



# 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*



Institute of Infectious and Tropical  
Diseases - University of Brescia



WHO Collaborating Centre for  
TB/HIV collaborative activities  
and for TB elimination

NDWG Annual Meeting 2016

## LTBI, an emergent condition ?

“Seedbeds of tuberculosis in the community”

William Osler

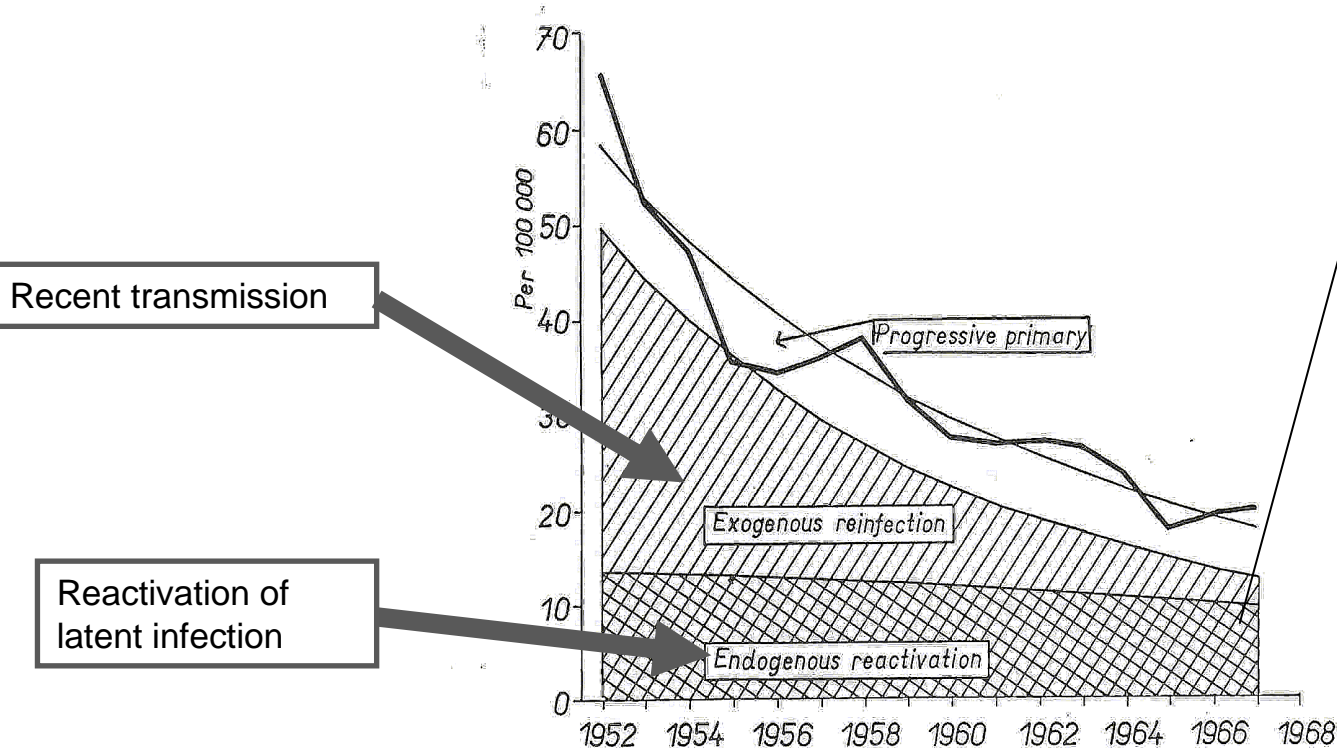
“Father of modern medicine”

1849-1919



# Managing LTBI: the backbone of ending TB

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.



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

Sutherland *Adv Tuberc Res* 1976;19:1  
Shea KM, *Am J Epidemiol.* 2014;179(2):216–225  
Heldal E, *Int J Tuberc Lung Dis.* 2000;4(4):300–307



# 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**

FRAMEWORK TOWARDS

**TB ELIMINATION**

IN LOW-INCIDENCE COUNTRIES

**Guidelines on the  
management of  
latent tuberculosis  
infection**

## **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 (%).

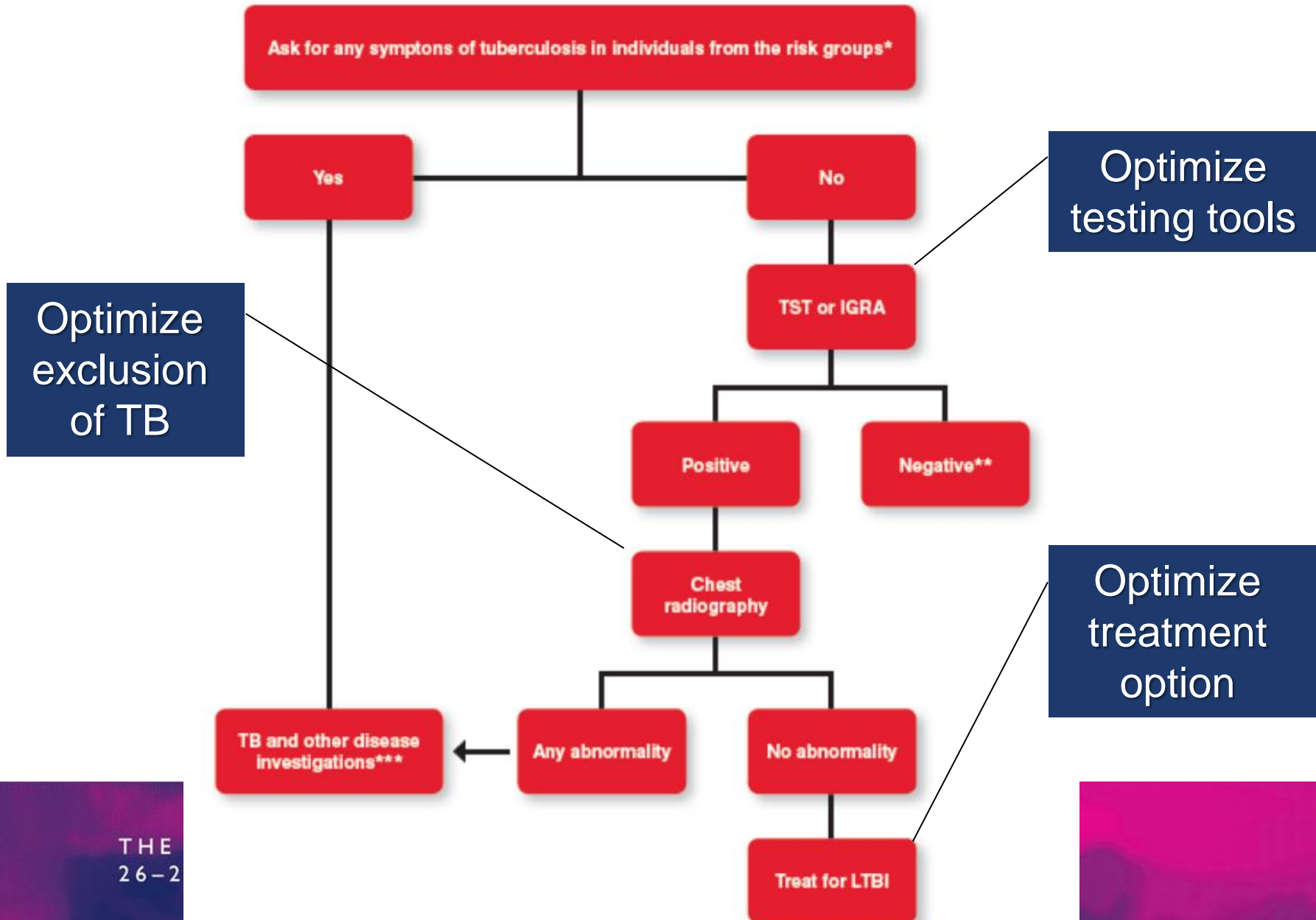
**≥ 90%**

**END TB**  
STRATEGY



World Health  
Organization

# Challenges to optimize the algorithm



# 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

Risk population groups	Strength of recommendation
<ul style="list-style-type: none"> <li>• People living with HIV</li> <li>• Adult and child PTB contacts</li> <li>• Patients initiating anti-TNF treatment</li> <li>• Patients receiving dialysis</li> <li>• Patients preparing for transplantation</li> <li>• Patients with silicosis.</li> </ul>	<b>Strong: systematic testing and treatment should be performed</b> <b>(Low to very low quality of evidence)</b>
<ul style="list-style-type: none"> <li>• Prisoners</li> <li>• Health workers</li> <li>• Immigrants from high burden countries</li> <li>• Homeless persons</li> <li>• Illicit drug user</li> </ul>	<b>Conditional: Systematic testing and treatment should be considered</b> <b>(Low to very low quality of evidence)</b>
<ul style="list-style-type: none"> <li>• Patients with diabetes</li> <li>• People with harmful alcohol use</li> <li>• Tobacco smokers</li> <li>• Under-weight people</li> </ul>	<b>Conditional: systematic testing and treatment is not recommended unless they belong in the upper two groups</b> <b>(Very low quality of evidence)</b>



# 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?

	Objective	Deliverable
Objective 1	Ensure that the critical knowledge enabling the development of new diagnostic tools and solutions is available	Develop a concept document on requirements for LTBI diagnostic tests
Objective 2	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	Produce a TPP for a test of progression
		Develop a guide for study design and protocols
		Scientific events organized at major tuberculosis conferences

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





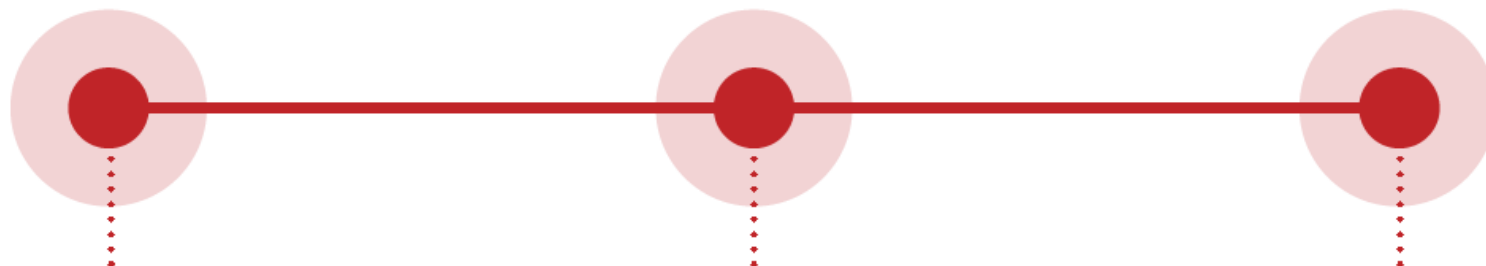
## New Diagnostics Working Group

**2<sup>nd</sup> Expert Workshop for the development of tests for progression of latent tuberculosis infection (LTBI) to active disease**

**1<sup>st</sup> 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

Accepted in Lancet Respiratory Medicine  
*Lead author Frank Cobelens*

development of the Target Product Profile for a test of progression of LTBI

Final round of revision  
*Lead authors Samuel Schumacher and Claudia Denkinger*

development of guidelines to design optimized studies that will produce data for policy evaluation

Final round of revision  
*Lead authors Sandra Kik and Frank Cobelens*

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