

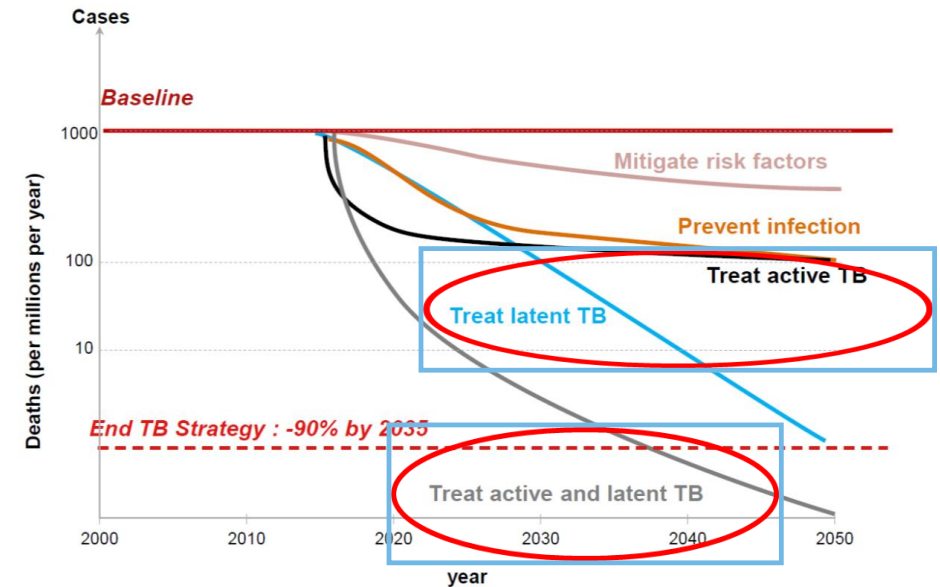
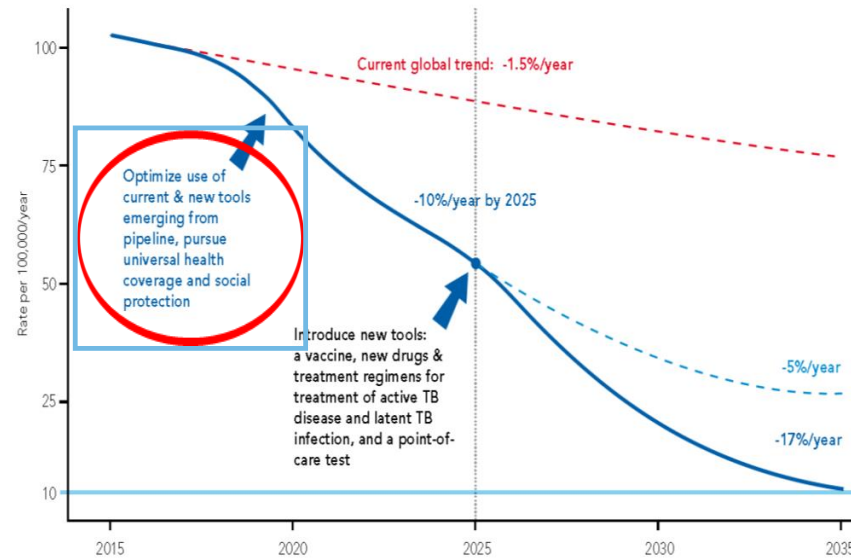
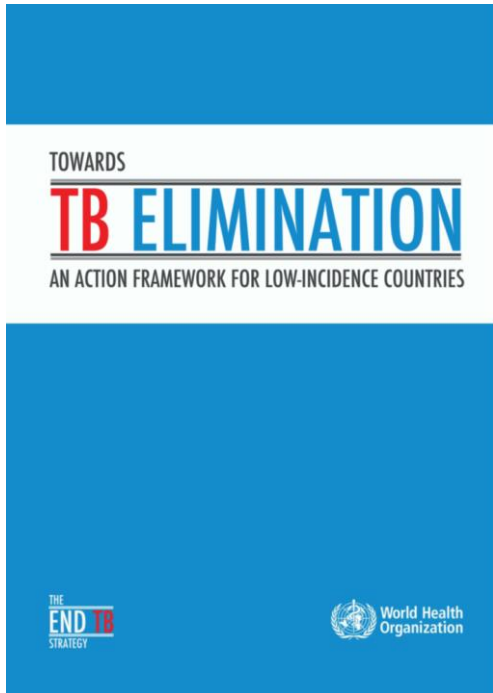


**SCREENING FOR LATENT  
TB INFECTION IN  
RESOURCE-LIMITED  
SETTINGS: NEED FOR  
INNOVATIVE SOLUTIONS  
TO MEET ENDTB GOALS.**

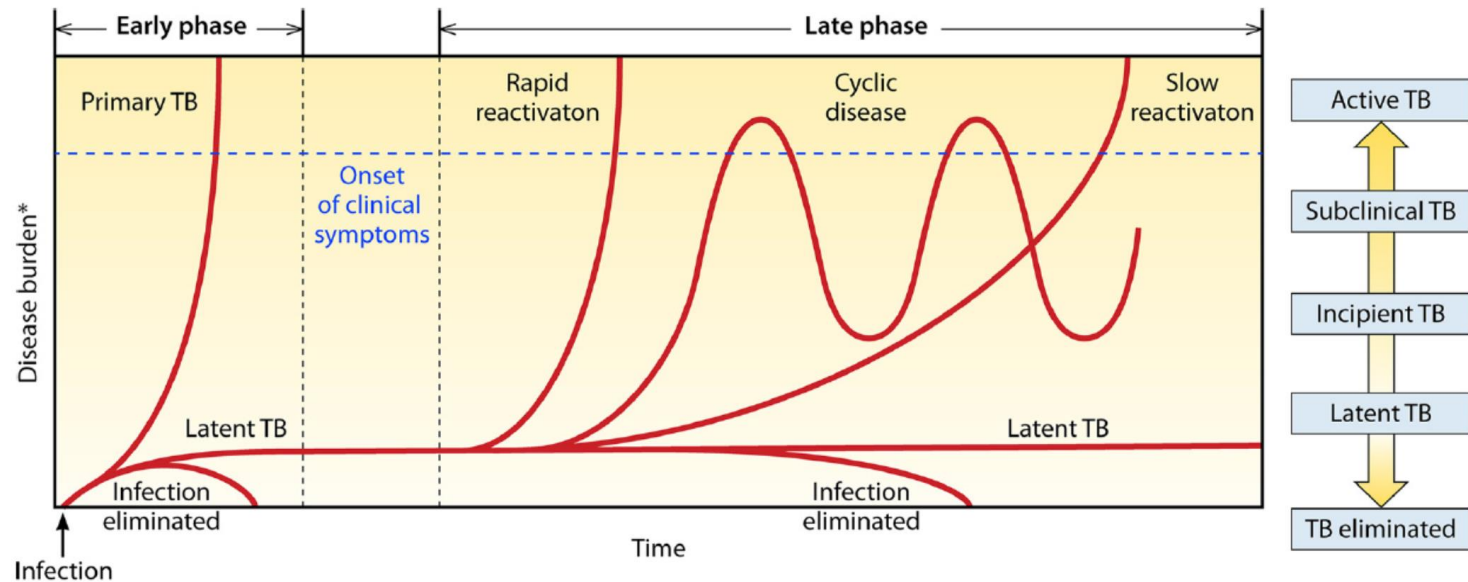
**ECHO SESSION ASLM  
OCTOBER 14<sup>TH</sup> 2021**

**DR . GIORGIO ROSCIGNO  
NEXT2PEOPLE**

# THE VISION OF WHO: TB ELIMINATION

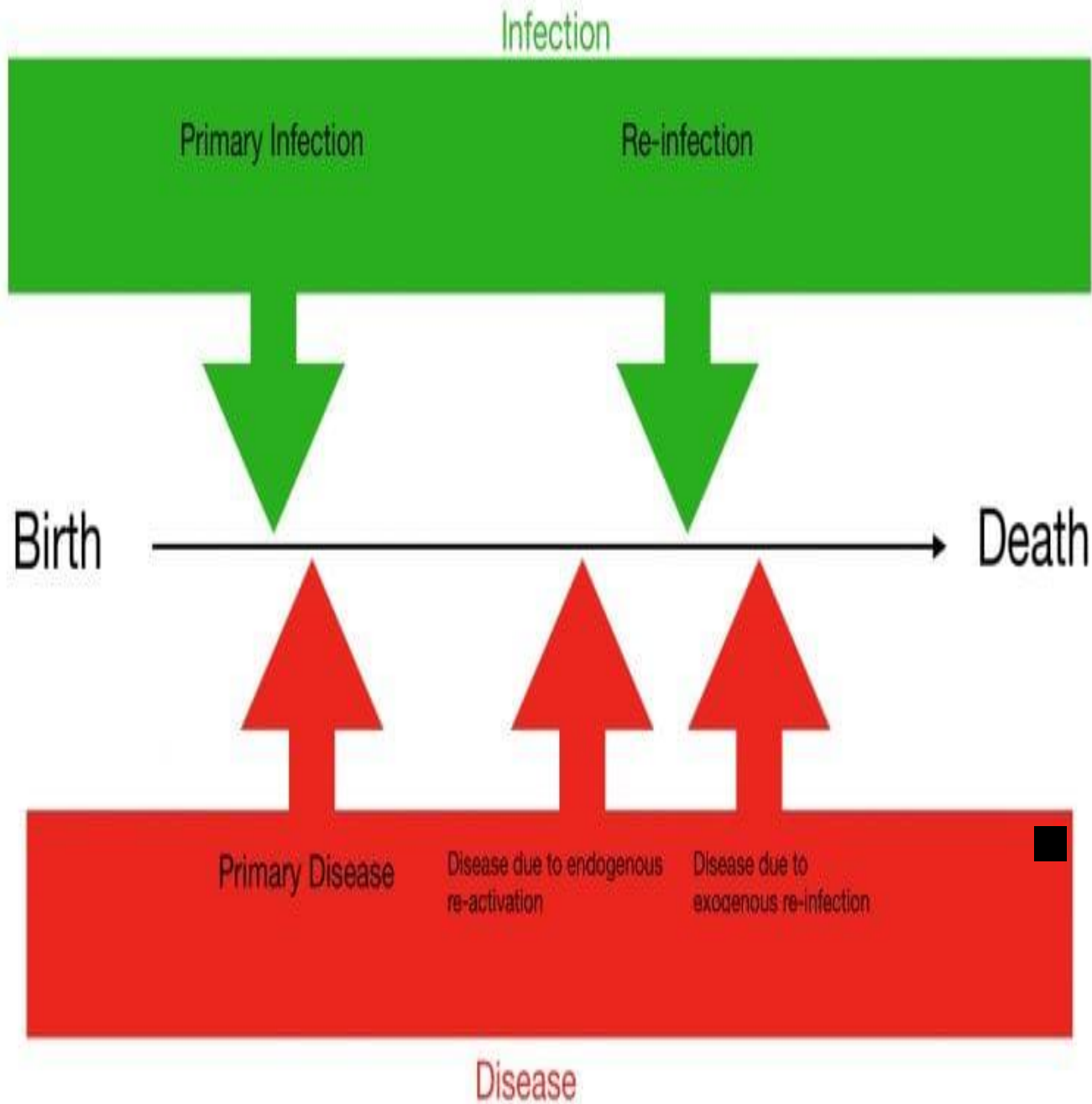


# PROGRESSION FROM LATENT TO ACTIVE TB



\*Rising TB burden implies an increase in abundance of TB and pathogen biomarkers, compartment-specific changes in immunological responses, and a decrease in the probability of disease resolution in the absence of treatment.

**FIG 1** Pathways of tuberculosis disease progression. After initial exposure, *M. tuberculosis* may be eliminated by the host immune response, persist as a latent infection, or progress to primary active disease. Following the establishment of latent infection, disease may persist in a latent form, naturally progress in a slow or rapid fashion to active tuberculosis, or cycle through incipient and subclinical states before developing into symptomatic disease or eventual disease resolution. Although not all possibilities for regression of disease burden are depicted, spontaneous recovery may occur in any of these clinical trajectories.



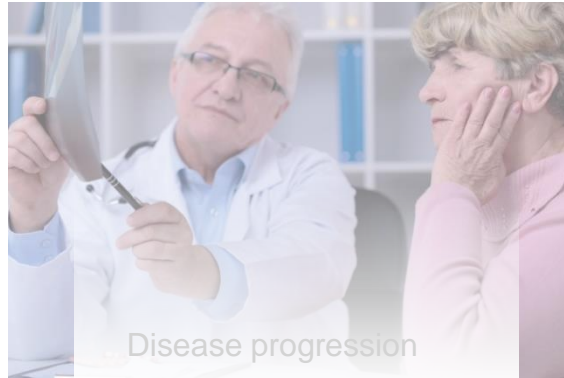
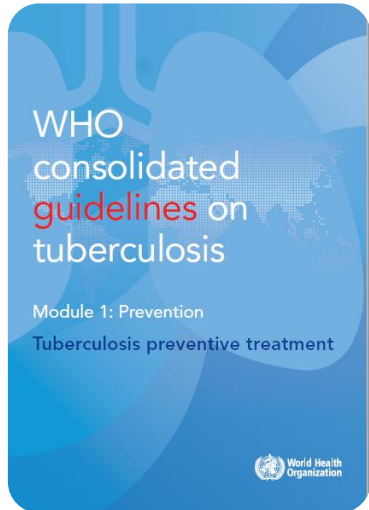
- Latent tuberculosis infection ( LTBI) is defined as a state of persistent immune response to stimulation by Mycobacterium Tuberculosis antigens with no evidence of clinically manifest active TB ( WHO).
- Up to one third of the world population is estimated to be infected with M. Tuberculosis the vast majority have no sign or symptoms of active TB disease and are not infectious although they are at risk of developing TB disease.
- 5 to 10% of those infected will develop active disease over the course of their lives usually within 5 years after infection.
- The risk for active disease after infection depends on multiple factors yet the most important being immunological status ( HIV and age).



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- Although individuals with LTBI are asymptomatic, however, they constitute an important reservoir contributing to the pool of active TB cases in future . As the success of global TB control will heavily depend upon the performance of TB control programs of high TB-burden countries (HBCs), it is imperative to treat LTBI individuals along with active TB cases.
- **Mass population LTBI screening and treatment are not feasible yet for infected individuals in population groups in which the risk for progression significantly exceeds that of general population the benefits exceed the potential harm ( drugs adverse events and costs).**

## ■ Targeting high-risk groups for TB detection



- HIV infected
- Immunosuppressive therapies
- End-stage renal disease
- Children under age 5
- Silicosis
- Organ or Hematological transplant
- Pregnant women

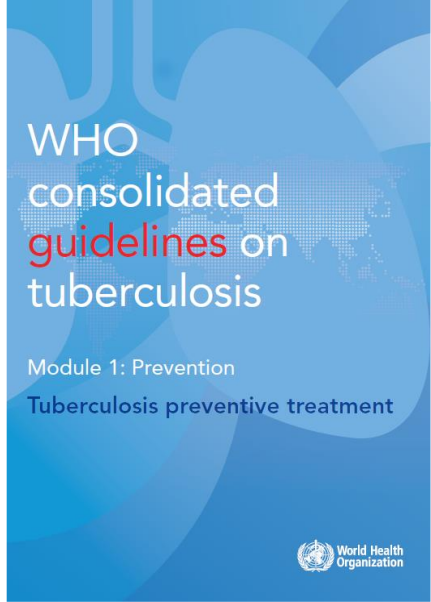


- Healthcare workers
- Immigrants from high TB-burden countries
- Prisoners
- Homeless
- Military
- All contacts of Active TB
- MDR Contacts



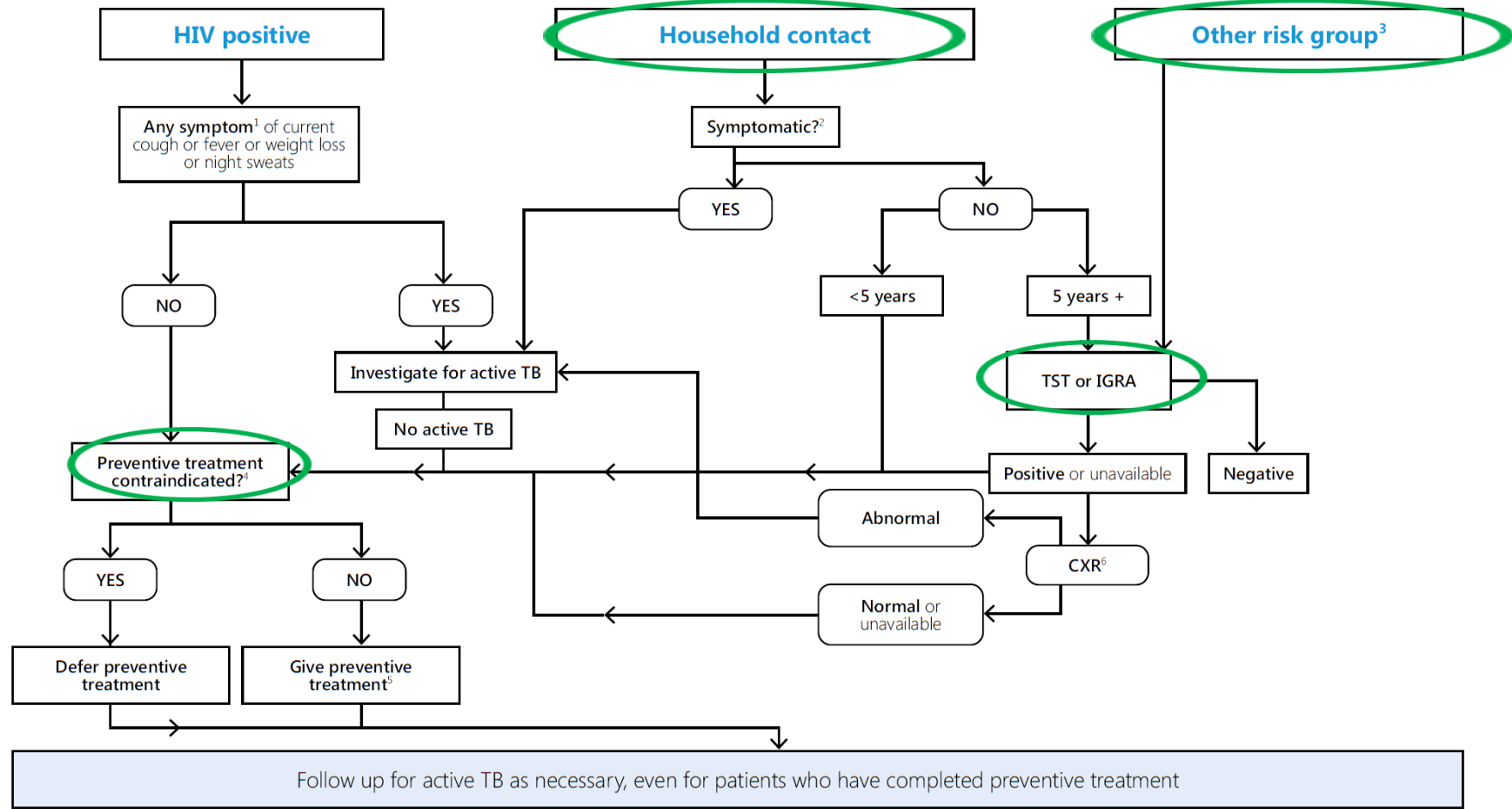
- Alcohol Abusers
- Diabetes
- Tobacco use
- Malnourishment
- Globalization and travel

—● Systematic testing is recommended in all settings regardless of background epidemiology of TB



2020

Fig. 1. Algorithm for LTBI testing and TB preventive treatment in individuals at risk

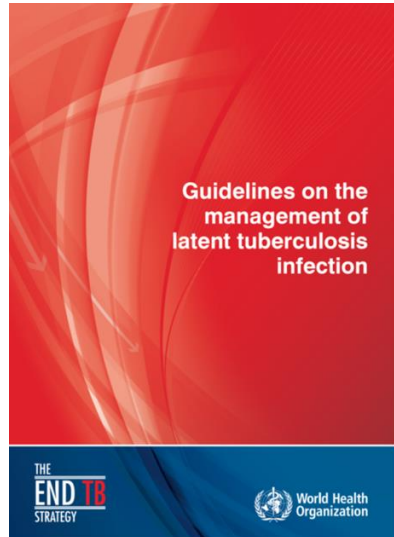


# SCREENING FOR LATENT INFECTION

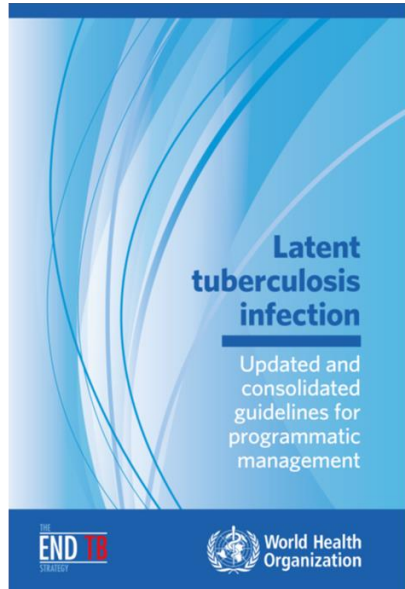
- Latent TB infection is asymptomatic
- Both available screening tests (tuberculin and IGRA) are indirect and rely on immunological response to TB antigens
- Infected persons who have a risk of progression to TB should benefit from a preventive treatment
- Screening is performed according to the national Guidelines
- Two pitfalls in practice:
  - Missing really infected persons with negative screening tests: immunocompromized persons may have a negative TST in spite of infection or TB
  - Overtreating uninfected persons with a false positive screening: a large proportion of positive TST are not confirmed by IGRA



# MANAGEMENT OF LTBI: THE POSITION OF WHO



2015



2018

Preventive treatment of infected people is **recommended** for :

- People living with HIV or under anti-TNF
- Recent contacts of pulmonary TB (all ages)
- Immunodeficiency from other origin (organ transplantation, renal dialysis, silicosis)

Screening and treatment of LTBI is **optional** for:

- Health-care workers exposed to TB
- Migrants from high-incidence countries
- Prisoners, homeless persons, users of illicit drugs

# THERE ARE TWO KINDS OF TESTS THAT ARE USED TO DETERMINE IF A PERSON HAS BEEN INFECTED WITH TB BACTERIA: THE TUBERCULIN SKIN TEST AND TB BLOOD TESTS.

## IGRA / Qiagen Quantiferon

- Requires a single patient visit to conduct the test.
- Results can be available within 24 hours.
- Does not boost responses measured by subsequent tests.
- Prior BCG (bacille Calmette-Guérin) vaccination does not cause a false-positive IGRA test result.
- Populations in which IGRAs are preferred for testing:
  - Persons who have received BCG (either as a vaccine or for cancer therapy); and
  - Persons from groups that historically have poor rates of return for TST reading.

## Tuberculin Skin Test (TST)

- Using a small needle, a health care provider injects a liquid (called tuberculin) into the skin of the lower part of the arm. When injected, a small, pale bump will appear. The person given the TST must return within 2 or 3 days to have a trained health care worker look for a reaction on the arm where the liquid was injected. The health care worker will look for a raised, hard area or swelling, and if present, measure its size using a ruler. Redness by itself is not considered part of the reaction.

## UNMET MEDICAL NEEDS (INFECTION SCREENING)

- 1) TST problems of availability in Country
- 2) quality control
- 3) BCG vaccination interference
- 4) two patients visits required

: No **alternative** to the tuberculin skin test (TST) in places without access to labs in High Burden Low Income countries. ■ Global shortage of tuberculin remains an ongoing problem

.1) **QuantiFERON ELISA and LIAISON too costly and complex for adoption**

2) **ELISA required which is too complex to decentralize.**

**Alternatives exist :**

Ellume Ultrasensitive Digital Detection System which is expected to address cost and complexity requirements .Eliminates need for lab based detection platforms • Single tube with CD4 and CD8 antigens • Acceptable IGRA performance • Increase cost effectiveness • Low complexity – digital immunoassay based • No cold chain • No equipment maintenance and calibration • No computer required • No continuous power supply requirement



## TST VS NEW IGRA ESTICK TEST

- Tuberculin skin test (TST) • Manual placement, reading and data entry – requires staff and RN time
- • False positive results caused by BCG vaccine and NTM • Two patient visits required, high no-show rate
- • Subjective test • Poor surveillance tool, manual documentation, errors
- • Two-step testing required for serial testing
- • Short expiration ~ 6 months unopened, 30 days if vial opened

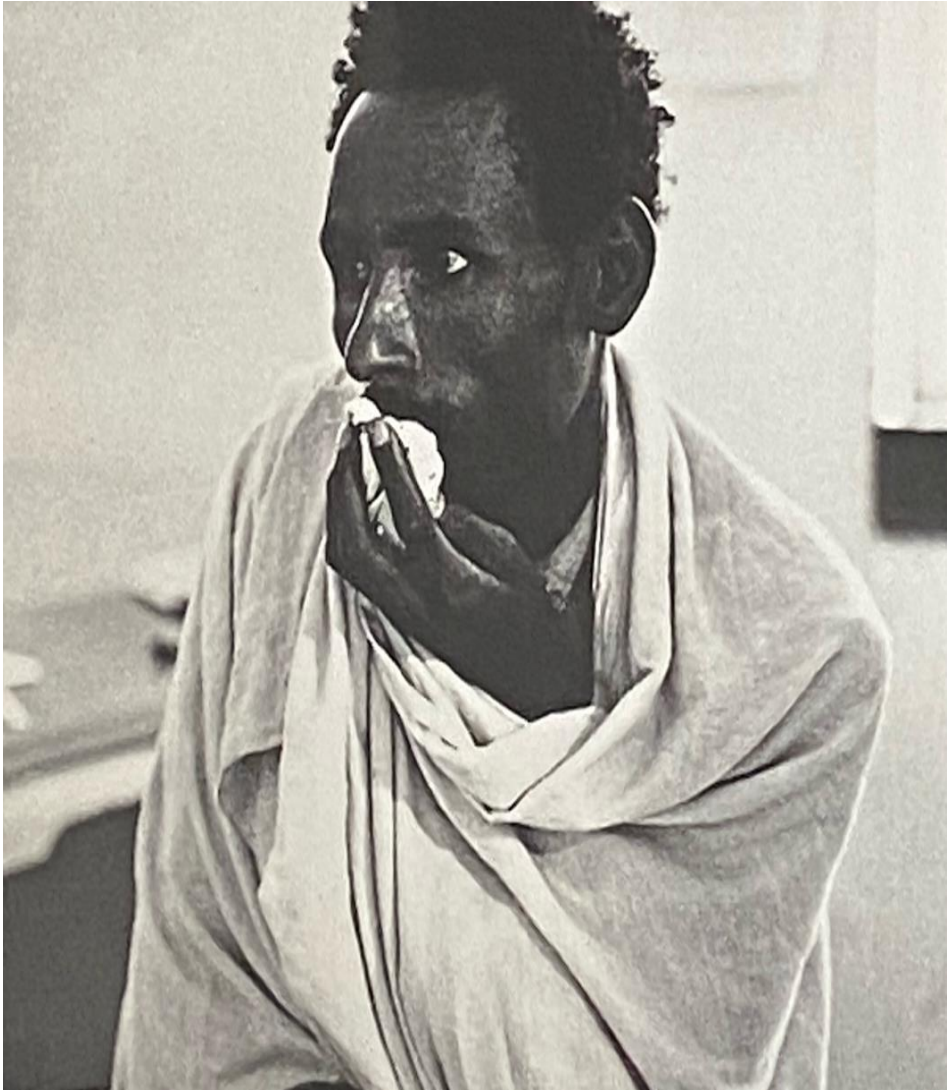
## IGRA: E- stick based test

- • Field friendly, portable
- , Quality assured
- • One tube, One mL of blood.
- • Highly specific, not affected by BCG
- • Results with one patient visit
- • Objective test • Electronic results – ideal surveillance tool
- • No cold chain requirement
- Tier 2 or reference lab requirement decentralized testing
- Ability to do single to high volume testing within 24 hours Electronic reporting designed for TB control programs

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## Key Recommendations from The Lancet Commission

The Commission estimates that 47% of the world's population has little to no access to diagnostic testing, leading to over one million unnecessary deaths globally every year. To address this situation, the Commission recommends that countries identify their most-needed tests, or Essential Diagnostics List (EDL), and use it to create a national diagnostics strategy to facilitate the implementation of diagnostics at each level of the healthcare system. The Commission highlighted the role of technology innovations, such as POC instruments and hand-held imaging devices, in improving access to diagnostics for communities.





Uganda Journalists Resource Center

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Key NEEDS for any new diagnostic introduced at community level

- Ability to use non sputum samples
- Ability to rule out TB/COVID 19 with confidence (true negatives)
- Low cost to allow for high-throughput screening/triage
- Can be used without electrical source
- Can detect TB infection and active disease in any at risk person
- Does not require a lab or highly trained technicians
- Linkages to follow-up care and treatment

Community Level

IGRA Peripheral Blood Tests. TST

TST IGRA



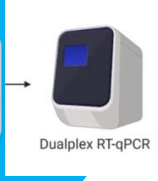
Marker Exposure  
Contact Tracing  
Surveillance Early  
Diagnosis



QiareachLAM/UI  
tra portable Xray  
/AI

-: High Throughput  
TrueNAT IGRA

Rural  
Level/GP Office  
**CONFIRM INFECTION**



Qiareach  
Molecular Test

District Lab  
Confirmatory IGRA  
MOLECULAR Genexpert

District &  
Private  
Laboratories  
Hospitals



District Lab Confirmation  
Genexpert

RT- PCR

Regional Level



RTPCR

Reference  
Laboratories



Surveillance Reference Methods.  
Network supervision Culture

Surveillance Reference Methods.  
Network supervision



next<sup>2</sup> people  
making possible healthcare for all today

**THANK YOU**





