


Challenges of TB detection in children: WHO guidance on stool-based testing and diagnostic approaches in children and adolescents

Sabine Verkuijl, WHO Global Tuberculosis Programme

Stool testing webinar, 16 January 2025

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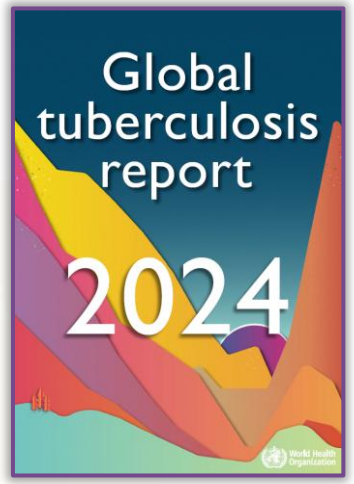
TB incidence and mortality in children and adolescents, 2023



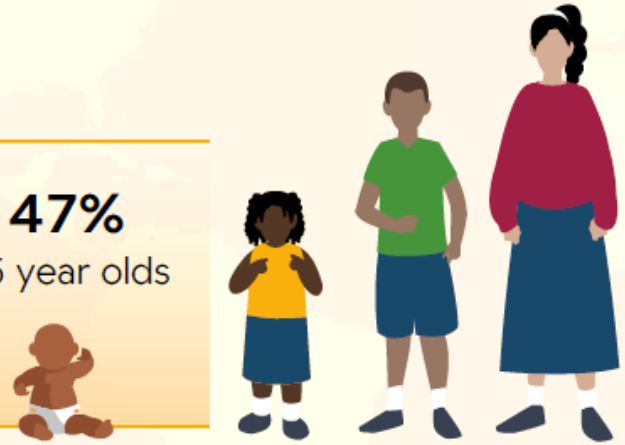
10.8 million
TB among all ages in 2023

1.25 million
TB deaths in 2023

1.25 million
children (0–14 years) developed TB in 2023 (12% of all TB)

191 000
TB deaths in 2023 (15% of all TB deaths)

47%
<5 year olds



727 000 adolescents
(10–19 year-olds) developed TB in 2012 (Snow et al, 2018)

Among deaths in HIV-negative children and young adolescents 0–14

73% were in children <5 years

96%
of deaths occurred in children who did not access TB treatment

(Dodd et al, 2017)

25 000
(14%) TB deaths in the 0–14 year age group were among children living with HIV

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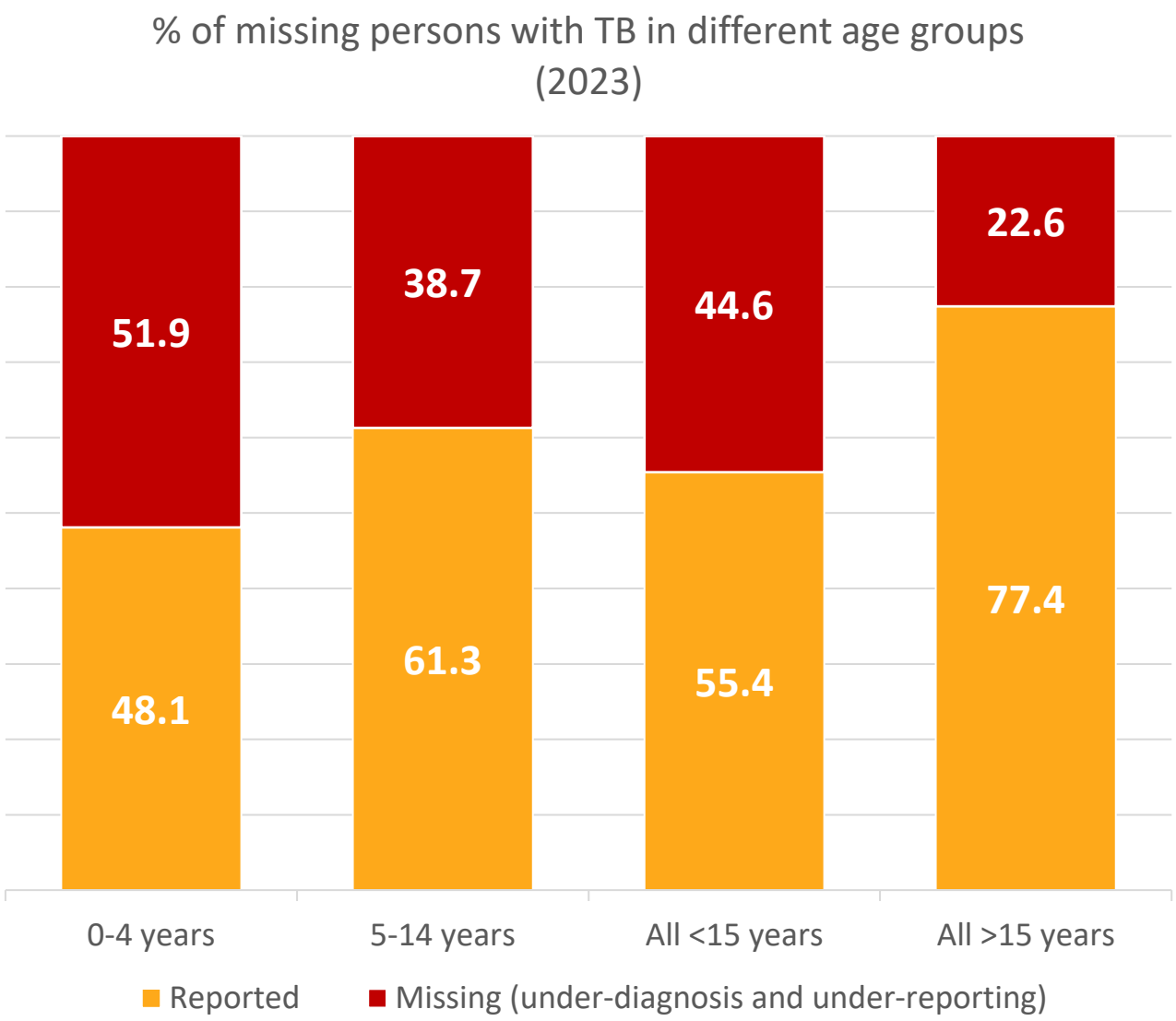
Treatment coverage gap (global)



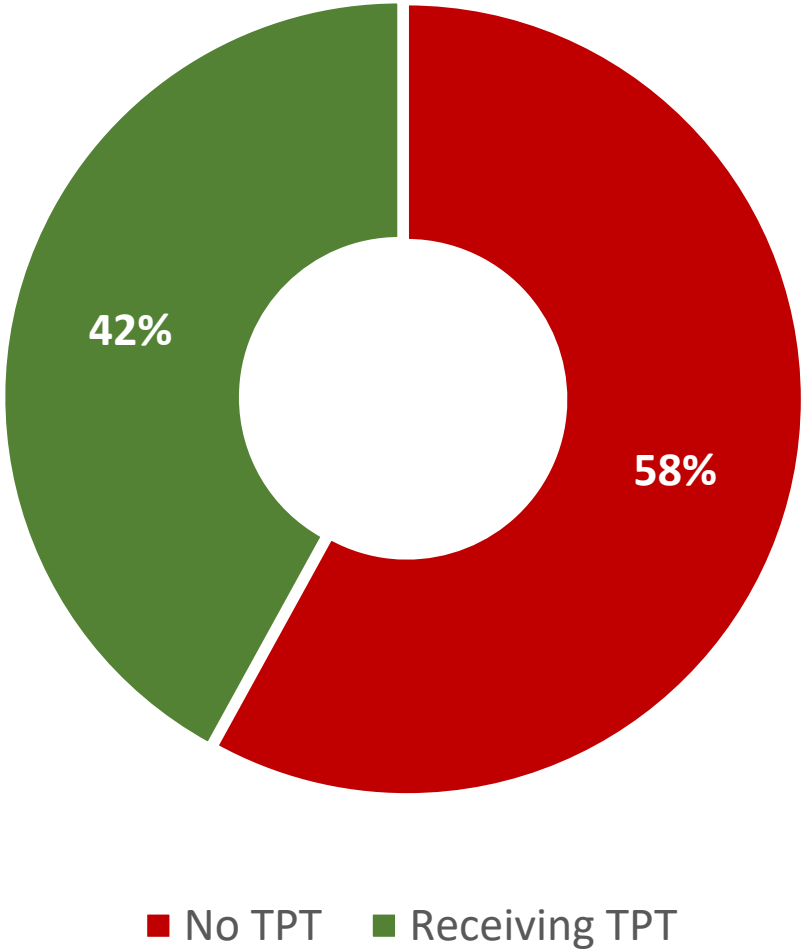
Reasons for the treatment Coverage gap:

- Paucibacillary TB
- Lack of a sensitive PoC test
- Challenges with collection of suitable respiratory samples
- Overlap of symptoms with other common childhood diseases
- Limited capacity to diagnose children with TB - sample collection, access to testing/CXR, confidence in clinical diagnosis

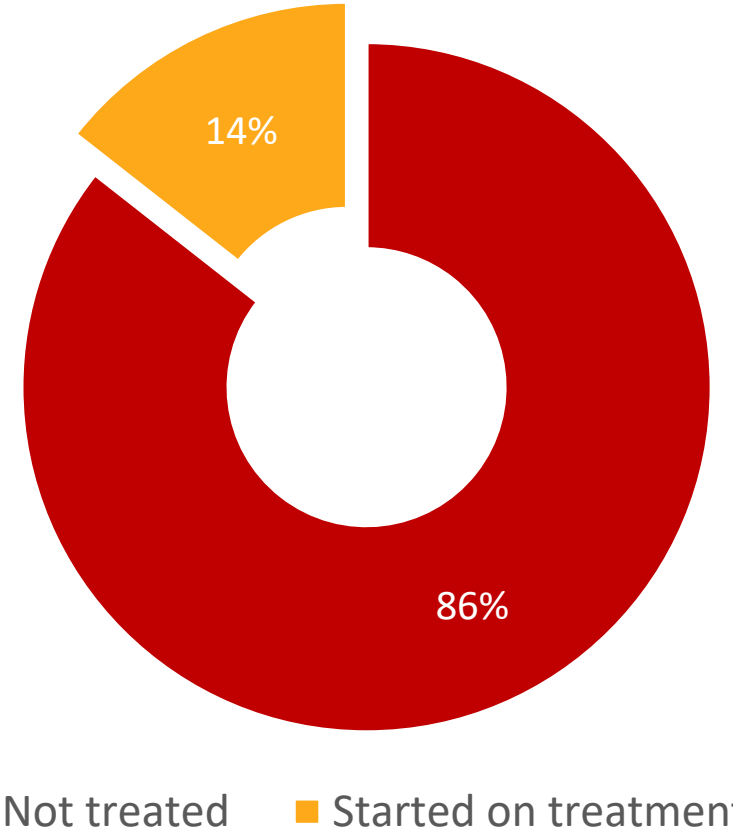
Gaps: TPT and MDR/RR-TB (global)

Global tuberculosis report 2024

Access to TPT in child contacts <5 years



MDR/RR-TB treatment initiation in children and young adolescents, average for 2018-2023 (out of an estimated 30 000 per year)



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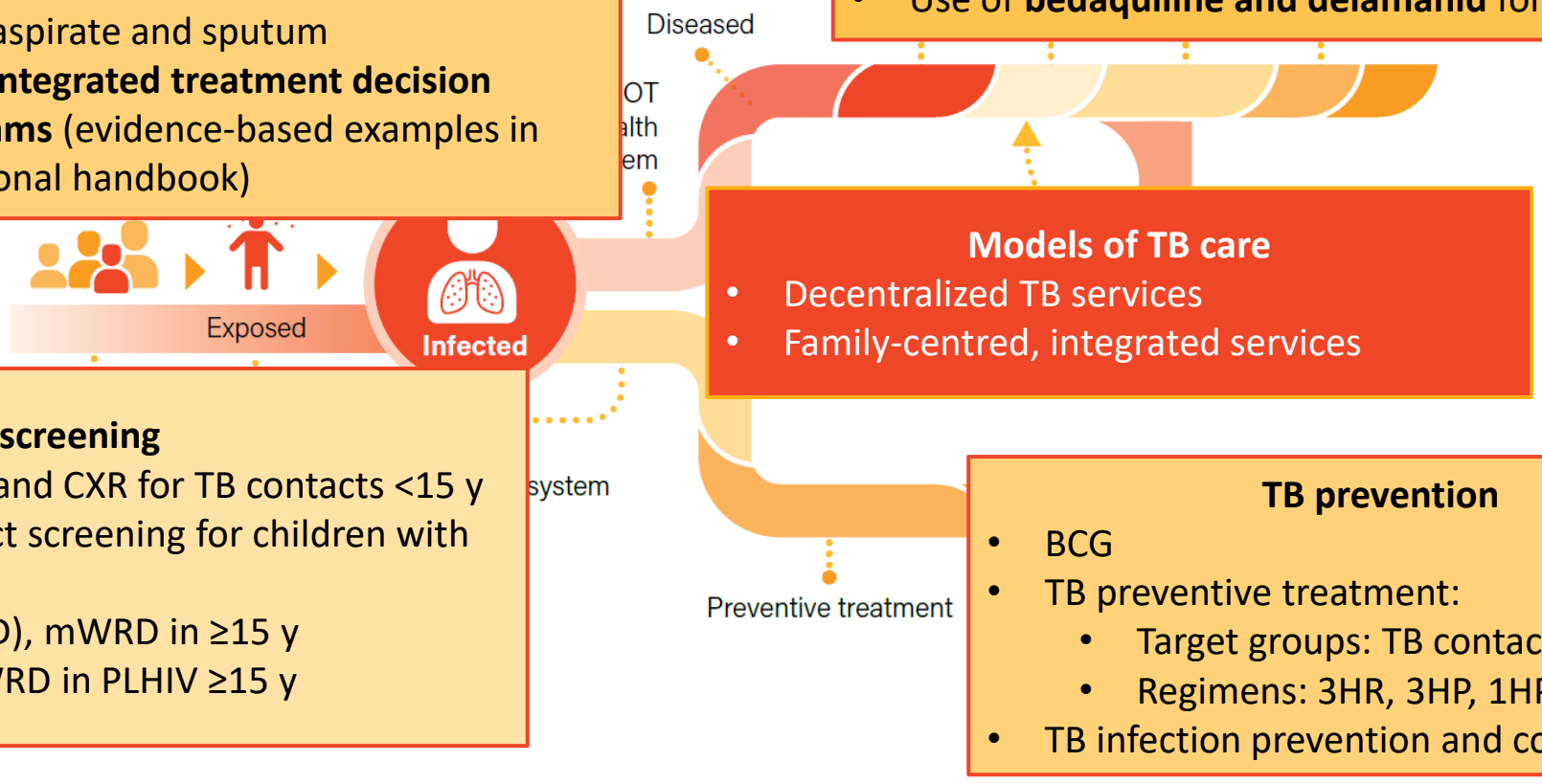
WHO policy guidance

TB treatment

- 4-month regimen (2HRZ(E)/2HR) for **non-severe TB** (3 months – 16 years) – eligibility criteria detailed in operational handbook
- Alternative regimens for **TB meningitis**: 6HRZEto and 2HRZ(E)/10HR
- Use of **bedaquiline and delamanid** for all ages (MDR/RR-TB)

TB diagnostic approaches

- Use of rapid diagnostic tests
- Xpert Ultra and MTB/RIF on **stool**, NPA, gastric aspirate and sputum
- Use of **integrated treatment decision algorithms** (evidence-based examples in operational handbook)



Models of TB care

- Decentralized TB services
- Family-centred, integrated services

TB screening

- Symptom screening and CXR for TB contacts <15 y
- Symptom and contact screening for children with HIV < 10 y
- Use of CXR (with CAD), mWRD in ≥15 y
- Use of CXR, CRP, mWRD in PLHIV ≥15 y

TB prevention

- BCG
- TB preventive treatment:
  - Target groups: TB contacts, CALHIV
  - Regimens: 3HR, 3HP, 1HP, 6-9H
- TB infection prevention and control

Guidelines: https://www.who.int/publications/i/item/9789240046764
Handbook: https://www.who.int/publications/i/item/9789240046832
WHO TB Knowledge Sharing Platform: https://extranet.who.int/tbknowledge

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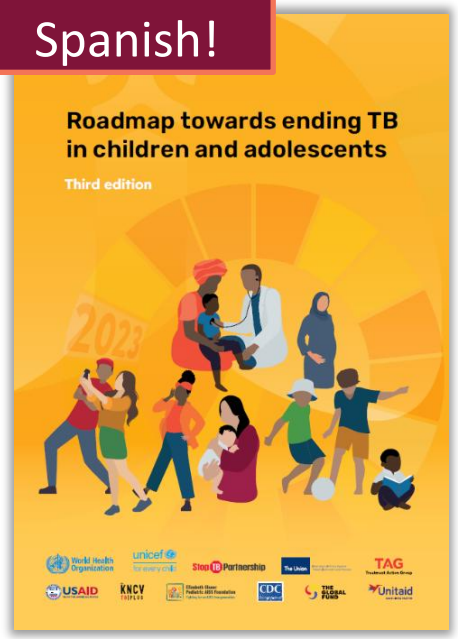
The third edition of the Roadmap (2023)

Available in French and Spanish!



- **Aim**: to define actions to be prioritized and implemented over the next 5 years to reduce TB-related morbidity and mortality in children and adolescents
- Aligned with the **UN HLM 2023** targets
- Ten key actions covering funding, accountability, social protection, advocacy, capacity building, prevention, optimal care (**including child-friendly diagnostic approaches**), integrated strategies, recording & reporting and TB R&D

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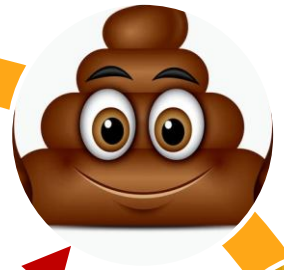
https://www.who.int/publications/i/item/9789240084254

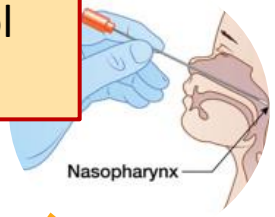
WHO guidance on diagnostic approaches



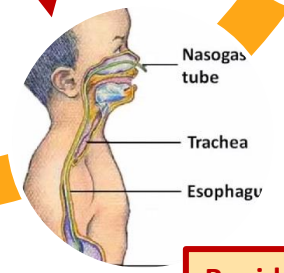
stool

(induced) sputum

Rapid communication Sept '24:
Parallel testing:
Respiratory specimen + stool
(+ LF-LAM if HIV pos)

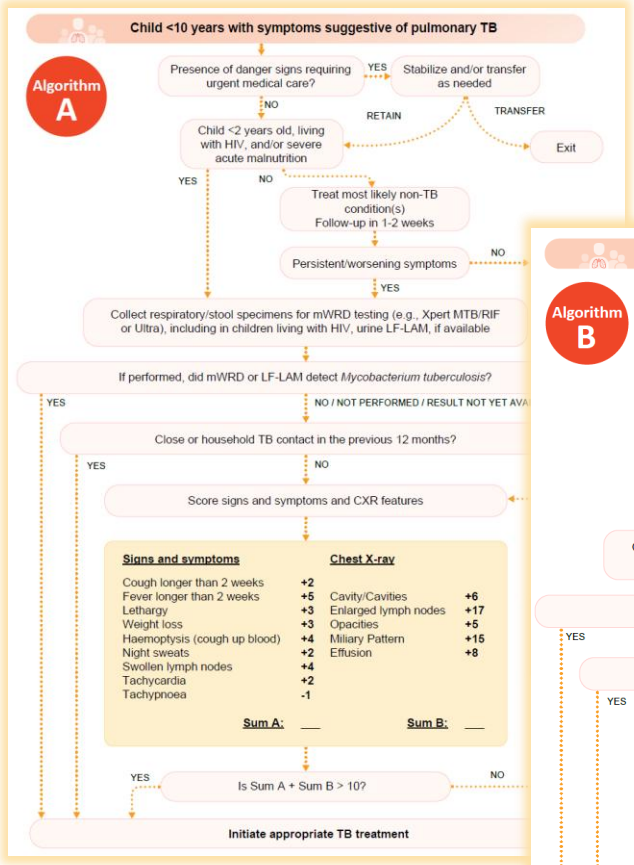


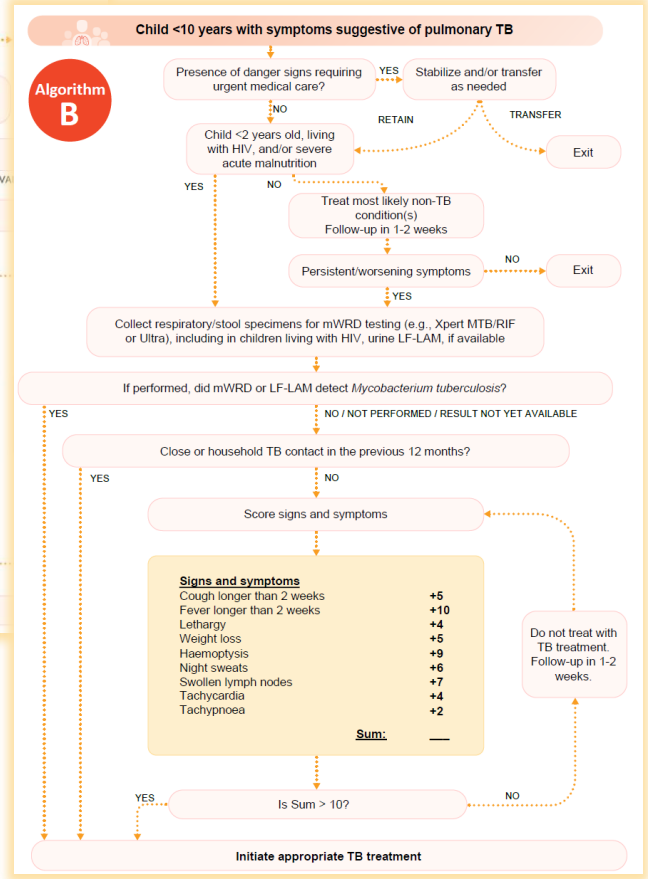
NPA

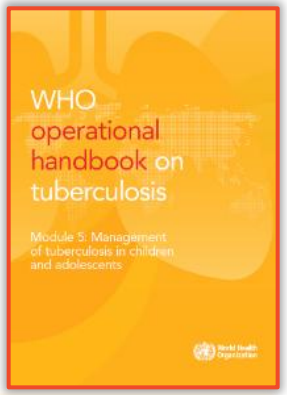


gastric aspirate

Rapid communication:
https://www.who.int/publications/i/item/B09111







Interim recommendation on **TDAs in general** with **evidence-based example TDAs** in the Module 5 Operational Handbook

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TDR For research on diseases of poverty
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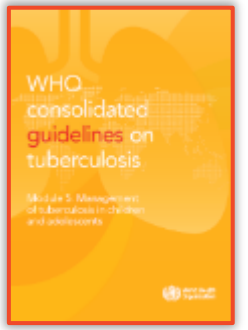
Use of mWRDs for the diagnosis of TB in children



In children with signs and symptoms of pulmonary TB:

- Xpert Ultra should be used as the initial diagnostic test for TB and RR detection in **sputum, gastric aspirate, nasopharyngeal aspirate and stool**, rather than smear microscopy/culture and phenotypic DST

- Xpert MTB/RIF should be used as an initial diagnostic test for TB and RR detection in **sputum, gastric aspirate, nasopharyngeal aspirate and stool** rather than smear microscopy/culture and phenotypic DST

Strength	Certainty of Evidence
Strong	Low for sputum Very Low for NPA** **Moderate for GA* (new 2022)** **Moderate for stool (new 2022)**
Strong	Moderate for sputum Low for GA*, NPA** and stool

* GA: Gastric aspirate
** NPA: nasopharyngeal aspirate

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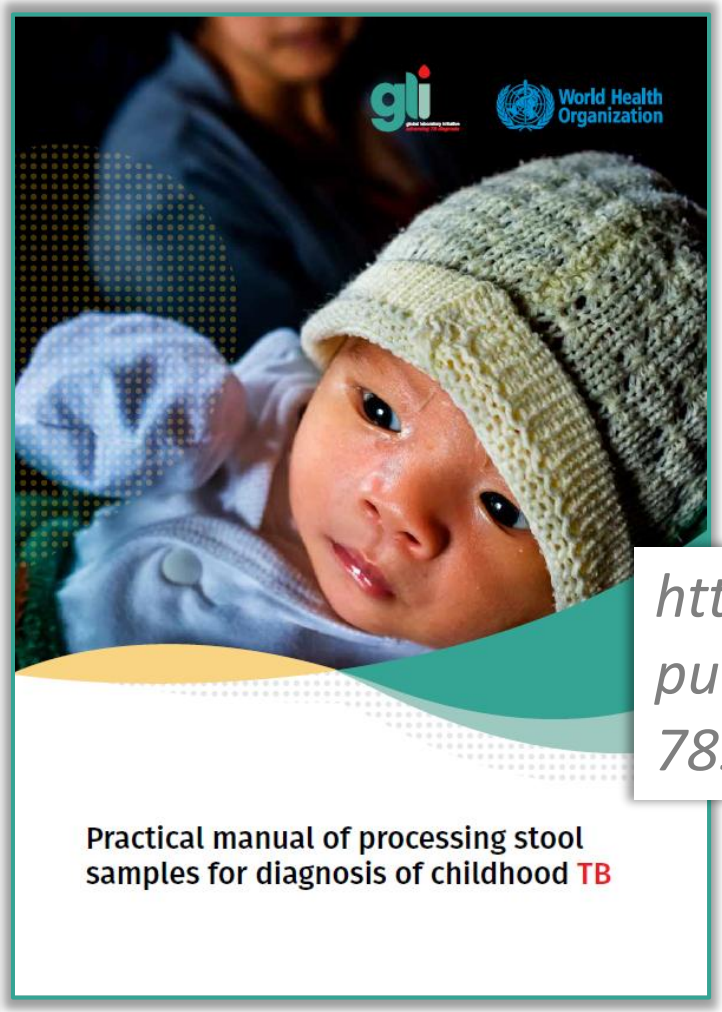
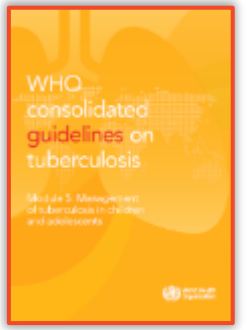
Use of mWRDs for the diagnosis of TB in children

Test	Acceptable specimen types	Rifampicin resistance detection
Xpert MTB/RIF	Sputum Gastric fluid NPA Stool Cerebrospinal fluid (CSF) Lymph node aspirate or biopsy Pleural fluid Peritoneal fluid Pericardial fluid Synovial fluid Urine Blood [a]	Yes
Xpert Ultra	Sputum Gastric fluid NPA Stool CSF Lymph node aspirate or biopsy	Yes
Truenat MTB and MTB Plus (Molbio Diagnostics, Goa, India)	Sputum	Yes
TB-LAMP	Sputum	No
LF-LAM	Urine [b]	No

[a] Use of a blood specimen is recommended for people living with HIV with signs and symptoms of disseminated TB.

[b] Use of urine is recommended for children and adolescents living with HIV (see specific recommendations in Box 4.4).





https://www.who.int/publications/i/item/9789240042650

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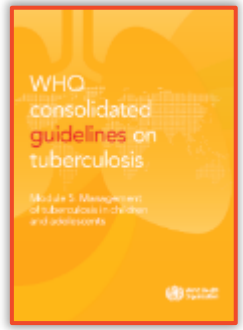
Diagnostic accuracy of LC-aNAATs in paediatric specimens



Specimen type (population)	Sensitivity	Specificity	Certainty of evidence
Xpert MTB/RIF			
Sputum	0.65	0.99	Moderate
Gastric aspirate	0.73	0.98	Very low (se) to low (sp)
NPA	0.46	1.00	Moderate (se) to high (sp)
Stool	0.61	0.98	Low (se) to moderate (sp)
Stool (HIV-positive)	0.70	0.98	Low (se) to high (sp)
Xpert Ultra			
Sputum	0.73	0.97	Low (se) to high (sp)
Gastric aspirate	0.64	0.95	Moderate
NPA	0.46	0.98	Very low (se) to low (sp)
Stool	0.53	0.98	Moderate

se: sensitivity; sp: specificity.

[a] Microbiological reference standard: TB culture on respiratory samples.

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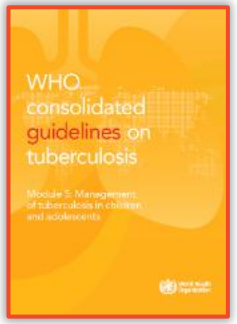
Integrated treatment decision algorithms



Algorithm A

Child <10 years with symptoms suggestive of pulmonary TB

Presence of danger signs requiring urgent medical care?

YES → Stabilize and/or transfer as needed

RETAIN / TRANSFER

NO

Child <2 years old, living with HIV, and/or severe acute malnutrition

→ Exit

YES

NO

Treat most likely non-TB condition(s)
Follow-up in 1-2 weeks

Persistent/worsening symptoms

NO → Exit

YES

Collect respiratory/stool specimens for mWRD testing (e.g., Xpert MTB/RIF or Ultra), including in children living with HIV, urine LF-LAM, if available

If performed, did mWRD or LF-LAM detect *Mycobacterium tuberculosis*?

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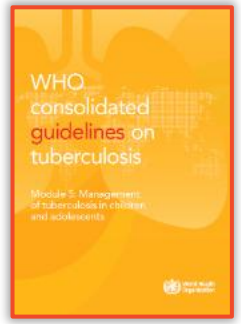
Integrated treatment decision algorithms



Algorithm A

If performed, did mWRD or LF-LAM detect *Mycobacterium tuberculosis*?

YES

NO / NOT PERFORMED / RESULT NOT YET AVAILABLE

Close or household TB contact in the previous 12 months?

YES

NO

Score signs and symptoms and CXR features

Signs and symptoms		Chest X-ray	
Cough longer than 2 weeks	+2		
Fever longer than 2 weeks	+5	Cavity/Cavities	+6
Lethargy	+3	Enlarged lymph nodes	+17
Weight loss	+3	Opacities	+5
Haemoptysis (cough up blood)	+4	Miliary Pattern	+15
Night sweats	+2	Effusion	+8
Swollen lymph nodes	+4		
Tachycardia	+2		
Tachypnoea	-1		

Sum A: ___ **Sum B:** ___

Is Sum A + Sum B > 10?

YES

NO

Initiate appropriate TB treatment

Scoring part only:
Sensitivity: 85%
Specificity:
Algorithm A: 37%
Algorithm B: 30%

Additional steps added to improve performance

Algorithms internally validated, external validation ongoing

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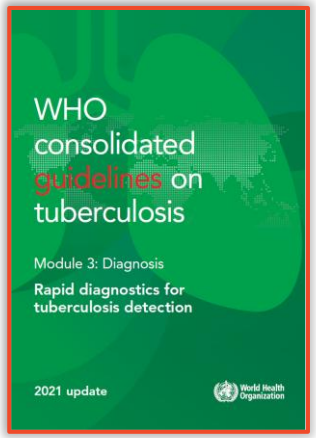
Updates on concurrent testing with LC-aNAATs



- **Children** with signs/symptoms or positive screening test: **LC-aNAAT on respiratory samples and stool** *(strong recommendation, low certainty evidence)*
  - Strong recommendation as large desirable effects: rapid and accurate diagnosis in highly vulnerable population (recognizing challenges and large gap)
  - Concurrent testing prioritized over the use of a single molecular test
  - **Evidence supports use of a single LC-aNAAT on sputum, gastric aspirate, stool and NPA as initial diagnostic test as well**

- **Children with HIV** with signs/symptoms or positive screening test: **LC-aNAAT on respiratory sample and stool and LF-LAM on urine** *(conditional recommendation, low certainty evidence)*

Rapid communication: https://www.who.int/publications/i/item/B09111
LC-aNAAT: Low complexity automated nucleic acid amplification test

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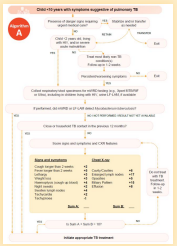
Implementation: concurrent testing

↑ **cost** (but cost-effective as earlier diagnosis)

Challenges of **respiratory sample** collection



Integration into treatment decision algorithms

Ultimate decision depending on feasibility, acceptability, budget, operational research

Decentralization & **integration** into child health and PHC needed

Capacity to make a **clinical diagnosis** (including for DR-TB)

Stool testing remains critical: non-invasive

Capacity building, mentoring, equipment & supplies

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E-courses on TB in children and adolescents

https://openwho.org/courses/TB-child-adolescent-EN

https://openwho.org/courses/TB-child-adolescent-programmatic

Courses being transferred to WHO Academy
(Links to be updated soon)

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Thank you for your attention!

verkuijls@who.int

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