Updated WHO guidance on the management of tuberculosis in children and adolescents

European Medical Consilium
Session 1: TB screening, prevention & new approaches to diagnosis in children and adolescents
1 June 2022

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Outline of sessions 1 and 2

Session 1 on 1 June 2022:
- Burden of TB in children and adolescents
- 2022 WHO Consolidated Guidelines and Operational Handbook on the Management of Tuberculosis in Children and Adolescents
- TB screening and contact investigation
- TB prevention: ruling out TB disease and provision of TB preventive treatment in children and adolescents
- New WHO guidance on diagnostic approaches

Session 2 on 24 June 2022:
- New WHO guidance on treatment and dosing of drug-susceptible TB, drug-resistant TB and on treatment of drug-susceptible TB meningitis
- Special situations (CALHIV, TB in pregnancy and management of newborns, Palliative care, care for adolescents, TB in children with severe acute pneumonia, and TB in children with malnutrition)
- Models of Care
The burden of TB in children and adolescents and main programmatic gaps
Global burden estimates (2021 Global TB report)

7.5 million children (0–14) infected with TB each year (Dodd et al., 2014)

9.9 million TB patients in 2020

1.09 million children (0–14 years) developed TB in 2020
- 47.5% <5 years olds

226,000 child (0–14) TB deaths in 2020
- 80% in children <5 years
- 96% of deaths in children who did not access TB treatment
- 21,000 (9%) deaths among children living with HIV

1.5 million TB deaths in 2020
- 1.3m in HIV-uninfected
- 215k in PLHIV

1.3 million
727,000 adolescents (10–19 year-olds) developed TB in 2012 (Snow et al., 2016)
The case detection and prevention gaps

**The case detection gap**

% of missing TB patients in different age groups

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Reported</th>
<th>Missing (under-diagnosis and under-reporting)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4 years</td>
<td>27.5</td>
<td>72.5</td>
</tr>
<tr>
<td>5-14 years</td>
<td>44.6</td>
<td>55.4</td>
</tr>
<tr>
<td>All &lt;15 years</td>
<td>36.5</td>
<td>63.5</td>
</tr>
<tr>
<td>All &gt;15 years</td>
<td>61.8</td>
<td>38.2</td>
</tr>
</tbody>
</table>

**The prevention gap**

In 2020, **almost two thirds** of 1.1 million eligible contacts <5 years* did **NOT** access TB preventive treatment (TPT)

* Estimated number of eligible children was reduced due to lower notifications of bacteriologically confirmed patients in 2020
No data collected on TPT for DR-TB
An introduction to the 2022 WHO Consolidated Guidelines and operational handbook on the Management of TB in Children and Adolescents
Development of updated guidelines on the management of TB in children and adolescents

- GDG meeting held in May/June 2021
- Evidence reviewed on the following PICO questions, using GRADE* methodology:
  - Use of Xpert Ultra in gastric aspirate and stool specimens
  - Integrated treatment decision algorithms
  - Treatment shortening in children with non-severe TB
  - In children with MDR/RR-TB: Use of bedaquiline in children under 6 and delamanid in children under 3 years
  - Short intensive treatment regimen for TBM
  - Models of care for case detection and provision of TPT (decentralized and family-centred, integrated approaches)
- **Rapid communication** published in August 2021
- **Consolidated guidelines** with operational handbook released at UN press conference on 21 March (Updated guidelines replace the 2014 second edition of the Guidance for National TB Programmes on the management of TB in children)

Guidelines: https://www.who.int/publications/i/item/9789240046764
Handbook: https://www.who.int/publications/i/item/9789240046832

*GRADE: Grading of Recommendations, Assessment Development and Evaluation*
Target audience and scope

- **Target audience:**
  - National programmes (TB, HIV, PHC, MCH), health care workers, education sector, NGOs, CSOs, CBOs, technical and implementation partners

- **Objective:**
  - Contribute to reductions in TB related morbidity and mortality in children and adolescents in line with global targets

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**Diagram:**

Cascade of care in children and adolescents exposed to and with TB, with broad topics of PICO questions (adapted from 2018 Roadmap)
The operational handbook on the management of TB in children and adolescents

Aim: provide practical guidance on implementation of WHO recommendations on prevention and management of TB in children and adolescents under programmatic circumstances and at different levels of the health system

- Chapters on: TB screening and contact investigation, prevention, diagnostic approaches, TB treatment (DS, DR-TB, PTB, EPTB), models of TB care, special situations such as TB/HIV, TB in pregnancy, palliative care, post TB care, care for adolescent with or at risk of TB
- Implementation tools: e.g. treatment decision algorithms, updated table on dosing of second-line medicines, a dosing table for the new TBM regimen, TST administration, sample collection procedures and more

<table>
<thead>
<tr>
<th>Weight band (kg)</th>
<th>Weight 3–&lt;5 kg using child-friendly formulations</th>
<th>Weight 25–&lt;35 kg using adult formulations (with Z 400 mg tablet)</th>
<th>Weight 25–&lt;35 kg using adult formulations (with Z 500 mg tablet)</th>
<th>Eto 250 mg tablet</th>
</tr>
</thead>
<tbody>
<tr>
<td>3–&lt;4</td>
<td>1.5</td>
<td>0.5</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>4–&lt;5</td>
<td>1.5</td>
<td>0.5</td>
<td>1</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Table 5.6: Dosing table: Short intensive TB meningitis regimen (6H/3RZE/10)

**Group** | **Medicine** | **Weight-based daily dose** | **Formulations (mg/mL as applicable)** | **Weight bands** | **Usual upper daily dose** |
<table>
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</thead>
<tbody>
<tr>
<td>A</td>
<td>Levofoxacin</td>
<td>15–20 mg/kg</td>
<td>100 mg/dt</td>
<td>5 mL (0.5 mg/mL)</td>
<td>3 to &lt;5 kg</td>
</tr>
</tbody>
</table>

| 250 mg tab (250 mg in | 10 mL = 25 mg/mL) | 2 mL | 5 mL (0.5 mg/mL) | 1 | 2 | 3 | 3 | 3 | 1.5 g |
Consolidation of recommendations from other WHO guidelines

WHO TB KNOWLEDGE SHARING PLATFORM

Access the modular WHO guidelines on tuberculosis, with corresponding handbooks and training materials.

https://tbksp.org/
TB Screening and contact investigation
TB screening and contact investigation

• **Systematic screening** for TB disease is conducted in a pre-determined target group at risk for TB disease

• **Contact investigation**: a form of systematic screening among close contacts (including children and adolescents), of a person with TB.
  - Helps to identify people with undiagnosed TB disease
  - Also key to prevent TB disease among those who are (likely) infected
Prioritizing household contacts and PLHIV

- 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

For these populations:
- Screening should always be conducted
- The operational handbook provides tools and algorithms, implementation models, and information on frequency
- In absence of disease, TPT should be provided when appropriate
Facilty- and community-based models of TB contact investigation: importance of careful planning and adequate resources

• Contact investigation should be a **standard component** of all national TB programmes

• Facilty- or community-based programmes or mixed models

• **Prerequisites for success**: adequate and dedicated human resources; coordination between actors at community and facility level; initial and refresher trainings, onsite coaching; diagnosis and dispensing of TB medicines or TPT at health facilities; provision of monitoring tools; reimbursement of transport costs for CHWs; sensitization in the community

• **Respect for privacy and human rights** is key!
Tools strongly recommended for screening child and young adolescent contacts (<15 years):

- **Symptom screening** (cough, fever, poor weight gain or weight loss)
- **Chest X-ray**

Tools strongly recommended for screening children living with HIV (<10 years):

- **Symptom screening** (cough, fever, weight loss)
- And/or **contact** with a person with TB
TB Screening algorithms for contacts ≤ 15 years

Algorithms with symptoms or CXR
TB screening algorithms for children living with HIV <10 years

Screening with symptoms
TB prevention: ruling out TB disease and provision of TB preventive treatment in children and adolescents
Importance of TB prevention

• ~ 7.5 million children and young adolescents (< 15y) are infected with TB every year \(^1\)

• People infected with TB: at ↑ risk of developing TB, especially if weakened immunity, e.g. PLHIV, children with SAM

• Young children (especially < 2y) at ↑ risk of progression to TB disease and of severe forms of TB disease (e.g. disseminated TB, TB meningitis) with ↑ risk of life-long sequelae or death

\(^1\) Dodd et al., 2016
TB Preventive Treatment (TPT): Target groups

• Children and adolescents with ↑ risk of progression from infection to disease
  • including CALHIV and adolescents with specific comorbidities or on specific treatment (e.g. anti-TNF treatment, dialysis, preparing for transplantation)

• Children and adolescents with ↑ likelihood of exposure to TB
  • including household contacts of people with bacteriologically confirmed TB and those living / working in institutional / crowded settings (e.g., recent immigrants from TB HBCs, homeless people, people who use drugs)
Ruling out TB disease before starting TPT

- **Clinical algorithm:** screening for symptoms of TB, history of contact with a person with TB, HIV status, age, TB infection test results and abnormal findings on CXR

- Either TST or IGRA can be used to test for TB infection and to find people more likely to benefit from TPT but non-availability should not pose a barrier to TPT

- Testing for TB infection is not required for asymptomatic household contacts < 5 years and for PLHIV (any age)
WHO recommendations on use of tests for TB infection

• In 2011 WHO issued recommendations on the use of IGRAs for the diagnosis of TBI, including the following technologies: TST; Qiagen QuantiFERON-Gold (QFT-G); QuantiFERON-TB Gold In- Tube (QFT-GIT); and Oxford Immunotec T-Spot.TB (T-Spot) assays.

• In 2018, WHO has updated the recommendations stipulating that both TST and/or IGRA can be used for TB infection. ¹

• In 2021, the WHO recommendations were extended for the below technologies: Beijing Wantai’s TB-IGRA; Qiagen QuantiFERON-TB Gold Plus (QFT-Plus).

• In 2022, WHO plans to issue recommendations on the use of TBST for the diagnosis of TBI including the following technologies: C-Tb (Serum Institute of India, India); Diaskintest (Generium, Russia); C-TST (formerly known as ESAT6-CFP10 test, Anhui Zhifei Longcom, China).

¹ WHO consolidated guidelines on tuberculosis, Module 1: Prevention – tuberculosis preventive treatment.
Rapid communication: TB antigen-based skin tests for the diagnosis of TB infection

• The TBST class is defined as skin tests for the detection of TB infection that use *Mtb* specific antigens (ESAT6 and CFP10)

• In 2021, WHO commissioned a systematic review of published and unpublished data on this new class of tests for TB infection that had not been previously reviewed by WHO

• A Guideline Development Group (GDG) was convened by WHO 31.01-3.02.22, to discuss the findings of the systematic reviews and to make recommendations on TBST for TB infection

• The following technologies were included in the evaluation: C-Tb (Serum Institute of India, India); C-TST (Anhui Zhifei Longcom, China); and Diaskintest (Generium, Russia)

• The objectives of the meeting were to assess the available data on TBST related to patient-important outcomes, diagnostic accuracy, safety, concordance, and economic and qualitative evidence, in comparison to TST and IGRA

https://www.who.int/publications/i/item/WHO-UCN-TB-2022.1
Key findings

• **TBST were found to be accurate**
  - Pooled sensitivity and specificity for TB infection detection were 76.0% (95% CI: 70.0 to 81.0) and 98.0% (95% CI: 94.0 to 99.0), respectively.
  - Difference in specificity between TBST and TST among those who were BCG vaccinated was 67.4% (95% CI: 24.0 to 110.7) and was higher for TBST.
  - However, difference in specificity between TBST and IGRA among those who were BCG vaccinated was 9.7% (95% CI: −31.2 to 11.8) and was lower for TBST, although the CIs overlapped.
  - Agreement with TST in people without TB disease was 59.4% (95% CI: 45.4 to 72.1) and in people with TB disease was 88.3% (95% CI: 82.1 to 92.5).
  - Agreement with IGRA in people without TB disease was 89.0% (95% CI: 82.6 to 93.2) and in people with TB disease was 85.7% (95% CI: 79.5 to 90.3).

• **TBST safety profile appeared similar to TST**

• **TBST were found to be cost-effective**

• **TBST were found to be acceptable and feasible**
Options for TPT to prevent DS-TB

- **6/9H, 3HP, 3HR** are strongly recommended for use in children and adolescents
- **1HP, 4R*** alternative options (all disease burden settings and target populations including PLHIV)

- choice depends on availability of appropriate formulations and considerations for age, safety, drug-drug interactions and adherence

- age limits: **3HP ≥2y; 1HP ≥13y**

*bold: strong; not bold: conditional recommendations
<table>
<thead>
<tr>
<th>Target group</th>
<th>Preferred regimen</th>
<th>Alternative regimen(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-negative children ≤2y</td>
<td>3HR if paediatric fixed-dose combination (FDC) available</td>
<td>If paediatric FDC not available, use 6H (preferably dispersible tablets)</td>
</tr>
<tr>
<td>HIV-negative children ≥2y and ≤25 kg body weight</td>
<td>3HR if paediatric FDC available</td>
<td>If paediatric FDC not available, use 3HP or 6H</td>
</tr>
<tr>
<td>HIV-negative children &gt;25 kg body weight</td>
<td>3HP using adult formulations</td>
<td>3HR using adult FDC 1HP using adult formulation (≥13y)</td>
</tr>
<tr>
<td>Children living with HIV</td>
<td>6H (preferably using dispersible tablets)</td>
<td>3HR for children on EFV-based ART 3HP for older children on EFV ART (and able to swallow tablets)</td>
</tr>
<tr>
<td>Adolescents living with HIV</td>
<td>3HP if on TDF, EFV, DTG or RAL-based ART</td>
<td>1HP (≥13y) if on TDF, EFV, DTG or RAL-based ART 6H</td>
</tr>
</tbody>
</table>
TPT for high-risk household contacts of patients with MDR-TB

- Contacts of people with MDR-TB or Hr TB: higher risk of TB infection, same risk of progression to TB disease as DS-TB contacts

- **Conditional recommendation on TPT for contacts exposed to MDR-TB**
  - Considerations: intensity of exposure, confirming source patient and their DST, confirmation of TB infection (TST or IGRA)

- Suggestion on drug choice: **6 months of daily levofloxacin** (unless source case resistant)
  - Use of *paediatric formulation* in children
  - With or without other medicines e.g. E (or Eto if tolerated)
  - Clinical follow-up for 2 years
  - Active evaluation for developing signs and symptoms suggestive of TB

- **RR-TB contacts**: same as MDR-TB; If source case H susceptible, 6-9H may be used; **Hr TB contacts**: 4R may be an option (but little evidence)

- 3 studies are ongoing and results awaited to inform further new TPT guidance:
  - **TB-CHAMP**: Lfx versus placebo daily for 6 months regardless of IGRA or HIV status (< 5 years; South Africa)
  - **PHOENIx**: Dlm versus standard dose INH daily for 26 weeks (<5 years, TST/IGRA + >5 years, 11 countries)
  - **V-QUIN**: testing 24 weeks of LFx vs placebo (all ages; with evidence of infection; Vietnam)
TPT completion criteria, adherence strategies and management of interruptions

- Children and adolescents on TPT should be reviewed every month for those on 3-months regimens (e.g. 3HR or 3HP) or every 2 months for those on a 6-month regimen (6H) or DR-TB TPT
- **Monitor** for symptoms suggestive of disease; weight to adjust TPT dosage; adverse events; treatment adherence & ensure R&R (TPT register; use of PREVENT-TB application)
- **Explain** the importance of adherence at every visit & take note of risk factors for poor adherence and address them
- **Young children refusing to take medicines**: offer TPT with food that masks the taste; provide a treat when treatment completion; in case of vomiting within 30 min of intake, provide a new dose and try to give TPT at a different time in the day
- **Shorter regimens** are associated with better adherence and higher treatment completion based on 80% or 90% (for 3HP) of recommended doses taken within 133% of the planned TPT duration

### Regimen Duration and Treatment Completion

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Total duration (months)</th>
<th>Expected number of doses</th>
<th>80% of recommended doses</th>
<th>Extended time for treatment completion (days): original treatment duration +33% additional time</th>
</tr>
</thead>
<tbody>
<tr>
<td>6H (daily)</td>
<td>6</td>
<td>182</td>
<td>146</td>
<td>239</td>
</tr>
<tr>
<td>3HR (daily)</td>
<td>3</td>
<td>84</td>
<td>68</td>
<td>120</td>
</tr>
<tr>
<td>3HP (weekly)</td>
<td>3</td>
<td>12</td>
<td>11 *</td>
<td>120</td>
</tr>
<tr>
<td>1HP (daily)</td>
<td>1</td>
<td>28</td>
<td>23</td>
<td>38</td>
</tr>
<tr>
<td>4R (daily)</td>
<td>4</td>
<td>120</td>
<td>96</td>
<td>160</td>
</tr>
</tbody>
</table>
New approaches to the diagnosis of TB in children and adolescents
In children with signs and symptoms of pulmonary TB, Xpert Ultra should be used as the initial diagnostic test for TB and detection of rifampicin resistance on sputum, nasopharyngeal aspirate, gastric aspirate or stool, rather than smear microscopy/culture and phenotypic DST

(UPDATED: strong recommendation, moderate certainty of evidence for test accuracy in stool and gastric aspirate; low certainty of evidence for test accuracy in sputum; very low certainty of evidence for test accuracy in NPA)

Remarks:

• Although no evidence was available on the accuracy of the detection of rifampicin resistance, the previous recommendation on the use of Xpert Ultra for the detection of rifampicin resistance in sputum samples and NPA was extrapolated to stool and gastric aspirate.

• Considerations regarding the acceptability and feasibility of implementation of both stool and gastric aspirate specimens need to be taken into account.
Xpert MTB/RIF, Xpert Ultra assays as the initial test to diagnose pulmonary TB and RR in children

- In children with signs and symptoms of pulmonary TB
  - 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
  - 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.

### Strength | Certainty of Evidence
---|---
Strong | Moderate for sputum
Strong | Low for GA*, NPA** and stool
Strong | Low for sputum
Strong | Very Low for NPA**
Strong | Moderate for GA*
Strong | Moderate for stool

* Gastric aspirate
** Nasopharyngeal aspirate
Xpert MTB/RIF, Xpert Ultra assays as the initial test to diagnose extrapulmonary TB and RR

- In adults and children with signs and symptoms
  - of TB meningitis, Xpert MTB/RIF or Xpert Ultra should be used in cerebrospinal fluid (CSF) as an initial diagnostic test for TB meningitis rather than smear microscopy/culture
  - of EP TB, Xpert MTB/RIF may be used in LNA, LNB, pleural fluid, peritoneal fluid, pericardial fluid, synovial fluid or urine specimens as the initial diagnostic test rather than smear microscopy/culture
  - of EP TB, Xpert Ultra may be used in LNA and LNB as the initial diagnostic test rather than smear microscopy/culture
  - of EP TB, Xpert MTB/RIF or Xpert Ultra should be used for RR detection rather than culture and phenotypic DST
  - of disseminated TB (HIV-positive), Xpert MTB/RIF may be used in blood, as an initial diagnostic test for disseminated TB

<table>
<thead>
<tr>
<th>Strength</th>
<th>CoE*</th>
</tr>
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<tbody>
<tr>
<td>Strong</td>
<td>Moderate for Xpert MTB/RIF Low for Xpert Ultra</td>
</tr>
<tr>
<td>Conditional</td>
<td>Moderate for pleural fluid; Low for LNA**, peritoneal fluid, synovial fluid, urine Very low for pericardial fluid, LNB***</td>
</tr>
<tr>
<td>Conditional</td>
<td>Low</td>
</tr>
<tr>
<td>Strong</td>
<td>High certainty for Xpert MTB/RIF Low certainty for Xpert Ultra</td>
</tr>
<tr>
<td>Conditional</td>
<td>Very Low</td>
</tr>
</tbody>
</table>

* Certainty of Evidence
** Lymph node aspirate
*** Lymph node biopsy
**** Rifampicin resistance
**Xpert MTB/RIF, Xpert Ultra assays for repeated testing in children**

- In children with signs and symptoms of PTB
  - in settings with **pretest probability** < 5%
    - and an Xpert MTB/RIF negative result on an initial test, repeated testing with Xpert MTB/RIF in sputum, gastric fluid, nasopharyngeal aspirate or stool specimens may not be used
    - and an Xpert Ultra negative result on an initial test, repeated testing with Xpert Ultra in sputum or nasopharyngeal aspirate specimens may not be used
  - in settings with **pretest probability** 5% or >
    - and an Xpert MTB/RIF negative result on an initial test, repeated testing with Xpert MTB/RIF (for total of two tests) in sputum, gastric fluid, nasopharyngeal aspirate and stool specimens may be used
    - and an Xpert Ultra negative result on an initial test, repeated one Xpert Ultra test (for a total of two tests) in sputum and nasopharyngeal aspirate specimens may be used

<table>
<thead>
<tr>
<th>Strength</th>
<th>CoE*</th>
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<tbody>
<tr>
<td>Conditional</td>
<td>Low for sputum</td>
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<td></td>
<td>Very low for other specimen types</td>
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<tr>
<td>Conditional</td>
<td>Very low</td>
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<tr>
<td>Conditional</td>
<td>Low for sputum</td>
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<tr>
<td></td>
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<tr>
<td>Conditional</td>
<td>Very low</td>
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* Certainty of Evidence
In children with presumptive pulmonary TB attending health care facilities, integrated treatment decision algorithms may be used to diagnose pulmonary TB.

*(INTERIM RECOMMENDATION - conditional recommendation, very low certainty of evidence)*

**Remarks:**

- Bacteriological confirmation needs to be sought whenever possible, using available and recommended diagnostic tests and appropriate paediatric specimens – especially in children with a high likelihood of DR-TB
- Newly developed treatment decision algorithms for different settings with detailed practical guidance on there are included in the operational handbook. Use of these evidence-based algorithms is encouraged.
- *Interim* recommendation: valid for 24 months, after which new evidence will be reviewed.
Background on the new treatment decision algorithms

• **2 algorithms** developed after the GDG meeting by evidence reviewers in consultation with a GDG sub-group, for inclusion in the handbook
  - **Algorithm A**: for settings with CXR; **Algorithm B**: for settings without CXR
  - Mainly aimed at **PHC level** to build confidence and capacity to make decisions on starting TB treatment

• Methodology: **prediction modelling** based on individual patient database (~ 5000 records from diagnostic studies)
  - Sensitivity cut-off: 85% for scoring section (yellow blocks only)
  - Corresponding specificity 37% (algorithm A) and 30% (algorithm B)
  - Additional steps in final algorithm (triage, risk assessment, treatment for alternative diagnosis if low risk, bacteriological testing) to **improve diagnostic accuracy**

• **Detailed guidance and examples** included in the handbook, with printable job aid in annex 5
Practical guidance on integrated treatment decision algorithms in children

• New evidence-based algorithms developed and featured in operational handbook
  - **A**: settings with CXR
  - **B**: settings without CXR
• Main characteristics:
  - Triage step
  - Assessment of risk for rapid disease progression (< 2 years, CLHIV, SAM)
    - High risk: continue next steps
    - Low risk: treat for most likely non-TB condition, next steps if no improvement after 1-2 wks
• mWRD (LF-LAM if CLHIV)
Practical guidance on the use of the algorithms in children (2)

• Scoring of signs and symptoms and CXR features

• **CXR features:**
  • Cavities; enlarged lymph nodes; opacities; miliary pattern; effusion

• If total score >10: decision to start TB treatment
  • Assessment of risk for DR-TB
  • Assessment of severity

• Detailed guidance and examples

• Job-aid in annex

In children <10 y: Intrathoracic LN TB now classified as PTB
Assessments after making a decision to treat a child for TB

1. **Assessment for risk factors for DR-TB:**
   - contact with a confirmed or presumed person with DR-TB
   - a poor response to first-line treatment after 2–3 months, or
   - previous TB treatment in the past 12 months
   → refer the child to the appropriate level of care as needed

2. **Assessment of severity of disease to inform duration of treatment:**
   - non-severe PTB: intrathoracic lymph node TB without airway obstruction; uncomplicated TB pleural effusion; or paucibacillary, non-cavitary disease confined to 1 lobe and without a miliary pattern
   - further details in treatment presentation
   → children with non-severe, presumed drug-susceptible TB should receive a 4-month treatment regimen (2HRZ(E)/2HR)
Practical guidance on the diagnosis of EPTB and DR-TB

Extrapulmonary TB
- WHO recommendations on use of Xpert MTB/RIF and Ultra on non-respiratory specimens
- Typical clinical features of different forms of EPTB
- Investigations depending on site of disease

Drug-resistant TB
- Clinical presentation similar to DS-TB
- Critical importance to attempt bacteriological confirmation using mWRD
- Clinical diagnosis based on suggestive signs/symptoms/CXR with history of contact with DR-TB (DST pattern of source case)

Suspect DR-TB in a child/adolescent if:
- contact with a person with confirmed DR-TB
- contact with a person with presumed DR-TB (e.g. failed treatment, retreatment or death from TB)
- Child/adolescent with TB not responding to first-line treatment after 2–3 months despite good adherence (and IRIS unlikely in CLHIV on ART)
- Child/adolescent previously treated for TB with recurrence of disease (true relapse or reinfection)
Acknowledgements and thanks

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• Experts who contributed to the development of the guidelines and handbook, including the GDG, ERGs, technical partners, funding partners, members of the Child and Adolescent TB Working Group

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