Programmatic management of LTBI : a two pronged approach for ending the TB epidemic

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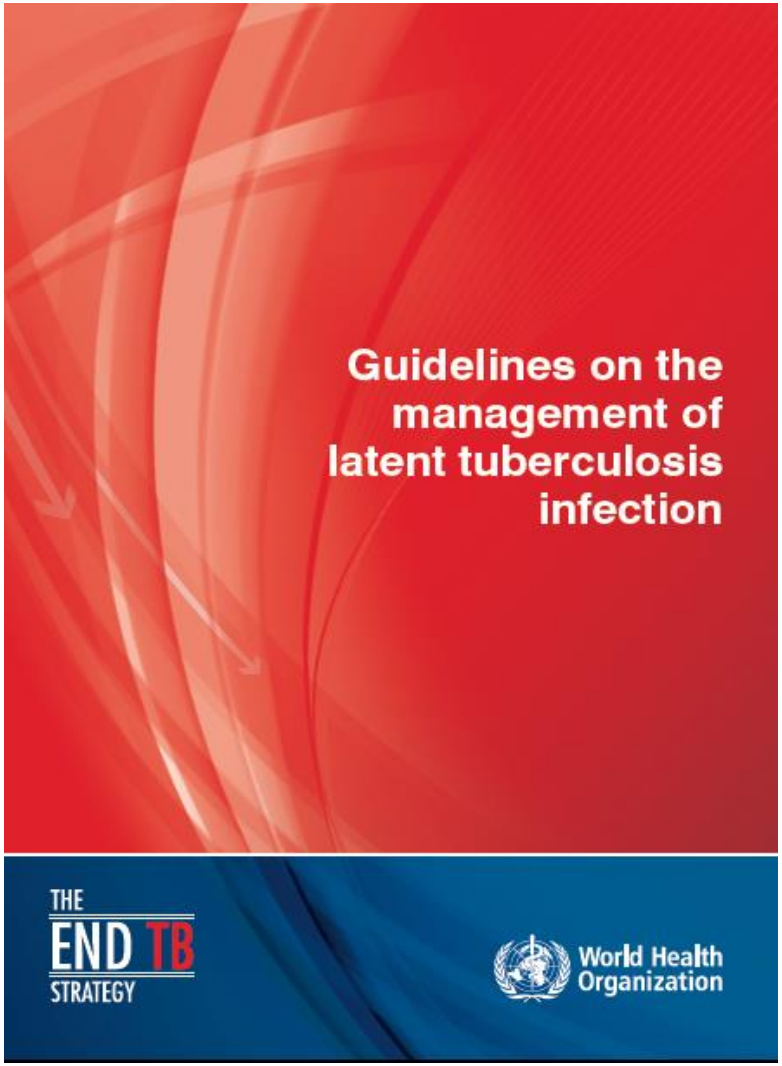
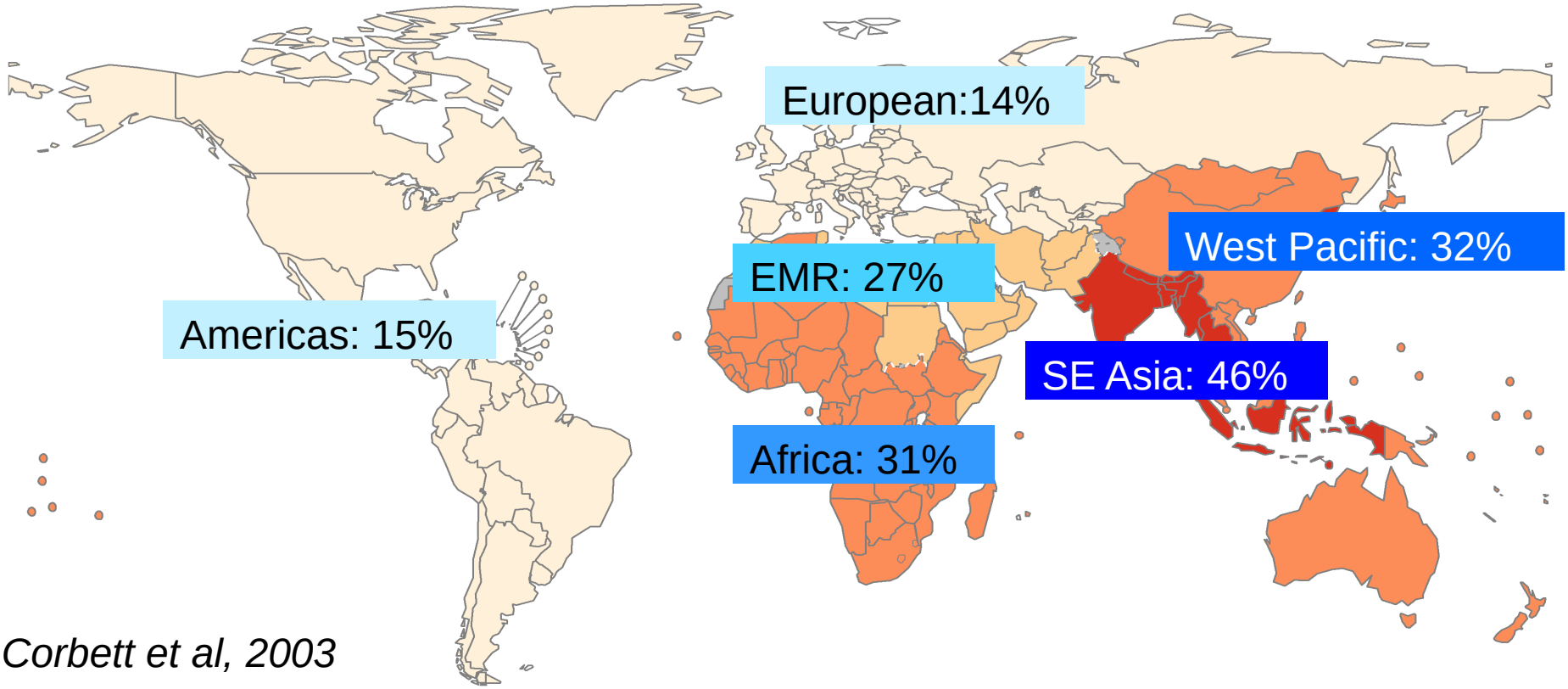
What is latent TB infection?

A state of persistent immune response to stimulation

by *Mycobacterium tuberculosis* antigens without evidence of clinically manifested active TB



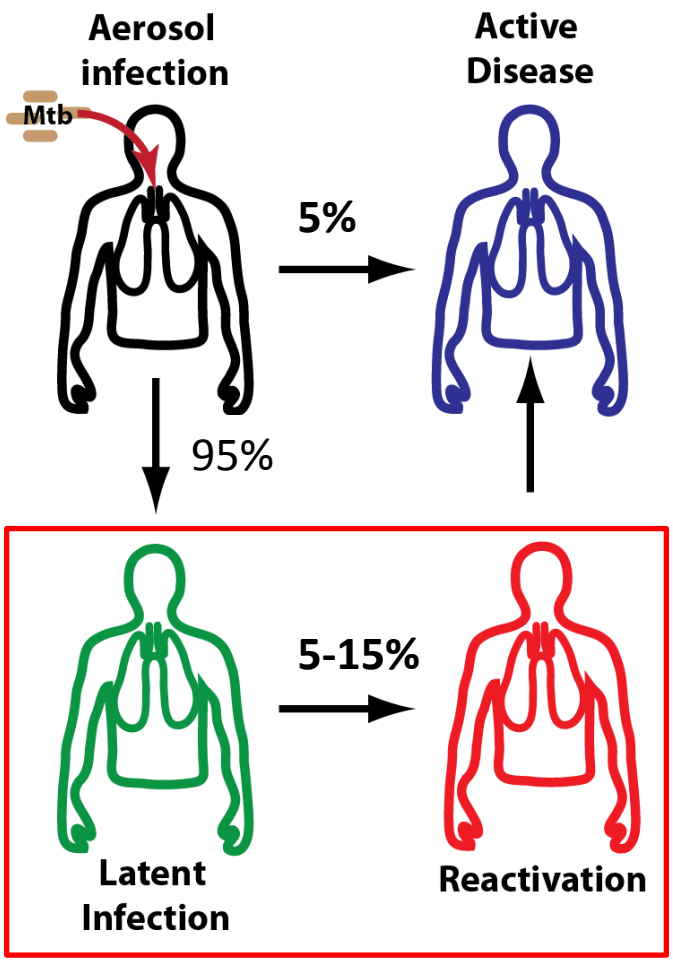
Estimated LTBI prevalence in general population



Corbett et al, 2003

Global estimate: 30%

LTBI represent the TB reservoir

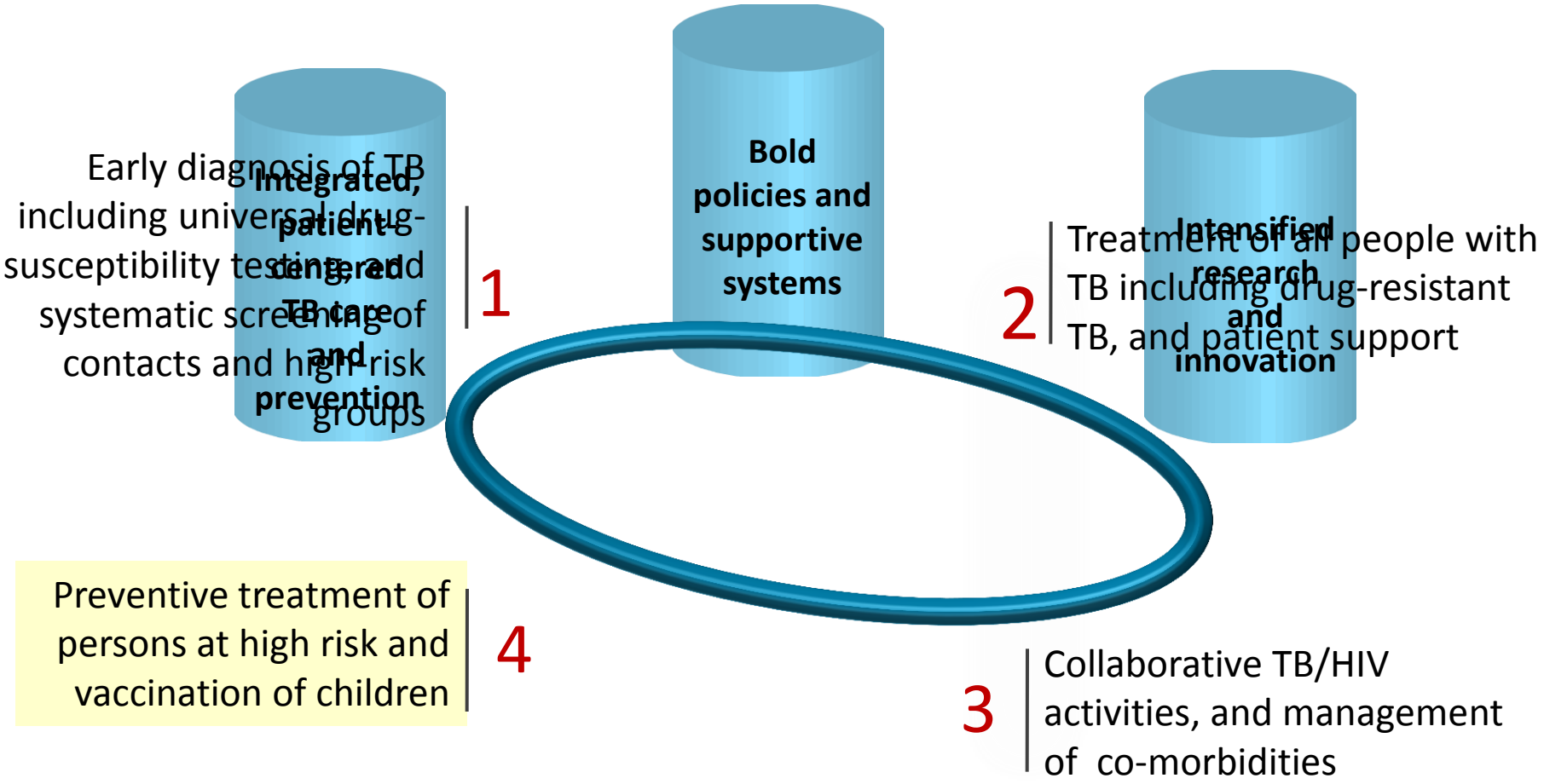


9.6 million TB cases /year

2 billion population with latent TB infection

End TB Strategy

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



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

1

2

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

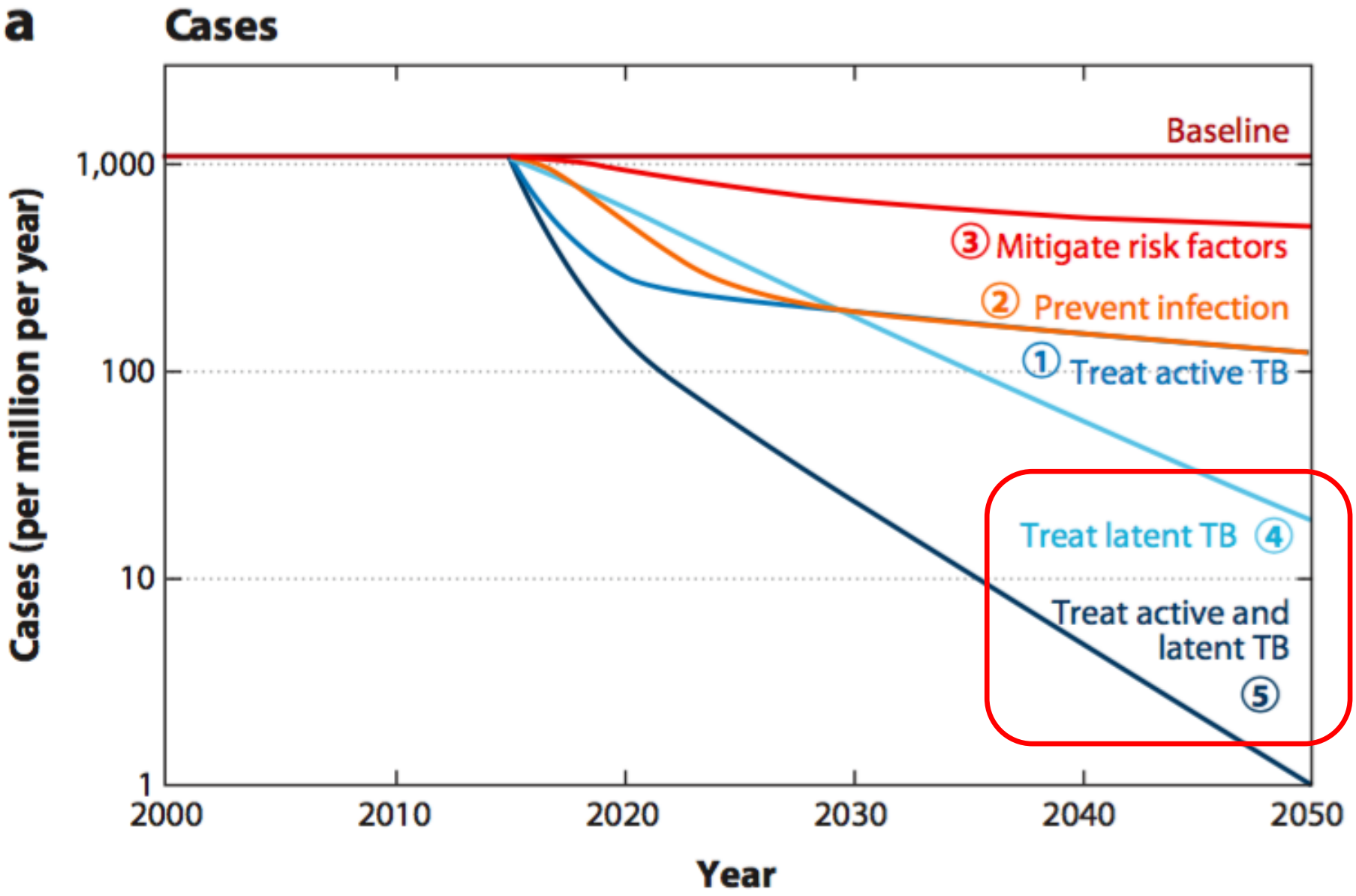
Preventive treatment of persons at high risk and vaccination of children

4

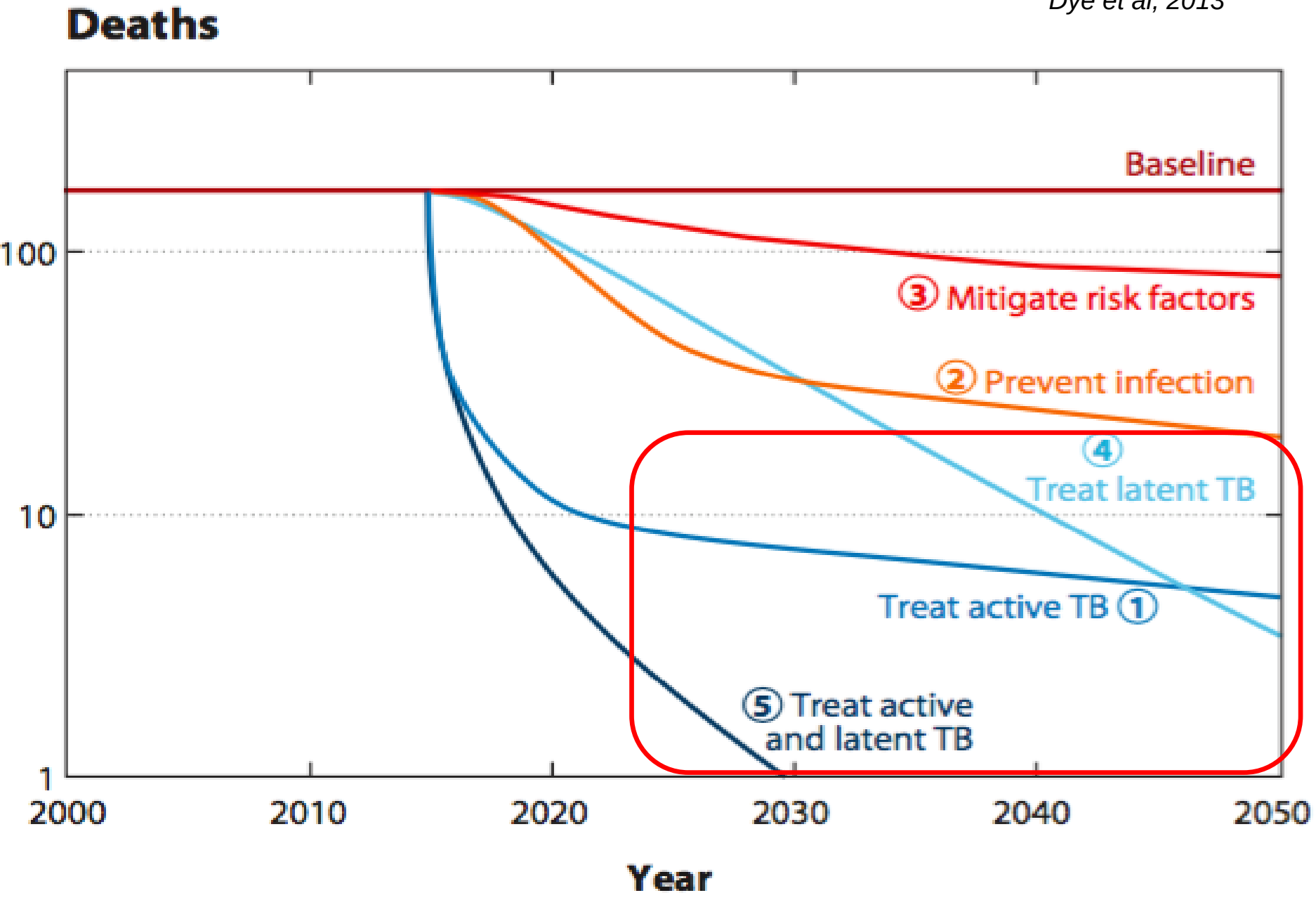
3

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

Dye et al, 2013

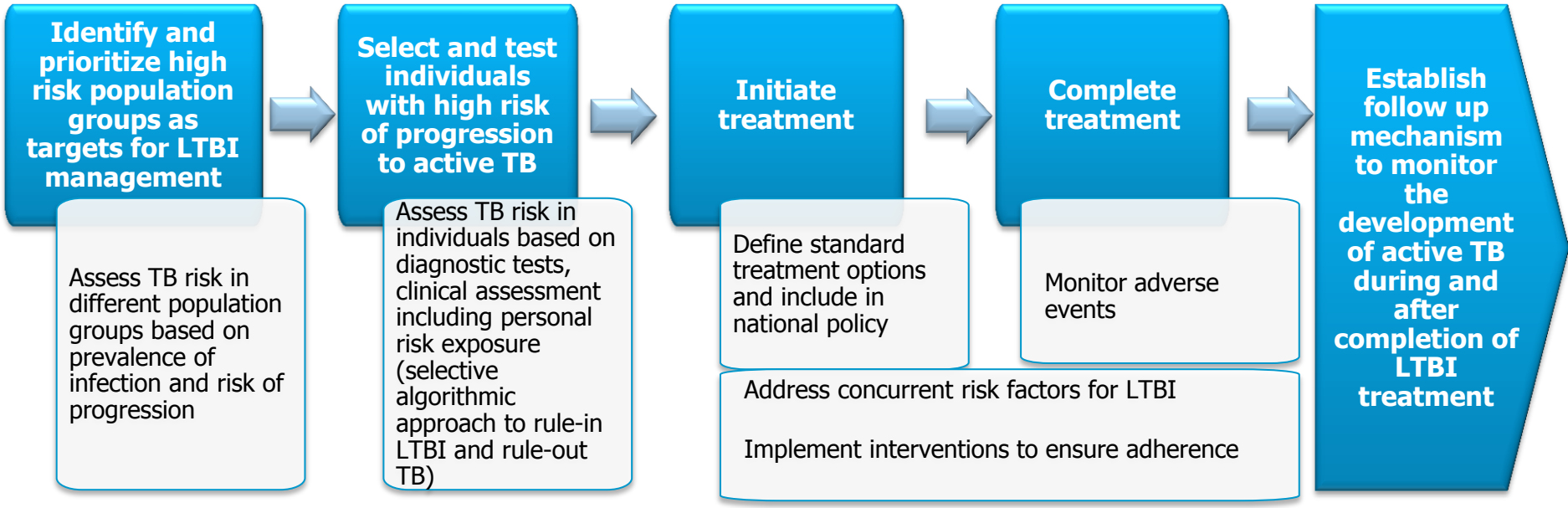


Dye et al, 2013



LTBI management is one of the priority actions for TB elimination

Approach for programmatic management of LTBI



Provide programmatic support: algorithm-based national guidelines targeting high risk population groups; proper documentation, reporting and monitoring of people receiving LTBI treatment; functional supply system for diagnostic tests, drugs and other treatments; promote implementation and basic science research to develop service delivery models and scale up novel evidence based interventions.

Principles of LTBI treatment and diagnosis

- Individual benefits should outweigh the risk
- Public health approach with individual benefit
- Complement active TB case finding activities

Considerations for recommendations

- Balance of benefits and harms
- Values and preferences of clients and healthcare providers
- Resource considerations

Two sets of countries for global LTBI response

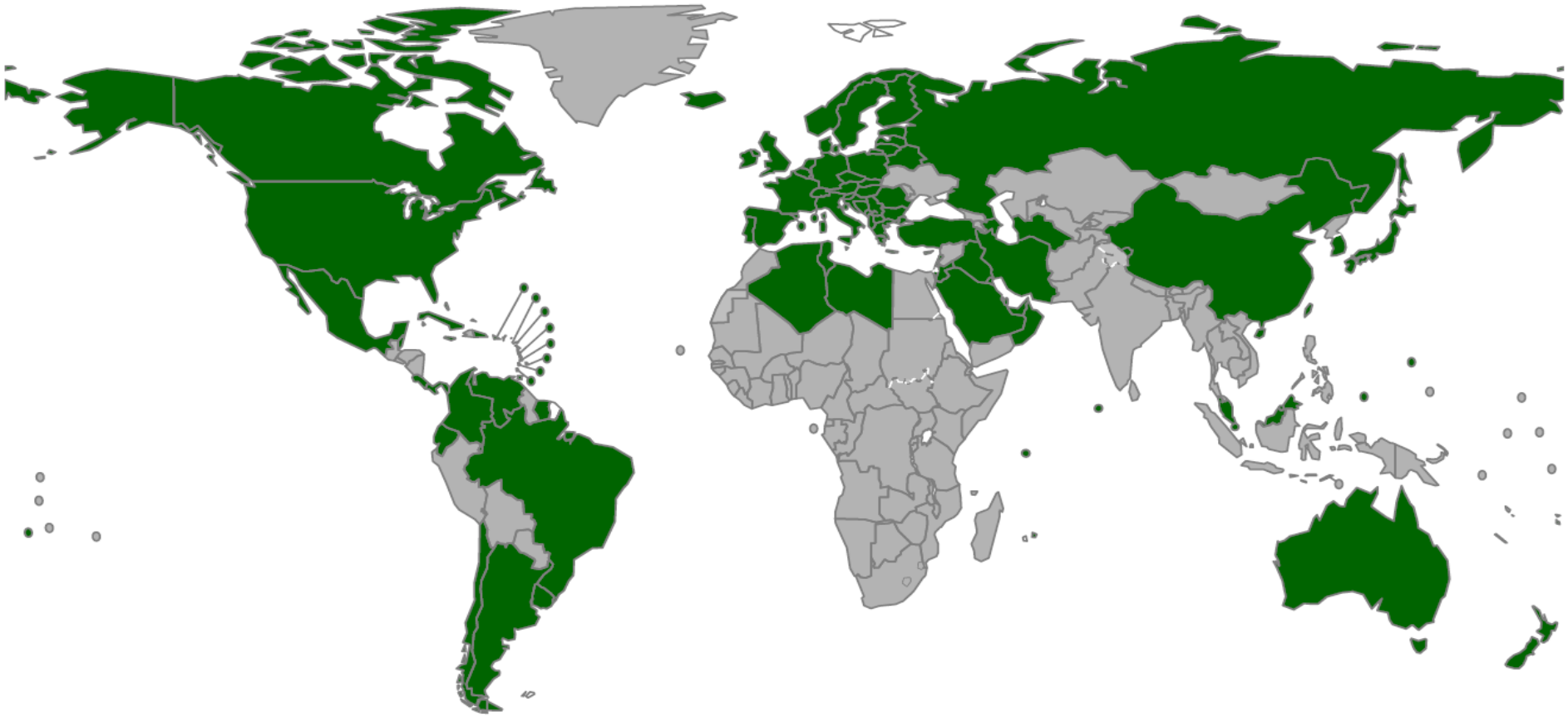
High-TB burden

- Estimated TB incidence >100 per 100,000
- LICs and LMICs
- Risk groups
  - PLHIV
  - Household child contacts (<5y)

Low-TB burden

- Estimated TB incidence <100 per 100,000
- UMICs and HICs
- Risk groups
  - PLHIV
  - Child and adult contacts
  - Clinical indications
    - Transplant
    - Dialysis
    - Anti-TNF
    - Silicosis

Primary targets for LTBI guidelines (low TB burden)



113 high or upper middle income countries with an estimated TB incidence rate of less than 100 per 100,000 population

LTBI treatment recommendations for low-TB burden

Risk population groups	Strength of recommendation
• Prisoners • Health workers • Immigrants from high burden countries • Homeless persons • Illicit drug user	Conditional: Systematic testing and treatment should be considered *(Low to very low quality of evidence)*
• Patients with Diabetes • People with harmful alcohol use • Tobacco smokers • Under-weight people	Conditional: systematic testing and treatment is not recommended unless they belong in the upper two groups *(Very low quality of evidence)*

Two sets of countries for global LTBI response

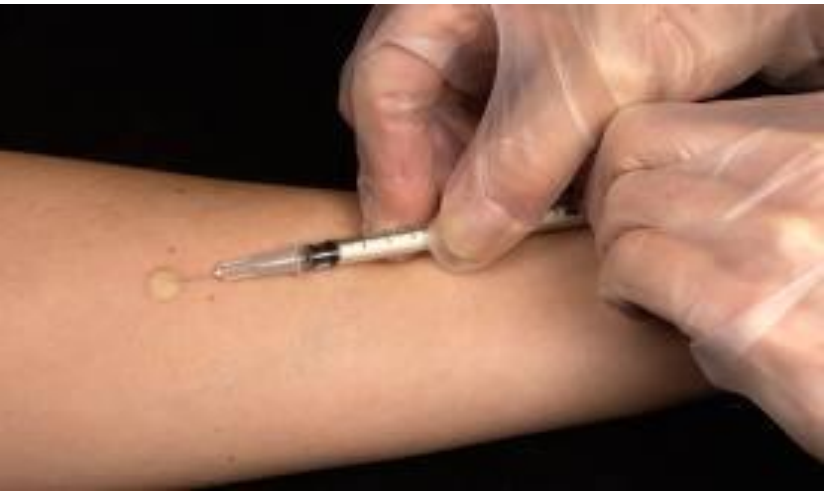
High-TB burden

- No TST or IGRA required
- INH 6 months recommended

Low-TB burden

- TST or IGRA required
- Multiple regimens
  - 6 months isoniazid (6H)
  - 9 months isoniazid (9H)
  - 3 months weekly rifapentine plus isoniazid (3HP)
  - 3 to 4 months isoniazid plus rifampicin (3-4 HR)
  - 3 to 4 months rifampicin alone (3-4R)

Diagnosis of LTBI: Tuberculin Skin Test



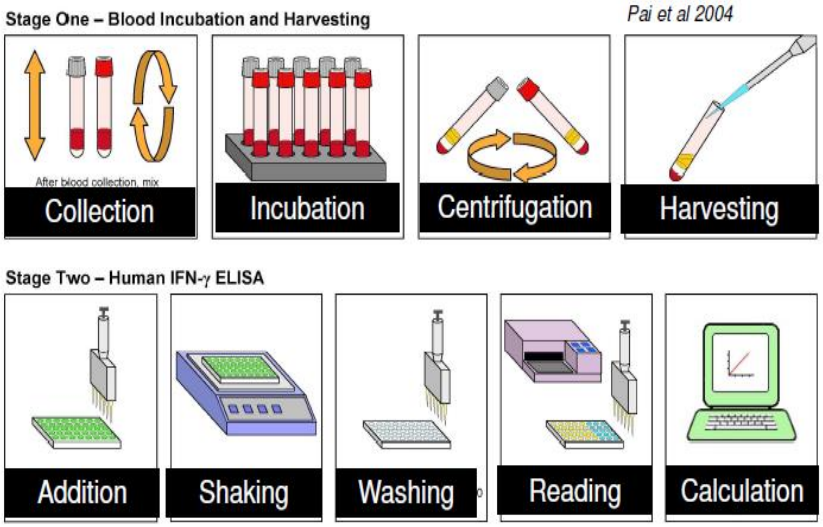
- Mix of several Antigens
- Cross reactivity with BCG
- Low specificity
- Anergy (e.g. PLHIV)

- Operational challenges
  - Return visit (48-72 hr)
  - Cold chain and dark room
  - Trained personnel to read
  - Reading problems

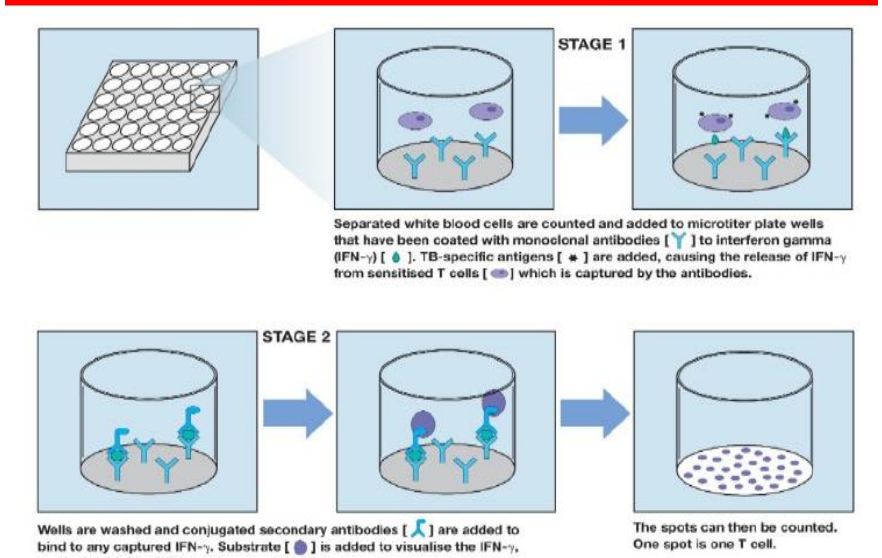
  (Under-reading and reader variability)

IGRAs: target MTB specific antigens
(ESAT-6;CFP-10; TB7.7)

Quanti FERON-TB Gold®

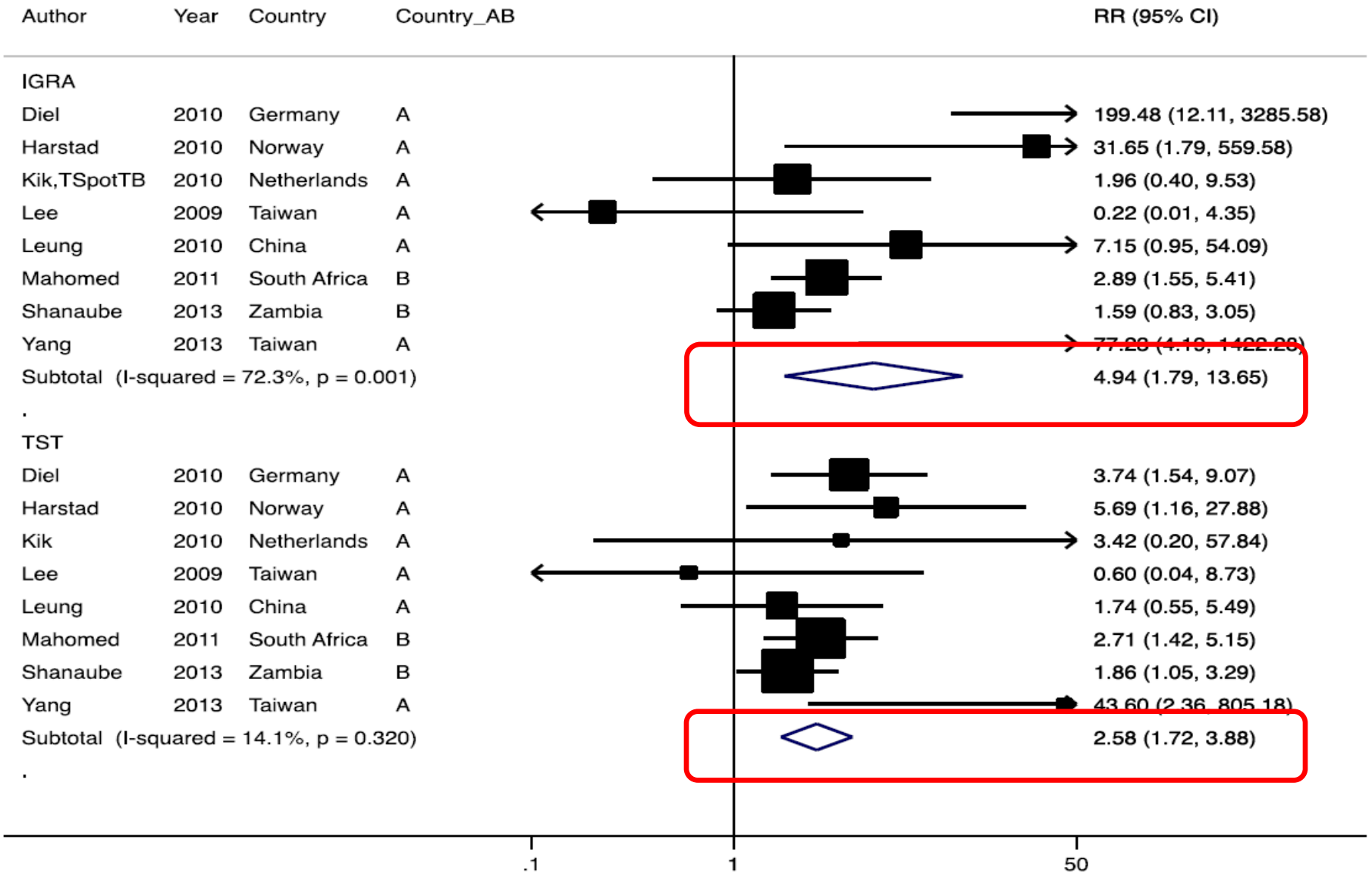


T-SPOT.*TB*®



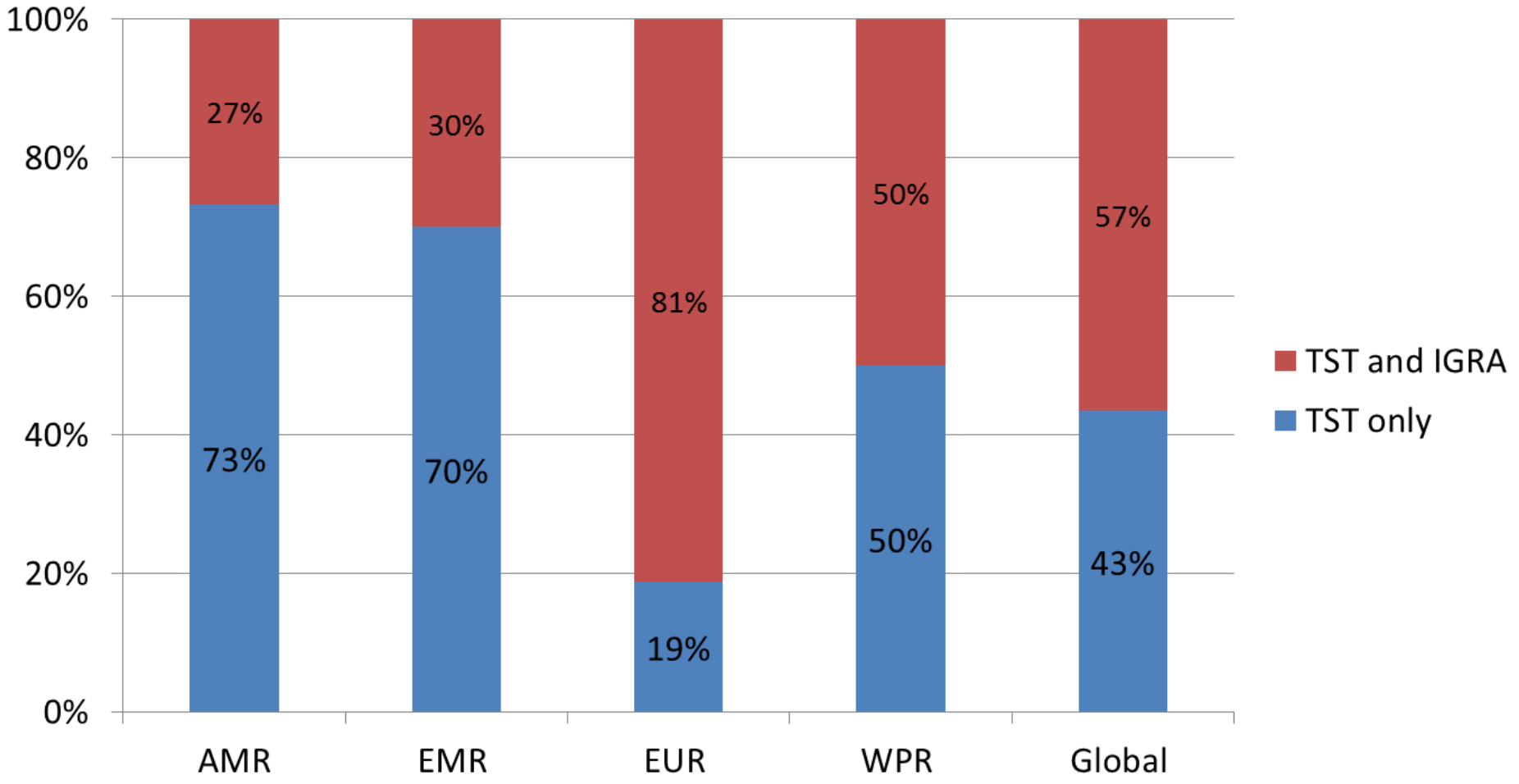
IGRAs are more costly and technically complex

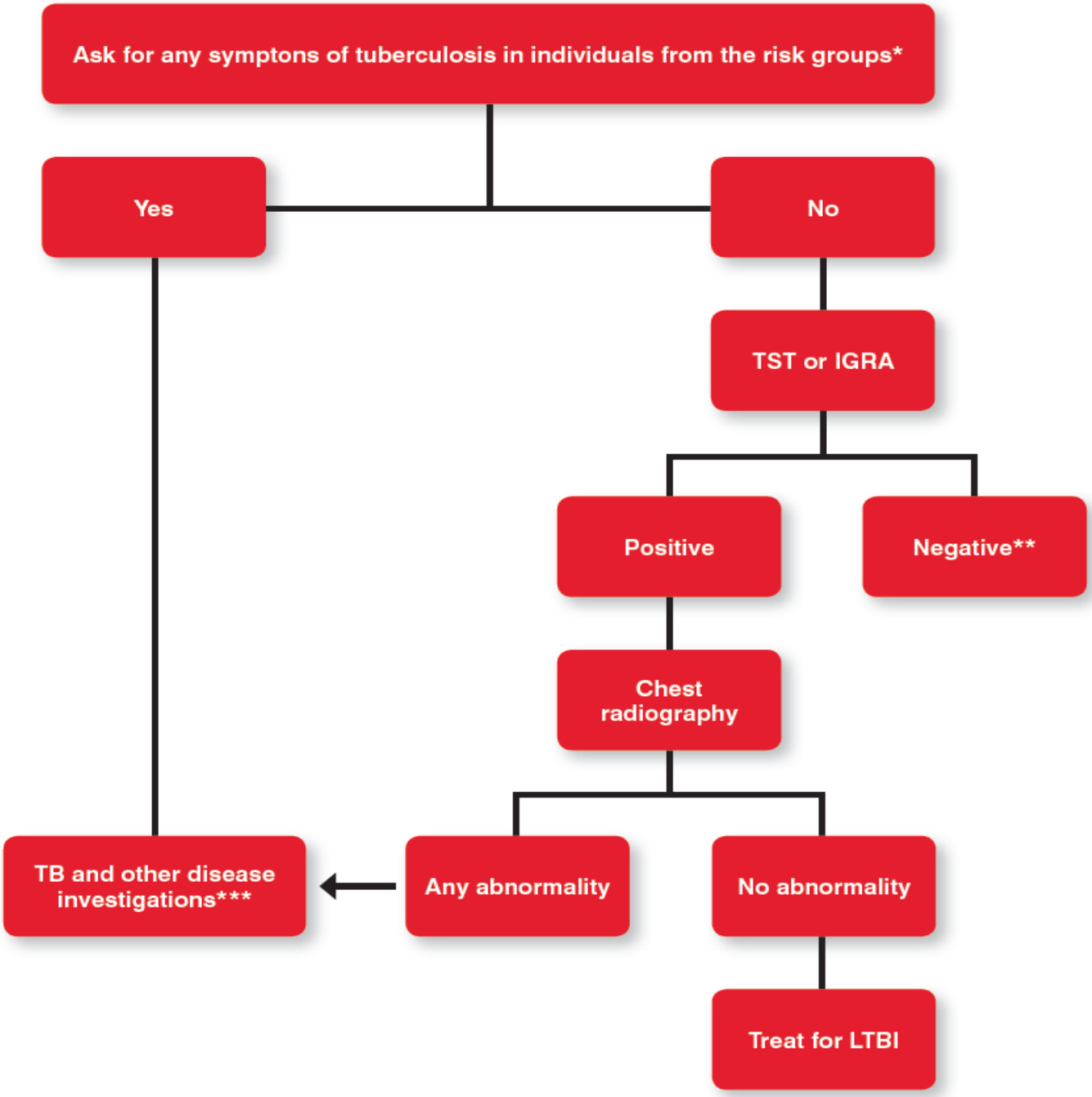
Head-to-head comparison of TST and IGRA for prediction of future TB disease



LTBI tests adopted by countries

(Survey among 74 low TB burden countries)



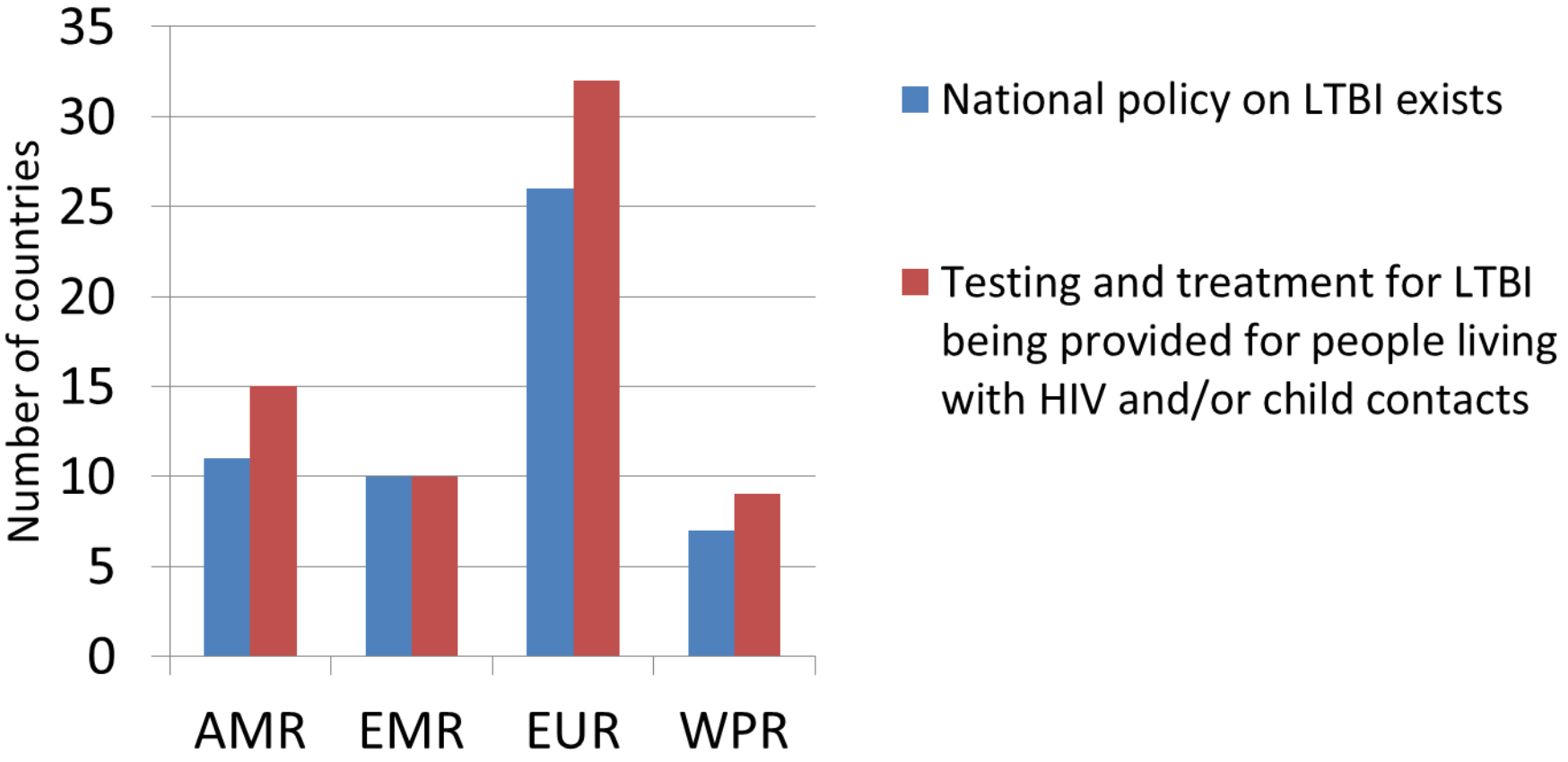

Ask for any symptons of tuberculosis in individuals from the risk groups*
Yes
No
TST or IGRA
Positive
Negative**
Chest radiography
TB and other disease investigations***
Any abnormality
No abnormality
Treat for LTBI

Rifapentine/INH (12 doses) for LTBI treatment

- FDA approval for LTBI: done and EML: ongoing
- Included in WHO essential medical list and expression of Interest for manufacturers
- Fixed dose combination of HP developed:300H/300P (adults) and 150H/150P (for children and solvable)
- Studies show no interaction with Efavirenz
- It is efficacious both in adults and children (>2y)

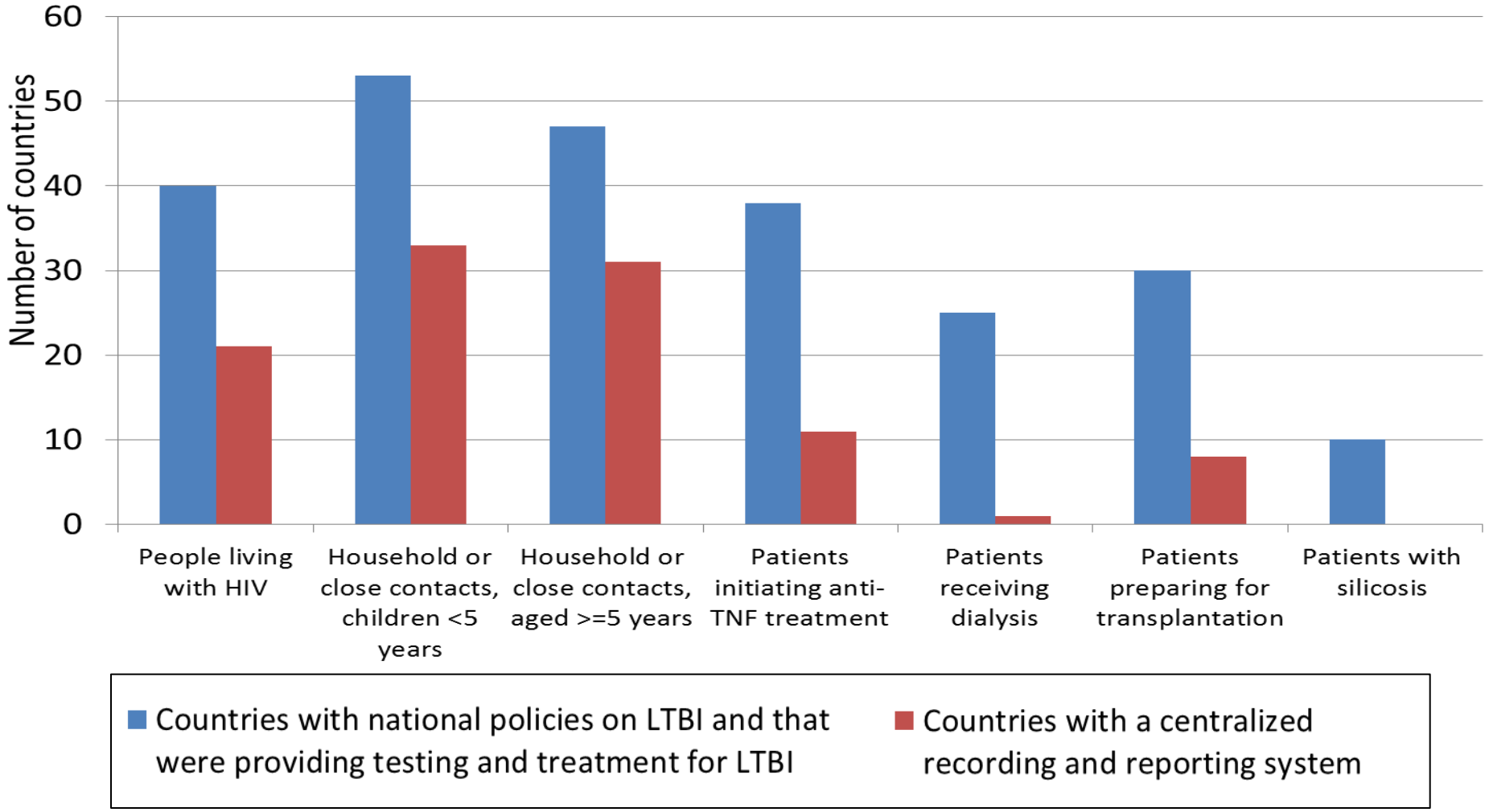
Challenge: Gap between policy and practice

(Survey among 74 low TB burden countries)



Challenge: Not all LTBI activities are recorded and reported

(Survey among 74 low TB burden countries)



Conclusion

- Programmatic management of LTBI is an integral part of End TB Strategy
- It has relevance for both high and low TB burden countries
- Efforts should intensify for the programmatic management of LTBI globally including M and E