World Health Organization

END TB

Programmatic management of latent TB infection: Global perspective and updates

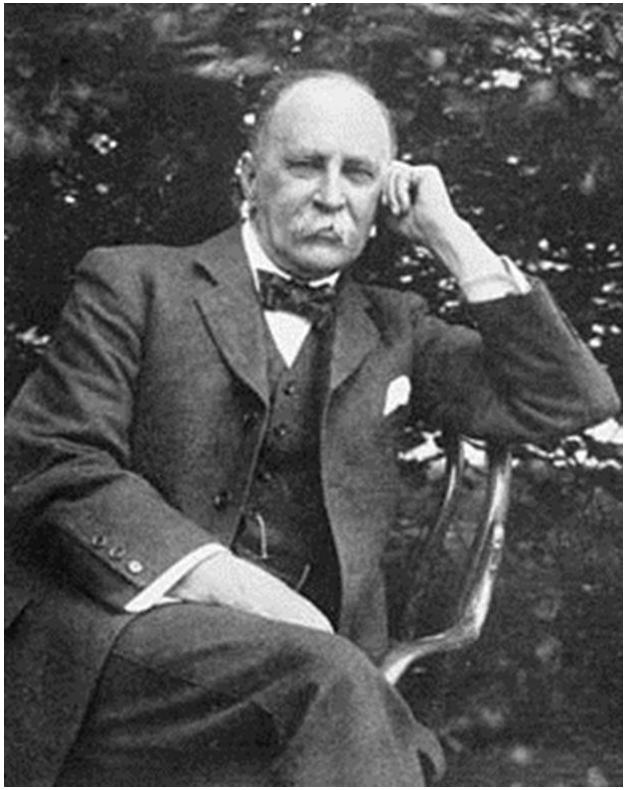
GLOBAL TB PROGRAMME

Haileyesus Getahun, MD, MPH, PhD.

What is latent TB infection?

A state of persistent immune response to stimulation by *Mycobacterium tuberculosis* antigens without evidence of clinically manifested active TB

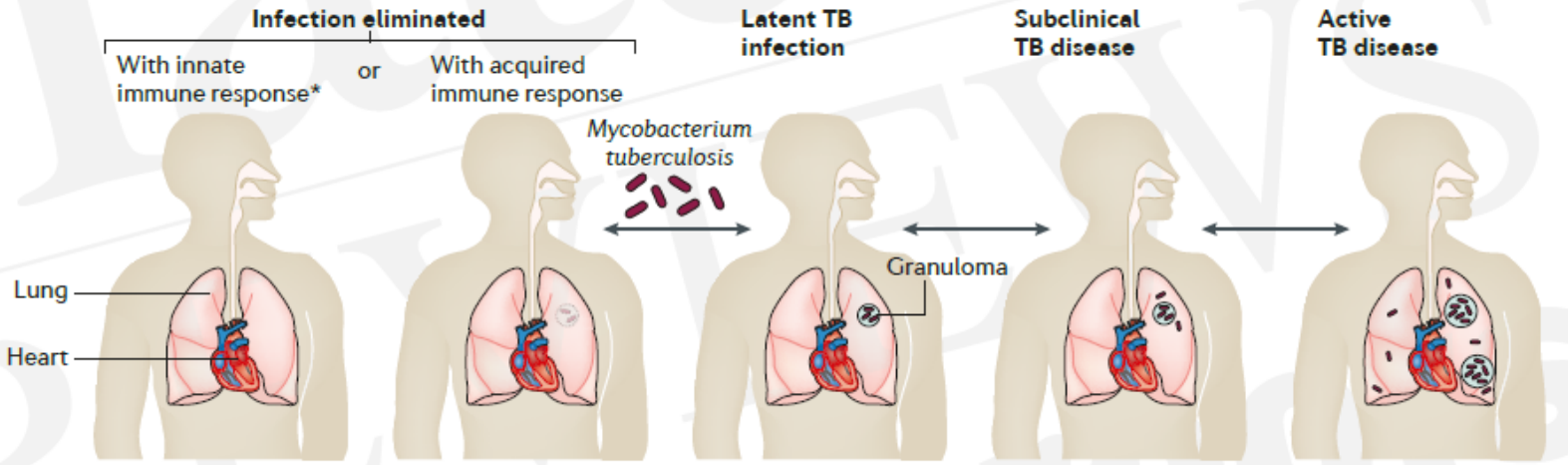
No gold standard test to diagnose LTBI



"Seedbeds of tuberculosis in the community"

William Osler

LTBI is part of Spectrum of TB disease

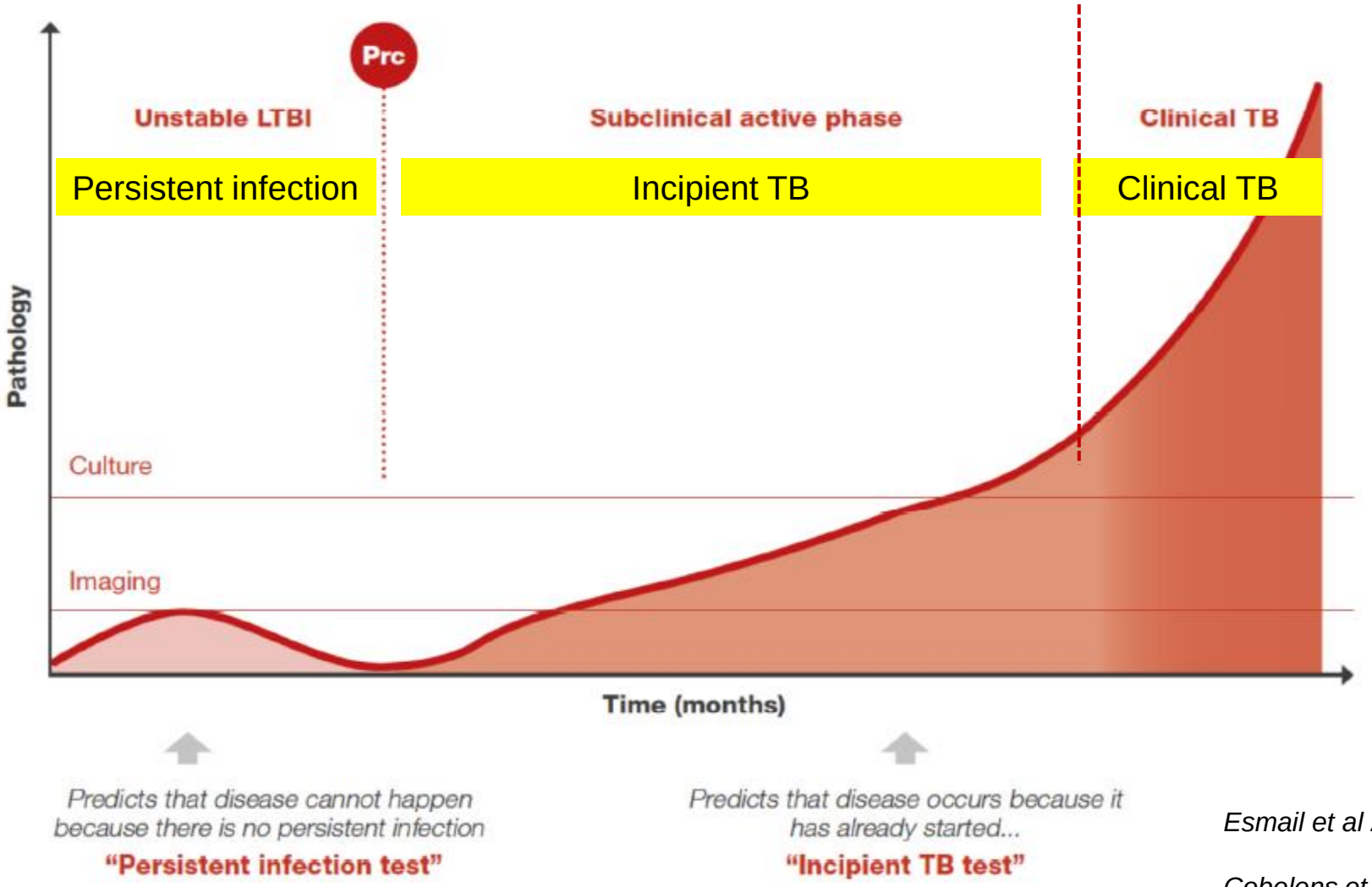


TST	Negative	Positive	Positive	Positive	Usually positive
IGRA	Negative	Positive	Positive	Positive	Usually positive
Culture	Negative	Negative	Negative	Intermittently positive	Positive
Smear	Negative	Negative	Negative	Usually negative	Positive or negative
Infectious	No	No	No	Sporadically	Yes
Symptoms	None	None	None	Mild or none	Mild to severe
Preferred treatment	None	None	Preventive therapy	Multidrug therapy	Multidrug therapy

Pai *et al* 2016

LTBI test concept: persistent infection and incipient TB

Figure 1. The postulated spectrum of TB infection and the progression to active TB disease
(adapted from Esmail *et al*. 2014)

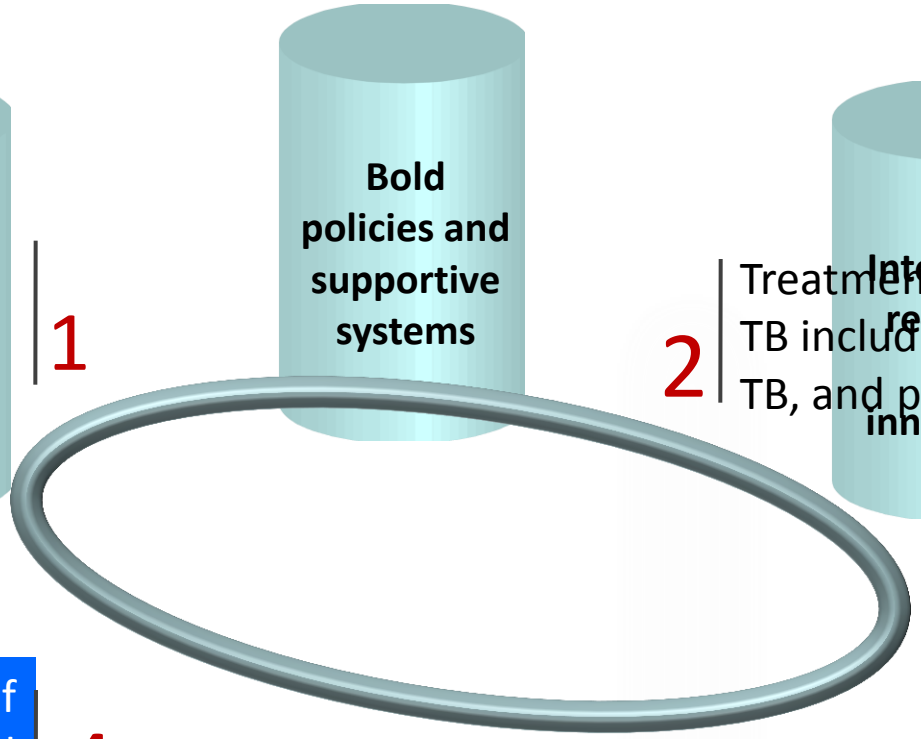


Esmail et al 2014

Cobelens et al 2016

WHO End TB Strategy

TARGETS: 90% reduction of deaths and 80% reduction in incidence by 2030



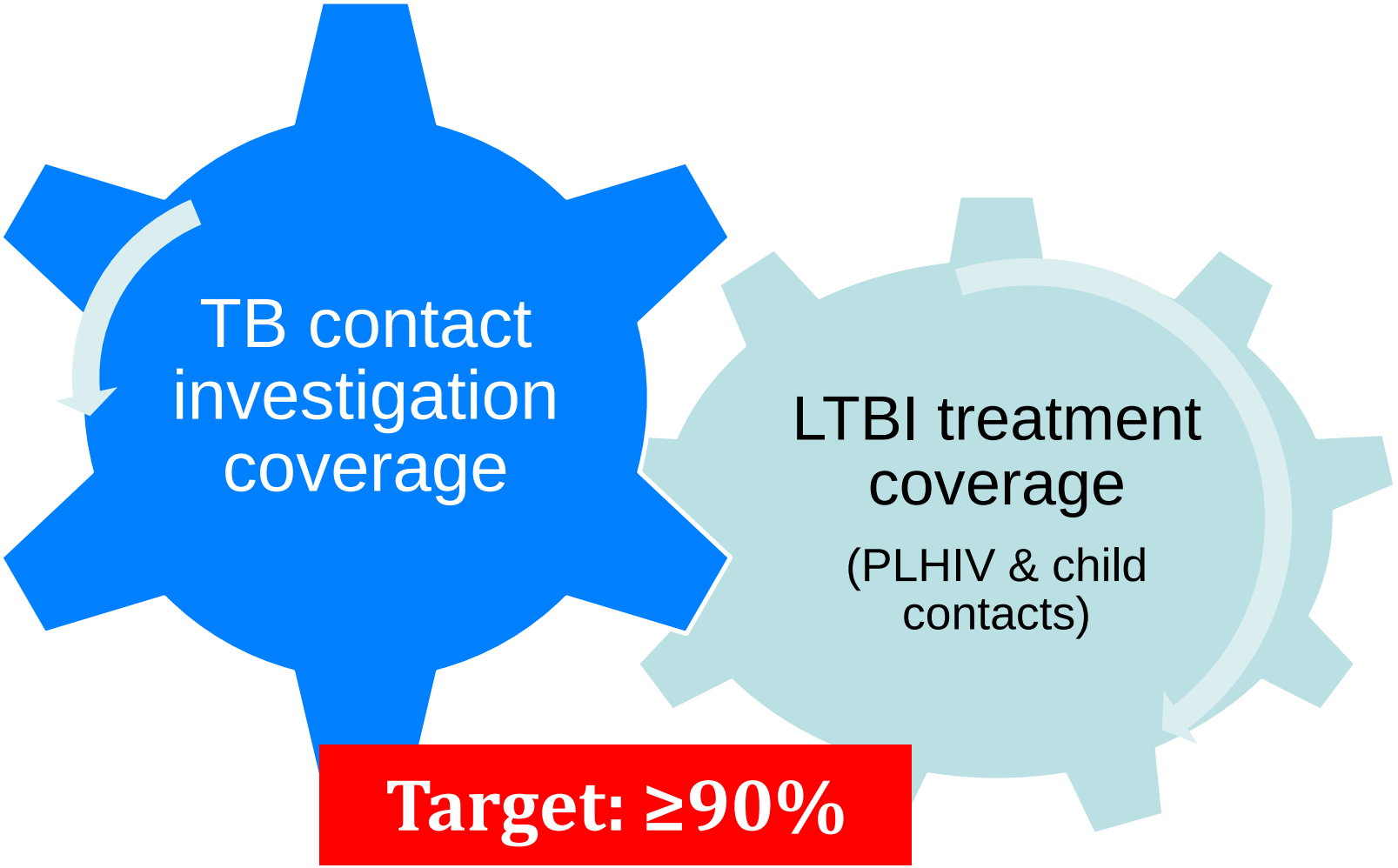
1 Early diagnosis of TB including universal drug-susceptibility testing, and systematic screening of contacts and high risk groups

2 Treatment of all people with TB including drug-resistant TB, and patient support

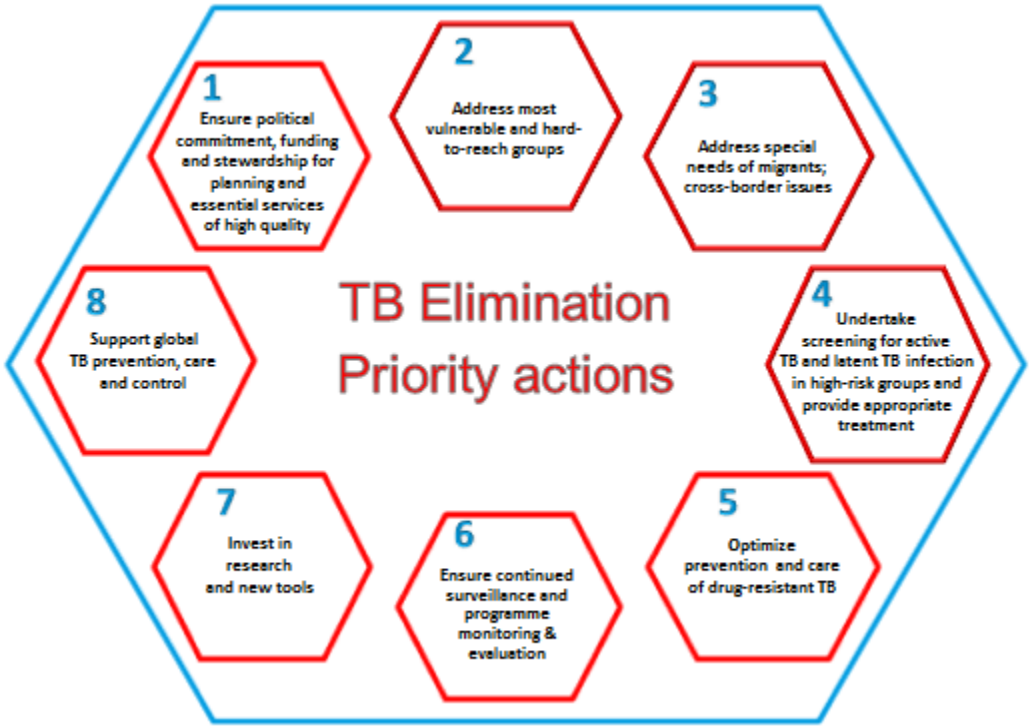
3 Collaborative TB/HIV activities, and management of co-morbidities

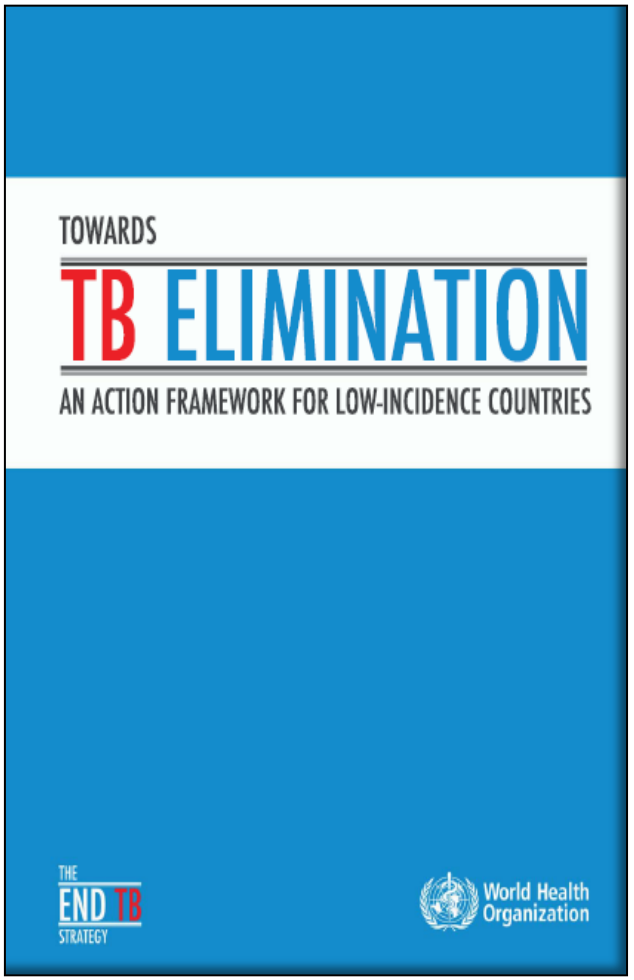
4 Preventive treatment of persons at high risk and vaccination of children

Two of 10 indicators to monitor the implementation of the End TB Strategy

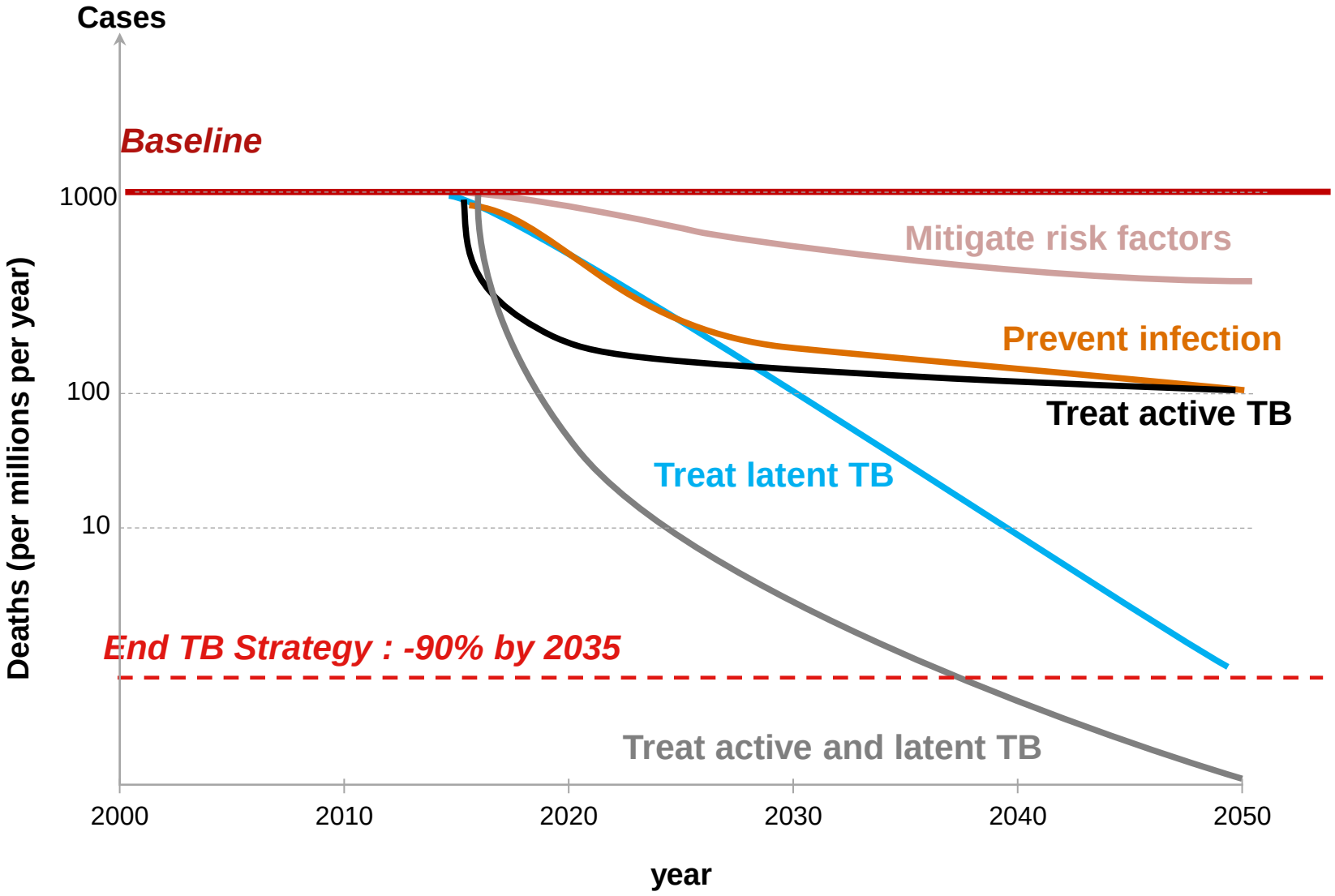


LTBI management- priority action for TB elimination



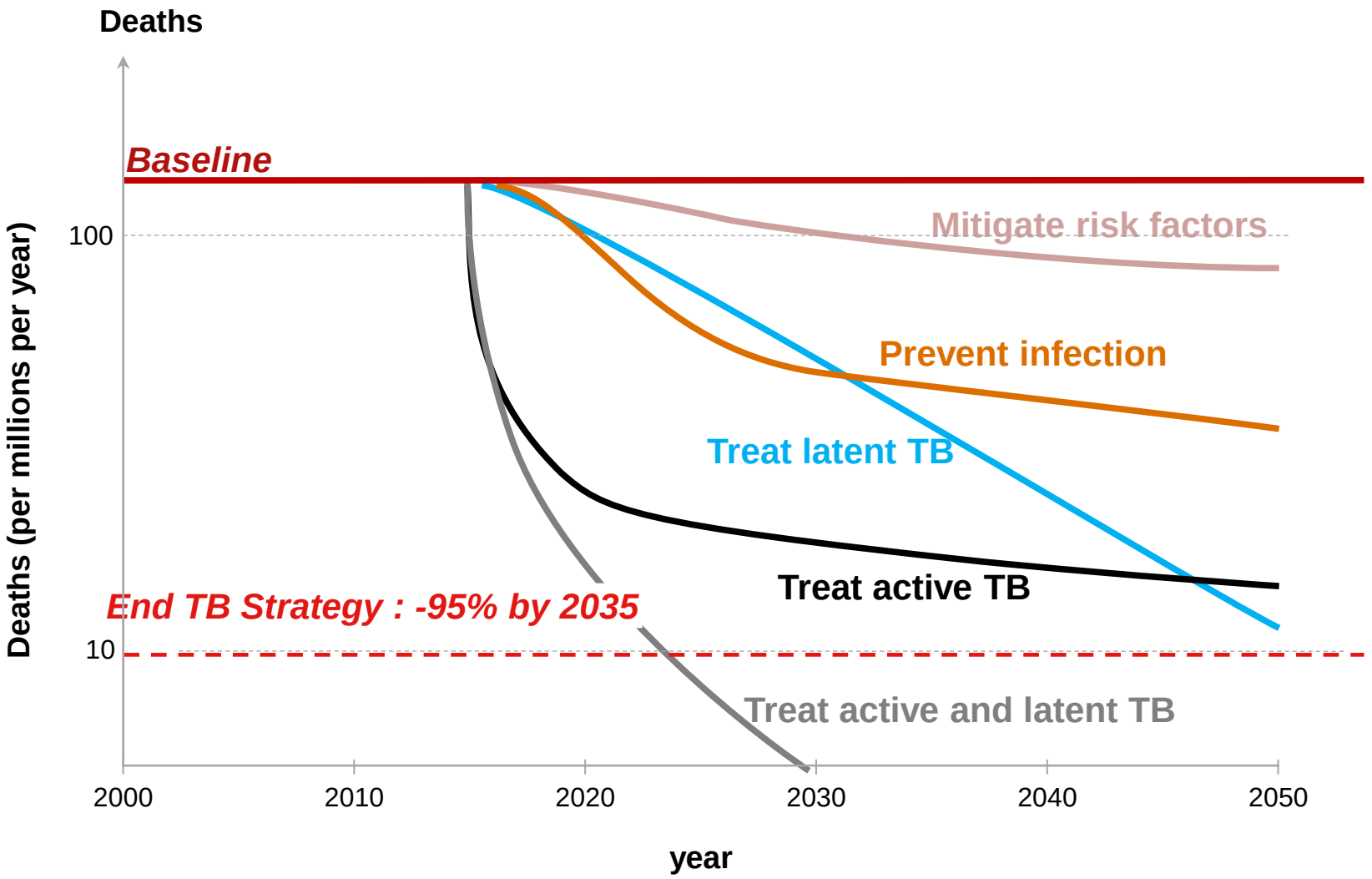


LTBI management contributes to the End TB Strategy targets (Incidence of TB)



Dye C et al., Prospects for Tuberculosis Elimination. Ann Rev Public Health 2013. 34:271-86

LTBI management contributes to the End TB Strategy targets (Deaths)



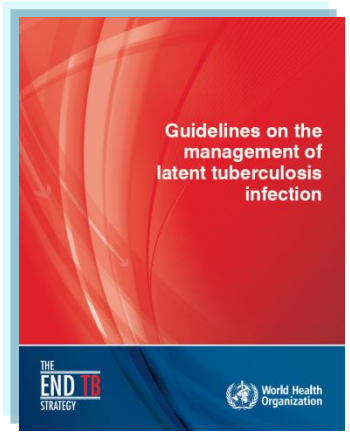
Dye C et al., Prospects for Tuberculosis Elimination. Ann Rev Public Health 2013. 34:271-86

Two-prong policy based on TB burden and income:

Recommeded risk groups

Low-TB burden

TB incidence <100 per 100,000
UMICs and HICs



Strong

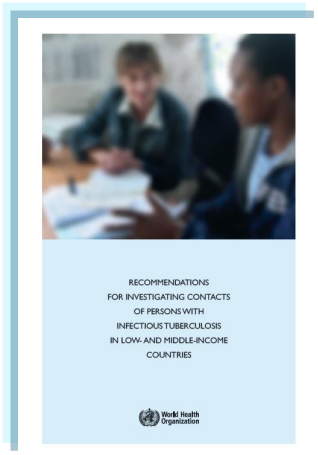
- Child and adult contacts
- PLHIV
- Transplant patients
- Silicosis patients
- Dialysis patients
- Anti-TNF patients

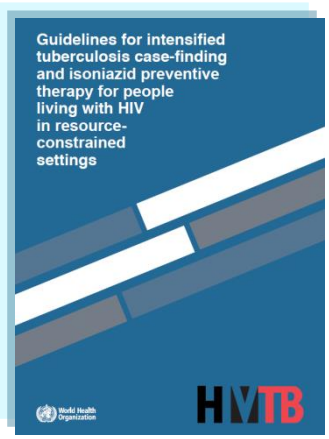
Conditional

- Prisoners
- HCW
- Immigrants from HBC
- Homeless persons
- Illicit drug users

High-TB burden

- TB incidence >100 per 100,000
- LICs and LMICs



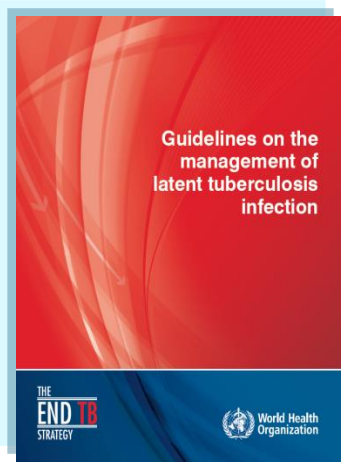


- PLHIV
- Household child contacts (<5y)

LTBI testing recommendation based on burden and income

Low-TB burden

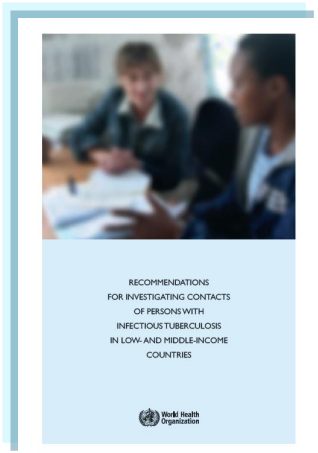
TB incidence <100 per 100,000
UMICs and HICs

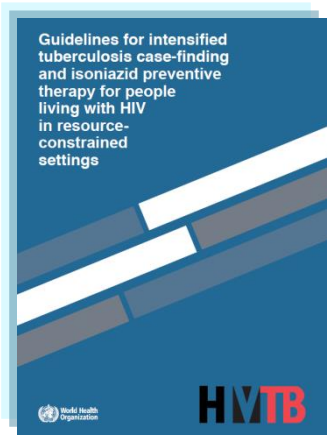


- LTBI testing (TST and/or IGRA) and a positive test is required
- Exclude active TB according to national guidelines

High-TB burden

- TB incidence >100 per 100,000
- LICs and LMICs

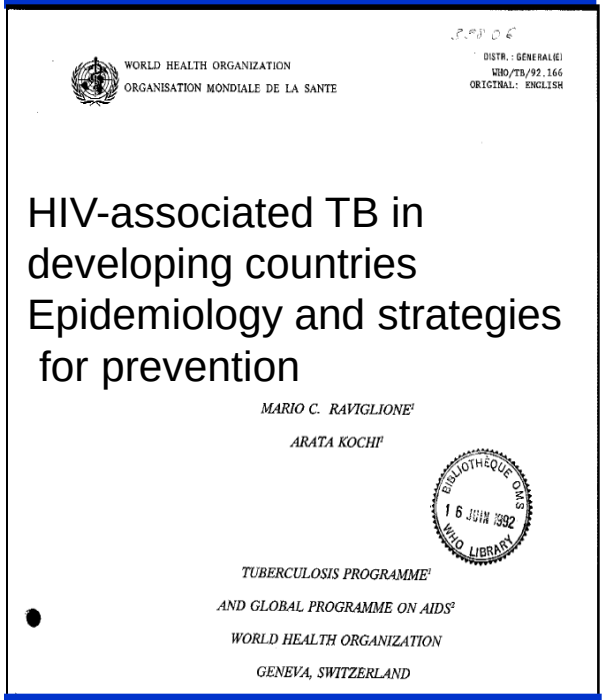




- LTBI testing (TST and/or IGRA) not a requirement
- TST is encouraged in PLHIV
- IGRA should not replace TST
- Exclude active TB with investigations according to national guidelines

Isoniazid preventive therapy has been recommended for PLHIV and child contacts for ages

WHO



WORLD HEALTH ORGANIZATION
ORGANISATION MONDIALE DE LA SANTE

DISTR.: GENERAL(E)
WHO/TB/92.166
ORIGINAL: ENGLISH

HIV-associated TB in developing countries
Epidemiology and strategies for prevention

MARIO C. RAVIGLIONE[1]
ARATA KOCHI[1]

BIBLIOTHEQUE OMS
16 JUIN 1992
WHO LIBRARY

TUBERCULOSIS PROGRAMME[1]
AND GLOBAL PROGRAMME ON AIDS[2]
WORLD HEALTH ORGANIZATION
GENEVA, SWITZERLAND

1992

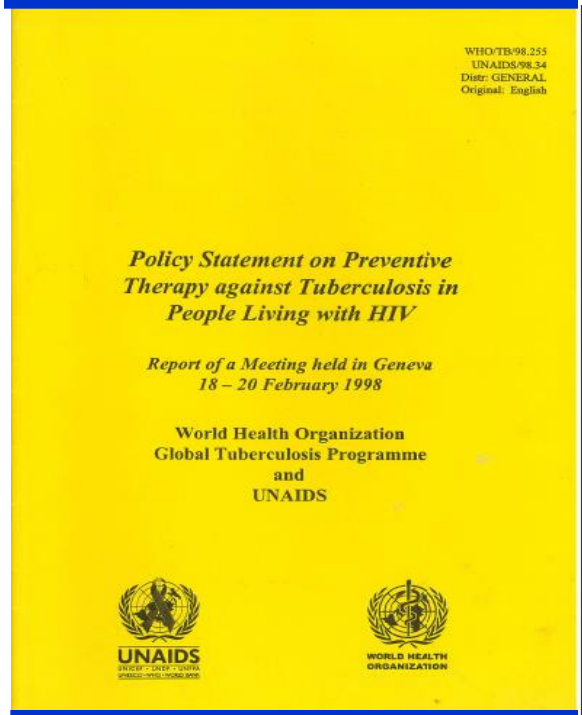
WHO & Union

Tuberculosis preventive therapy in HIV-infected individuals. A Joint Statement of the WHO and IUATLD

Wkly Epidemiol Rec 1993,68:361-364.

1993

WHO & UNAIDS



WHO/TB/98.255
UNAIDS/98.34
Distr: GENERAL
Original: English

Policy Statement on Preventive Therapy against Tuberculosis in People Living with HIV

Report of a Meeting held in Geneva 18 – 20 February 1998

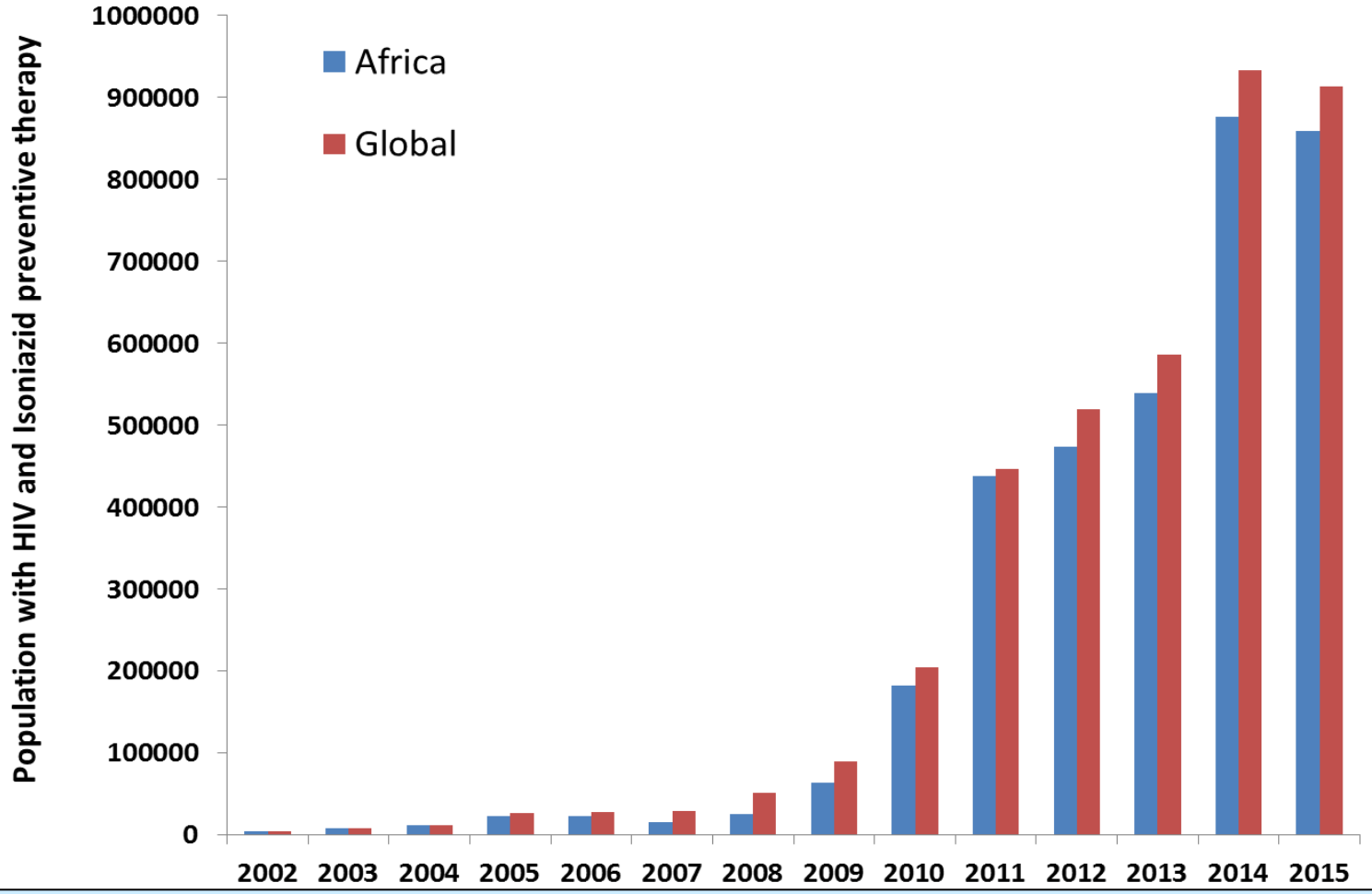
World Health Organization
Global Tuberculosis Programme
and
UNAIDS

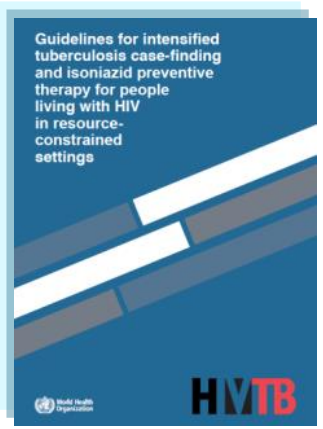
UNAIDS

WORLD HEALTH ORGANIZATION

1998

Progress of implementation of IPT in PLHIV

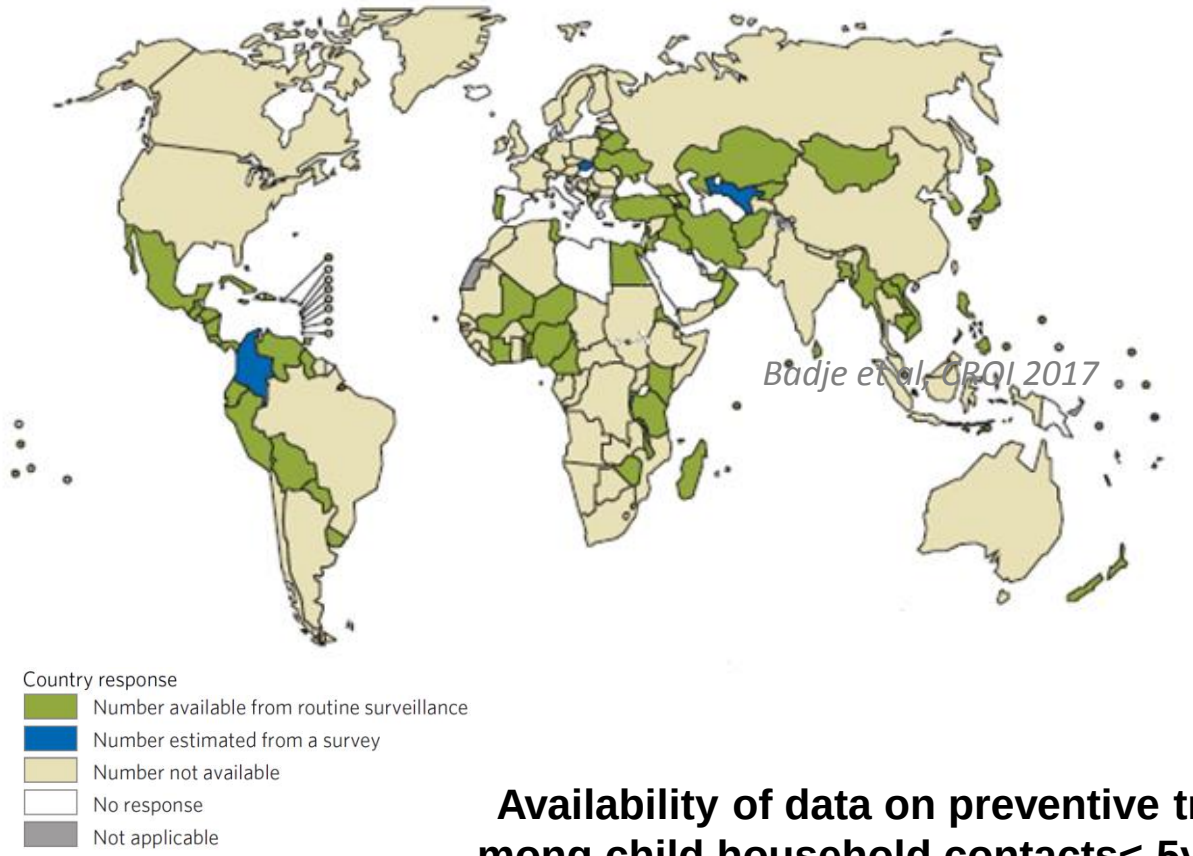


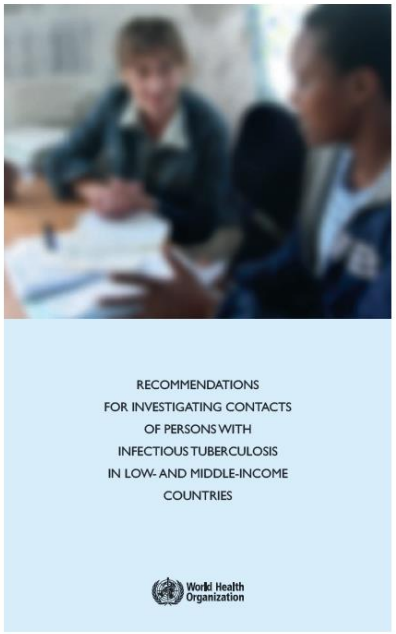


Nearly 1M PLHIV received IPT in 2015

Only 57 countries report implementation in 2015

Preventive treatment for child household contacts<5yrs





Availability of data on preventive treatment among child household contacts< 5years, 2015

87,000 (7% of estimated eligible) in 88 countries received PT

Challenges

Implementation of isoniazid preventive therapy for people living with HIV worldwide: barriers and solutions

Haileyesus Getahun[a], Reuben Granich[b], Delphine Sculier[a], Christian Gunneberg[a], Leopold Blanc[a], Paul Nunn[a] and Mario Raviglione[a]

AIDS 2010, **24** (suppl 5):S57–S65

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http://dx.doi.org/10.5588/ijtld.16.0241

Policies and practices on the programmatic management of latent tuberculous infection: global survey

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Key barriers for TB prevention scale up

- Does it really work?
  - Reluctance of programme managers and health workers
  - Are we not doing harm?

- Difficulty to exclude active TB and drug resistance fear
  - Inadvertent mono-treatment

- Operational barriers
  - Poor adherence of clients
  - Access to INH and who owns it

Risk of drug resistance following LTBI treatment

- No significant association of risk of drug resistance.
  - INH – RR (95%CI) = 1.45 (0.85,2.47)
  - Rifamycin – RR (95%CI) = 1.12 (0.41,3.08)

Challenge: multiple service provider units with no harmonisation of data and practice

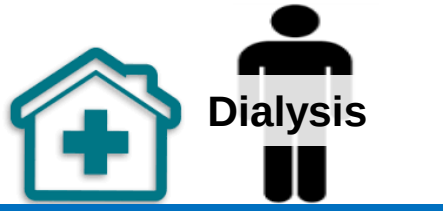
ID services

TB services

Public health services

Rheumatology units

HIV services



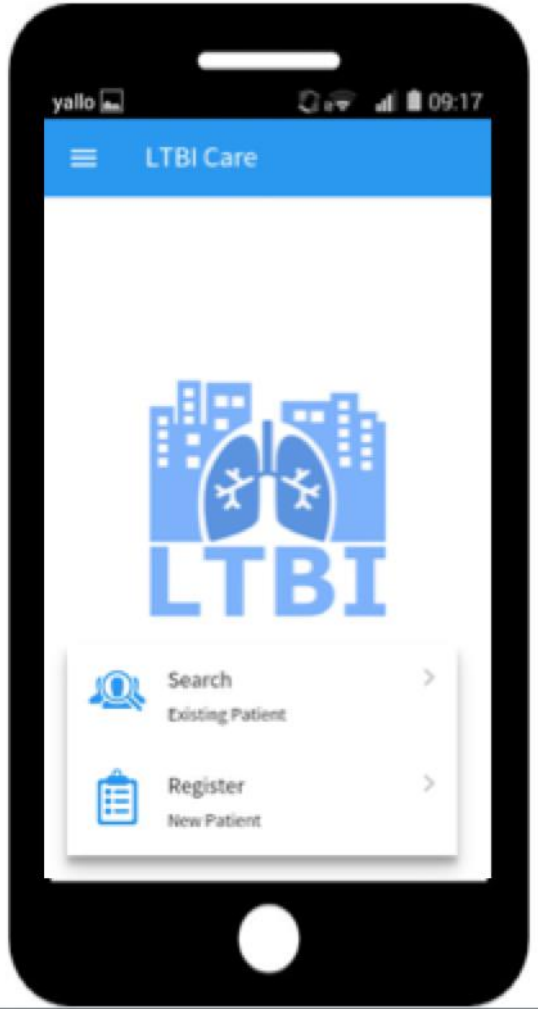
Nephrology units

Pneumology units

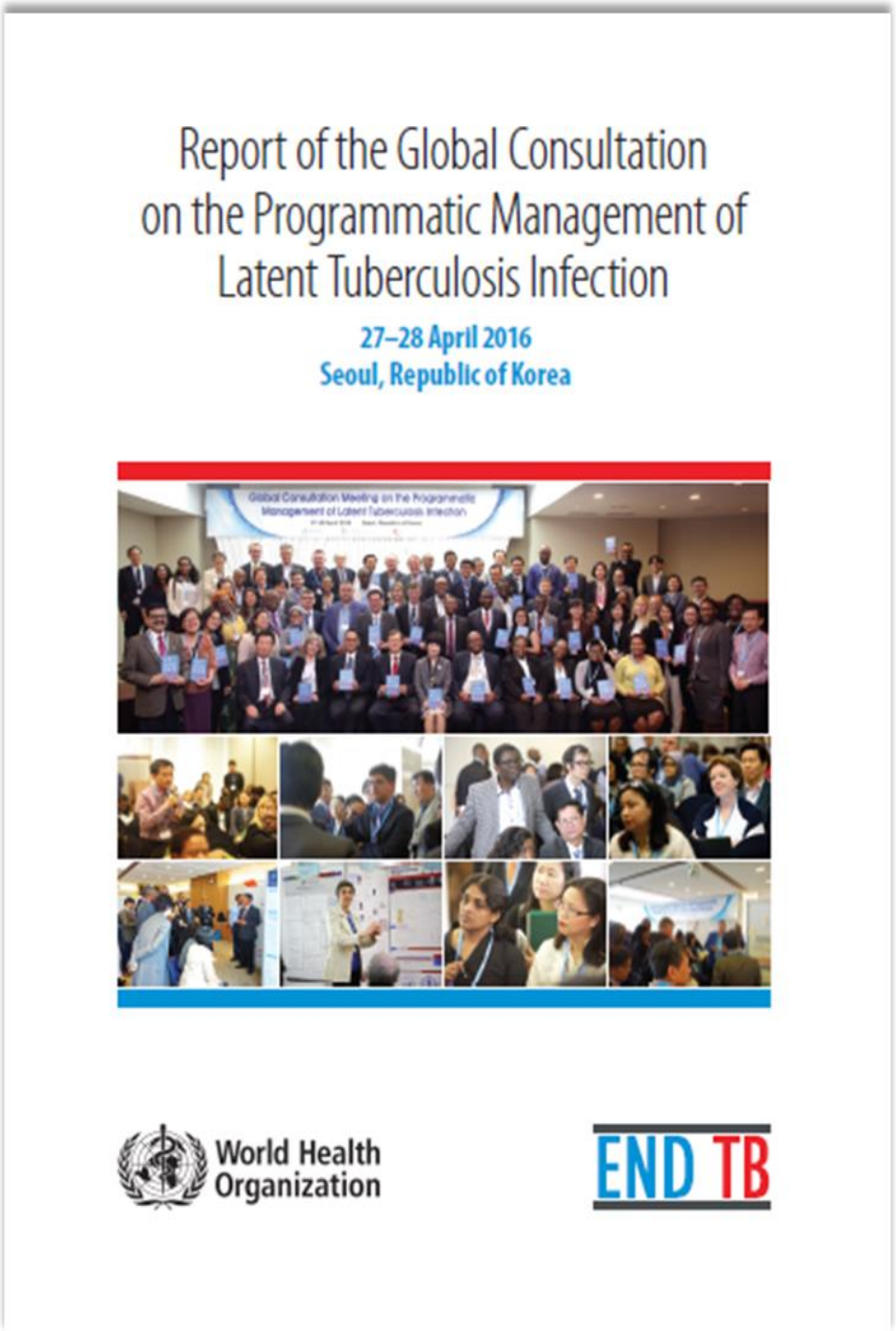
MCH services

LTBI digital tool key characteristics

- Free – downloadable from WHO website
- Adaptable - to country specific context and needs
- Functional - on mobile devices
- Flexible - record data off line and synchronise later and use local server



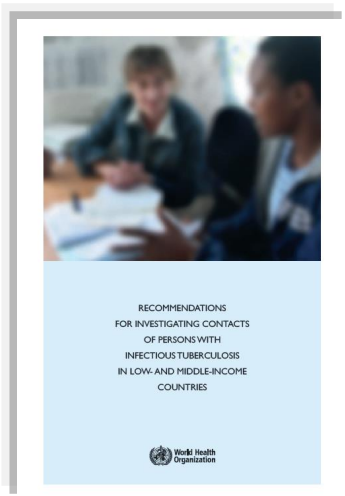
https://www.youtube.com/watch?v=QxJknYG53jM

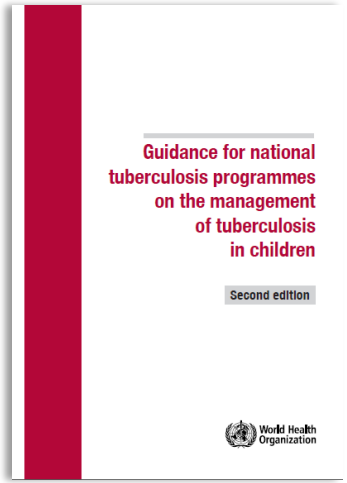


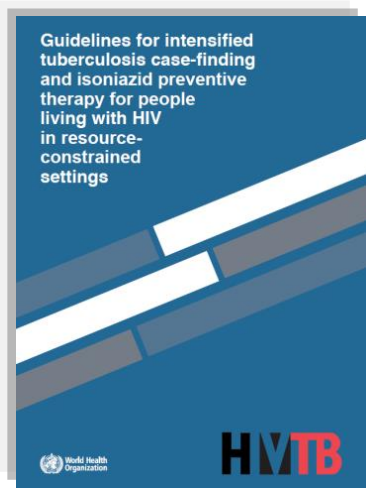
Support the harmonization of policy recommendations across countries,

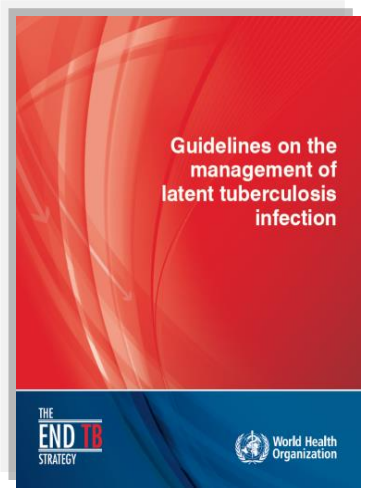
regardless of the burden of TB.

Consolidated and updated LTBI guidelines









Consolidated WHO LTBI guidelines - 2017

Seven PICO questions examined for high burden countries

- Preventive treatment for HIV negative household contacts
- Screening to exclude TB in HIV negative household contacts
- Accuracy of WHO 4 symptomatic to exclude TB in PLHIV on ART
- IGRA as alternative to tuberculin skin tests
- 3 month daily rifampicin plus INH for children and adolescents
- 3-month weekly rifapentine and INH as an alternative to IPT
- Preventive treatment recommendation for MDR-TB contacts

Conclusions

- Programmatic management of LTBI is essential component of End TB Strategy and TB elimination
- Research for best test and treatment should be integral to the programmatic implementation
- WHO guidelines are being updated and large scale changes anticipated

Acknowledgment: Yohhei Hamada