



# CQUIN 5<sup>th</sup> Annual Meeting

Virtual: November 16-19, 2021

## Systematic screening for TB disease

Updated WHO recommendations and screening algorithms for  
people living with HIV

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HIV Learning Network  
The CQUIN Project for Differentiated Service Delivery

# Rationale

- TB is a primary cause of AIDS-related death
  - In 2020, about 215 000 **people died** of **HIV-associated TB**
  - HIV **post-mortem studies** find **TB prevalence of 40%**
  - **TB was undiagnosed prior to death** in close to **50%** of cases<sup>1</sup>
- Large case detection gap among people living with HIV
  - An estimated **44%** of people living with HIV-associated TB are **not diagnosed**
- Therefore early detection and treatment are essential to reducing mortality among people living with HIV



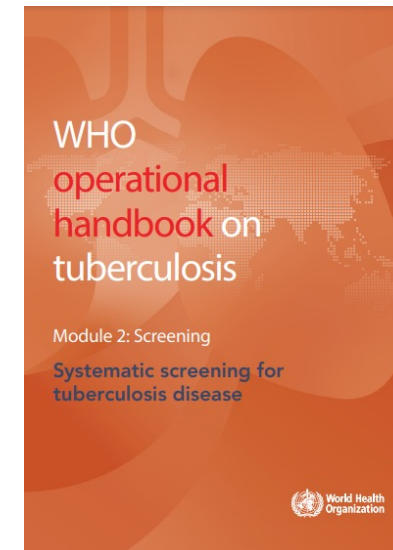
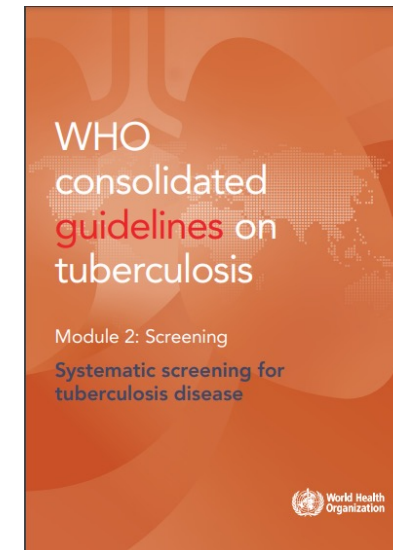
# TB screening guidelines – update process

## Goals of update:

- Consolidate and update recommendations to bring them in line with most recent evidence
- Evaluate **novel screening tools** and **technologies**
- Provide more guidance on use of screening tools and algorithms for specific risk groups and populations

## New guidelines, operational guide:

- Released March 22, 2021
- Now available: <https://www.who.int/activities/screening-for-tb>



# Recommendations

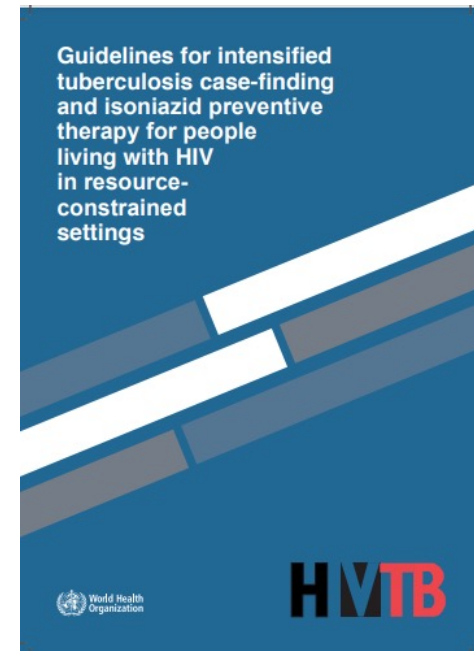
## Tools for screening adults and adolescents 10 years and older living with HIV



### ■ WHO-recommended 4 symptom screen (W4SS)

- Cough
- Fever
- Night sweats
- Weight loss

- Strong recommendation
- Recommended since 2011 for screening all PLHIV at every healthcare visit
- Has limited specificity in some subgroups, making clinical implementation difficult due to the high proportion of patients that screen positive
- Remains the cheapest and most feasible screening test
- Issues of quality of implementation



Population	No. of studies (no. of participants)	Sensitivity (95% CI)	Specificity (95% CI)
WHO target product profile	NA	> 0.90	> 0.70
All people living with HIV	23 (16 269)	0.83 (0.74–0.89)	0.38 (0.25–0.53)
Inpatients	4 (672)	0.96 (0.92–0.98)	0.11 (0.08–0.14)
Outpatients on ART	9 (4 309)	0.53 (0.36–0.69)	0.70 (0.50–0.85)
Outpatients not on ART	19 (11 159)	0.84 (0.75–0.90)	0.37 (0.25–0.50)
CD4 ≤ 200 cells/μL	22 (5 956)	0.86 (0.77–0.92)	0.30 (0.18–0.45)
Pregnant women living with HIV	8 (1 937)	0.61 (0.39–0.79)	0.58 (0.39–0.75)



# Recommendations

## Tools for screening adults and adolescents 10 years and older living with HIV



### ▪ C-Reactive Protein (cutoff of 5mg/L)

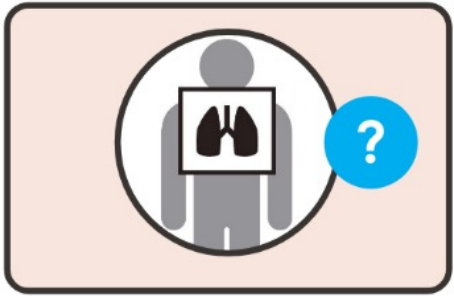
- Conditional recommendation
- A general marker for inflammation, can be performed as a point-of-care test in some settings
- Has similar sensitivity and similar or improved specificity to W4SS in all subgroups of PLHIV, depending on cut-off
- **Represents an improvement in accuracy (particularly specificity) over the W4SS for people living with HIV not on ART**

Population	No. of studies (no. of participants)	Sensitivity (95% CI)	Specificity (95% CI)
WHO target product profile	NA	> 0.90	> 0.70
All people living with HIV	6 (3 971)	0.90 (0.78–0.96)	0.50 (0.29–0.71)
Inpatients	1 (400)	0.98 (0.93–1.00)	0.12 (0.09–0.17)
Outpatients on ART	1 (381)	0.40 (0.10–0.80)	0.80 (0.75–0.84)
Outpatients not on ART	4 (3 186)	0.89 (0.85–0.92)	0.54 (0.45–0.62)
CD4 ≤ 200 cells/μL	6 (1 829)	0.93 (0.87–0.97)	0.40 (0.22–0.62)
Pregnant women living with HIV	2 (62)	0.70 (0.12–0.97)	0.41 (0.12–0.78)



# Recommendations

## Tools for screening adults and adolescents 10 years and older living with HIV



- **Chest X-ray (any abnormality)**

- Conditional recommendation
- CXR used alongside W4SS increases sensitivity of screening, to help detect TB and rule out prior to TPT
- CXR and W4SS combined (parallel screen) provides improved sensitivity and similar specificity to W4SS alone for all subgroups of PLHIV
- **Most sensitive screening strategy for PLHIV on ART**

Population	No. of studies (no. of participants)	Sensitivity (95% CI)	Specificity (95% CI)
WHO target product profile	NA	> 0.90	> 0.70
All people living with HIV	8 (6 238)	0.93 (0.88–0.96)	0.20 (0.10–0.38)
Inpatients	1 (52)	0.90 (0.33–0.99)	0.07 (0.03–0.19)
Outpatients on ART	4 (2 670)	0.85 (0.69–0.94)	0.33 (0.15–0.58)
Outpatients not on ART	8 (3 516)	0.94 (0.89–0.96)	0.19 (0.09–0.34)
CD4 ≤ 200 cells/μL	8 (2 232)	0.94 (0.90–0.97)	0.14 (0.07–0.25)
Pregnant women living with HIV	1 (8)	0.75 (0.11–0.99)	0.56 (0.24–0.84)



# Recommendations

## *Tools for screening adults and adolescents 10 years and older living with HIV*



- **Molecular WHO-recommended rapid diagnostic tests**

- **Strongly recommended** for medical inpatients with HIV in high-burden settings (medical wards with a TB prevalence of  $\geq 10\%$ ) as a “screen and treat” strategy, no need for further diagnostic testing
- **Conditionally recommended** for all other people living with HIV
- Priority should be made to ensuring universal access to mWRD as a diagnostic test.
- Diagnostic workup recommended if used for screening.

Population	No. of studies (no. of participants)	Sensitivity (95% CI)	Specificity (95% CI)
WHO target product profile	NA	> 0.90	> 0.70
All people living with HIV	14 (9 209)	0.69 (0.60–0.76)	0.98 (0.97–0.99)
Inpatients	4 (639)	0.77 (0.69–0.84)	0.93 (0.89–0.96)
Outpatients on ART	4 (2 645)	0.54 (0.20–0.84)	0.99 (0.97–1.00)
Outpatients not on ART	10 (5 796)	0.72 (0.64–0.79)	0.98 (0.98–0.99)
CD4 $\leq$ 200 cells/ $\mu$ L	12 (3 422)	0.76 (0.68–0.82)	0.97 (0.95–0.98)
Pregnant women living with HIV	4/4/3	0.55 (0.33–0.75)	0.99 (0.97–0.99)

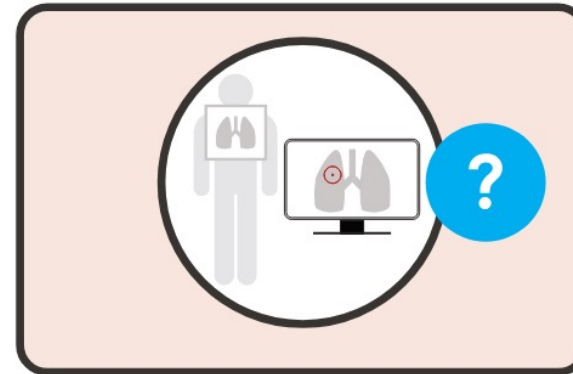
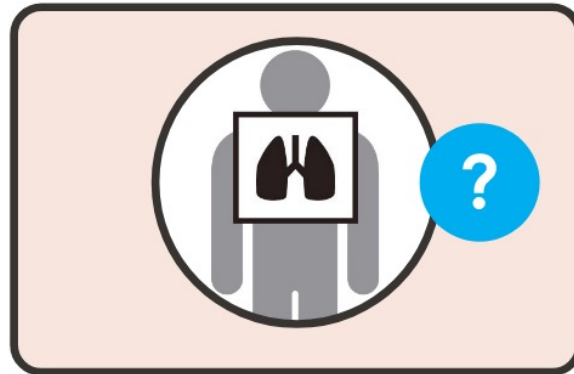


# Recommendations

## *Tools for screening*

Computer-aided detection (CAD) for automated interpretation of chest X-ray is now recommended conditionally as an alternative to human interpretation for TB screening and triage for all adults aged 15 years and older

– **INCLUDING** people living with HIV



Landscape of CAD software - <https://www.ai4hlth.org/>

CAD for TB detection - <https://tdr.who.int/activities/calibrating-computer-aided-detection-for-tb>

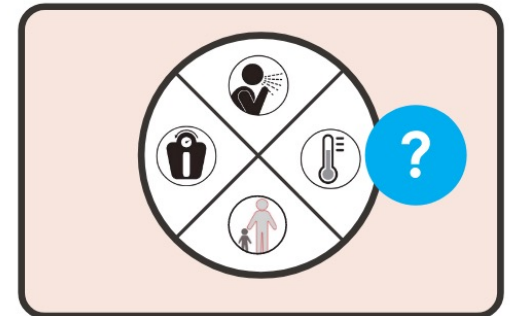




# Recommendations

## *Tools for screening children*

- Two groups of children in whom TB screening is strongly recommended
  - Child contacts of TB patients
  - Children living with HIV
- Tools strongly recommended for screening child contacts (up to 15 years)
  - Symptom screening (cough, fever, weight loss)
  - Chest X-ray
- Tool strongly recommended for screening children living with HIV (up to 10 years)
  - Symptom screening (current cough, fever, poor weight gain, or close contact with a TB patient)



## Algorithms for screening



Adults and adolescents living with HIV

2015

2021 2022

2030

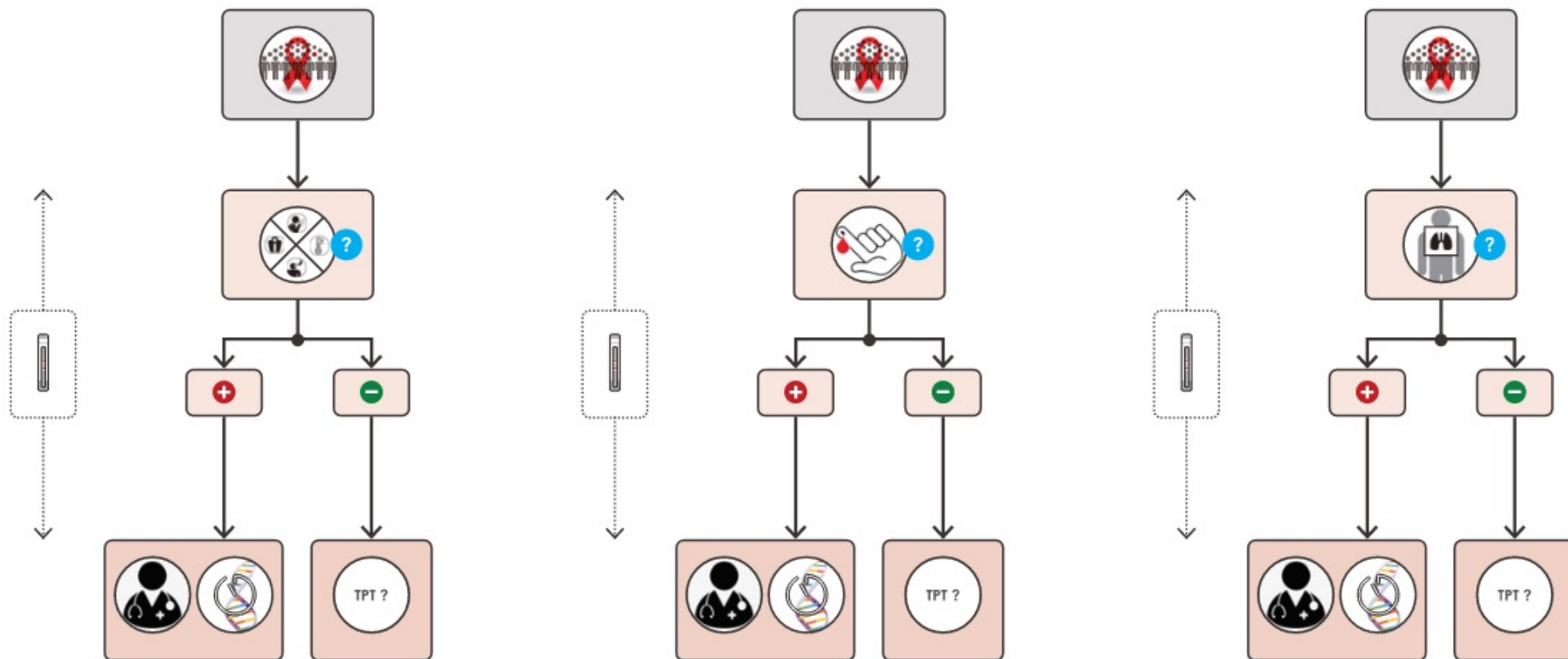


THE CLOCK IS TICKING



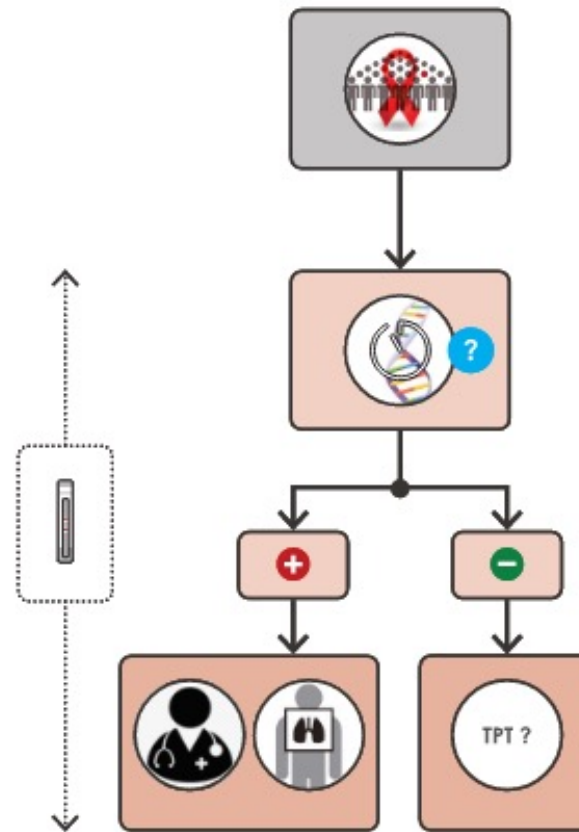
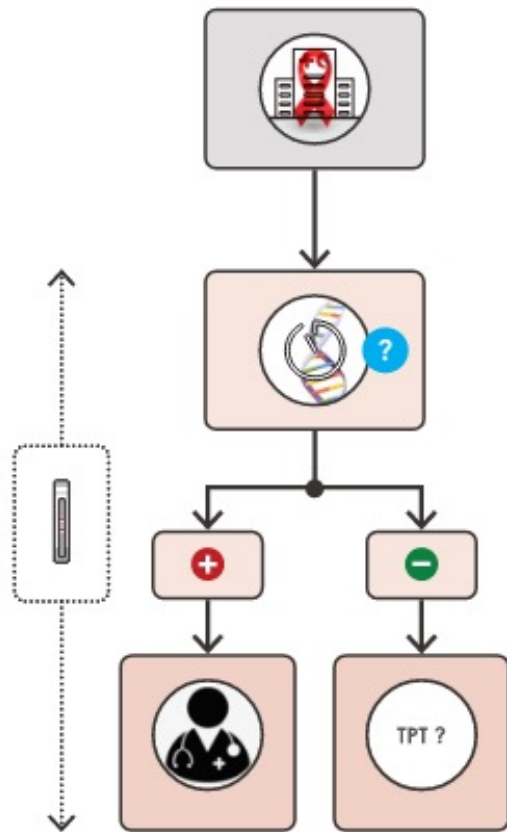
# Adults and adolescents living with HIV

## Single screening algorithms – W4SS, CRP, CXR



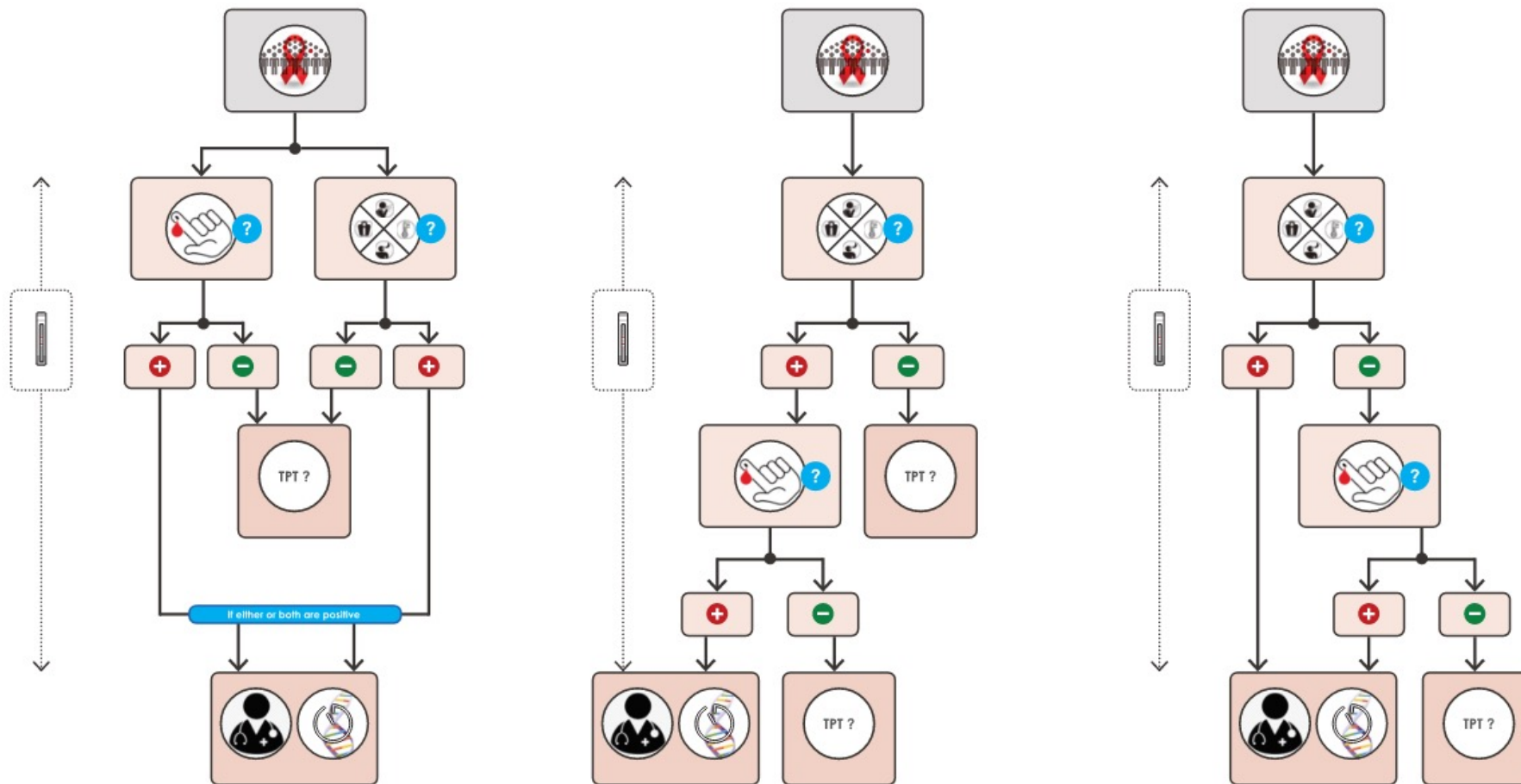
# Adults and adolescents living with HIV

## Single screening algorithms - mWRDs



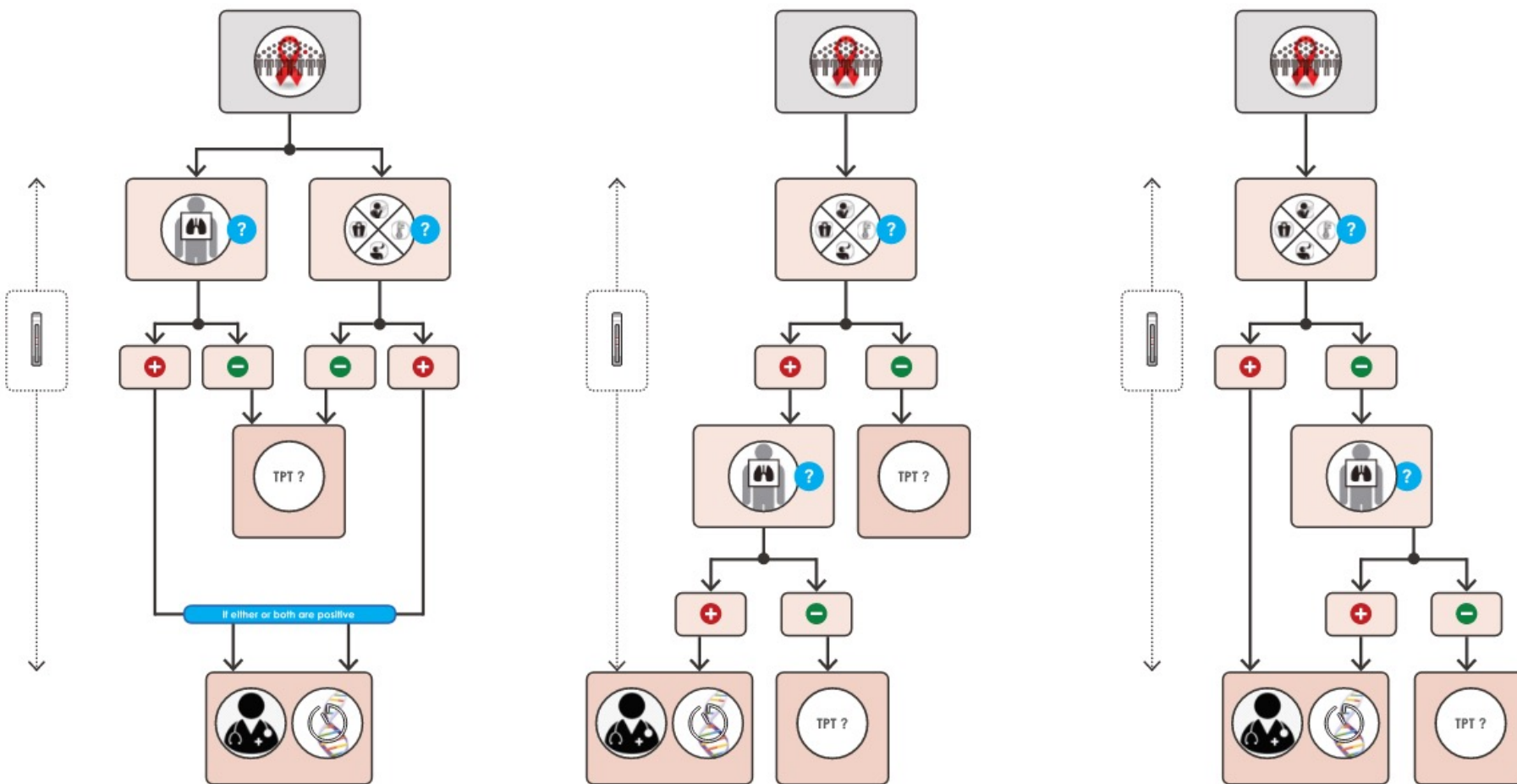
# Adults and adolescents living with HIV

## Algorithms with W4SS and CRP



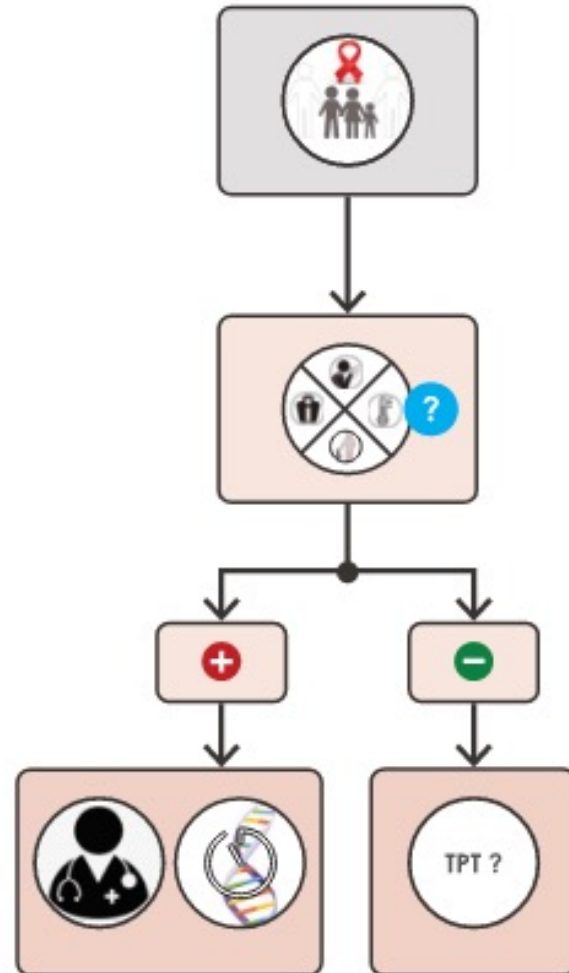
# Adults and adolescents living with HIV

## Algorithms with W4SS and CXR



# Children living with HIV < 10 years

Screening with symptoms

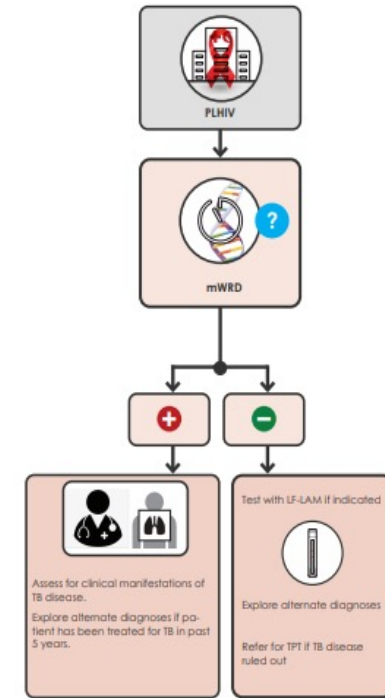
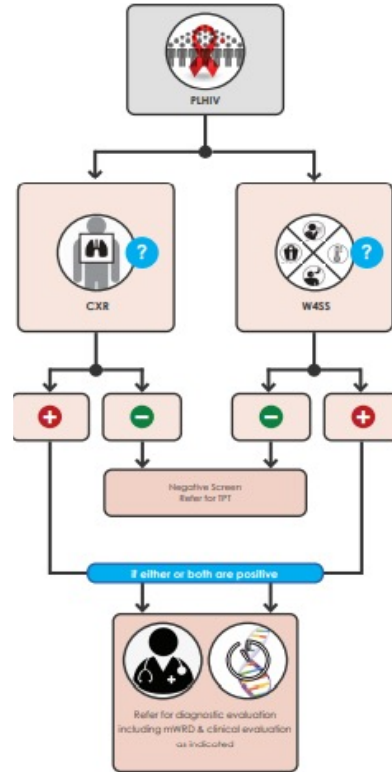
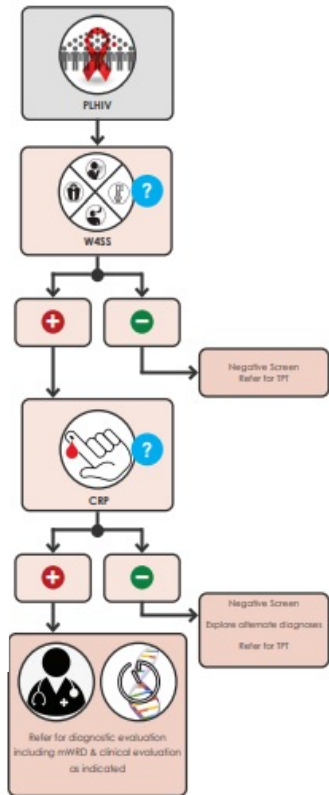


Outpatients not on ART W4SS+ then CRP ( $\geq 5$ mg/L)	Outpatients on ART Parallel W4SS + X-ray	Medical Inpatients $>10\%$ TB prevalence - mWRD alone
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<b>Sens:</b> 0.84 (0.73-0.90) <b>Spec:</b> 0.64 (0.55-0.72)	0.85 (0.69-0.94) 0.33 (0.15-0.58)	0.77 (0.69-0.84) 0.93 (0.89-0.96)
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**Compared with W4SS alone**

<b>Sens:</b> 0.84 (0.75-0.90) <b>Spec:</b> 0.37 (0.25-0.50)	0.53 (0.36-0.69) 0.70 (0.50-0.85)	0.96 (0.92-0.98) 0.11 (0.08-0.14)
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# THANK YOU!



THE CLOCK  
IS TICKING  
It's time to **END TB**



2015

2021 2022

2030



# Guideline update – PICO questions

Diagnostic accuracy (sensitivity, specificity) of screening tools:

- For screening the general population and high-risk groups:
  - Symptoms screening
  - Chest X-ray (CXR)
  - Molecular WHO-recommended rapid diagnostic tests (mWRDs)
- For screening people living with HIV
  - WHO-recommended 4-symptom screen
  - CXR
  - mWRDs
  - C-reactive protein (CRP)
- For screening children at high risk of TB (contacts, children living with HIV)
  - Symptoms,
  - Chest X-ray (CXR),
  - Molecular WHO-recommended rapid diagnostic tests (mWRDs)
- What is the performance of computer-aided detection (CAD) software for automated reading of digital CXR for the detection of TB disease, for screening and triage?

