Xpert MTB/RIF Implementation: Results, Impact and Lessons Learned for the Next Generation of Tests

Advanced TB Diagnostic Research
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Outline

• Background on TB REACH
• Rationale for using Xpert MTB/RIF
• Xpert in TBR-supported projects
• Impact of Xpert on TB case detection
• M&E and DR-TB
• Conclusions
Why TB REACH?

New and Relapse TB Case Notifications Since 2008

![Bar chart showing notified, estimated, and prevalence cases from 2008 to 2012.](chart.png)

- **Notified**
- **Estimated**
- **Prevalence**

Transforming the Fight
TOWARDS ELIMINATION OF TUBERCULOSIS
TB REACH

- Promotes **early** and **increased** TB case detection using **innovative** approaches
  - Especially in poor, underserved & vulnerable
- Supported by Canada (UNITAID for Waves 3 & 4)
- Administered by the Stop TB Partnership
- Provides grants to projects selected on a competitive basis
- External M&E using project and NTP data
- Provides programmatic evidence introducing new approaches in different settings
4 Funding Waves 46 Countries
142 Grants and over 90 Million USD Committed

51 Projects reporting Xpert testing data
Reaching the Missed Cases

- Active TB
- Infection
- Exposure
- Patient recognizing symptoms
- Accessing care
- HW recognizing symptoms
- TB Diagnosis
- Treatment and notification

Better Diagnostics
SS+TB increased 36.9% in intervention areas and decreased 3.6% in control populations.

Slightly higher number of additional cases for all forms TB.
Using Xpert to Improve Case Detection
Xpert General Results

• Data from 51 projects
• Data reported to TB REACH through March 31, 2014
• 386,263 tests performed
• Programmatic evidence in a variety of settings

*Results from early programmatic implementation of Xpert MTB/RIF testing in nine countries*

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*BMC Infectious Diseases 2014, 14:2*
Xpert Placement

- Mobile vans
- Chest camps
- Private labs
- Prisons
- ART centers
- Health centers
- District hospitals
- Reference labs
- Private clinics
Testing Algorithms

- All with symptoms
- All HIV+
- All SS- (some using LED Mx)
- SS- with suggestive CXR
- SS- and HIV+
- All with abnormal/suggestive CXR
- Seriously ill, hospitalized
• Maximize throughput?
• Increase % yield?
• Conserve tests?
• Improve Turn-Around-Time?
• Detect Rif Res?
• POC test?
Xpert Test Results

• Highly heterogeneous
• Detected 48,705 MTB+ individuals
• Overall Crude Positivity 12.6%
• Rif Resistant 6,215 (1.7% of individuals tested)
  – Range per quarter (0-14.2%) - Median 0.9%
• Failed test Rate 7.9%
  – Decreasing (5.9% in last quarter) but variable
  – Range - project/quarterly (1.2-28.4%) - Median 6.9%
Cartridges and Calibration

• Biggest problem so far is expired tests
  – Restrictive algorithms, poor planning
  – Customs clearance – and storage
  – Sharing tests among sites is being done
• Failed tests have a large cost, tracking user stats and error codes is critical, sputum quality
• Calibration compliance has improved but still not 100%
• Vast variations in module failure (5-100%)
  – Depends on infrastructure, location, dust, electricity?
Automated Reporting

- Test with a computer
- Delivers rifampicin resistance results
- Increasingly decentralized
- Many partners supporting
- Short shelf life of cartridges
- Potential – and need for networked machines and reporting
- Current Cepheid system is difficult (terrible) for informing programs
Automated Reporting
What Happened?
Recoding and Reporting

• As more machines are placed in service, recording and reporting becomes more challenging
• Paper systems are cumbersome, slow and error-prone
• Automated reporting systems are needed – with useful data
• Important to link test/lab and clinical data
Xpert Impact on TB Notifications
Two Case Studies

DRC
• Covering 15 facilities and 7 more with referrals
• Algorithm: 3 SSM Neg -> Xpert

Nepal
• Covering 9 districts and 9 more with referrals
• Algorithm: 3 SSM Neg -> CXR Sug -> Xpert
Quarterly B+ Case Notifications with Xpert MTB/RIF Introduction, Kinshasa

<table>
<thead>
<tr>
<th>Year</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
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<td>2013</td>
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</tbody>
</table>

Evaluation pop

Control pop

TB REACH Begins
DRC and Xpert

• ~45% of people eligible were tested with Xpert
• 8,770 Xpert tests – 1,254 MTB+
  – 140 Rif+
• 24% improvement on B+ cases on treatment
• 51% of results were returned during the same day
• ~25% of patients received results 3 or more days after sputum collection
• Intervention area All forms increased 6% while in the control areas increased 13%
Nepal: Historical pTB Notifications

![Graph showing historical pTB notifications in Nepal with notations for T1 to T14 and trend SS+]

- Historical SS+
- Historical Trend SS+
pTB Notification - new reporting system

Notified Patients

- Bac+
- Bac-
- Xpert MTB+ Patients
Historical pTB Notifications

![Historical pTB Notifications Graph](image)
pTB Notifications

Notified Patients

- All pTB
- Bac+
- Xpert MTB+ Patients
pTB Notifications

Notified Patients

- All pTB
- Bac+
- Bac-
Nepal Summary

- 9,723 tests performed
  - 1,878 MTB+ tests including
  - 123 Rif Resistant results
- 1,530 (81.5%) were enrolled on treatment in intervention areas
- 21% increase in B+ notifications
- Proportion of B+ among pulmonary TB increased from 66% -> 86%
- However – no impact overall on people on ATT
Programmatic M&E for Xpert

• Different systems, algorithms are found within same areas - inhibits proper monitoring of impact

• TB REACH projects were among first implementers in many countries – guinea pigs
  – Steep learning curve
  – Restrictive algorithms

• No standard recording and reporting
  – Yield is easy (% positive)
  – Tracking patients is hard (linking to treatment)
Basic Indicators to Monitor

A. Number of people eligible for screening
B. Number of people screened
   • Proportion of people screened among those eligible (B/A)
C. Number of suspected TB patients identified
   • Proportion of people suspected TB patients identified among those screened (C/B)
D. Number of people tested/evaluated for TB disease
   • Proportion of people tested/evaluated for TB among suspected patients (D/C)
E. Number of people diagnosed with TB and
   • Proportion of people diagnosed among those screened (E/B) and tested (E/D)
F. Number of patients initiated on treatment
   • Proportion of people initiated on treatment among those diagnosed (F/E)
G. Number of patients successfully completing treatment
   • Proportion among those initiated (G/F)
Basic Indicators to Monitor

- Quarterly number of diagnostic tests conducted (historical and prospective)
- Quarterly historical and prospective disaggregated notification data (SS+, Bac+, SS-, EPTB)
- Quarterly cohort treatment outcomes
Xpert and DR-TB

• Clearly a possible game changer for improving detection
  – Impact on mortality? Treatment outcomes?
  – Scale up for MDR is a clear global and country priority but…
  – Need smart testing strategies – and…
• Links to DST and treatment are a challenge
• Treatment capacity, drugs, as well as laboratory capacity are still issues
• Cost?
A Note on Costs

• Not 9.98 USD
• Costs include machine and tests +, +, +
  – Port clearance, infrastructure, warranty, training, maintenance, reporting, transport networks
• How many tests do you do a year per machine?
• How many machines do you have?

<table>
<thead>
<tr>
<th>Country</th>
<th>Retreatment Cases</th>
<th>HIV+ TB Inc (Est)</th>
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<tbody>
<tr>
<td>DRC</td>
<td>7,492</td>
<td>16,000</td>
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<tr>
<td>Ethiopia</td>
<td>4,089</td>
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<tr>
<td>Nigeria</td>
<td>7,548</td>
<td>46,000</td>
</tr>
</tbody>
</table>

Running 500 tests a year costs you easily 60 USD per test in year one

Most machines are not running at full capacity (or even near it)
Testing Strategies for DR-TB

Retreatment Patients:
- 20% of All DR-TB Patients

New Patients:
- 3.6% of All DR-TB Patients
- 30% Retreatment
- 70% New
Conclusions

• Many lessons learned for next generation of rapid tests
• Training – automated reporting - and good algorithms are critical
• NTPs need to be able to access useful data that may not always be RCTs
• Lab interventions alone are unlikely to increase number of people put on TB treatment - unless it allows greater access than SSM
• Who are we missing? People in or outside of health care system?
• Adjunct strategies are needed to test more people to increase case detection
Thank You!