WHO update on progress towards UNGA HLM on TB targets and new policy recommendations

Annual meeting of the child and adolescent TB working group

Annemieke Brands and Sabine Verkuijl, 16 October 2020
Outline

• Child and adolescent TB data in the Global TB Report 2020
• Progress against UNGA HLM TB targets related to children
• WHO policy updates
  – TB preventive treatment (TPT)
  – Rapid diagnostics
  – DR-TB treatment
• Updating of the 2014 childhood TB guidelines
• Impact of COVID-19
What is new for children and adolescents?

- Countries with electronic case based systems requested to report in age bands 0-4, 5-9, 10-14, 15-19 years (2019)

- Treatment initiation for MDR/RR-TB in children and young adolescents 0-14 years (2018 and 2019)

- Treatment outcomes in children/young ado’s 0-14 years (2018 cohort) – mainly treatment success rate

- Box 5.3 on “Strengthening data collection for children and adolescents with TB” (Chapter 5, TB diagnosis and treatment, page 79-81)
Global burden estimates (2020 Global TB report)

- **TB patients in 2019**:
  - 10 million overall
  - 47% <5 years olds
  - 1.2 million children (0-14 years) developed TB in 2019
    - 727,000 adolescents (10-19 year-olds) developed TB in 2012
      - (Dodd et al., 2018)
  - 80% in children <5 years

- **TB deaths in 2019**:
  - 1.4 million
  - 230,000 child (0-14) TB deaths
    - 96% of deaths in children who did not access TB treatment
    - 36,000 (16%) deaths among children living with HIV

- **Children living with HIV**:
  - 36,000 deaths in 2019

- **Children infected with TB each year**:
  - 7.5 million children (0-14) infected with TB each year
  - (Dodd et al., 2014)
Detailed age-disaggregated reporting

• 10 TB HBCs reported fully age disaggregated notifications: Brazil, China, India, Kenya, Lesotho, Myanmar, Namibia, Philippines, Thailand, Zimbabwe
• These ten countries represent almost 45% of all notifications in the 0-14y age group
• First time to receive data on adolescents aged 10-19 years
• Data largely in line with estimates by Snow et al (2018)*

* Snow KJ, Sismanidis C, Denholm J, Sawyer Susan M, Graham SM. The incidence of tuberculosis among adolescents and young adults: a global estimate. Eur Respir J. 2018;51(2)
Treatment initiation in children with MDR/RR-TB

- Countries were requested to report on the number of children/young ado’s (0-14y) initiated on second-line treatment for MDR/RR-TB
  - Backdated for 2018, and for 2019
- **165 countries** reported **at least 1 child** started on second-line treatment in 2019
- **6 countries** (India, Russian Federation, South Africa, Ukraine, Pakistan and Kazakhstan) reported **≥100 children** started on second-line treatment (covering 81% of all cases) in 2019

<table>
<thead>
<tr>
<th>Year</th>
<th>MDR/RR-TB (all ages)</th>
<th>MDR/RR-TB (0-14y)</th>
<th>% children among all MDR/RR-TB</th>
<th>% of estimated annual burden*</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018</td>
<td>156 205</td>
<td>3 398</td>
<td>2.2%</td>
<td>10.6%</td>
</tr>
<tr>
<td>2019</td>
<td>177 099</td>
<td>5 588</td>
<td>3.2%</td>
<td>17.5%</td>
</tr>
</tbody>
</table>

* Estimated annual burden 32 000 (Dodd, 2016; Jenkins, 2018)

<table>
<thead>
<tr>
<th>Country</th>
<th>Children with MDR/RR-TB started Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>India</td>
<td>3360</td>
</tr>
<tr>
<td>Russian Federation</td>
<td>476</td>
</tr>
<tr>
<td>South Africa</td>
<td>332</td>
</tr>
<tr>
<td>Ukraine</td>
<td>161</td>
</tr>
<tr>
<td>Pakistan</td>
<td>110</td>
</tr>
<tr>
<td>Kazakhstan</td>
<td>100</td>
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</tbody>
</table>
TB treatment outcomes in children 0-14y

- 123 (of 215) countries reported treatment success rate in children and young adolescents 0-14y), including 19 (of 30) TB HBCs (N=347,909, 67% of total notifications in 0-14y in 2018)
  - Overall 85% success (similar to adults), range 73-97%
- 99 countries in European and American regions reported all outcomes for children/young ado’s (N=13,185)
  - Relatively high % not evaluated (9.5% versus 6% in adults)
Trends in provision of TPT to eligible <5 contacts

- Eligible: 1,200,000 (2015), 1,300,000 (2016), 1,300,000 (2017), 1,269,527 (2018), 1,308,122 (2019)
The case detection and prevention gaps remain...

The case detection gap

% of missing TB patients in different age groups

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Missing (under-diagnosis and under-reporting)</th>
<th>Reported</th>
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<tbody>
<tr>
<td>0-4 years</td>
<td>65</td>
<td>35</td>
</tr>
<tr>
<td>5-14 years</td>
<td>49</td>
<td>51</td>
</tr>
<tr>
<td>All &lt;15 years</td>
<td>56</td>
<td>44</td>
</tr>
<tr>
<td>All &gt;15 years</td>
<td>25</td>
<td>75</td>
</tr>
</tbody>
</table>

The prevention gap

In 2019, two thirds of over 1.3 million eligible contacts <5 years did NOT access TB preventive treatment (TPT)

WHO recommends TB prevention including:
- Preventive therapy
- Infection control measures
- BCG vaccination

In the 158 countries for which data on BCG coverage are available, 120 reported coverage of at least 90% in 2017.
Progress against UNGA HLM targets

Case detection and treatment

1,040,000 children notified with TB in 2018 and 2019

- 30% of the 2022 target (3.5m)

8,984 children started on second-line treatment for MDR/RR-TB in 2018 and 2019

- 7.8% of the 2022 target (115,000)

Provision of TB preventive treatment

782,952 contacts < 5y initiated on TPT in 2018 and 2019

- 20% of the 2022 target (4m)

178,051 contacts ≥5y initiated on TPT in 2018 and 2019

- 0.9% of the 2022 target (20m)

5.3 million PLHIV initiated on TPT in 2018 and 2019

- 88% of the 2022 target (6m)
Policy updates relevant for children and adolescents

TB Preventive Treatment, rapid diagnostics, DR-TB treatment; Child and adolescent TB guideline update; Impact of COVID
• 6/9H, 3HP, 3HR, 4R, 1HP* 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
• pregnancy does not disqualify women living with HIV from receiving IPT. More research needed but automatic deferral of IPT to postpartum may not be justified.
• no grounds to support dose changes when RPT and DTG are used together in adults (dose of DTG needs to be increased when it is given with RIF) – data on children awaited

*bold: strong; not bold: conditional recommendations
TPT – which regimens to use in which situations?

**Children <2 years***
- Preferred regimen: **3RH**
- If paediatric FDC not available: **6H**

**Children <25 kg** (up to 8-10 years)
- Preferred regimen: **3RH**
- If paediatric FDC not available: **6H** (dispersible tab) or **3HP** (adult formulations)

**Older children** (over 25 kg)
- **3RH** (adult FDCs)
- **3HP (>2y) / 1HP (>13y)** (adult formulations)

**Children living with HIV**
- **6H** (dispersible tab)
- For children on EFV-based ART only: **3RH**
- If able to swallow tablets: **3HP (>2y) / 1HP (>13y)**

* Neonates: No data available, expert opinion recommended
Guidelines on Rapid Diagnostics for TB detection (1)

• Strong recommendations on the use of Xpert MTB/RIF in children with signs and symptoms of pulmonary TB: as **initial diagnostic** test for TB and **rifampicin-resistance detection** in sputum, gastric aspirate, nasopharyngeal aspirate and stool.

• Strong recommendation on the use of Xpert Ultra in children as initial diagnostic test for TB and detection of RIF resistance in **sputum or nasopharyngeal aspirate**.

• Strong recommendation on use of Xpert MTB/RIF or Ultra in CSF as initial diagnostic test for **TBM**.

Guidelines: [https://apps.who.int/iris/rest/bitstreams/1284627/retrieve](https://apps.who.int/iris/rest/bitstreams/1284627/retrieve)
Handbook: [https://apps.who.int/iris-rest/bitstreams/1284635/retrieve](https://apps.who.int/iris-rest/bitstreams/1284635/retrieve)
Guidelines on Rapid Diagnostics for TB detection (2)

• Conditional recommendations on:
  – Use of Xpert MTB/RIF in lymph node aspirate, lymph node biopsy, pleural, peritoneal, pericardial or synovial fluid or urine specimens as the initial diagnostic test for extrapulmonary TB
  – Use of Xpert Ultra in lymph node aspirate or biopsy for lymph node TB
  – Use of Xpert MTB/RIF in blood for disseminated TB in CLHIV

• Conditional recommendations on repeat testing:
  – Pretest probability < 5% and initial test (Xpert or Ultra) negative: no repeat testing
  – Pretest probability ≥ 5%
    • and initial Xpert negative: repeat Xpert (for total of 2 tests) in sputum, gastric fluid, NPA and stool specimens may be used
    • and initial Ultra negative: repeat Ultra (for a total of 2 tests) in sputum and NPA may be used

Guidelines: https://apps.who.int/iris/rest/bitstreams/1284627/retrieve
Handbook: https://apps.who.int/iris/rest/bitstreams/1284635/retrieve
LF-LAM in children and adolescents living with HIV

- **Inpatient settings**: Strong recommendation to use LF-LAM to assist in diagnosis of active TB in HIV+ children and adolescents:
  - with signs and symptoms of (E)PTB or
  - with advanced HIV disease or who are seriously ill* or
  - irrespective of signs and symptoms of TB and with a CD4 cell count of less than 200 cells/mm³

- **Outpatient settings**: Suggestion to use LF-LAM to assist in diagnosis of active TB in HIV+ children and adolescents:
  - with signs and symptoms of (E)PTB or seriously ill* or
  - irrespective of signs and symptoms of TB and with a CD4 cell count of less than 100 cells/mm³

- **Outpatient settings**: LF-LAM should not be used without assessing TB symptoms; without TB symptoms and unknown CD4 cell count/CD4 cell count ≥200 cells/mm³; and without TB symptoms and with a CD4 cell count of 100–200 cells/mm³

- **Algorithms** for both settings available
  - Use of LF-LAM in conjunction with Xpert / Ultra

* “Seriously ill”: based on four danger signs: respiratory rate >30/minute, temperature >39 °C, heart rate >120/minute and unable to walk unaided
DR-TB treatment guidelines update 2020

- Shorter all **oral BDQ-containing regimen**:
  - 4–6 Bdq (6 m)-Lfx-Cfz-Z-E-H\(^{h}\)-Eto / 5 Lfx-Cfz-Z-E
  - Eligibility: no extensive TB disease; no severe EPTB (any forms other than TB LN); **children ≥6 years**
  - Child-friendly formulations to be used whenever possible; reference to BDQ crush study
  - Children < 6y: BDQ not yet recommended - lack of safety data and data on use as part of the shorter all-oral regimens
    - FDA approval of BDQ 20 mg based on RTC by J&J for children ≥ 5y - data not yet assessed by WHO

- **Longer individualized regimens** for those not eligible for shorter regimen above, including **children <6y and with EPTB other than TB LN**
  - DLM in children ≥3y, shortening of duration to <18m in children without extensive disease
  - **BPaL under OR conditions** in ≥14y in MDR-TB with FQ resistance

https://www.who.int/activities/tackling-the-drug-resistant-tb-crisis
Updating the 2014 child TB guidelines

- Target audience beyond NTPs
- Expansion to include adolescents (10-19 years)
- Consolidated document to include new recommendations but also updated recommendations relevant to children and adolescents from other WHO TB, HIV and other guidelines
- Accompanying operational handbook, with practical “how to” guidance on all topics, including those without evidence-based recommendations

- Developments so far:
  - Input from CAWG core team on topics to include in call for data
  - Call for data issued on 24 July; Responses received and categorized
  - Emerging scope:
    - Treatment shortening in children with non-severe TB
    - Diagnostic approaches in (vulnerable) children
    - Treatment of children with drug-resistant TB with all oral regimens
    - Models of care for TB prevention, case detection, treatment and care
    - Possibly treatment of congenital TB/TB in infants; Treatment of TB meningitis
  - First internal steering group meeting conducted

- Next steps:
  - Finalization of scope and PICO questions
  - Commissioning of systematic reviews
  - Establishment of GDG
  - Target date for publication: end 2021
Impact of COVID-19 on child and adolescent TB services

- Isolation of children with features of respiratory infection
- Lockdowns, closed TB facilities, reassignment of staff – delays in TB diagnosis and treatment
- Increased household exposure to TB
- Competing needs for diagnosis of COVID-19 over TB (e.g. GeneXpert)
- Indirect: reduced household income, increased poverty, food insecurity, malnutrition, vulnerability to other diseases, missed health checks and vaccinations

WHO publications
- Information note on TB and COVID
- Q&A on TB and COVID
- Scientific brief on BCG and COVID
- Maintaining essential health services: operational guidance for the COVID-19 context

https://www.who.int/teams/global-tuberculosis-programme/covid-19

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