Scaling Up Xpert MTB/RIF as Part of HIV Care: Progress, Challenges, and the Way Forward?

Heather Alexander, PhD
TB/OI Unit Lead, International Laboratory Branch

19th Core Group Meeting of the Global TB/HIV Working Group
11-12 February 2014
XPERT MTB/RIF SCALE UP:
PROGRESS
Global Implementation Landscape

Q1 2011
- 23 countries
- 99 GeneXpert instruments
- 524 modules

Q3 2013
- 95 countries
- 1843 GeneXpert instruments
- 9625 modules
Global Scale-Up

Cumulative number of GeneXpert instrument modules and Xpert MTB/RIF cartridges procured under concessional pricing

Data provided by FIND
2013 Revised WHO Definitions and Reporting Framework

- Revised forms and registers
- Bacteriological confirmation rather than smear-positivity
- Revised definitions to be used by WHO in 2014 for 2013 data
Xpert MTB/RIF for the diagnosis of pulmonary TB and RIF resistance in adults and children

- Xpert MTB/RIF **should be used** rather than conventional microscopy, culture and DST as the initial diagnostic test in **adults** presumed to have MDR-TB or HIV-associated TB (strong recommendation, high-quality evidence)

- Xpert MTB/RIF **should be used** rather than conventional microscopy, culture and DST as the initial diagnostic test in **children** presumed to have MDR-TB or HIV-associated TB (strong recommendation, very low-quality evidence)
October 2013 Policy Update

Xpert MTB/RIF for the diagnosis of extrapulmonary TB and RIF resistance in adults and children

- **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)
Interpretation of Test Results

- **WHO Xpert MTB/RIF implementation manual. Technical and operational ‘how-to’: practical considerations. 2nd Ed.**

  - In groups with high risk of MDR-TB
    - MTB detected; R resistant
      - WHO recommended regimen for MDR-TB with H; Registration as RR-TB
      - DST to at least H; Quinolones; SL injectable
    - Repeat Xpert MTB/RIF
      - MTB detected; R resistant
      - Modify MDR-TB treatment based on the DST results; Update registration
      - MTB detected; R sensitive
      - WHO recommended regimen for MDR-TB with H; Registration as RR-TB
      - DST to at least R; H; Quinolones; SL injectable
      - Modify MDR-TB treatment based on the DST results; Update registration
    - MTB not detected
      - WHO recommended first-line treatment; Registration as bacteriologically confirmed TB
      - If TB still suspected
        - Further investigation (CXR, repeat Xpert MTB/RIF, culture, etc.)
      - In case of discordance on R result, refer sample for sequencing

* Done on a fresh sample. If LPA is available at the site and sample is smear positive, LPA can be used for the repeated testing

* WHO Xpert MTB/RIF implementation manual. Technical and operational ‘how-to’: practical considerations. 2nd Ed.
XPERT MTB/RIF SCALE UP: CHALLENGES
Challenges with TB/HIV Diagnostic Evaluation

• One patient two parallel care systems
  ▪ Limited dialogue among TB clinics, HIV clinics, and laboratories
  ▪ Inadequate tracking of referred patients

• Inadequacies in recording & reporting systems
  ▪ TB and HIV systems do not communicate
  ▪ HIV M&E does not capture TB screening/ diagnostic cascade

• Limitations of current TB/HIV indicators
  ▪ Monitor only TB screening and TB treatment initiation
  ▪ Measuring delays in the diagnostic cascade requires additional resources (i.e., special studies)
  ▪ TB treatment initiation influenced by multiple factors and difficult to interpret
Laboratory Testing is One Component of Diagnostic Cascade

Pre-laboratory:
- Symptom Identification
- Specimen Collection
- Specimen Transport

Laboratory:
- Laboratory Testing

Post-laboratory:
- Result Transmission
- Treatment Initiation
Introduction and Scale-Up are Multi-Phase Processes

- Coordinate Stakeholders
- Develop Implementation Plan and Revise Tools
- Prepare Testing Sites and Network
- Procurement and Inventory Management
- Training and Installation
- Supervision and Quality Assurance
- Monitoring and Evaluation/Revise Strategy
Initial Testing Algorithms Focused on Presumptive MDR TB Cases

Xpert MTB/RIF testing at 9 sites in Nigeria (January – December 2012)

XPERT MTB/RIF SCALE UP:
WAY FORWARD
Coordination Among Ministries of Health, Donors, and Partners

- Implementation efforts led by national TB and HIV programs
- Prevent overlap in planned support
- Identify gaps in systems and support
- Facilitate linkage to and retention in treatment and care
- Facilitate sustainability
- Share tools, innovations, and best practices
Priority Areas for Support and Technical Assistance

- Coordination with national TB and HIV program staff, partners, and donors
  - Through national Xpert MTB/RIF advisory groups
- Selection and prioritization of testing sites
  - Emphasis on high-burden HIV care and treatment facilities
- Revision of algorithms, registers, and reports
- Strengthening specimen referral networks
  - Leveraging investments in CD4, VL, and EID networks
- Comprehensive quality assurance programs
- Systems for timely reporting of results
- Monitoring and evaluation
  - To assess programmatically-relevant and patient-important outcomes
  - To inform future decision making and policies
GLI Xpert MTB/RIF Training Package Roll-Out

- 12 module workshop-in-a-box
- CDC, Cepheid, FIND, TB CARE I, USAID, WHO collaboration
- Pilots in progress
- GLI endorsement anticipated mid-2014
Point of Care Testing for Reduced Time to Treatment?

* Theron Lancet 2014
Integrated Sample Referral Networks for Hub-Based Testing

* Slide Credit: Moses Joloba, Uganda SRL
Comprehensive Quality Assurance Programs to Ensure Accurate Results

Xpert MTB/RIF Quality Assurance Cycle

- SOPs, Registers, Report Forms
- Instrument Verification
- Training Materials and Competency Assessments
- Routine Maintenance Tasks
- Corrective Action/Quality Improvement
- External Quality Assessment (EQA)
Tools for Linking TB and HIV Program Data, Real-Time Result Reporting, and M&E
Summary

• Unprecedented collaborative efforts to date
• Funding changes will facilitate further coordination
• Complexity of diagnostic cascades present implementation challenges
• Implementation approaches must be tailored to local context
• New tools and innovations hold promise for addressing key hurdles
• Systems strengthening will lay the foundation for introduction of additional new diagnostic tests
• The role of robust monitoring and evaluation systems cannot be overestimated