessed if there is a strong mechanism for monitoring and evaluation;
- 8) A strong referral systems leads to accessibility, which leads to increased utilization;
- 9) A cartridge management system prevents expiry, stock-outs, and wastage;
- 10) Quality assurance measures using well documented supervision and maintenance activities lead to an effective testing programme; and
- 11) Scale-up activities require a focal person for coordination and management.

As next steps, TB CARE I aims to intensify active case finding via alternative mechanisms, include paediatric and extrapulmonary TB into national diagnostic algorithms, strengthen national specimen referral, improve data recording systems, support PMDT developments, evaluate impact and cost-effectiveness, and identify mechanisms for sustainability.

## SESSION 4: Best practices in monitoring & evaluation (Chair: Dennis Falzon)

### [Using M&E to guide scale-up of Xpert MTB/RIF in Tanzania](#) (presented by Heidi Albert)

Monitoring entails routine data collection, and evaluation entails the analysis of routine data and collection and analysis of additional data. M&E findings should provide the evidence base to guide the planning process for further scale up and improved quality of Xpert MTB/RIF implementation.

M&E can be used to answer key questions guiding programme implementation, including:

- How many instruments are in the country? Where are they?
- Who put them there? When?
- Where to place new instruments?
- Have Xpert users received training? What curriculum? Were they certified as competent?
- Who is responsible for conducting site assessments, training, site monitoring, collecting lab indicators? Has it been done according to plans?
- How do we ensure uninterrupted cartridge supply and avoid expiry of cartridges?
- Who is responsible for equipment maintenance and calibration? When does it need doing?
- What level of unsuccessful tests? What causes?
- Has the rate of errors reduced since mentoring and refresher training was given?
- Has use of Xpert increased TB and drug resistance detection rate compared with microscopy?
- What proportion of patients diagnosed with Xpert are put on appropriate treatment within 7 days?
- Are data reported to MOH?

Monitoring of lab indicators, including numbers of MTB and rifampicin resistance results, shows overall test consumption, answers whether instruments are over- or under-utilized, shows rates of MTB positive and rifampicin-resistant results, variation in numbers of tests per month (including possible stockouts) and variations in rates of MTB and resistance.

Monitoring of unsuccessful test rates (errors, invalids, no results) shows whether a machine or module is experiencing technical problems or whether particular users are responsible for high numbers of unsuccessful tests.

Staff must be trained and competent. In addition to MOH qualification requirements for testing personnel, standardized and documented M&E training should be tailored to the responsibilities that a staff member will have, whether it be as a test operator, an advanced user (country expert) or a regional/district supervisor. A competency assessment should be performed, there should be ongoing mentoring and monitoring for M&E, and SOPs should be up-to-date and available at point-of-testing.

Reliable data collection requires standardized tools, trained assessors, direct observation of data, internal and external M&E and integrated data management tools. Basic data skills are required at site and district/regional level, with more advanced data skills required at national level.

## Moving towards systematic M&E

- Establish mechanisms for flow of information between users to supervisors to regional and central focal persons to NTP management
- Systems approach – integrated data collection, automated basic analysis across different tools, option for advanced data analysis
- Integrate into existing NTP/lab M&E activities
- Practical training in basic data skills
- Advanced data skills training for supervisors/ national focal persons/planning
- Partner coordination – develop and use single set of tools, report near real time to MOH
- Leveraging connectivity to improve data collection
- Donors providing whole package for implementation, not just instruments and cartridges
- Ongoing mentoring in M&E

Regular on-site supervision must be organized to ensure quality of performance of Xpert MTB/RIF testing and all processes.

### Panel: Advancements in electronic recording and reporting systems for Xpert MTB/RIF

This panel was organized to present the different tools available for electronic recording and reporting, allowing for remote monitoring as well as rapid return of results to clinicians and/or patients.

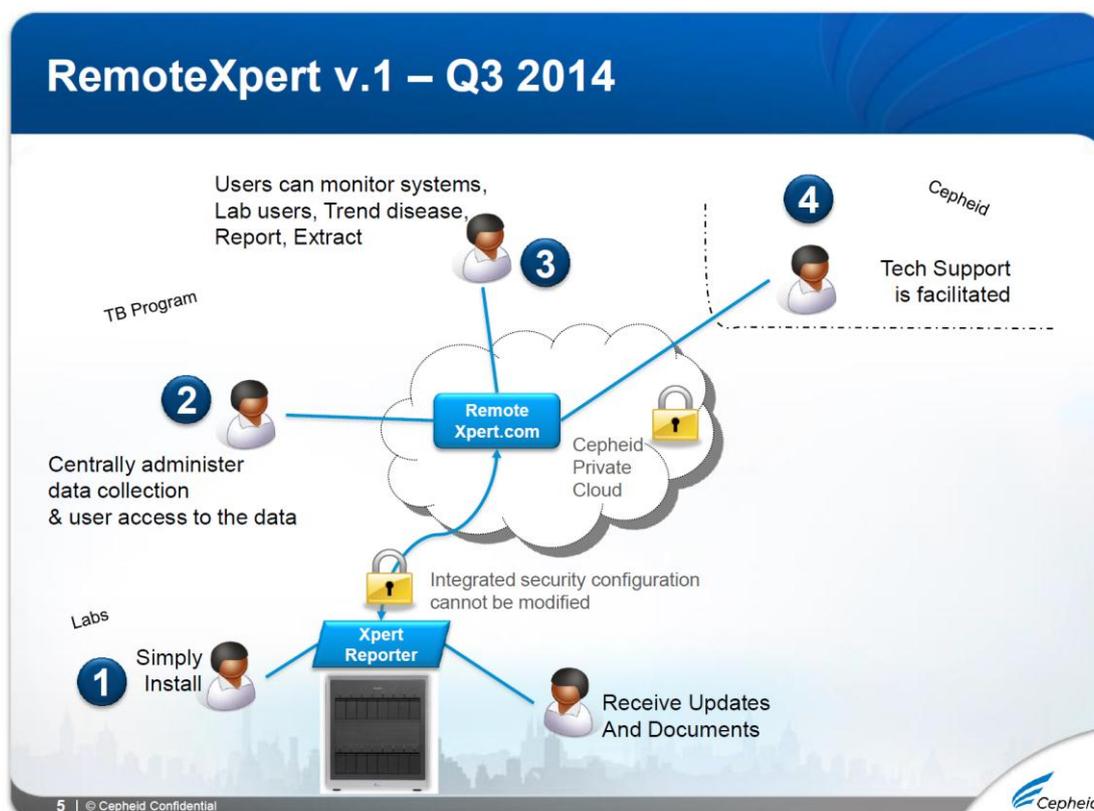
#### [Cepheid – RemoteXpert program](#) (presented by Martin Colla)

Cepheid's RemoteXpert program is being developed to allow for the remote monitoring of how many tests are being performed, to identify system or user training issues, and to monitor disease / resistance treatment logistics. A pilot package is being tested by South Africa NHLS and FIND India. It allows for geographic disease trending, error trending per operator and module, aggregate reports per region, exporting of test results to Excel, control reporting for each GeneXpert, provides user access rights. There is pilot reporter software on the GeneXpert system, and a RUO web application.

Version 1 of RemoteXpert will be launched in Q3 2014. The platform will have the following features:

- Collects and aggregates test results from GeneXpert systems
- The customer controls what is collected and who can access
- Automated, requires minimal user action on the GeneXpert
- Provides historical and geographic trending
- Provides error trending
- Append data to test results (demographics, algorithm used, etc)
- Share data with authorized institutions (full or summary level)

- Data export for authorized users
- Tech support tools for most frequent cases (logs, test data, etc)
- Push document to GeneXpert system (user training)
- Supports GeneXpert system replacement or relocation to a different lab
- Remote upgrade of the Reporter application



**[Abt Associates: GxAlert](#) (presented by Jeff Takle)**

**[Interactive Health Solutions: XpertSMS](#) (presented by Aamir Khan)**

**[GenXchange in the Democratic Republic of Congo](#) (presented by Emmanuel André)**

GxAlert and Xpert SMS are open source software that:

- Centrally collects data to provide a real-time dashboard that displays rates of errors by machine, as well as cartridge supply by site to help prevent stockouts or expiry
- Can automatically send messages via SMS or email (including by USB modem) to clinicians informing them of results and/or to patients informing them of availability of results
- Can provide real-time test results, stratified by numerous variables, including reason for testing (patient group) if indicated in the comments field, age, sex, etc.
- Can store data either in external servers (GxAlert or XpertSMS server) or on a national-based server, depending on MOH preference

Specific details can be received about GxAlert by contacting Jeff Takle ([Jeff\\_Takle@abtassoc.com](mailto:Jeff_Takle@abtassoc.com)) and about XpertSMS by contacting Ali Habib ([ali.habib@irdresearch.org](mailto:ali.habib@irdresearch.org)).

GenXchange was presented as a customized open source software developed for the Democratic Republic of Congo to remotely monitor machine performance by site and automatically send messages via SMS to

patients and clinicians. It has allowed the programme to target centres with high rates of errors or dysfunctional modules for troubleshooting. The software can also monitor various pre-analytical indicators by linking to the lab register, including the time between microscopic analysis and Xpert MTB/RIF testing or patient-related data such as history of TB, age, sex, etc. Data are stored locally on the GeneXpert laptop. Anonymized database is then continuously uploaded in an external server. More information can be received on this experience by contacting Emmanuel André ([emmanuel.andre@uclouvain.be](mailto:emmanuel.andre@uclouvain.be)).

Costs for electronic recording & reporting systems (including RemoteXpert, GXAlert, RemoteXpert and GenXchange) vary and can include modems, connectivity, installation and data hosting costs.

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### **Connected Diagnostics "Interoperability through Standards" (presented by Tobias Broger)**

WHO and the International Telecommunications Union have been working to improve the standardization of electronic health (eHealth) solutions, including the compatibility between systems ("interoperability") and advocating to graduate pilot projects to full-scale interventions (see [http://www.itu.int/pub/D-STR-E\\_HEALTH.05-2012](http://www.itu.int/pub/D-STR-E_HEALTH.05-2012)). As a result, Ministries of Health have started to develop national eHealth strategies. However these strategies now need to be operationalized and implementation manuals and other tools will be needed for service providers and programme staff. There are several things which need to happen. End-users need to start envisioning how eHealth could help them in their day-to-day activities; to reach interoperability of eHealth systems it is critical at this point in time to start large scale implementation of widely-accepted eHealth standards before further isolated eHealth pilots occur; freely available application programming interfaces (API) can help manufacturers and eHealth providers to define how their systems need to interact with each other; in the long-term an eHealth system-testing and certification programme is required to ensure interoperability, scalability, sustainability and patient rights like privacy.

In-country implementers can play an active part in the process by implementing diagnostic systems and eHealth solutions that are in line with the national eHealth strategy, think about the different information technology requirements across diseases and health conditions, provide FIND with the specific requirements and scenarios, and implement diagnostic systems and eHealth solutions that employ widely-accepted standards that enable connection with other eHealth systems. Manufacturers and eHealth/mHealth providers can take part in the development of the API and the selection of the appropriate interface and terminology standards, test the interoperability of the system/application and implement the API. Policymakers should promote global eHealth standards and promote the development of eHealth certification and accreditation schemes.

## SESSION 5: Expanding access (Chair: Fuad Mrzayev)

### [The critical role of technical assistance in expanding access to Xpert MTB/RIF: MSH's experience in 5 countries in Sub-Saharan Africa](#) (presented by [Alaine Nyaruhirira](#))

MSH has provided short technical assistance for implementation and scale-up of Xpert MTB/RIF in 5 sub-Saharan African countries. This support has included providing technical assistance to develop scale-up plans, increase awareness of global policy guidance, supporting training (including sensitization of medical doctors, nurses and other health care workers) and installation in collaboration with Cepheid, support development of QA systems and mechanisms for troubleshooting and maintenance, and support development of tools to monitor the consumption and procurement of cartridges.

Challenges encountered that targeted technical assistance can overcome include:

- Countries do not use the WHO checklist of prerequisites as a guide to assess readiness and appropriateness of selected sites for placement of GeneXpert. As a result, epidemiological data is not used to make correct decisions on placement and optimization of machine use, case finding practices of clinicians are not aligned to the recommended use of Xpert MTB/RIF, correct supplies and transport are not available, proper specimen referral systems are not implemented, and power outages interrupt use of Xpert MTB/RIF.
- Lack of MoH/NTP leadership, resulting in poor coordination of donors and partners, and differing algorithms and referral systems. Some countries purchase machines and cartridges without having first made an implementation plan and budget.
- WHO policies and accompanying materials are not adequately disseminated in countries
- Linkages between Xpert MTB/RIF test results, and other technologies and treatment are not always assured. This can result in rifampicin-resistant cases not always being linked to treatment, and not having follow-up culture and DST.

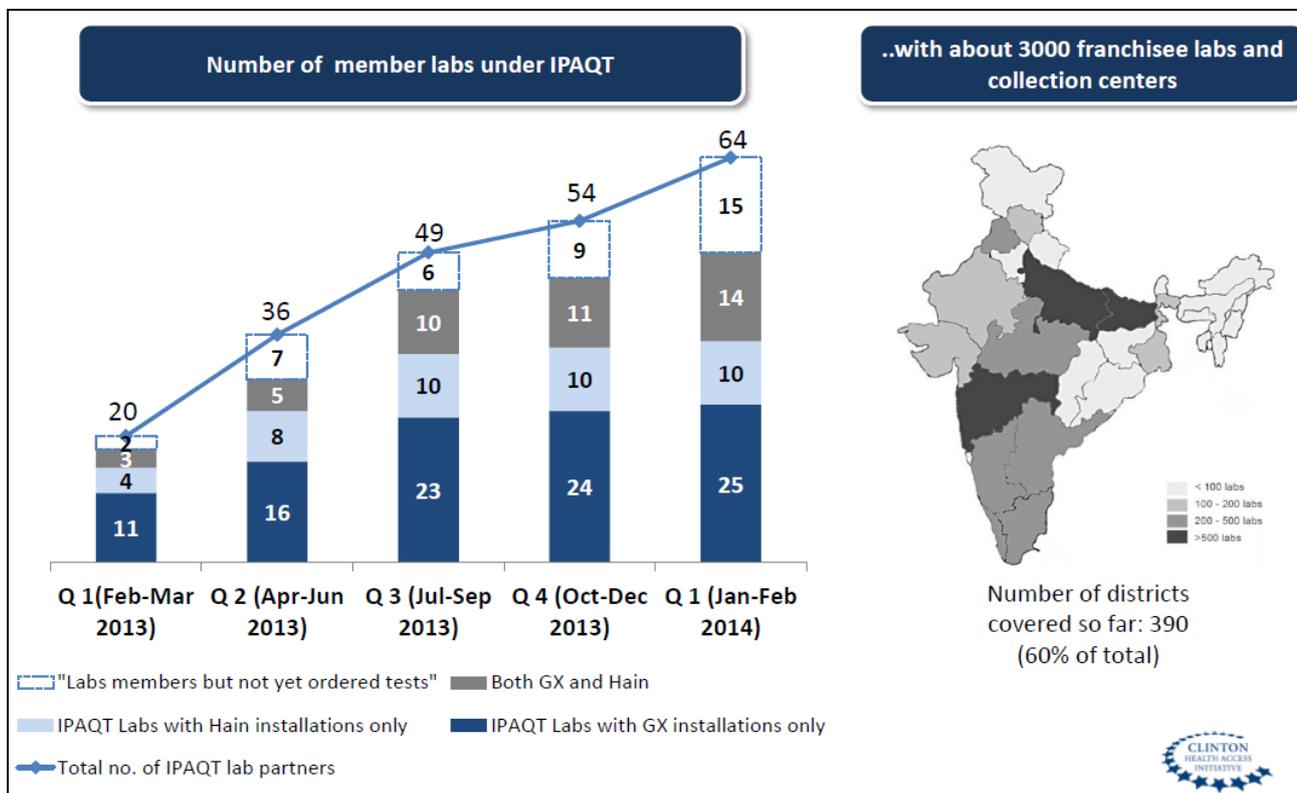
Introduction of Xpert MTB/RIF requires funding for strong technical assistance, and support during implementation is also required to monitor progress and impact on case detection, PMDT and TB/HIV integration. Countries must plan and budget for technical assistance, ensure a TB lab strategic plan is developed with an integrated and budgeted Xpert MTB/RIF roll-out plan, and coordinate donors' and partners' financial and technical support. WHO/GLI needs to ensure an efficient mechanism for disseminating Xpert MTB/RIF guidance and accompanying materials, and support is needed for countries to customize the WHO implementation manual for local use.

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### [IPAQT – Initiative for Promoting Affordable & Quality TB Tests](#) (presented by [Harkesh Dabas](#))

TB diagnosis in India is characterized by private sector dominance despite a strong national TB programme. The private healthcare market is complex and layered, and the diagnostic market ranges from accredited large lab networks to non-accredited small local labs. Poor testing practices abound, including use of serology and in-house PCR tests.

IPAQT provides private labs with access to quality tests at lower prices, allowing patients to access affordable quality diagnostics and better treatment through the public sector. The RNTCP benefits from gaining access to data on positive cases in the private sector for treatment follow-up. Only WHO/RNTCP-approved tests are included in IPAQT, all member labs must undergo periodic EQA, and only accredited labs may join. The partners labs charge patients below a ceiling price for the technologies, currently including Xpert MTB/RIF, Hain LPA and MGIT. All stakeholders in the value chain have agreed to drop their margins, translating into lower prices for the TB patient.

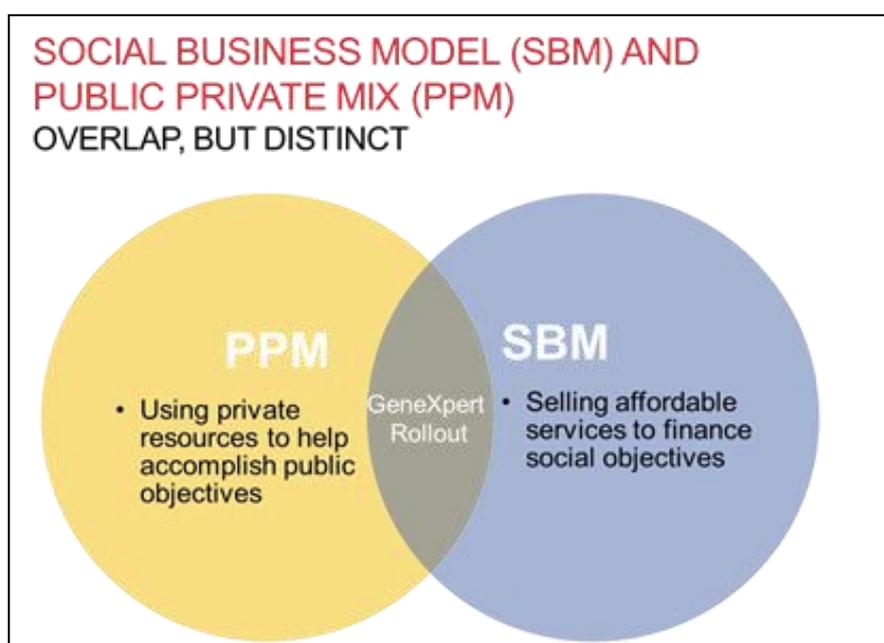


The number of member labs has grown, and included 64 labs as of Q1 2014, covering about 3,000 franchisee labs and collection centers in 390 districts across India. Linkages to treatment need to be ensured, to ensure MDR cases are followed up by state TB teams, and those patients opting for public sector treatment are initiated on DOTS plus treatment. Under IPAQT, it is estimated that the fraction of the market able to afford an Xpert MTB/RIF test has increased from 3.7% to 15%. However, in order to address the infirmities in diagnosis and treatment in the private sector at scale, stakeholders need to deliberate and institute more market-based sustainable solutions; further, since the private sector caters to close to 15% of the global burden, access to affordable diagnostics is a critical must. Towards that end, interventions such as a volume-based subsidy to labs private laboratories or public sector leveraging the reach of these laboratories to improve access to affordable quality tests need to be explored could further increase the fraction of the market.

More information on IPAQT is available at: [www.IPAQT.org](http://www.IPAQT.org)

### Establishment of social business models using Xpert MTB/RIF in three Asian megacities: TBXpert and TB REACH projects (presented by Aamir Khan)

The social business models developed by IRD aim to scale Xpert MTB/RIF testing by providing free Xpert MTB/RIF testing and treatment to patients seeking care in the private sector, while ensuring sustainability by generating revenue through adjunct tests and services. The projects are focused on lung health and diabetes- not just TB- and engage GPs, hospital OPDs, private laboratories and public hospitals. The projects have fully integrated digital radiology and automated chest X-ray reading, automated reporting of TB results to programme managers, screeners and doctors, glucometers and HbA1C, desktop spirometry, and other tests. The social business model price for diagnostic and treatment services (USD 5) covers a lease-to-own X-ray machine, screener incentives, screening center operations, GP treatment incentives, mobile phone data system, and profit for reinvestment.



The experience with development and implementation of social business models has found:

- Mass screening permits high utilization of GeneXpert modules and rapid increases in case-notification
- Moderate-risk, high-gain investments in social business models for the private sector have the potential to be sustainable and to improve standards of lung health and diabetes care
- Social business models have been acceptable to government programs (NTPs)
- Approach based upon incremental experience gained through TB REACH investments in private sector
- Investments focused on the public health system miss large numbers of patients in the private sector

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### Getting to Zero TB deaths: a patient centered approach to diagnosis (presented by Colleen Daniels)

Funding for R&D for TB diagnostics is grossly insufficient, linkages should be strengthened between researchers and developers, as there is still a crucial need for point-of-care tests.

A patient-centered approach entails accurate diagnosis leading to rapid treatment initiation, active management of co-morbidities and symptoms, and follow-up to ensure adherence and cure. It ensures access to care, strong systems of care and support, empowering patients and sustainability.

