Supporting TB elimination: Advances towards delivering new diagnostics for LTBI
Setting the scene for LTBI diagnostics

Alberto Matteelli
University of Brescia, Brescia, Italy - WHO Collaborating Centre for TB/HIV and TB Elimination

NDWG Annual Meeting 2016
“Seedbeds of tuberculosis in the community”

William Osler

“Father of modern medicine”

1849-1919

LTBI, an emergent condition?
Managing LTBI: the backbone of ending TB

In some low-burden countries, reactivation accounts for about 80% of new cases of disease.

Fig. 2. Contribution of the three different types of infection to the total morbidity from pulmonary tuberculosis at ages 45-49 in the Netherlands from 1952 to 1967.

Sutherland Adv Tuberc Res 1976;19:1
## Evolution of global TB strategies

### 1994-2005

**The DOTS Strategy**
1. Government commitment
2. Case detection through passive case finding
3. Standardized chemotherapy to all sputum smear positive TB cases of under proper case management conditions
4. Establishment of a system of regular supply of anti-TB drugs
5. Establishment of a monitoring system, for programme supervision and evaluation

### 2006-2015

**The Stop TB Strategy**
1. Pursue high-quality DOTS expansion and enhancement
2. Address TB/HIV, MDR-TB and other challenges
3. Contribute to health system strengthening
4. Engage all care providers
5. Empower people with TB and communities
6. Enable and promote research

### 2016-2035

**The End TB Strategy**
1. Integrated, patient-centred TB care and prevention
2. Bold policies and supportive systems
3. Intensified research and innovation
Preventive treatment coverage
Number of people living with HIV and children who are contacts of cases who were started on preventive treatment for latent TB infection, out of all those eligible (%).

≥90%
Challenges to optimize the algorithm

Ask for any symptoms of tuberculosis in individuals from the risk groups*

Yes

No

TST or IGRA

Positive

Negative**

Chest radiography

TB and other disease investigations***

Any abnormality

No abnormality

Treat for LTBI

Optimize testing tools

Optimize exclusion of TB

Optimize treatment option
Tests and treat at-risk only or all those who are infected?

With current diagnostic tools most of those treated would not need it. Benefits and harms trade-out unfavourable

→ limit testing and treatment to high-risk groups and discourage mass testing and treatment
## Recommendations on at-risk populations

<table>
<thead>
<tr>
<th>Risk population groups</th>
<th>Strength of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>• People living with HIV&lt;br&gt;• Adult and child PTB contacts&lt;br&gt;• Patients initiating anti-TNF treatment&lt;br&gt;• Patients receiving dialysis&lt;br&gt;• Patients preparing for transplantation&lt;br&gt;• Patients with silicosis.</td>
<td>Strong: systematic testing and treatment should be performed (Low to very low quality of evidence)</td>
</tr>
<tr>
<td>• Prisoners&lt;br&gt;• Health workers&lt;br&gt;• Immigrants from high burden countries&lt;br&gt;• Homeless persons&lt;br&gt;• Illicit drug user</td>
<td>Conditional: Systematic testing and treatment should be considered (Low to very low quality of evidence)</td>
</tr>
<tr>
<td>• Patients with diabetes&lt;br&gt;• People with harmful alcohol use&lt;br&gt;• Tobacco smokers&lt;br&gt;• Under-weight people</td>
<td>Conditional: systematic testing and treatment is not recommended unless they belong in the upper two groups (Very low quality of evidence)</td>
</tr>
</tbody>
</table>
Tests and treat at-risk only or all those who are infected?

With current diagnostic tools most of those treated would not need it. Benefits and harms trade-out unfavourable.

- limit testing and treatment to high-risk groups and discourage mass testing and treatment
- reduce Number Needed to Treat by improving testing
- reduce treatment duration and side effects
LTBI Task Force of the NDWG
key objectives

Enhance the **knowledge** base and support **consensus-building** by engaging participation of key experts and stakeholders towards further development and finalization of:

- Concept document on diagnostic tests required to comprehensively accomplish LTBI management, including: a) a test for progression; b) a test of cure; c) a test for recent infection

- Target Product Profiles for a test of progression of latent tuberculosis infection

- A guide for the preparation of study design and protocols for testing the performance of assays targeting latent TB and progression from latent infection to active disease
## How will the Task Force support NDWG priorities and Global Plan targets?

<table>
<thead>
<tr>
<th>Objective</th>
<th>Deliverable</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Objective 1</strong></td>
<td>Ensure that the critical knowledge enabling the development of new diagnostic tools and solutions is available</td>
</tr>
<tr>
<td><strong>Objective 2</strong></td>
<td>Develop a portfolio of new diagnostic tools coupled with a package of accompanying solutions to ensure that results translate into patient treatment, with a focus on tests for prediction of the risk of disease progression</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# LTBI Task Force of NDWG established in December 2015

<table>
<thead>
<tr>
<th>First name</th>
<th>Name</th>
<th>Institution</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Coordinator</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alberto</td>
<td>Matteelli</td>
<td>University of Brescia</td>
<td>Italy</td>
</tr>
<tr>
<td><strong>Members</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gavin</td>
<td>Churchyard</td>
<td>Aurum Institute</td>
<td>South Africa</td>
</tr>
<tr>
<td>Frank</td>
<td>Cobelens</td>
<td>AIGHD / KNCV</td>
<td>The Netherlands</td>
</tr>
<tr>
<td>Claudia</td>
<td>Denkinger</td>
<td>FIND</td>
<td>Switzerland</td>
</tr>
<tr>
<td>Christopher</td>
<td>Gilpin</td>
<td>WHO</td>
<td>Switzerland</td>
</tr>
<tr>
<td>Delia</td>
<td>Goletti</td>
<td>INMI, Rome</td>
<td>Italy</td>
</tr>
<tr>
<td>Amita</td>
<td>Gupta</td>
<td>Johns Hopkins</td>
<td>United States</td>
</tr>
<tr>
<td>Sandra</td>
<td>Kik</td>
<td>KNCV</td>
<td>The Netherlands</td>
</tr>
<tr>
<td>Dick</td>
<td>Menzies</td>
<td>McGill</td>
<td>Canada</td>
</tr>
<tr>
<td>Christian</td>
<td>Lienhardt</td>
<td>WHO</td>
<td>Switzerland</td>
</tr>
<tr>
<td>Lele</td>
<td>Rangaka</td>
<td>University College London</td>
<td>UK</td>
</tr>
<tr>
<td><strong>Extended membership</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daniela</td>
<td>Cirillo</td>
<td>San Raffaele Scientific Institute</td>
<td>Italy</td>
</tr>
<tr>
<td>Alessandra</td>
<td>Varga</td>
<td>FIND</td>
<td>Switzerland</td>
</tr>
<tr>
<td>Susanna</td>
<td>Capone</td>
<td>University of Brescia</td>
<td>Italy</td>
</tr>
</tbody>
</table>
Stop TB Partnership

New Diagnostics Working Group

2nd Expert Workshop for the development of tests for progression of latent tuberculosis infection (LTBI) to active disease

1st July 2016

Organized by the New Diagnostics Working Group
Hosted by San Raffaele Hospital, Milan, Italy
Where are we now

- New evidence on the nature and significance of LTBI, and its relevant implications on the conceptualization of diagnostics
- Development of the Target Product Profile for a test of progression of LTBI
- Development of guidelines to design optimized studies that will produce data for policy evaluation

- Accepted in Lancet Respiratory Medicine
  *Lead author Frank Cobelens*
- Final round of revision
  *Lead authors Samuel Schumacher and Claudia Denkinger*
- Final round of revision
  *Lead authors Sandra Kik and Frank Cobelens*

Meeting hosted by WHO Geneva to finalize and endorse planned in early 2017.