



CQUIN 5th Annual Meeting

Virtual: November 16-19, 2021

Session 3c: Differentiated TB/HIV: Implementing WHO's
new TB/HIV Screening Guidance

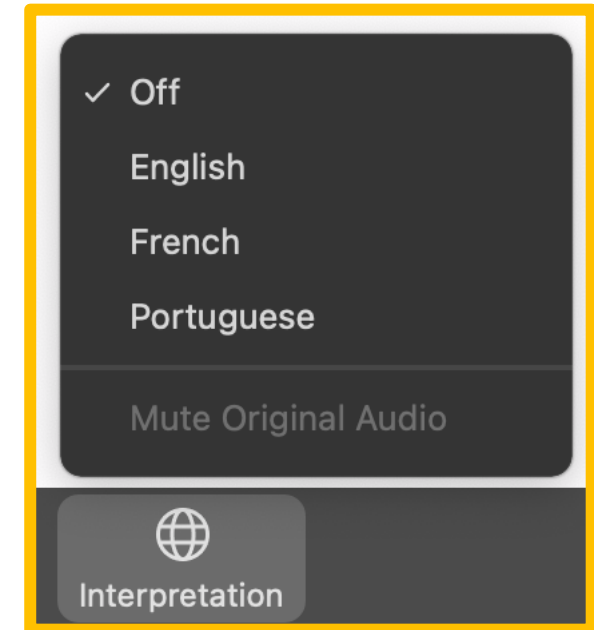
Tuesday, November 16, 2021



HIV Learning Network
The CQUIN Project for Differentiated Service Delivery

Welcome/Bienvenue/Bem-vindos

- Be sure you have selected the language of your choice using the “Interpretation” menu on the bottom of your screen.
- Assurez-vous d’avoir sélectionné la langue de votre choix à l’aide du menu <<Interprétation>> en bas de votre écran Zoom.
- Certifique-se de ter selecionado o idioma à sua escolha usando o menu de interpretação na parte inferior do seu ecrã



Plenary Moderators



Andrea Howard
Director of the Clinical & Training Unit
ICAP at Columbia University



Puneet Dewan
Senior Program Officer in TB Delivery
Bill & Melinda Gates Foundation

Poll 1

Are you familiar with the 2021 WHO consolidated guidelines on TB screening?

- Yes
- No

Connaissez-vous les directives consolidées de l'OMS de 2021 sur le screening de la tuberculose ?

- Oui
- Non

Poll 2

Has your country modified the national TB screening guidelines for people living with HIV based on the new WHO consolidated guidelines on TB screening?

- Yes
- No, but we are planning to do so
- No, and we do not have plans to do so

Votre pays a-t-il modifié les directives nationales de screening de la tuberculose pour les personnes vivant avec le VIH suite aux nouvelles directives consolidées de l'OMS sur le screening de la tuberculose ?

- Oui
- Non, mais nous prévoyons de le faire
- Non, et nous n'avons pas planifié de le faire pour le moment

Poll 3

- Which TB screening tests will your country include in the revised TB screening guidelines for people living with HIV? (Choose all that apply)
- Symptoms
- Chest x-ray
- Computer-aided detection for automated interpretation of chest x-rays
- C-reactive protein
- Molecular rapid diagnostic test
- Undecided

Quels tests de screening de la tuberculose votre pays inclura-t-il dans les directives révisées de screening de la tuberculose pour les personnes vivant avec le VIH ? (Choisissez tout ce qui correspond)

- La symptomatologie
- La radiographie pulmonaire
- La détection assistée par ordinateur pour l'interprétation automatisée des radiographies pulmonaires
- La protéine C-réactive
- Test de diagnostic moléculaire rapide
- Pas encore décidé



CQUIN 5th Annual Meeting

Virtual: November 16-19, 2021

Framing Remarks

Andrea A. Howard, MD, MS

Clinical & Training Unit Director

ICAP at Columbia University

16 November 2021



HIV Learning Network
The CQUIN Project for Differentiated Service Delivery

TB remains a leading cause of death

- TB remains the second leading cause of death from an infectious disease
 - >1.2 million TB deaths in 2019
- Leading cause of death among PLHIV
 - ~30% AIDS-related deaths in 2019
- TB is largely curable and preventable



TB case detection is a major challenge to ending the TB epidemic

- In 2019, ~2.9 million of 10 million people with TB were not diagnosed or reported
- Gap in TB case detection greater in PLHIV
 - ~44% of people with HIV-associated TB are not diagnosed
- 18% ↓ in number tested and treated for TB from 2019-2020 due to COVID-19
 - 19% decline for DR-TB
 - 37% decline for XDR-TB



TB screening is an essential component of the End TB Strategy

- Early identification of individuals with presumptive TB, followed by prompt diagnosis and treatment initiation, improves patient outcomes and reduces transmission
- TB screening also used to rule out active TB prior to initiating TB preventive treatment
- TB screening has largely relied on use of the symptom screening tool
- WHO consolidated guidelines on TB screening 2021
 - Incorporates new evidence on novel screening tools and technologies
 - Accompanying operational handbook to support policy makers in choosing screening algorithms for specific populations



Session Objectives

- Summarize WHO TB screening guidelines for PLHIV
- Discuss plans for modifying country TB screening guidelines and implementing new TB screening tools / algorithms
- Describe plans to support dissemination and implementation of new TB screening tools / algorithms for PLHIV
- Identify common gaps, challenges and opportunities for TB/HIV CoP to support future joint learning, co-creation of tools and resources, and exchange visits

Plenary Presentation



Fabrizia del Greco
Technical Specialist, TB/HIV
World Health Organisation



CQUIN 5th Annual Meeting

Virtual: November 16-19, 2021

Systematic screening for TB disease

Updated WHO recommendations and screening algorithms for
people living with HIV

Dr. Fabrizia Del Greco

Consultant, WHO HHS Programme

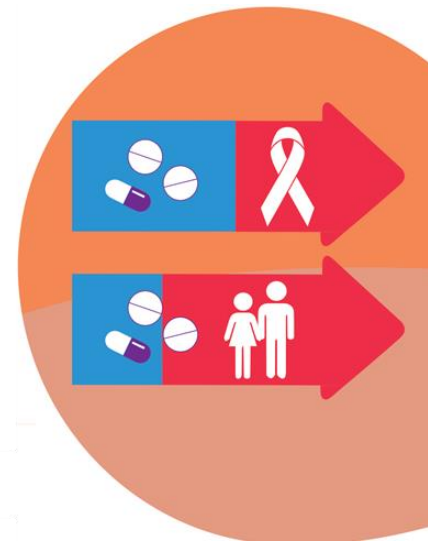
16 November 2021



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 cases¹
- 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



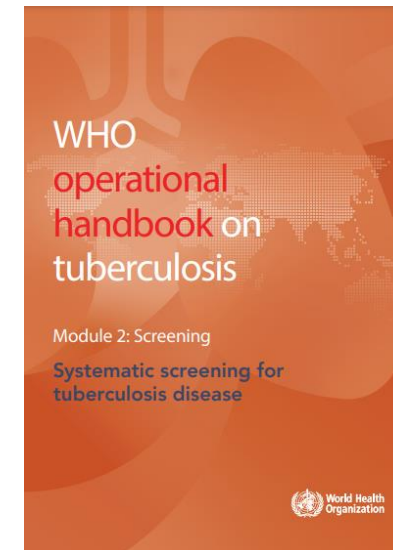
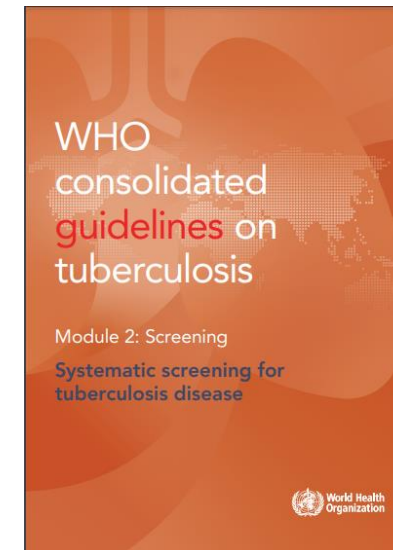
TB screening guidelines – update process

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

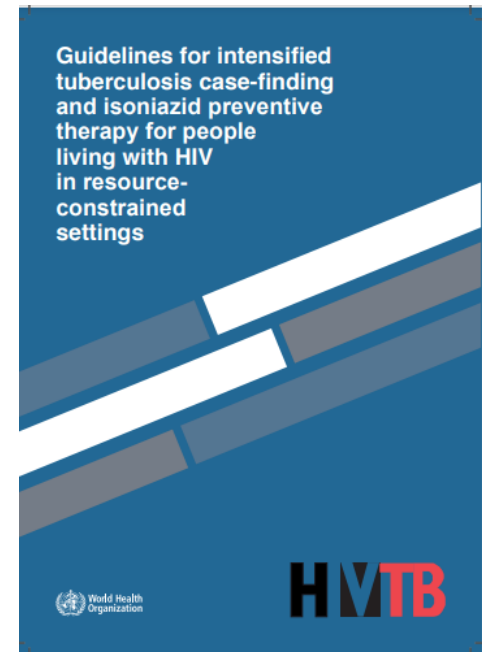
Tools for screening adults and adolescents 10 years and older living with HIV



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/ μ 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)

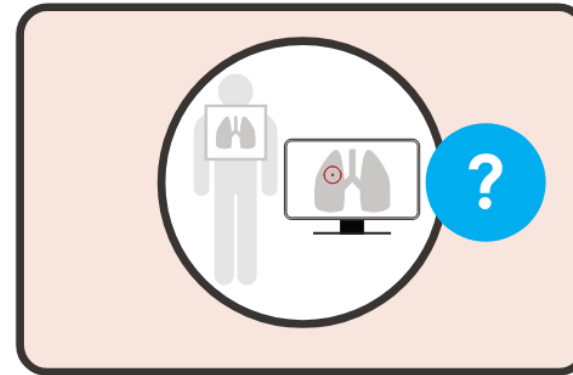
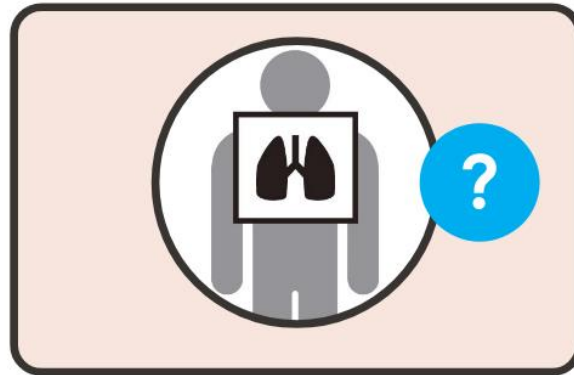


Recommendations

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/>

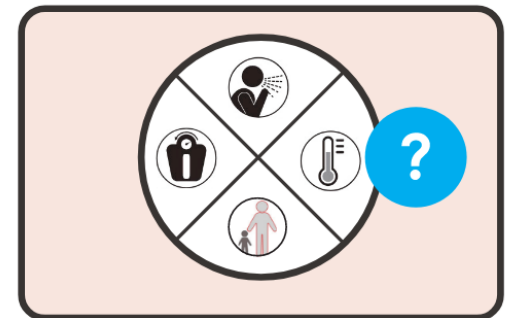
CAD for TB detection - <https://tdr.who.int/activities/calibrating-computer-aided-detection-for-tb>



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

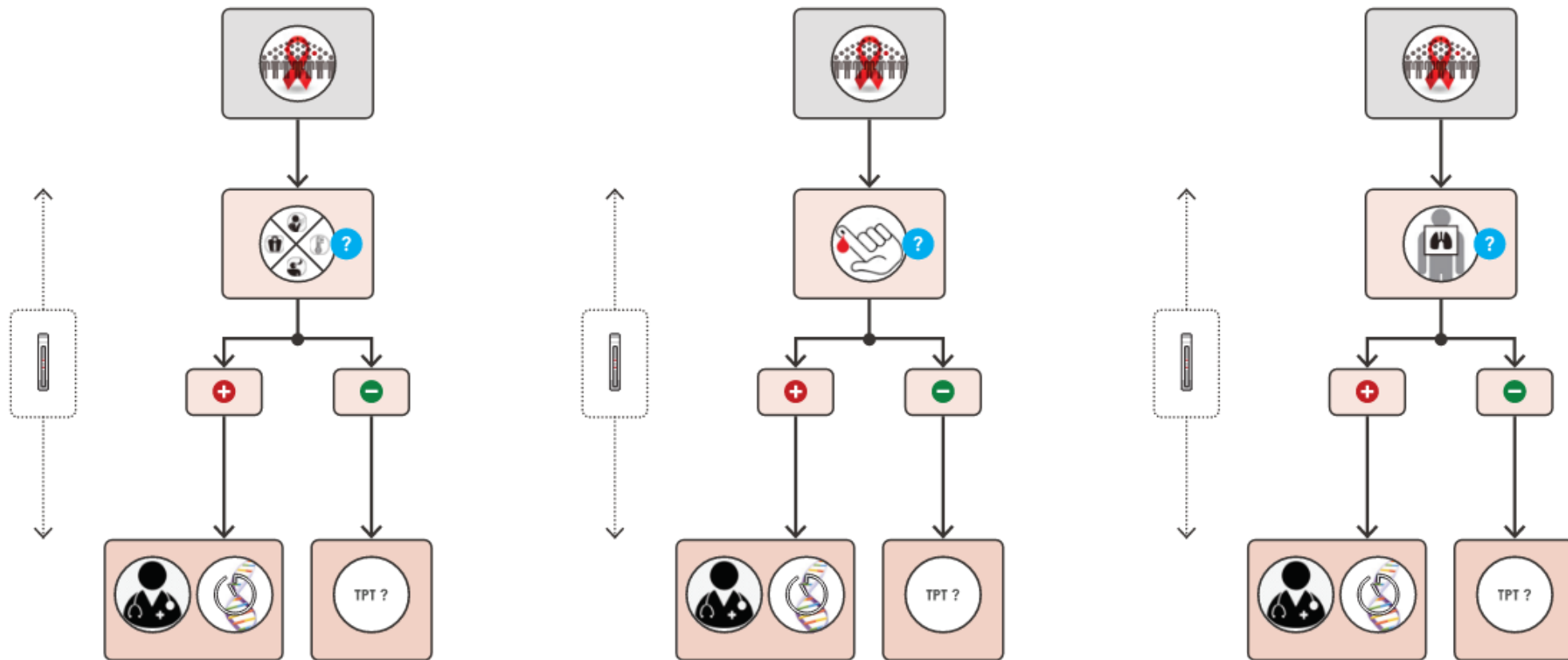


THE CLOCK IS TICKING



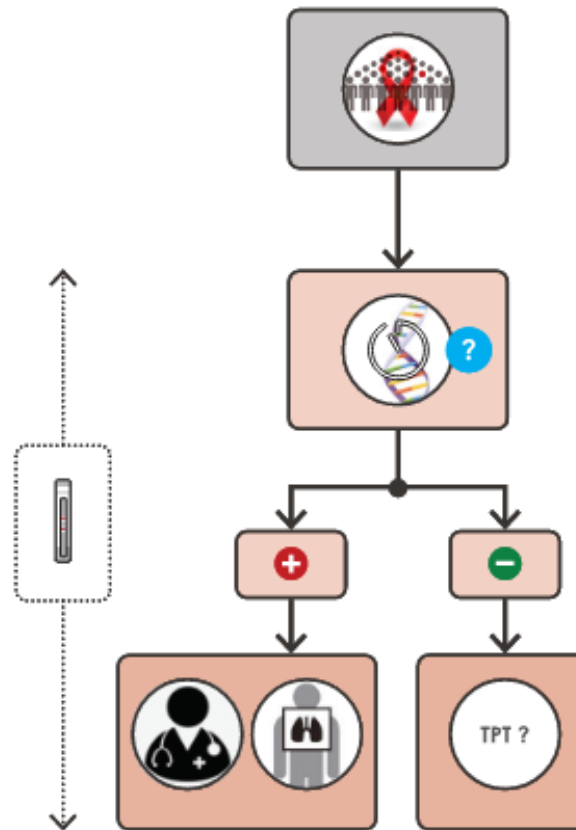
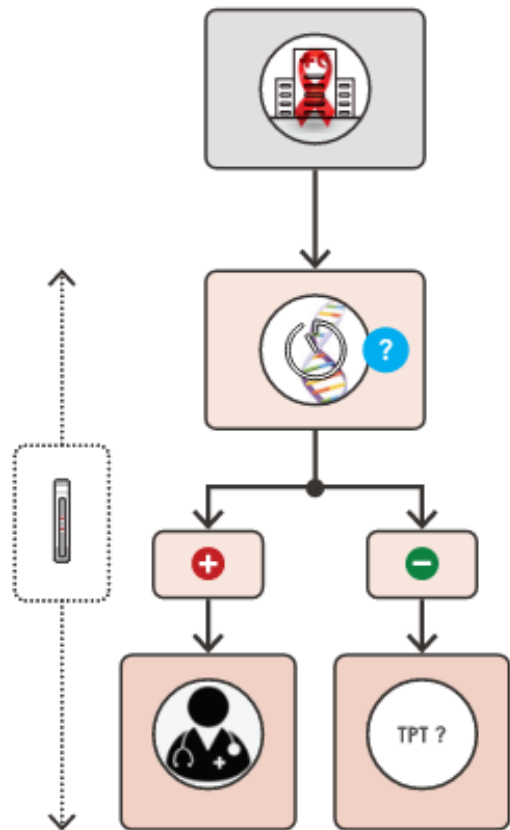
Adults and adolescents living with HIV

Single screening algorithms – W4SS, CRP, CXR



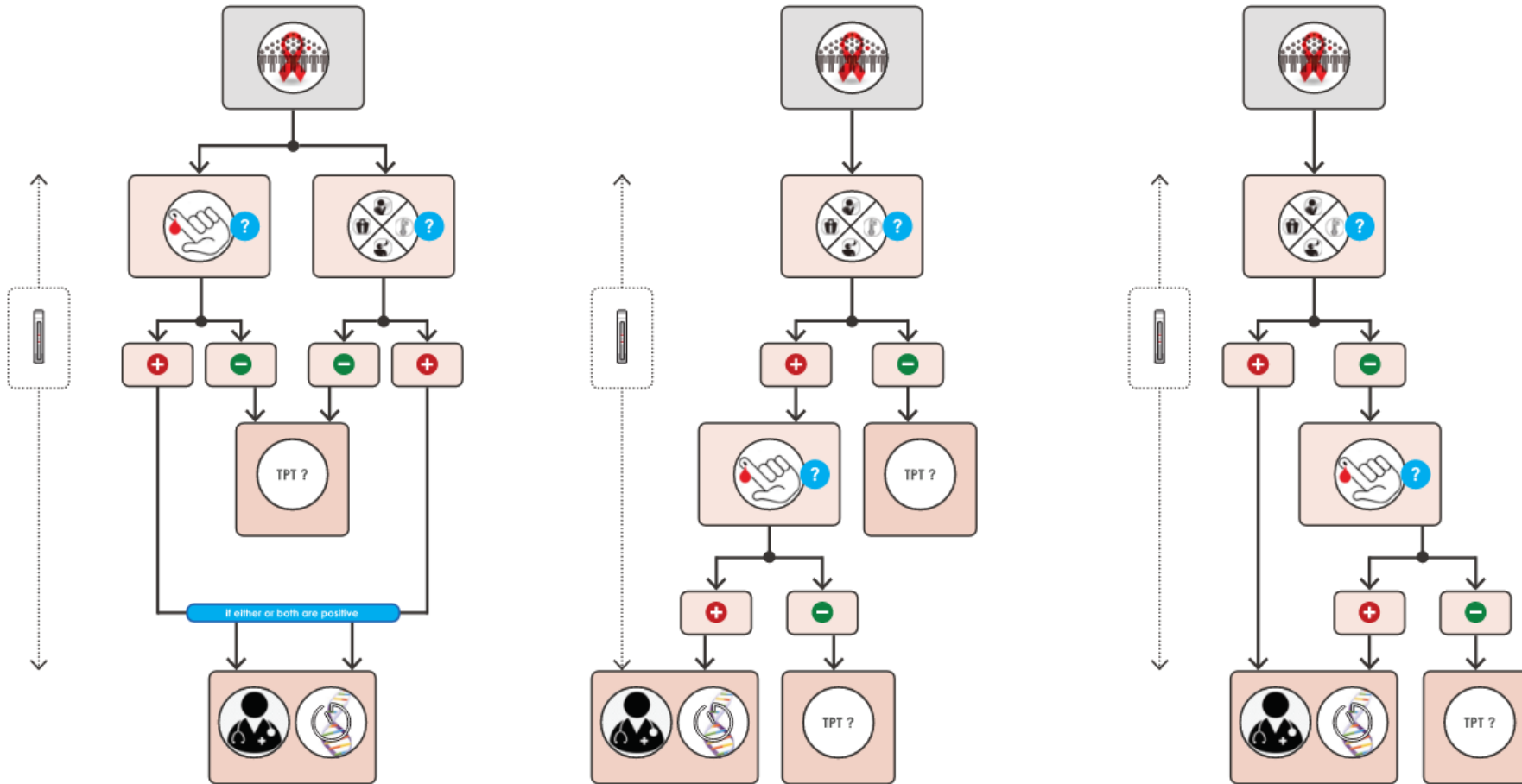
Adults and adolescents living with HIV

Single screening algorithms - mWRDs



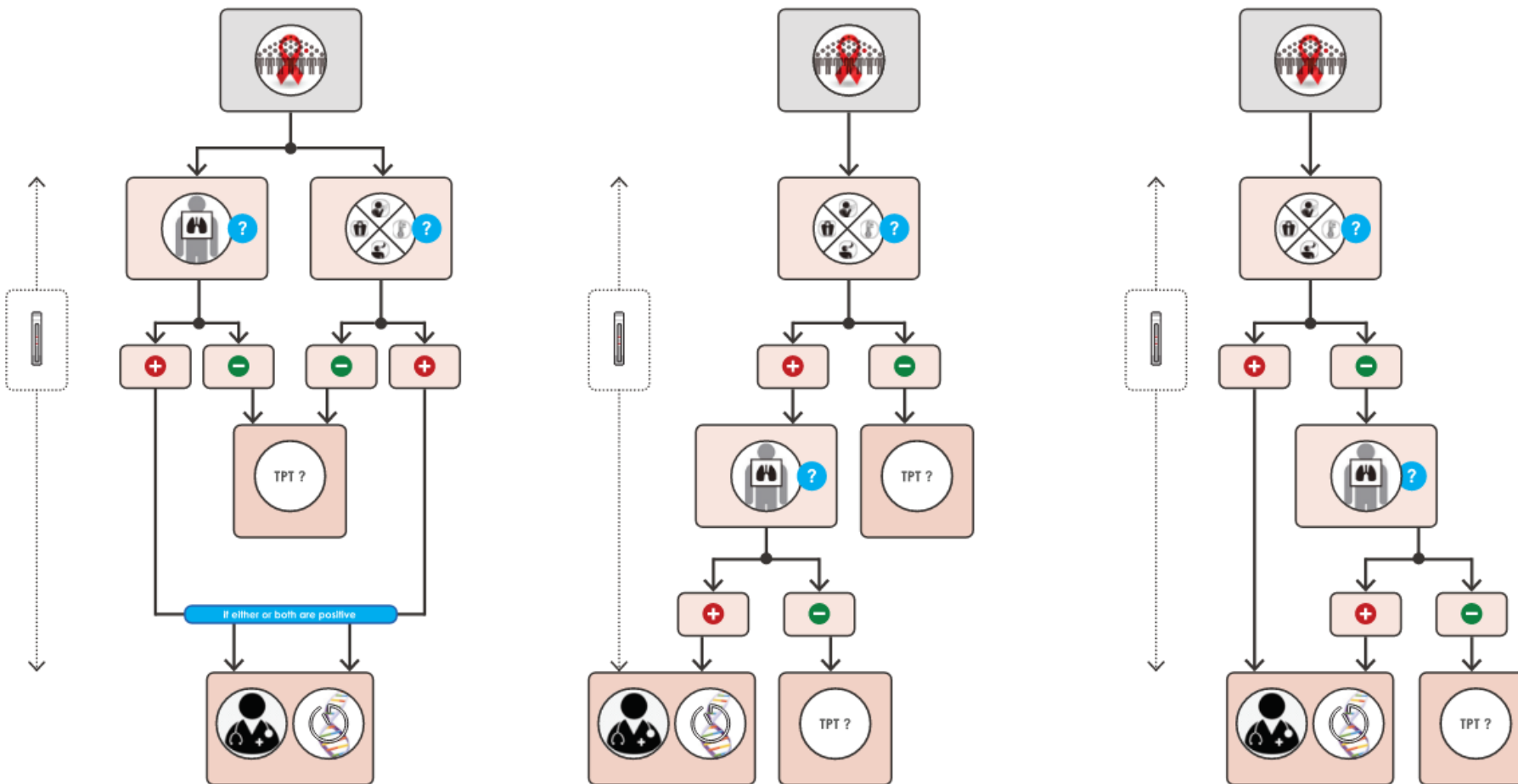
Adults and adolescents living with HIV

Algorithms with W4SS and CRP



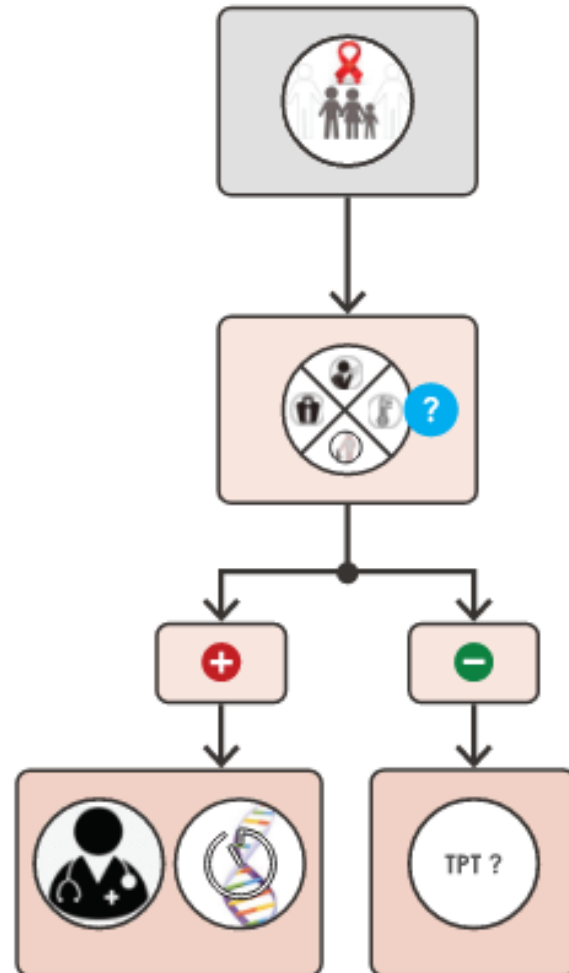
Adults and adolescents living with HIV

Algorithms with W4SS and CXR



Children living with HIV < 10 years

Screening with symptoms



Outpatients not on ART W4SS+ then CRP (≥ 5 mg/L)

Sens: 0.84 (0.73-0.90)
Spec: 0.64 (0.55-0.72)

Outpatients on ART Parallel W4SS + X-ray

0.85 (0.69-0.94)
0.33 (0.15-0.58)

Medical Inpatients $>10\%$ TB prevalence - mWRD alone

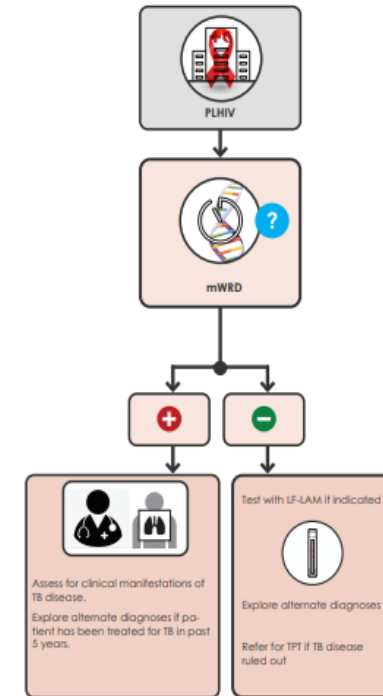
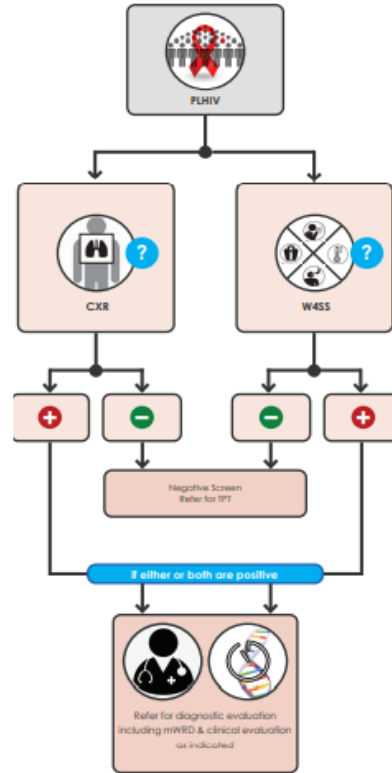
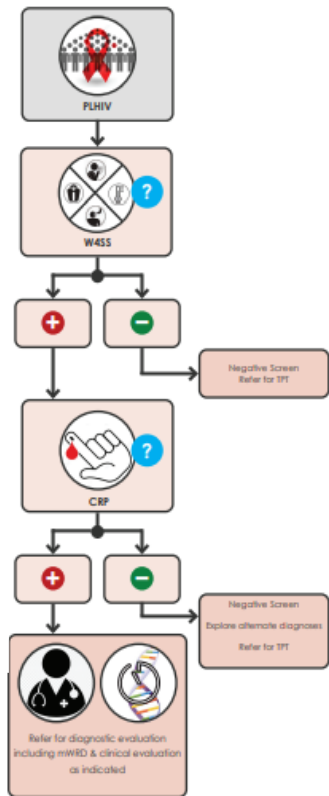
0.77 (0.69-0.84)
0.93 (0.89-0.96)

Compared with W4SS alone

Sens: 0.84 (0.75-0.90)
Spec: 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)





Acknowledgements

Saskia den Boon, Dennis Falzon, other WHO staff at HQ, Regional, Country Offices
Evidence Reviewers – especially Gary Maartens, Ashar Dhana - IPD team, University of Cape Town
Patients who contributed to studies and reviews
National TB and HIV Programmes
Guideline Development Group, External Review Group
FIND, Stop TB Partnership, IoM
TAG, civil society
USAID
Other experts and funding agencies





© WORLD HEALTH ORGANIZATION 2021

All rights reserved. Publications of the World Health Organization can be obtained from WHO Press, World Health Organization, 20 Avenue Appia, 1211 Geneva 27, Switzerland (tel: +41 22 791 3264; fax: +41 22 791 4857; email: bookorders@who.int). Requests for permission to reproduce or translate WHO publications – whether for sale or for noncommercial distribution – should be addressed to WHO Press, at the above address (fax: +41 22 791 4806; email: permissions@who.int).

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by the World Health Organization to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall the World Health Organization be liable for damages arising from its use.



THANK YOU!



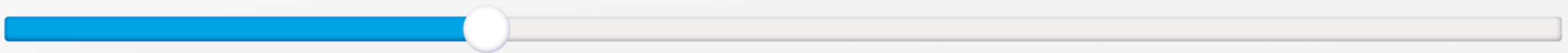
THE CLOCK
IS TICKING
It's time to **END TB**



2015

2021 2022

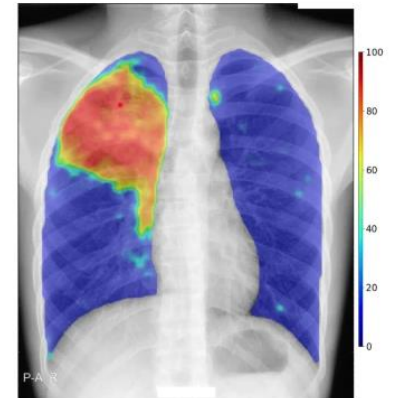
2030



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?



Panelists/Panélistes/Painelistas



Macarthur Charles
Medical Officer
Division of Global HIV and TB
Centers for Disease Control
Atlanta



Gugulethu Madonsela
AHD Focal Person
Eswatini National AIDS Program
Ministry of Health
Eswatini



Lawrence Khonyongwa
Executive Director
Network of People Living with HIV
Malawi



Benedita Jose
Director of the National TB
Control Program
Ministry of Health
Mozambique



CQUIN 5th Annual Meeting

Virtual: November 16-19, 2021

Session 4 starts Wednesday 17 November at 7:00am EST/12.00noon
West Africa/1:00pm Geneva/2:00pm Pretoria/3:00pm Nairobi



HIV Learning Network
The CQUIN Project for Differentiated Service Delivery