Xpert MTB/RIF: Evidence, WHO Policy Recommendations and Roadmap

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Assoc Prof, Dartmouth and Medical Scientist, FIND
Partnering for better diagnosis for all
Disclosure

• I have no personal financial conflict of interest to disclose. However, I contract for FIND, which has a contractual relationship with Cepheid
• This agreement calls for FIND to support development work and undertake studies of Cepheid’s TB diagnostic assay
• In turn, Cepheid is to provide their tests at favorable prices to the public sector in developing countries
• Thanks to C Boehme, CN Paramasivan, L Sundaram and M Perkins at FIND and K Weyer for slides
• Thanks to CORE Group
TB: Major Cause of Suffering and Death

- First human case 3400 BC
- Consumption, White Plague, scrofula, King’s Evil, pthisis
- England 1815: 1 in 4 deaths
- France 1918: 1 in 6 deaths
- During 20thC, TB killed ~100 million
- In 2009, estimated 9.4 million incident cases, and 1.68 million deaths
Timothy Cratchit aka Tiny Tim

- Tiny Tim known based on invalid son of Dicken’s friend
- 1997 Excavation at St. Andrew’s Church found 19C gravesite
- “In Memory. Timothy Cratchit. 1839–1884, Beloved Husband of Julia, Father of Robert, and Son of Robert and Martha.”
- Skeletal remains of 40yo man wearing metal frame and leather on legs and back
- PCR confirmed TB*

*CW Callahan. JID 1997;176:1653–4
Evolution of TB diagnostics in the public sector
Evolution of TB diagnostics in the public sector

Fundamental diagnostic: 1882
Evolution of TB diagnostics in the public sector

Fundamental diagnostic: 1882

Fundamental diagnostic: 2010
The Slow Road to Microscopy Diagnosis of TB

Threshold for visibility of AFB by smear microscopy

Number of TB bacilli per millilitre (mL) of sputum

- Infection of healthy patient
- Patient visits clinic: no diagnosis made
- First smear: AFB negative
- Blood appears in sputum; infant daughter infected with TB

Patient feels unwell
Night cough begins
Cough worsens: patient returns to clinic

Too weak to work

Patient returns to clinic

AFB+: TB diagnosis made

first month second month third month fourth month fifth month
About FIND

Vision is of a world where everyone will have equitable access to high quality diagnosis.

Mission is to drive the development and implementation of accurate and affordable diagnostic tests that are appropriate to patient care in low-resource settings.
Simple Standards for New TB Diagnostics

- Higher sensitivity than microscopy
  - >85% true positive rate
  - Not impaired by HIV
- Comparable specificity to microscopy
  - >95% true negative rate
- Limited additional workload
- Practicability of use in the field
**FIND’s Focus in Value Chain**

**Upstream**
- Liaise with funders, pharmaceutical and biotech companies, research institutions, academia

**FIND’s focus**
- Development
- Evaluation
- Demonstration
- WHO policy, market access and distribution

**Downstream**
- Liaise with funders, multi-lateral agencies, NGOs, health ministries, and agencies like GDF and GFATM

**Development**
- Proof of principle
- Facilitate, co-fund, co-develop

**Evaluation**
- Product in box
- Regulatory-quality lab & field trials
- Efficacy Data

**Demonstration**
- Large-scale projects measuring feasibility & impact on disease control programs
- Effectiveness Data

**WHO Policy**
TB Diagnostic Testing at Different Levels of Health System

Types of testing | Health system levels | Fraction of patients seen at given level
---|---|---
Surveillance, Reference methods, Network supervision | National reference laboratory | 5%
Resolution testing (current test: culture, drug-susceptibility) | Referral laboratory | 10%
Passive case finding (current test: microscopy), Detect and treat | Microscopy centre | 25%
Screening, Primary care (current test: none) | Peripheral health clinic | 60%
New Technologies for Reference Level

- Automated liquid culture and DST
  - WHO endorsement 2007
- Rapid species identification
  - WHO endorsement 2007
- Line-probe assays for MDR TB
  - WHO endorsement 2008
- Noncommercial culture and DST
  - MODS and Colour Test
  - WHO policy July 2010
New Technologies for Microscopy Level

- iLED fluorescent microscopy
  - WHO endorsement 2009
  - Policy July 2010
- Manual DNA detection
  - LAMP (in evaluation)
- Automated DNA detection
GeneXpert MTB/RIF

- Automated, real-time molecular diagnostic
  - PCR technology
  - Simultaneous detection of TB and rifampicin resistance
- Simple process depends on acquiring sputum
- 100 min to result
- No need for biosafety cabinet
  - For use at district and sub-district
- Modular system
  - Cartridges for other diseases
From Bench to Bedside

- WHO Expert Group assessment: 1 Sept 2010
- STAG-TB evaluation: 27 Sept 2010
- WHO Global Consultation: 30 Nov-2 Dec 2010
- WHO Policy announcement: 7 Dec 2010
How Does Xpert MTB/RIF Work in the Lab?
Simple Sample Processing – Direct Sputum

1. Add 2:1 Sample Buffer to sample
2. Shake then stand 10 minutes
3. Shake then stand further 5 minutes
4. Transfer 2ml to cartridge
   Begin Test…
GeneXpert

Xpert
MTB/RIF

5  20  80  Samples per shift  500-1000
Xpert MTB/Rif Molecular Beacon Assay

The PCR target is the 81 bp region of the rpoB gene: 5 probes bind to wildtype, but not mutant target.

Each probe is labeled with a different fluorescent dye, permitting simultaneous detection.

Example of Rif-Sensitive Profile – 5 probes & SPC show fluorescence.
The Evidence for Xpert MTB/RIF
### Multicenter Evaluation Study

- 5 reference laboratories with high quality gold standard
- Geographically diverse populations
- 1,730 patients suspected of pulmonary TB or MDR-TB (4,386 samples)

#### Countries

<table>
<thead>
<tr>
<th>Country</th>
<th>HIV</th>
<th>TB (C+)</th>
<th>MDR TB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peru</td>
<td>2%</td>
<td>61%</td>
<td>7%</td>
</tr>
<tr>
<td>South Africa</td>
<td>Cape Town</td>
<td>77%</td>
<td>Durban</td>
</tr>
<tr>
<td></td>
<td>TB (C+)</td>
<td>39%</td>
<td>MDR TB</td>
</tr>
<tr>
<td></td>
<td></td>
<td>13%</td>
<td>9%</td>
</tr>
<tr>
<td>Azerbajan</td>
<td>HIV</td>
<td>5%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TB (C+)</td>
<td>42%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MDR TB</td>
<td>31%</td>
<td></td>
</tr>
<tr>
<td>India</td>
<td>HIV</td>
<td>5%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TB (C+)</td>
<td>60%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>MDR TB</td>
<td>67%</td>
<td></td>
</tr>
</tbody>
</table>
**Single, Direct Xpert:**

**Performance Similar to Solid Culture**

<table>
<thead>
<tr>
<th>Site</th>
<th>TP</th>
<th>FP</th>
<th>FN</th>
<th>TN</th>
<th>Sensitivity in C+ (95 CI)</th>
<th>Specificity in C- (95 CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lima, Peru</td>
<td>201</td>
<td>0</td>
<td>8</td>
<td>101</td>
<td>96 (93-98)</td>
<td>100 (96-100)</td>
</tr>
<tr>
<td>Baku, Azerbaijan</td>
<td>123</td>
<td>1</td>
<td>24</td>
<td>68</td>
<td>84 (77-89)</td>
<td>99 (92-100)</td>
</tr>
<tr>
<td>Cape Town, SA</td>
<td>136</td>
<td>1</td>
<td>10</td>
<td>185</td>
<td>93 (88-96)</td>
<td>99 (97-100)</td>
</tr>
<tr>
<td>Durban, SA</td>
<td>36</td>
<td>3</td>
<td>7</td>
<td>215</td>
<td>84 (70-92)</td>
<td>99 (96-99)</td>
</tr>
<tr>
<td>Mumbai, India</td>
<td>179</td>
<td>0</td>
<td>8</td>
<td>35</td>
<td>96 (92-98)</td>
<td>100 (90-100)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>675</td>
<td>5</td>
<td>57</td>
<td>604</td>
<td><strong>92 (90-94)</strong></td>
<td><strong>99 (98-100)</strong></td>
</tr>
</tbody>
</table>

**Patient group**

<table>
<thead>
<tr>
<th></th>
<th>Single LJ</th>
<th>Single MGIT</th>
<th>Single, direct Xpert</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smear-positive, Culture-positive</td>
<td>93.0% (1016/1092)</td>
<td>97.7% (1104/1130)</td>
<td>98.2% (551/561)</td>
</tr>
<tr>
<td>Smear-negative, Culture-positive</td>
<td>69.3% (205/296)</td>
<td>84.4% (276/327)</td>
<td>72.5% (124/171)</td>
</tr>
<tr>
<td>All Culture-positive</td>
<td>88.0% (1221/1388)</td>
<td>94.7% (1380/1457)</td>
<td>92.2% (675/732)</td>
</tr>
</tbody>
</table>
Rifampicin Resistance Detection: Performance Similar to Phenotypic Standard

<table>
<thead>
<tr>
<th>Site</th>
<th>TP</th>
<th>FP</th>
<th>FN</th>
<th>TN</th>
<th>Sensitivity (95 CI)</th>
<th>Specificity (95 CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lima, Peru</td>
<td>16</td>
<td>3</td>
<td>0</td>
<td>190</td>
<td>100</td>
<td>98</td>
</tr>
<tr>
<td>Baku, Azerbaijan</td>
<td>47</td>
<td>4</td>
<td>2</td>
<td>90</td>
<td>96</td>
<td>96</td>
</tr>
<tr>
<td>Cape Town, SA</td>
<td>15</td>
<td>0</td>
<td>1</td>
<td>126</td>
<td>94</td>
<td>100</td>
</tr>
<tr>
<td>Durban, SA</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>38</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Mumbai, India</td>
<td>119</td>
<td>3</td>
<td>2</td>
<td>61</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Total</td>
<td>200</td>
<td>10</td>
<td>5</td>
<td>505</td>
<td>98 (94-99)</td>
<td>98 (96-99)</td>
</tr>
</tbody>
</table>

- Compared to sequencing: 99% sens, 100% spec
- 98% of RIF resistant cases were confirmed MDR-TB
# Implications of Rifampicin Resistance Testing According to Prevalence

<table>
<thead>
<tr>
<th>% RMP Resist</th>
<th>TP</th>
<th>FP</th>
<th>FN</th>
<th>TN</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>1%</td>
<td>9.5</td>
<td>19.8</td>
<td>0.5</td>
<td>970.2</td>
<td>32.4%</td>
<td>99.9%</td>
</tr>
<tr>
<td>5%</td>
<td>47.5</td>
<td>19</td>
<td>2.5</td>
<td>931</td>
<td>71.4%</td>
<td>99.8%</td>
</tr>
<tr>
<td>10%</td>
<td>95</td>
<td>18</td>
<td>5</td>
<td>882</td>
<td>84.1%</td>
<td>99.4%</td>
</tr>
<tr>
<td>15%</td>
<td>142.5</td>
<td>17</td>
<td>7.5</td>
<td>833</td>
<td>89.3%</td>
<td>99.1%</td>
</tr>
</tbody>
</table>

- Due to high spec, NPV >99% in settings with both high and low RMP resistance
- In low RMP resistance settings, PPV is reduced
  - Careful risk assessment in patients
Operational Considerations of Xpert MTB/RIF
Multicenter Implementation Studies

- 9 settings of intended use in 6 countries
  - District/sub-district (3), microscopy centers (3), MDR screening/ER (3)
  - Diverse lab conditions (temp up to 42C, space, staff background)
  - 7000 TB or MDR-TB suspected patients screened from diverse populations

<table>
<thead>
<tr>
<th>Location</th>
<th>Country</th>
<th>HIV</th>
<th>TB (C+)</th>
<th>MDR TB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baku</td>
<td>Azerbaijan</td>
<td>6%</td>
<td>47%</td>
<td>22%</td>
</tr>
<tr>
<td>Vellore</td>
<td>India</td>
<td>&lt;1%</td>
<td>10%</td>
<td>7%</td>
</tr>
<tr>
<td>Lima</td>
<td>Peru</td>
<td>3%</td>
<td>17%</td>
<td>8%</td>
</tr>
<tr>
<td>Cape Town</td>
<td>South Africa</td>
<td>77% (K), 30% (P)</td>
<td>26%</td>
<td>4%</td>
</tr>
<tr>
<td>Manila</td>
<td>Philippines</td>
<td>&lt;1%</td>
<td>20%</td>
<td>54%</td>
</tr>
<tr>
<td>Kampala</td>
<td>Uganda</td>
<td>100%</td>
<td>42%</td>
<td>2%</td>
</tr>
<tr>
<td>Manila</td>
<td>Philippines</td>
<td>&lt;1%</td>
<td>20%</td>
<td>54%</td>
</tr>
</tbody>
</table>
Partners and Study Design

**Lima, Peru**
- INS
- NTP / DISA IV Lima Este
- Instituto A. v. Humboldt
- UPCH

**Manila, Philippines**
- Lung Institute
- TDF
- CDC

**Cape Town, South Africa**
- MOH / NTP
- NHLS
- MSF
- UCT

**Vellore, India**
- Central TB Division
- Community Health Dep.
- Christian Medical College

**Kampala, Uganda**
- NRL
- Makerere University
- Mulago Hospital
- University of California

**Baku, Azerbaijan**
- MOH
- MOJ
- STI/Main Medical Dep.

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**Validation Phase**
- 1 Xpert added to routine examinations;
- Culture / DST added as reference standard;
- Patient management on smear/culture;

**Implementation Phase**
- Patient management on Xpert

**Continuation Phase**
- Culture dropped
# Operational Performance and Robustness

<table>
<thead>
<tr>
<th>Variable</th>
<th>Performance / outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indeterminate rate</td>
<td>2.5% and 0.3% after repetition. Culture indeterminate rate 4.7%</td>
</tr>
<tr>
<td>DNA contamination events</td>
<td>None observed (swabs, neg controls)</td>
</tr>
<tr>
<td>Operating and short term storage temperature</td>
<td>High lab temperature = no effect on performance</td>
</tr>
<tr>
<td>Training needs</td>
<td>2 days for non-experienced lab techs</td>
</tr>
<tr>
<td>User appraisal</td>
<td>Less difficult than microscopy; user friendly; user-independent read-out</td>
</tr>
</tbody>
</table>
Considerations for Implementation

<table>
<thead>
<tr>
<th>Variable</th>
<th>Performance / outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preventive maintenance</td>
<td>Annual calibration (logistics and costs)</td>
</tr>
<tr>
<td>Storage</td>
<td>2-28°C; cartridges require substantial storage space</td>
</tr>
<tr>
<td>Electrical supply and back-up power</td>
<td>power outage reported; uninterruptable power supply with UPS (400 VA) for 20 min. Serial car batteries tested</td>
</tr>
<tr>
<td>Biosafety requirements</td>
<td>Same as smear microscopy*</td>
</tr>
<tr>
<td>Waste management</td>
<td>As for sputum containers; additional waste volume compared to smear microscopy</td>
</tr>
</tbody>
</table>

Current Temperature Recommendations

• Recommended cartridge storage temp 2-28°C
• Max recommended operating temp 30°C
  – If exceeds by 5-10°C
    o Module becomes unavailable for use
    o Any test in process is reported as ERROR
• Once temperature drops to recommended returns to normal function
• Investigating extending temperatures
  – Note similar or lower temperature requirements for tests currently in use for other diseases
Current Negotiated Prices for ~150 Countries

- Capital costs > microscopy lab but < culture lab
  - GeneXpert GXIV-4 configuration $17,000-$17,500
- MTB/RIF test costs > than single microscopy test
  - Per cartridge is $16.86
  - Cost of culture/drug susceptibility testing similar to Xpert MTB/RIF test
- Annual calibration and maintenance $1,400
- Xpert MTB/RIF implementation likely cost-effective for NTPs*
  - Prices ≤ tests such as HIV viral load or CD4+ that have been successfully rolled out

*Amsterdam Institute of Global Health and Development
## FIND-negotiated prices for estimated volumes

### Forecasted per-test cost for FIND markets

<table>
<thead>
<tr>
<th></th>
<th>FIND-negotiated price</th>
<th>FIND-negotiated price</th>
<th>FIND-negotiated price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated annual global volumes (cartridges)</td>
<td>&gt; 600,000</td>
<td>&gt;1,700,000</td>
<td>&gt;3,700,000</td>
</tr>
<tr>
<td>Estimated year</td>
<td>2011</td>
<td>2012</td>
<td>2014</td>
</tr>
<tr>
<td>Price (Ex Works)</td>
<td>US$ 16.86</td>
<td>US$ 14.00</td>
<td>US$ 10.72</td>
</tr>
<tr>
<td>Ave % reduction over EU*</td>
<td>75%</td>
<td>79%</td>
<td>84%</td>
</tr>
</tbody>
</table>

*Average cost per cartridge in EU €50
FIND-negotiated maintenance and calibration costs (approximate)

Standard: one-year warranty; 24-hour hotline and e-mail support

**Scenarios for after-sales service, support, maintenance and calibration**

<table>
<thead>
<tr>
<th></th>
<th>Model 1: Cepheid Toulouse</th>
<th>Model 2: Distributor</th>
<th>Model 3: NTP staff</th>
<th>Model 4: Web-based</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Estimated year</strong></td>
<td>Now</td>
<td>Now</td>
<td>2012</td>
<td>2014</td>
</tr>
<tr>
<td><strong>Calibration (4 modules)</strong></td>
<td>US$ 1,400</td>
<td>US$ 1,400</td>
<td>US$ 1,000</td>
<td>US$ 500</td>
</tr>
<tr>
<td><strong>Description</strong></td>
<td>In Toulouse (requires 2 shipments: site-Toulouse)</td>
<td>Local distributor basis (requires 2 local shipments: site-distributor)</td>
<td>On-site (no swap out)</td>
<td>Remotely, using a calibration kit (no swap out)</td>
</tr>
<tr>
<td><strong>Shipment (4 modules)</strong></td>
<td>US$ 400</td>
<td>US$ 200</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>US$ 1,800</strong></td>
<td><strong>US$ 1,600</strong></td>
<td><strong>US$ 1,000</strong></td>
<td><strong>US$ 500</strong></td>
</tr>
</tbody>
</table>
Rapid Implementation and Roll-out of Xpert MTB/RIF
WHO Expert Group Review

Findings

- Test accuracy high, single test detecting 91% of culture-confirmed TB patients (99% smear-pos and 80% smear-neg), unaffected by HIV. R resistance detected with 95% sensitivity and 98% specificity;

- Time to detection <1 day, compared to 17 days (liquid culture); >30 days (solid culture); >75 days (phenotypic DST). Smear-negative TB patients started Rx after 4 days vs 58 days when Xpert not used;

- TB and MDR-TB case detection significantly increased, cost-comparison favourable to phenotypic culture and DST; cost-effectiveness highest when used as add-on to microscopy, but impact highest when used as initial diagnostic test in high-risk groups;

- Operational findings confirmed robustness, safety, minimal training needs, high user satisfaction. Relatively stable power supply, security against theft, annual validation, adequate storage capacity and waste disposal management required.

Courtesy: Dr. Karin Weyer
## WHO Expert Group Meeting: Grade Summary

<table>
<thead>
<tr>
<th>Xpert MTB/RIF</th>
<th>Absolute difference per 1000 persons</th>
<th>Quality of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-test prevalence 10%</td>
<td>TP 92</td>
<td>TN 891</td>
</tr>
<tr>
<td>TB detection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R detection</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Overall quality of evidence: Moderate

Desirable vs undesirable effects: Highly favourable

Patient values and preferences: No data

Cost and requirements: Moderate cost

Added value to conventional methods: Significant

Courtesy: Dr. Karin Weyer
WHO Expert Group Recommendations

1. Xpert MTB/RIF should be used as the initial diagnostic test in individuals suspected of having MDR-TB or HIV-associated TB (strong recommendation)

2. Xpert MTB/RIF may be used as a follow-on test to microscopy where MDR and/or HIV is of lesser concern, especially in smear-negative specimens (conditional recommendation, recognising major resource implications)

Courtesy: Dr. Karin Weyer
WHO Expert Group Recommendations (continued)

- **Recommendations also apply to children**, based on generalisation of data from adults and acknowledging the limitations of microbiological diagnosis of TB (including MDR-TB) in children;

- **Access to conventional microscopy, culture and DST is still needed** for monitoring of therapy, for recovering isolates for drug susceptibility testing other than rifampicin (including second-line anti-TB drugs); and for prevalence surveys and/ or surveillance;

- **Recommendations apply to the use of Xpert MTB/RIF in sputum specimens** (including pellets from decontaminated specimens), as data on the utility of Xpert MTB/RIF in extra-pulmonary specimens are still limited;

- **Recommendations support the use of one sputum specimen** for diagnostic testing, acknowledging that multiple specimens increase the sensitivity of Xpert MTB/RIF but have major resource implications.
Figure 1. Selection of individuals to test with Xpert MTB/RIF based on risk assessment

A. Individuals at risk of MDR-TB
- Diagnosed with TB or
- Suspected of having TB

B. HIV (+) individuals (or HIV unknown in high HIV settings) suspected of having TB

Primary considerations

Secondary considerations

Individuals accessing health centre

Xpert MTB/RIF

TB, Rif resistance
- Enrol on MDR-TB regimen
  - DST FLD and SLD
  - ART if HIV +

TB, no Rif resistance
- Treatment regimen based on patient history
  - ART if HIV +

No TB detected
- Appropriate further clinical management
  - IPT if HIV +
Collecting Evidence for Scale up

Operational research agenda:

1. Cost and cost-effectiveness of the algorithms in different epidemiological and risk settings
2. Additional yield, sensitivity, specificity, and predictive values
3. Impact on treatment and patient management
4. Impact on access to care by different socio-economic groups
5. Performance of Xpert MTB/RIF in remote and peripheral settings
6. Performance of Xpert MTB/TB in extra-pulmonary and paediatric TB
7. Models to engage the private sector and strengthen linkages with national TB programmes
Moving forward

WHO endorsement 2010

- Global Consultation
- WHO Policy Guidance
- Roadmap for implementation

Phased implementation 2011

- Through EXPAND-TB, TBREACH, TBCARE, PEPFAR
- Selected countries, different health service levels

Scale up 2012

- EXPAND-TB, Global Fund R11, TBREACH, TBCARE, PEPFAR, country budgets, etc
Mission Accomplished?
Does it Meet the Simple Standards for New Diagnostic?

- “Higher sensitivity than microscopy”
  - For TB, performance similar to culture
  - For RIF-res, sensitive and specific

- “Comparable specificity to microscopy”

- “Limited additional workload”

- “Practicability of use in the field”
TB Diagnostic Testing at Different Levels of Health System

<table>
<thead>
<tr>
<th>Types of testing</th>
<th>Health system levels</th>
<th>Fraction of patients seen at given level</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Surveillance</td>
<td>National reference laboratory</td>
<td>5%</td>
</tr>
<tr>
<td>• Reference methods</td>
<td>Referral laboratory</td>
<td>10%</td>
</tr>
<tr>
<td>• Network supervision</td>
<td>Microscopy centre</td>
<td>25%</td>
</tr>
<tr>
<td>• Resolution testing</td>
<td>Peripheral health clinic</td>
<td>60%</td>
</tr>
<tr>
<td>(current test: culture, drug-susceptibility)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Passive case finding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(current test: microscopy)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Detect and treat</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Screening</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Primary care</td>
<td></td>
<td></td>
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<tr>
<td>(current test: none)</td>
<td></td>
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</tr>
</tbody>
</table>
New Point-of-Care Technologies

• Antigen detection
  – LAM
  – Volatile organic compounds
• Antibody detection
FIND Strategic Evolution

Prioritize problems
- Disease-centered approach
  - Smear positive
  - Smear negative
  - DST
  - Latent TB infection

Co-invest with industry on existing technologies

Prioritize technologies
- Patient-centered approach
  - Integrated molecular platforms
    - Liquid culture - DST
    - Line-probe assay
    - Automated molecular detection
    - Manual DNA amplification

Identify / select platforms with potential for integration

Prioritize solutions
- People-centered approach
  - Community-based
    - Health centers
    - District level
    - Regional lab
    - Reference lab

Translate platforms into Point-Of-Care solutions

Decentralize technologies at community level and institutionalize approach

60%

5%

35%

malaria HIV HAT TB STD M&C care

TB

malaria
HAT
EID/HIV
Leish

TB

viral load

Integrated molecular platforms
Summary

- Improved TB diagnosis is cornerstone of TB control
- Effective use of new technologies requires
  - Demonstration at program level
  - Implementation at appropriate level of healthcare system
  - Continued commitment toward people-centered approach to reach those most in need