WHO Policy Update on TB Screening for Early Case Finding: Recommended Tools and Algorithms

MODULE 1

Stop **TB** Partnership

Introduction

This module discusses the World Health Organization's (WHO) recommended tools and algorithms for systematic screening for TB in different populations.

Course Outline

→ Overview of WHO recommendations on systematic screening for TB

→ Introduction to WHO-recommended screening tools for TB

→ Review of TB screening algorithms for the general population

→ Recommended screening tools and algorithms for people with HIV

→ Recommended screening tools and algorithms for children

→ Scoping the national TB context

Summary

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Learning Objectives

By the end of this module, participants should be able to:

- Understand the requirements and role of systematic screening in the global TB response.

- Describe the advantages and disadvantages of each of the WHO-recommended screening tools.

- Recognize the different TB screening algorithms appropriate for the general population, persons living with HIV, and children.

- Describe the current TB situation in the country, including screening and diagnostic practices.

TB Context

Global TB Situation
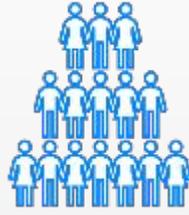
10 million people fall ill with TB every year.

Only 5.8 million people were diagnosed and notified in 2020.

1.5 million people die from TB each year—making it the world's top infectious killer.

TB is the leading cause of death of people with HIV and a major contributor to antimicrobial resistance.

WHO Recommendations
for Systematic Screening

WHO Guidelines on Systematic Screening

Systematic screening for TB disease is defined as:

> *The **systematic identification of people at risk for TB disease,** in a predetermined target group, by assessment using tests, examinations, or other procedures that can be applied **rapidly.***

From the WHO Consolidated Guidelines on Tuberculosis

- Screening tests should efficiently distinguish people likely to have TB disease from those who are unlikely to have TB disease.
- In those screened positive, diagnosis needs to be established by **evaluation using one or more diagnostic tests** and by **clinical assessment,** which together have high accuracy.

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Role of TB Screening in Overall TB Care

- Addressing the case detection gap—finding the "missing millions"
  - Globally in 2020, 5.8 million people were diagnosed and treated for TB, out of estimated 10 million cases—**significant 18% drop from 2019.**
  - The COVID-19 pandemic has made the problem much worse, with a predicted 4 to 16 percent increase in TB deaths over the next 5 years, according to a modeling study done by Stop TB.
  - Progress still lags in achieving targets from the UN High Level Meeting, 2018.
- Reaching the most vulnerable groups
  - Those with highest risk for TB often have the least access to care.
- Initiating TB preventive treatment
  - Systematic screening for TB disease is an essential first step in initiating TB preventive treatment in eligible populations.

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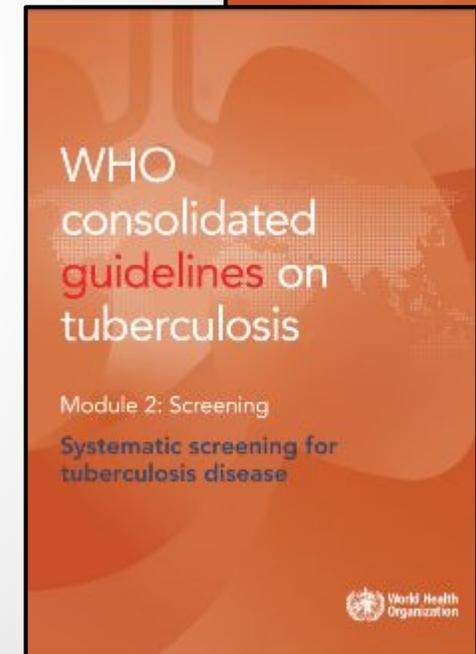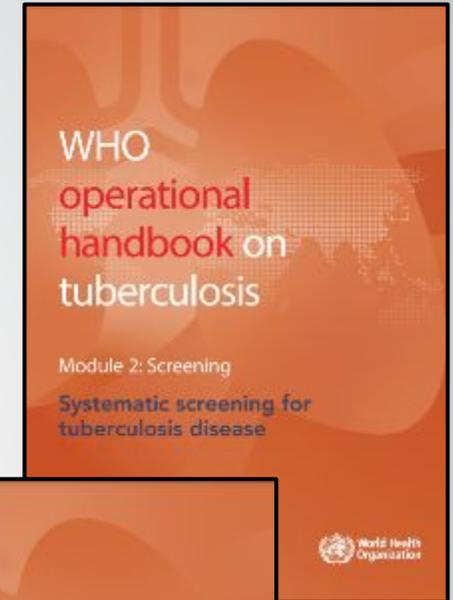# WHO Recommendation on Population to be Screened

New WHO guidelines and an operational handbook were released on March 22, 2021.

Systematic screening for TB disease is **strongly** recommended among:

Household and close contacts of TB patients	People living with HIV	Miners exposed to silica dust	Prisoners	Internally Displaced Persons (IDP)

The question is: using what tools, algorithms, and implementation models; **and** how often should screening occur?

TB treatment should be provided to those identified to have TB through subsequent diagnosis and clinical evaluation.
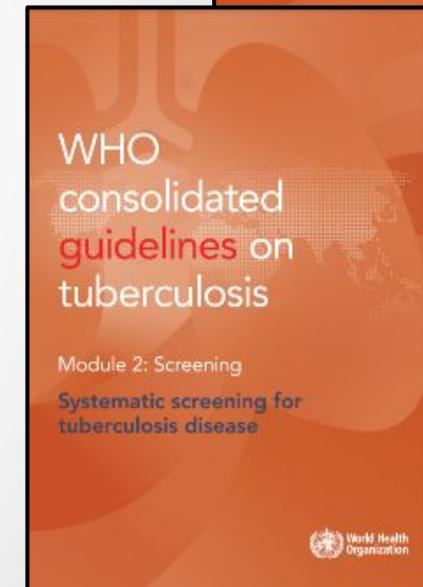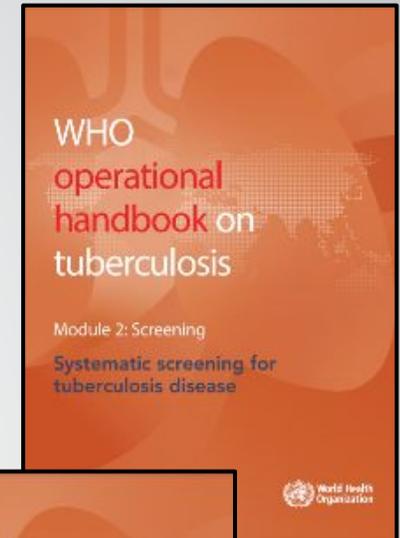
WHO operational handbook on tuberculosis
Module 2: Screening
Systematic screening for tuberculosis disease
World Health Organization

WHO consolidated guidelines on tuberculosis
Module 2: Screening
Systematic screening for tuberculosis disease
World Health Organization

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WHO Recommendation on Population to be Screened

Systematic screening for TB disease is also **conditionally** recommended among:

➔ People with untreated fibrotic lesions on a chest X-ray

➔ People with TB risk factors who are seeking health care, in settings with ≥0.1 percent TB prevalence

➔ People with malnourishment, diabetes, history of TB, chronic lung disease, and others

➔ Populations with structural risk factors for TB and limited access to health care

➔ Urban poor, homeless, refugees, migrants, and other vulnerable or marginalized groups

➔ General population in settings with ≥0.5 percent TB prevalence

For these populations, consideration should be given to:

✓ **Weighing** the benefits and risks of screening

✓ **Considering** opportunity costs for other TB and health interventions

✓ **Prioritizing** risk groups that represent the greatest burden or have the greatest vulnerability in a particular setting

WHO **operational handbook** on **tuberculosis**

Module 2: Screening

Systematic screening for tuberculosis disease

WHO **consolidated guidelines** on **tuberculosis**

Module 2: Screening

Systematic screening for tuberculosis disease

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TB Screening Tools Overview
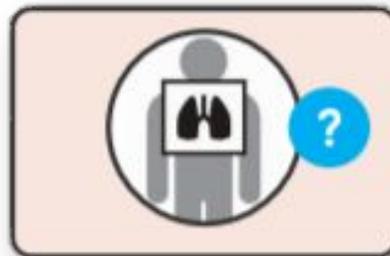
Recommended Tools to Screen
General Population (aged 15+) and High-risk Groups (not HIV+)

There are **four recommended screening tools** for TB in high-risk populations (and the general population in high burden settings) that are recommended by WHO for all individuals aged 15 years and older:
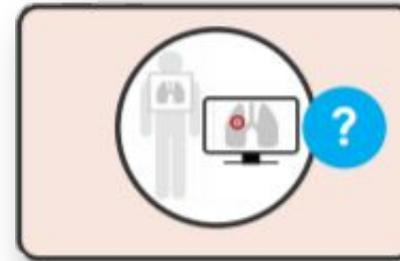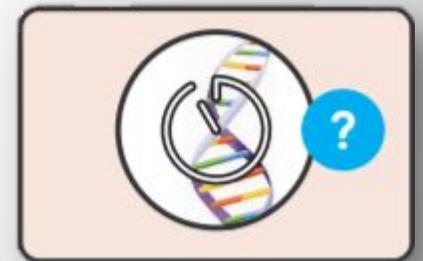
1.
Symptom screening

Cough | Any TB symptom
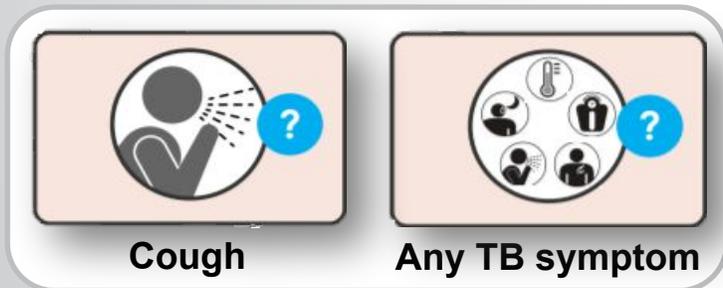
2.
Chest X-ray

3.
Computer-aided detection

4.
Molecular WHO-recommended rapid diagnostics

Symptom Screening

Screening individuals for symptoms of TB. This could be **any cough, prolonged cough,** or **any TB-associated symptom,** including any cough, hemoptysis, weight loss, fever, or night sweats.
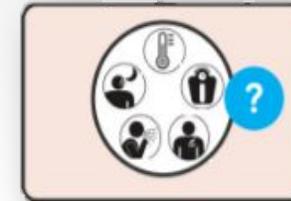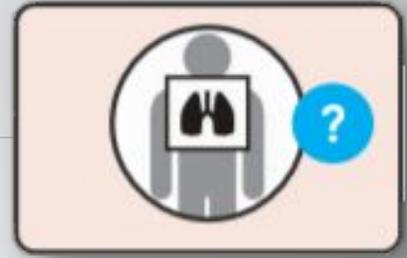
Benefits:

✔ A suitable and acceptable screening tool in most settings and risk groups

✔ May be more feasible to implement (fewer resources needed and less costly)

✔ Non-invasive

Limitations:

✔ Less sensitive than chest X-ray or molecular tests

✔ Does not identify asymptomatic or pre-symptomatic individuals, nor people with atypical symptoms.

Screening test	No. of studies (no. of participants)	Sensitivity	No. of studies (no. of participants)	Specificity
WHO target product profile	NA	> 0.90	NA	> 0.70
Prolonged cough (≥ 2 weeks)	40 (6 737)	0.42	40 (1 284 181)	0.94
Any cough	21 (2 734)	0.51	21 (768 291)	0.88
Any TB symptom (cough, haemoptysis, fever, night sweats, weight loss)	28 (3 915)	0.71	28 (460 878)	0.64
Chest radiography (any abnormality)	22 (4 243)	0.94	22 (1 012 752)	0.89
Chest radiography (suggestive abnormality)	19 (2 152)	0.85	19 (464 818)	0.96
Molecular WHO-recommended rapid diagnostic test	5 (337)	0.69	5 (8 619)	0.99

Chest X-ray

Chest X-ray (CXR) is an imaging tool for identifying lung abnormalities. The role of CXR is improving TB notification in high-prevalence settings.
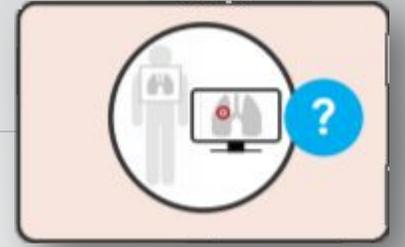
Benefits:

✔ A sensitive tool for screening and detecting active pulmonary TB

✔ Can identify asymptomatic or presymptomatic people with TB

✔ Useful triage tool to improve efficiency of molecular diagnostic testing

✔ Can provide differential diagnosis of other lung conditions outside of TB

✔ Potential in treatment monitoring

Limitations:

✔ Cannot detect extra-pulmonary TB

✔ Not very specific

✔ Involves exposure to radiation (although risk is minimal)

✔ Use and access to CXR is hampered by:

- Insufficiently trained radiologists
- Shortage of trained readers (usually physician radiologists) to interpret the images.
- Intra- and inter-reader variability
- Limited access to high-quality digital CXR imaging in low-resource settings

WHO recommends the use of CXR as an effective screening test for pulmonary tuberculosis, as well as an aid in the diagnostic pathway to complement bacteriological tests.

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Computer–aided Detection Software

> Computer-aided detection (CAD) is an interpretation tool for chest X-ray that can provide rapid, automatic interpretation of x-ray results and be used in addition to or in place of human readers.

Benefits:

✔ Validation studies have shown that CAD performance is similar to, or **better than,** human readers.

✔ Can be used **in absence** of trained human reader (if not available) and thereby increase case detection from CXR screening interventions

✔ Can enhance and facilitate human resources capacity when used **with** trained human reader (decision support, prioritization, workflow management)

✔ Results are provided rapidly (<1 minute), allowing for quick clinical decision-making

✔ Standardized reporting reduces inter- and intra-reader variability

✔ Can be used to meet different programmatic goals (e.g., halving the number of confirmation tests required or increase yields)

Limitations:

✔ Not yet validated nor recommended for use in children <15 years

✔ May not be as accurate in people with TB scarring but no active disease

✔ Further research is needed to ensure that CAD performs as well in key populations, such as persons living with HIV.

✔ A TB CAD product may not give an indication on the presence or absence of other diseases. Even if it does, the accuracy of differential diagnosis is not validated.

✔ High price and complex pricing structures

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Molecular WHO–recommended Rapid Diagnostics
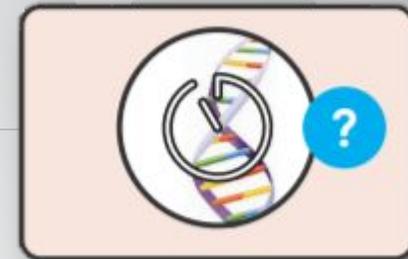
> Molecular WHO-recommended rapid diagnostics (mWRDs) are rapid and sensitive molecular tests suitable for screening. mWRDs include Xpert MTB/RIF, Xpert MTB/RIF Ultra, Truenat, etc.
>
> When used for screening, mWRDs have different accuracy than when they are used for diagnosis, and different predictive values are associated with a positive test and a negative test due to differences in the prevalence of TB in the populations being tested.

Benefits:

✔ Highly specific when used for screening (99 percent)

✔ Some mWRDs are becoming more decentralized.

Limitations:

✔ Require significant resources (machines, cartridges, consumables)

✔ Limited in individuals who cannot produce sputum

✔ Can result in false positives when used alone in low-prevalence setting for people living with HIV

✔ A negative mWRD cannot be used to exclude TB for people living with HIV.

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Tools for Screening People Living with HIV

> The following tools are recommended for screening people living with HIV (for adults and adolescents 10 years and older):

- WHO-recommended four symptom screen (W4SS)
  - Cough, fever, night sweats, weight loss
- C-Reactive Protein (CRP)
  - A point-of-care blood test measuring the occurrence of an indicator (CRP) in the blood.
  - Improves on the accuracy (particularly specificity) of the W4SS for people living with HIV not on antiretroviral therapy (ART)
- Chest X-ray
- Molecular WHO-recommended rapid diagnostic tests

Fever

Current cough

Weight loss

Night sweats
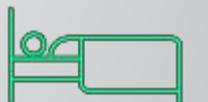
C–Reactive Protein

- A general marker for inflammation, can be performed as a point-of-care test in some settings

- Has similar sensitivity and similar or improved specificity to W4SS in all subgroups of people living with HIV, depending on cut-off

- Represents an improvement in accuracy (particularly specificity) over the W4SS for people living with HIV not on ART

Population	Cut-off > 5 mg/L		Cut-off > 10 mg/L	
	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
All people living with HIV	90	50	83	65
Inpatients	98	12	97	21
Outpatients on ART	40	80	20	90
Outpatients not on ART	89	54	82	67
≤ 200 CD4 cells/μL[a]	93	40	90	54
Pregnant women living with HIV	70	41	70	54

Tools for TB Screening in Children

> There are two groups of children in whom TB screening is **strongly** recommended:

Child contacts of people with TB

Tools **strongly** recommended for screening child contacts (up to 15 years) include:

- Symptom screening (cough, fever, poor weight gain)
  - In young children, reduced playfulness or lethargy may also be considered a symptom.
- Chest X-ray

Children living with HIV

Children with HIV (<10 years) should be screened for TB at every encounter with a health care worker given the risk of TB and of mortality in this group

Screening is **strongly** recommended for children living with HIV (up to 10 years) who:

- Show signs and symptoms indicative of TB such as cough, fever, poor weight gain

- Are close contacts of someone with TB

Children frequently have extrapulmonary TB disease, **health care workers must be aware of symptoms that indicate TB at other sites,** such as lymphatic, abdominal, meningeal, and osteoarticular TB.

TB Screening Algorithms Overview

Overview of TB Screening Algorithms

Screening algorithms **combine one or several screening tests and diagnostic evaluation** for TB disease. Different configurations of screening tests have different implications for the sensitivity, specificity, and costs of the algorithm.

There are four general types of screening algorithms to be aware of:

1. Single screening algorithm: Uses **only one screening test.** A positive screen result requires diagnostic evaluation.

2. Parallel screening algorithm: Uses **two screening tests in parallel.** A positive result on either or both requires diagnostic evaluation.

3. Sequential positive serial screening algorithm: Uses **two screening tests in sequence.** A positive result on the first screen results in referral to the next screening test.
- Diagnostic evaluation for anyone screening positive on both screening tests.

4. Sequential negative serial screening algorithm: Uses **two screening tests**
- A positive result on the first screening test results in referral to diagnostic evaluation.
- A negative result on the first screening test results in referral to the second screening test and diagnostic evaluation if positive on the second screening test.
- It is similar to, but reduces the cost of, parallel and sequential positive screening by limiting the numbers of people referred for a second screening test.

General Population (aged 15+) and High-risk Groups (not HIV+)

**Initial screen: Cough and all symptoms
CXR is used as secondary screen and mWRD/clinical evaluation as diagnosis**

Single screening algorithm
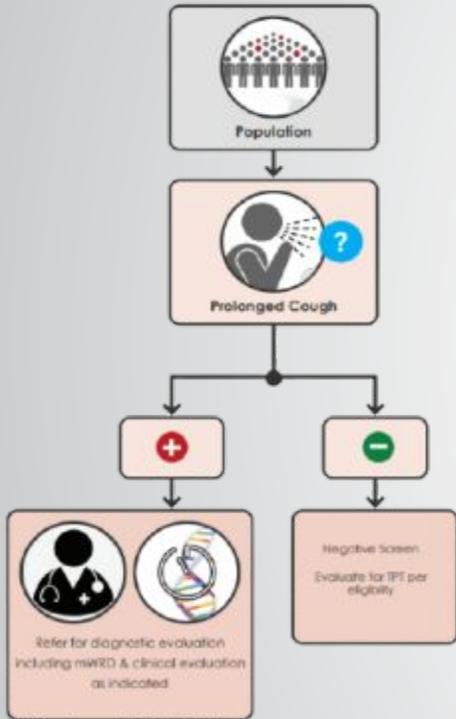
Parallel screening algorithm with CXR
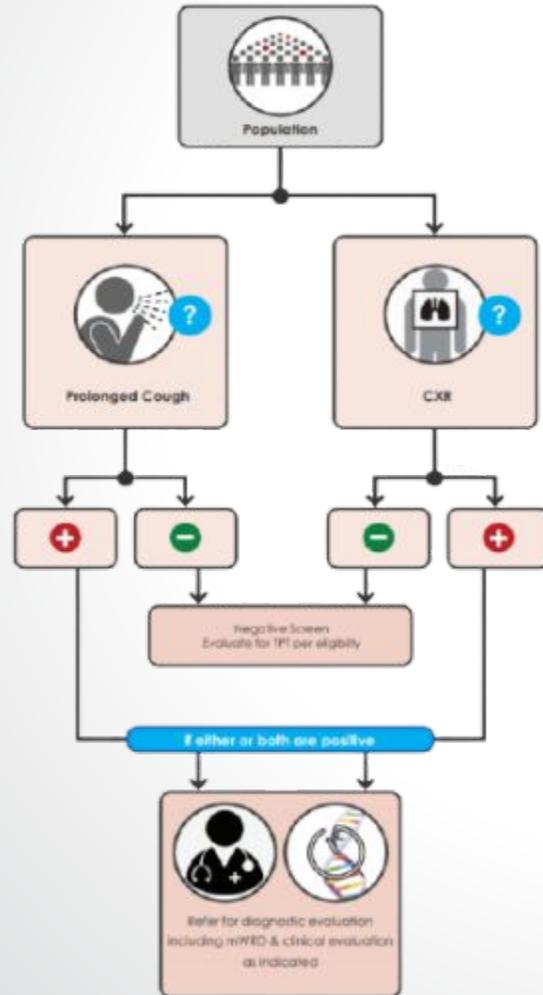
Sequential positive serial screening algorithm
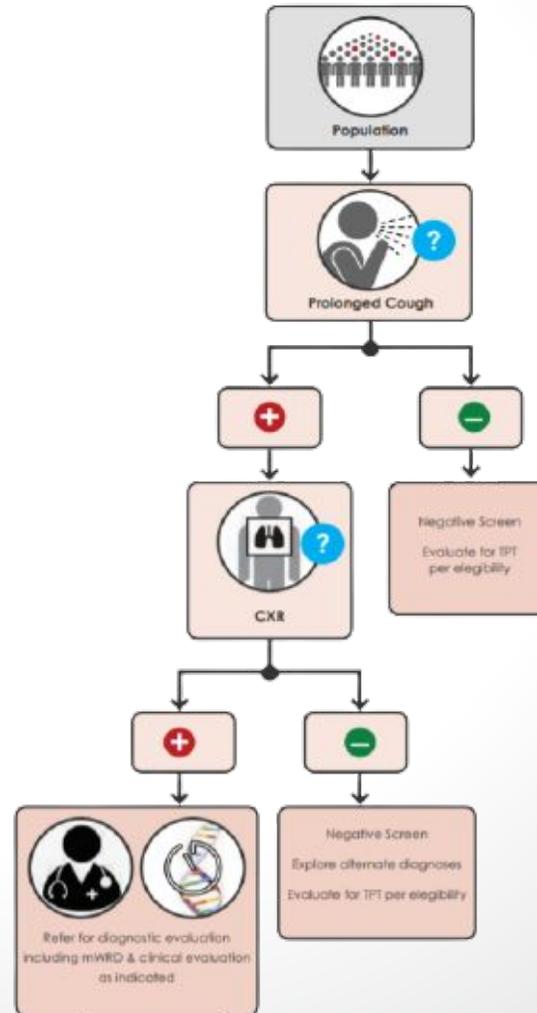
Sequential negative serial screening algorithm
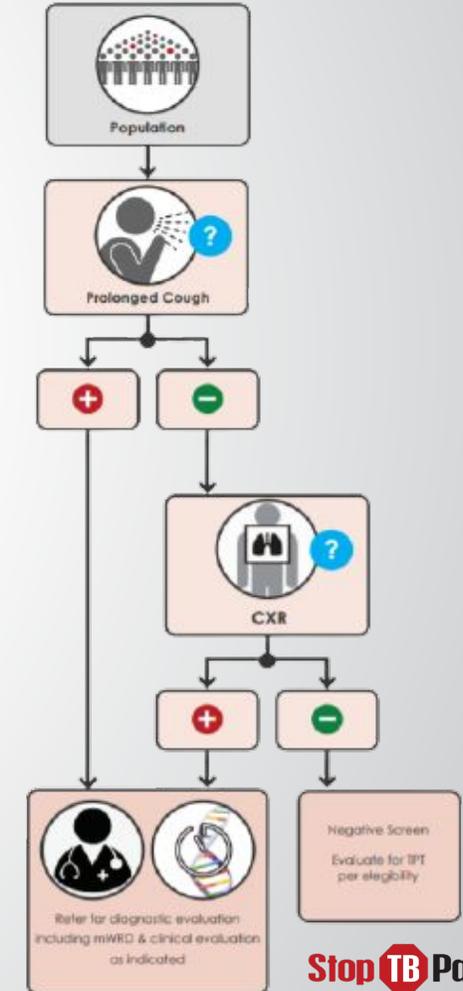
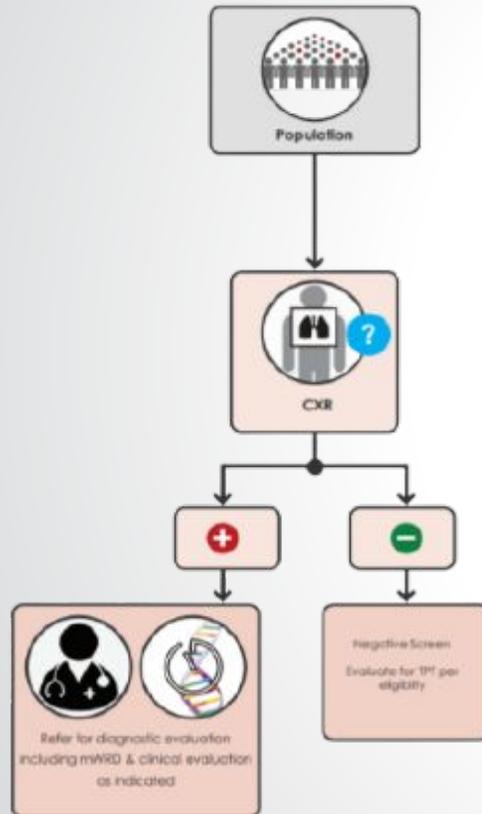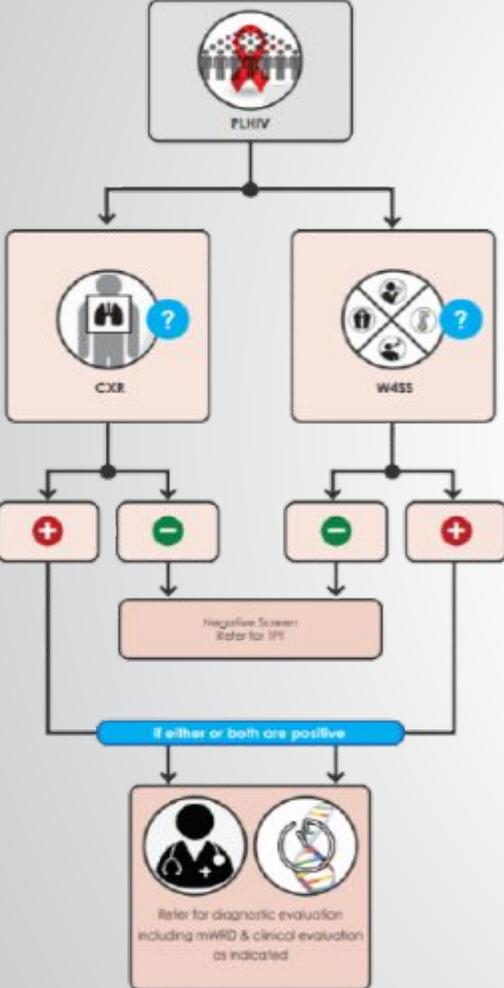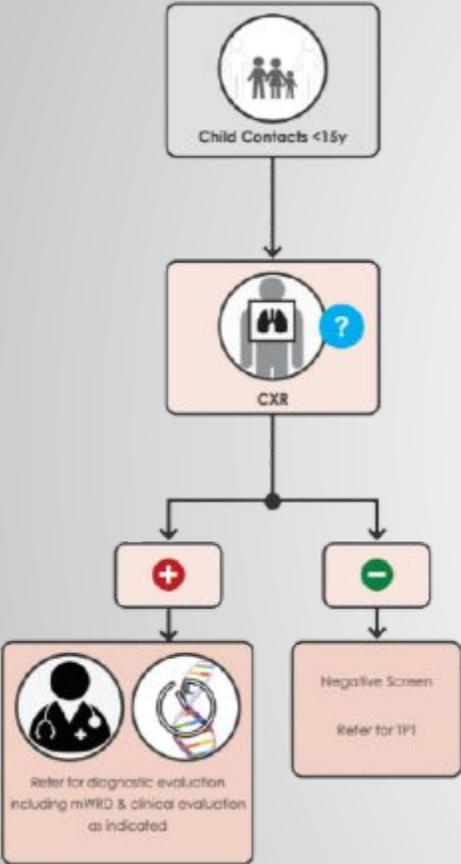*Source: WHO Operational Handbook on Tuberculosis: Systematic Screening for Tuberculosis Disease*

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General Population (aged 15+) and High-risk Groups (not HIV+)

Initial screen: CXR	Initial screen: mWRD

Single screening algorithm

Single screening algorithm
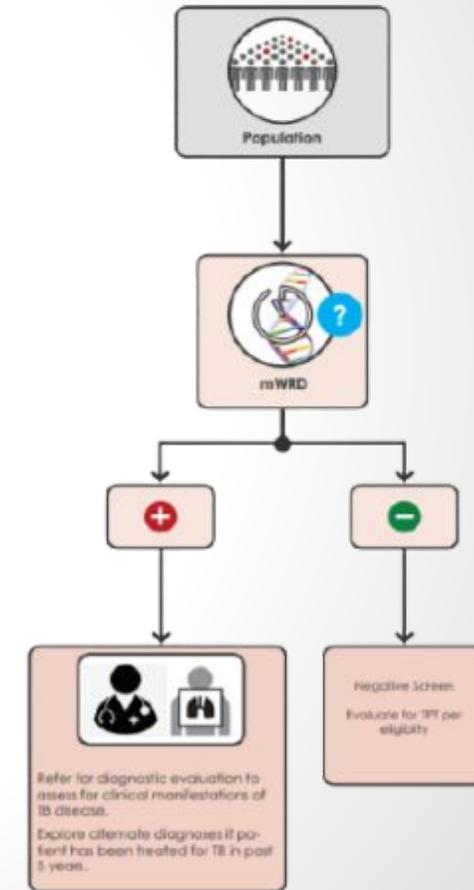
Screening Algorithms for Adults and Adolescents Living with HIV involving X-ray

Parallel screening with W4SS and CXR

Sequential positive screening with W4SS and CXR
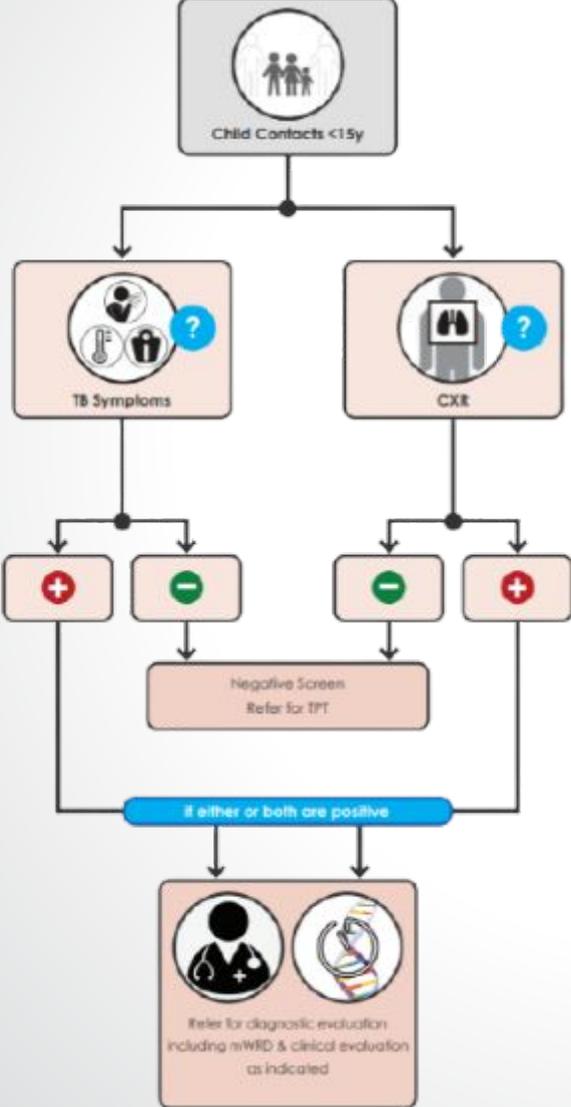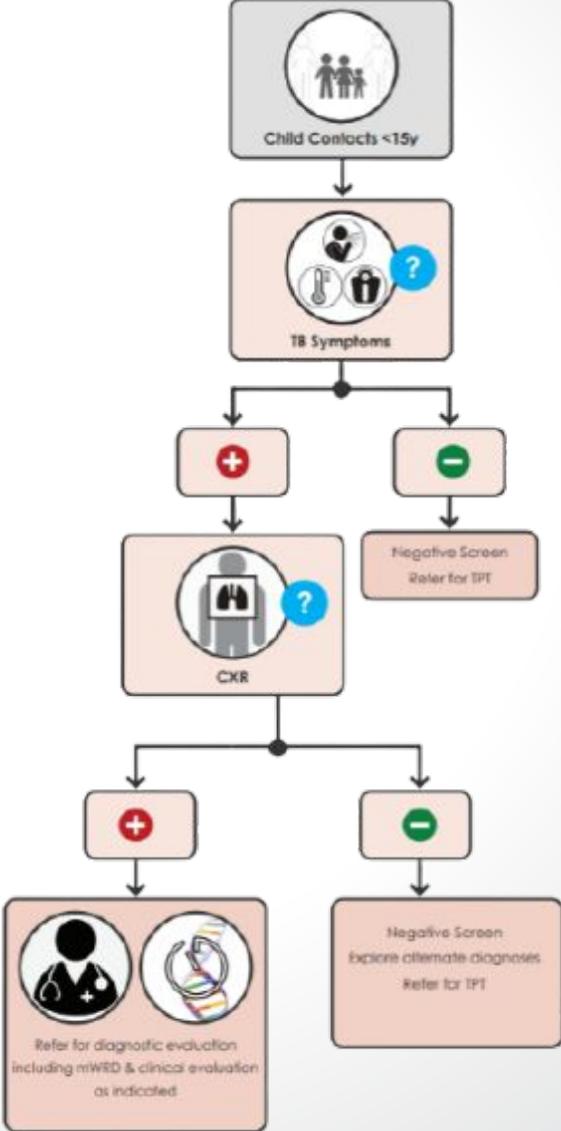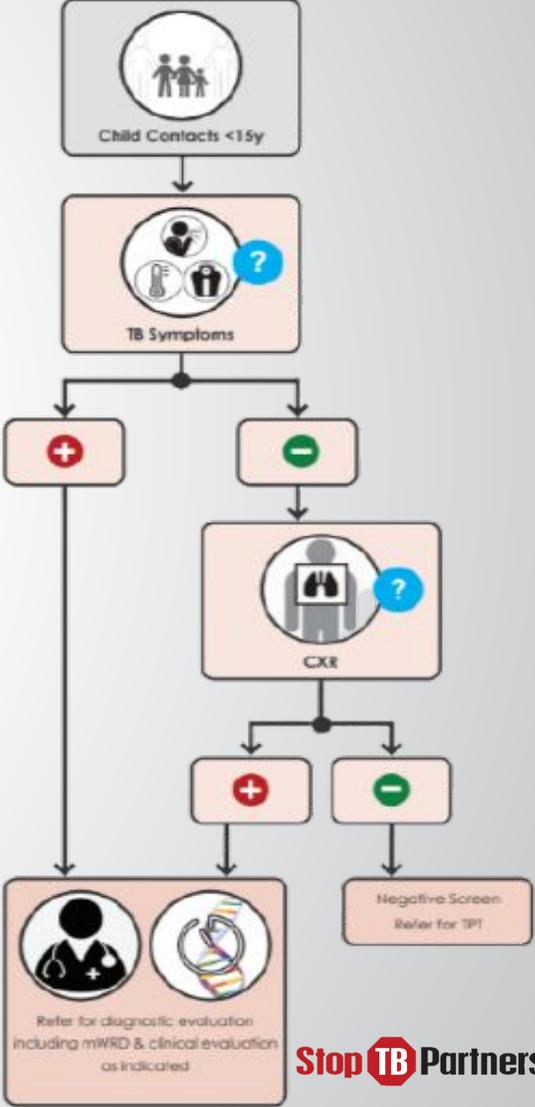
Sequential negative screening with W4SS and CXR
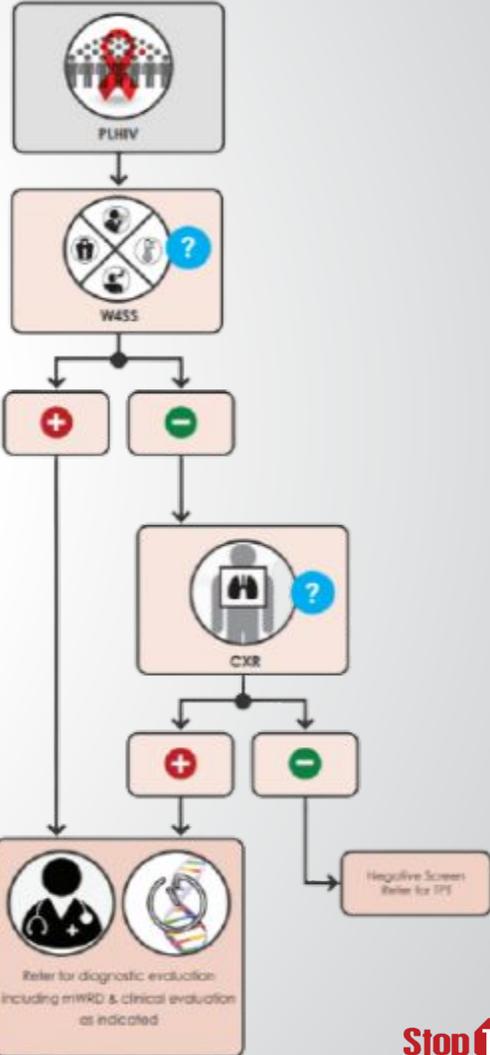
Screening Algorithms for Children involving X-ray

Single screening with CXR

Parallel screening with symptom and CXR

Sequential positive screening with symptoms and CXR

Sequential negative screening with symptoms and CXR

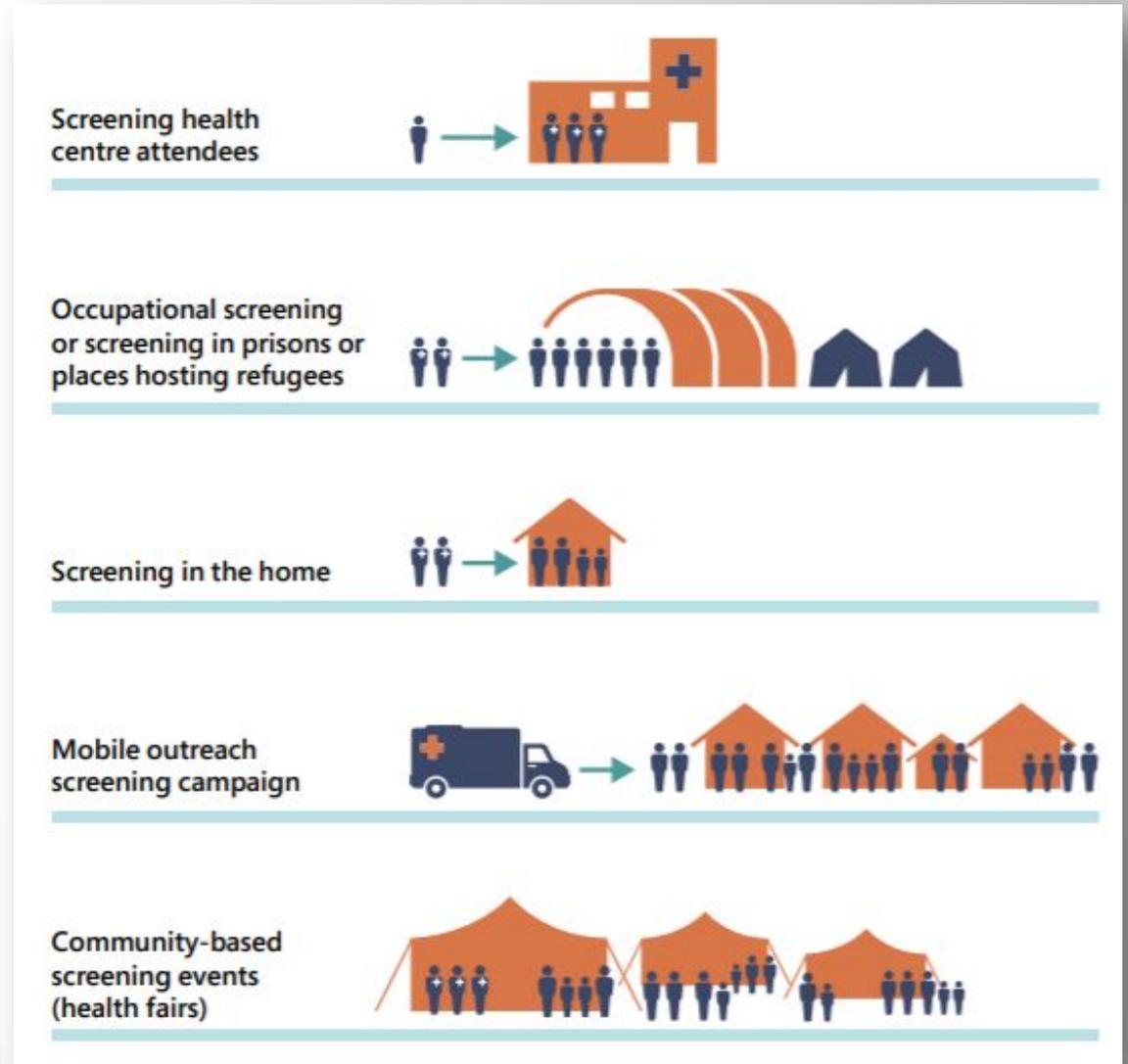*Source: WHO Operational Handbook on Tuberculosis: Systematic Screening for Tuberculosis Disease*

Different Screening Program Models

There are a number of established screening program models. Which model is used should be tailored to the **target population,** with **consideration for the available resources.**

- Offering screening where the target population lives or works may be particularly important in target populations that face barriers to accessing health care.
  - But this may require **more resources,** like a mobile van and radiography system.
- Depending on resources and need, programs may be **continuous** or **event-based.**

Barriers to accessing health care services may also apply to diagnostic and treatment services.
- How screen positive people will access these services should also be planned for.

Screening health centre attendees

Occupational screening or screening in prisons or places hosting refugees

Screening in the home

Mobile outreach screening campaign

Community-based screening events (health fairs)

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Algorithm Considerations for Risk Groups

Miners

High risk of transmission

↓

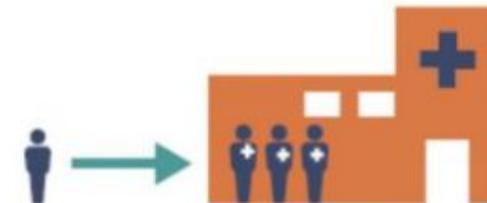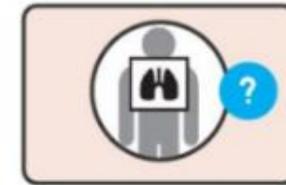Highly sensitive algorithms

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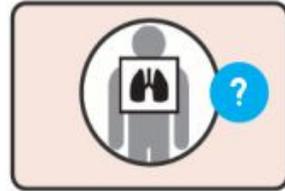
CXR preferred

Contacts

High prevalence of TB - high risk of TB - eligible for TPT

Goal of screening: identify TB disease early and rule out TB
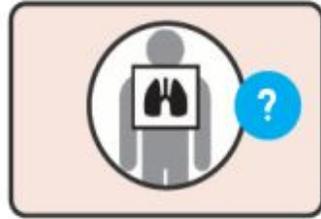
↓

High sensitivity

↓

CXR preferred

Algorithm Considerations for Risk Groups

Prisons

High risk of transmission

↓

Highly sensitive algorithms
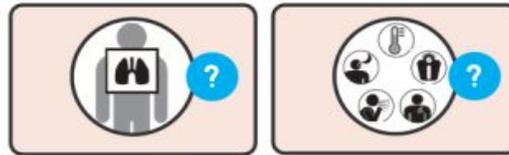
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CXR preferred

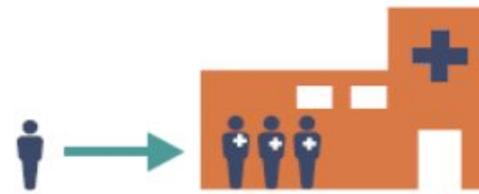## People with clinical risk factors

Setting with TB prevalence > 100 / 100 000

TB screening in people seeking healthcare or who are in medical care

CXR screening for increased sensitivity
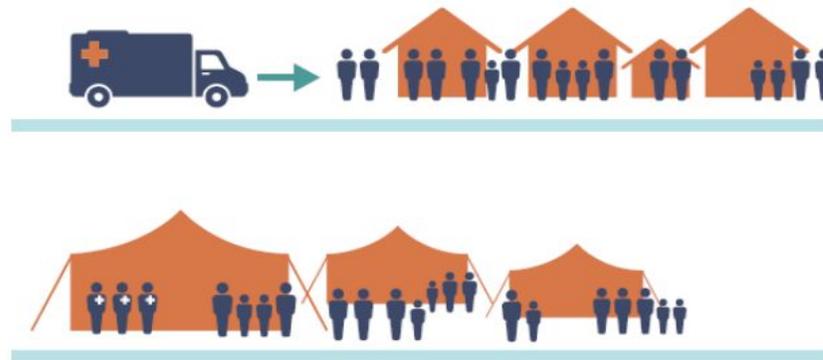
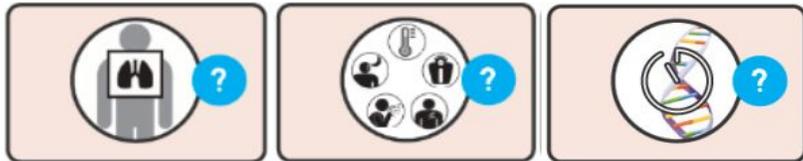Symptom screening for triage and infection control

Algorithm Considerations for Risk Groups

General population & high risk communities

If TB prevalence is ≥ 0.5%

Depending on required sensitivity, resources and feasibility of implementations

Summary

Summary

- Systematic screening plays a key role in the global TB response, especially for identifying the "missing cases" of TB.

- A screening intervention should be tailored to the barriers and needs of the target population.

- There are four WHO-recommended screening tools for TB in general population (aged 15+) and high-risk groups (not HIV+). These can be used alone, in parallel, or in sequence in screening algorithms.

- Different screening tools and algorithms are recommended for screening people living with HIV and children for TB.