Role of network optimisation to achieve 95-90-0 for MTB disease elimination: Scaling up testing

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Tuberculosis
Snapshot through 2020

Recorded Stats:

- Second most infectious killer in the world
- Over 1.5 million deaths per year
- Over 10 million new cases
- Over 1.9 billion people with Latent TB infection
- Over 815,000 co-infected patients
- Over 214,000 HIV patients died with TB coinfection

Additional Information:

- 3 out of 4 new cases in SEA (44%) or Africa (25%)
- 2021 World Health Organization Global Tuberculosis Report
- 57% of those treated were treated successfully
- COVID-19 may lead to additional 6.3 million TB cases between 2020-25

Impact of COVID on TB services
Programmes are re-thinking the diagnostic future post-pandemic

Advocates from global fund eligible countries reported resources for people with TB being diverted to respond to COVID-19

Reported people with TB to be facing significant challenges accessing treatment and care

Newly diagnosed patients fell from 7.1 million in 2019 to 5.8 million in 2020

Policy and program officers reported healthcare facilities to be reducing TB services during the pandemic

Diagnosis and screening FELL OVER 40% due to Covid-19 Disruptions

Diagnosing tuberculosis is multi-faceted and complex

Managing respiratory diagnosis

Multiple progression pathways make tuberculosis challenging to diagnosis

- Clinical phases influenced by predisposing factors and access to care
- Imaging, smear, culture and PCR commonly used in combination with physician diagnosis

Esmail et al Philos Transact Royal Soc 2014

Traditional raw sputum sample collection is challenging for some patients

- Swab studies to evaluate alternative sample types ongoing
- Goal to reach more patients with an easier to collect, transport and process sample
WHO Guidelines to Support Scale-Up
From treatment algorithms to diagnostic products

Expanding Testing Options Can Support Eradication Efforts

- Cross-Program testing can make all programmes more resilient to disruptions
- Investing in alternative sample types to reach more people
- Installation base already exists in urban areas for high volume testing

WHO operational hand book on Tuberculosis: Rapid diagnostics for TB detection
WHO Operational Handbook on Tuberculosis updated

New test options in the guidance

Table 2.1. New classes of technologies recommended and associated products evaluated

<table>
<thead>
<tr>
<th>Technology class</th>
<th>Products included in evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate complexity automated NAATs for detection of TB and resistance to rifampicin and isoniazid</td>
<td>Abbott RealTime MTB and Abbott RealTime MTB RIF/INH (Abbott)</td>
</tr>
<tr>
<td></td>
<td>BD MAX MDR-TB (Becton Dickinson)</td>
</tr>
<tr>
<td></td>
<td>cobas MTB and cobas MTB-RIF/INH (Roche)</td>
</tr>
<tr>
<td></td>
<td>FluoroType MTBDR and FluoroType MTB (Bruker/Hain Lifescience)</td>
</tr>
<tr>
<td>Low complexity automated NAATs for detection of resistance to isoniazid and second-line anti-TB agents</td>
<td>Xpert MTB/XDR (Cepheid)</td>
</tr>
<tr>
<td>High complexity reverse hybridization-based NAATs for detection of resistance to pyrazinamide</td>
<td>Genoscholar PZA-TB II (Nipro)</td>
</tr>
</tbody>
</table>
Lab ecosystems include a testing continuum

Network optimisation around systems built for specific environments creates service delivery efficiencies

Leveraging near-patient and POC solutions

Leveraging med-high throughput solutions

Molecular Dx can move closer to culture lab

Sample transport mechanisms in place / strengthened

Efficiently service larger populations while adding capacity
Scaling testing with a multiple partner approach
Supporting the creation of program dynamics with broader diagnostic options

**Dynamic flexibility for the program**

**Reduced risk of sole supplier**

**Benefit to patients in all settings**

**True Point of Care** (Rural)
- 10,000 sites
- 2 x 10,000 technicians

**Near Patient** (Hub & Spoke)
- 200 sites
- 3 x 200 technicians

**Urban/Peri-urban** (More populated areas)
- 10 sites
- 5 x 10 technicians

Samples can be reallocated to high volume laboratories during spikes in demand as well.

| Values are representative.

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Optimised Diagnosis - Three TB tests in the portfolio

**cobas® MTB**
Detects *M. tuberculosis* in raw and processed sputum using two selective sets of primers and two probes uniquely targeting separated regions (**dual-target** - 16S rRNA gene and esx genes esxJ, esxK, esxM, esxP, and esxW) with 86.6% smear-negative sensitivity.

**cobas® RIF/INH**
Designed as a reflex test together with cobas® MTB to detect Rifampicin-resistance associated mutations of the rpoB gene and Isoniazid-resistance associated mutations in the katG and inhA genes, of *M. tuberculosis* to enable rapid treatment optimization.

**cobas® MAI**
Duplex test designed to detect and differentiate *M. avium* and *M. intracellulare* DNA directly in respiratory specimens. Targets two prevalent species of the Mycobacterium avium complex (MAC) that are commonly associated with pulmonary nontuberculous mycobacterial disease.
Flexibility with three sample types

**Raw Sputum**
Un-processed sputum. Sometimes used for direct AFB smear.

**Sputum Sediment**
Sputum pre-treated by the NALC-NaOH method, which kills accompanying bacterial flora while keeping mycobacteria alive. Typically used for routine testing including AFB smear, culture verification and PCR.

**Bronchoalveolar Lavage (BAL) Sediment**
BAL pre-treated by the NALC-NaOH method, which kills accompanying bacterial flora while keeping mycobacteria alive.
One Patient sample, 1 pre-analytic treatment, 2 results

1 Patient Sample  
1 MIS treatment  
1 Sonication  
2 results

cobas MIS = microbial inactivation solution
Differential diagnosis to support clinical decisions

If patient presents with TB symptoms

[Diagram: Flowchart showing cobas® MTB followed by cobas® RIF/INH if positive, with an option for Reflex MDR testing]

Evaluate for drug resistance
Integrated RIF/INH testing to help identify MDR-TB

Global surveillance on MDR TB based on RIF resistance

About 8% of TB patients worldwide are estimated to have rifampicin susceptible, isoniazid-resistant TB (Hr-TB)

Globally, Hr-TB is more prevalent than MDR-TB. Efforts need to be made by all countries to move towards universal testing of both isoniazid and rifampicin at the start of TB treatment

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No extra sample
Same sample from cobas® MTB

No extra cost.
Included in the USD 9.90 Cobas MTB, reagents and consumables pricing model.*

*Pre-analytic instrument (sonicator) also included
# cobas® MTB test performance

Dual target MTB tests typically have approximately 85% smear-negative sensitivity

<table>
<thead>
<tr>
<th>Firm</th>
<th>Optimal Capacity per Run</th>
<th>MTB Smear Negative</th>
<th>LoD</th>
<th>Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roche cobas® MTB</td>
<td>94</td>
<td>86.6% (IFU)</td>
<td>7.6 – 8.8 CFU/mL (IFU)</td>
<td>MDR Same collection</td>
</tr>
<tr>
<td>Abbott m2000 MTB</td>
<td>94</td>
<td>81% (IFU)</td>
<td>17 CFU/mL (IFU)</td>
<td>MDR Depends</td>
</tr>
<tr>
<td>BD MAX MTB/XDR</td>
<td>24</td>
<td>81.5-85.1% (IFU)</td>
<td>20 CFU/mL (IFU)</td>
<td>MDR Same collection</td>
</tr>
<tr>
<td>Cepheid MTB/RIF Ultra</td>
<td>4 – 16</td>
<td>84% (+17%) (WHO publication)</td>
<td>16 CFU/mL (WHO publication)</td>
<td>MDR, XDR Depends</td>
</tr>
</tbody>
</table>

Note: Performance data is for information purposes only and cannot be directly compared because a head-to-head study was not done.
External publications for cobas® MTB
Demonstrated performance in sensitivity and accuracy in various contexts

- **FIND study assessed 4 platforms**
- **Roche has similar or lower LoD for MTBC compared to Xpert MTB/RIF**

- **Performance of MTB assay in high HIV burden settings (South Africa)**
- **cobas MTB sensitivity was unaffected by HIV coinfection**

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Margaretha de Vos et al.
Lesley Scott et al.
Nadarajan et al.

- **Performance evaluation**
- **Accurate detection of MTBC DNA and resistance-associated mutations in respiratory samples**
The new cobas® 5800 System to expand reach of testing

Compact footprint with flexible sample processing, integrated testing and full automation

Source: cobas® 5800 brochure
Supporting integrated testing & end to end solutions

Consideration for sample collection, transport to result return approaches customised for country needs

**Sample collection**
- Oral swabs* (MTB)
- Self collection* (HPV)
- cobas® Plasma Separation Card (HIV, HCV*)

**Disease management**
- HIV
- SARS-CoV-2
- HBV*, HCV*
- HPV*
- MTB*

**+LIS capabilities**
- HIV
- SARS-CoV-2
- HPV*
- MTB*
- HBV*, HCV*

**+ Capacity building initiatives to strengthen diagnostic systems**

*Under investigation and/or development; currently not part of claims
Roche experience, presence and commitment across Africa

Decades of support in scaling up HIV VL and EID programs can be leveraged to support TB programs

>450 Roche representatives across Sub Saharan Africa

Support network optimisation for TB programs to complement current approaches building capacity, scale and reach

Reduce risk for programs and laboratories creating more testing options and ability to integrate TB testing with existing systems

Support patient disease management (adherence for treatment success & MDR) with digital solutions (eg iThemba Life)

Create programs that are resilient and can scale to focus on sustainable TB eradication

Install base as of December 2021 which represents significant testing capacity
Beyond test performance to address challenges along the patient journey

End-to-end solutions to support sustainable programs and build local capacity

- **Inconvenience**
  - Few rural HCPs
  - Transport challenges

- **Sample Collection**
  - Stigma
  - Misinformation
  - Lack awareness

- **Laboratory Capacity & Efficiency**
  - Low automation
  - Lab inefficiency
  - Stock-outs

- **Healthcare Professionals Training**
  - Lack HCPs
  - Untrained HCPs
  - Medical Guidelines

- **Result Delivery**
  - Slow Turn-Around-Time
  - Loss follow up

- **Disease Management**
  - Lack counselling
  - Few Tx options

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Patient centered approach to improve health outcomes

HCP: Health Care Professionals, Tx: Treatment

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Partnering to support scale up of testing for TB elimination

End to end solutions and expanded diagnostic options support eradication efforts

An approach that strengthens the ecosystem for all

High impact program

- Optimized Dx networks: Near-patient & High volume testing
- More sample type options to reach more patients
- MDR testing for all who are TB positive
- iThemba supporting drug adherence and patient education
- Healthy people create strong economies
Doing now what patients need next