WHO Policy Updates on child and adolescent TB

Annual meeting of the Child and Adolescent TB working group

The Hague, The Netherlands, 24 October 2018

Malgosia Grzemska
Global TB Programme
WHO/HQ
Outline

• Child TB notification in high burden countries
• 2018 Roadmap towards ending TB in children and adolescents
• Global targets 2023
• Quick updates on prevention, diagnosis, and treatment of DS-TB and DR-TB
• Plans for 2019-21
% children with TB notified in 30 HBCs

Suggestive of over-diagnosis

Suggestive of under-diagnosis and/or under-reporting

No data available: Angola and PNG
Missing child TB cases in the 30 high burden countries

- **Russia**: 2% (2%)
- **Pakistan**: 45% - 4%
- **Bangladesh**: 95% - 46%
- **China**: 100% - 90%
- **Myanmar**: -8% - 39%
- **DPR Korea**: 64% - 64%
- **Thailand**: 92% - 90%
- **Vietnam**: 89% - 89%
- **Philippines**: 56% - 32%
- **Papua New Guinea**: no data
- **Cambodia**: 48% - 66%
- **Indonesia**: -8% - 8%

**Average (30 HBCs):**

- 63%
- 43%

**Missing children with TB aged 0-4 years**

- Nigeria: 92% - 80%
- Sierra Leone: 3% - 35%
- Liberia: 99% - 89%
- Brazil: 79% - 79%
- DR Congo: 70% - 19%
- Angola: no data
- Zambia: 82% - 58%
- South Africa: 54% - 63%

**Missing children with TB aged 5-14 years**

- Central African Republic: 49% - 33%
- Ethiopia: 68% - 4%
- Congo: 79% - 53%
- Lesotho: 86% - 79%
- Zimbabwe: 82% - 66%
- Kenya: 67% - 59%
- Uganda: 67% - 59%
- Mozambique: 70% - 26%

Source: WHO Global TB Report, 2018

*Data suggest over-diagnosis in 5-14 year olds*
% eligible children <5y on preventive treatment (2017)

Mozambique, Russia and DPRK reported >100%

No data available: Angola, CAR, Lesotho, Sierra Leone, Brazil, Pakistan, China, PNG
Major detection and prevention gaps remain due to persistent challenges and missed opportunities

- Insufficient advocacy, political leadership and stakeholder engagement
- Persistent policy-practice gaps in developing, implementing and scaling up evidence-based programmatic approaches (including prevention and finding the missing children with TB)
- Lack of implementation of integrated, family and community-centered strategies
- Inadequate recording and reporting systems
- Insufficient research on child and adolescent TB
Committing to end TB in Children, Adolescents and Families, 24 September 2018, Scandinavia House, New York, USA

- Roadmap towards Ending TB in Children and adolescents
- Best Practices in Child and Adolescent Tuberculosis Care
- Research Priorities for Paediatric Tuberculosis

Photo credit: Anne Detjen, UNICEF
Child and Adolescent TB Roadmap: 10 key actions

1. Strengthen advocacy at all levels
2. Foster national leadership and accountability
3. Foster functional partnerships for change
4. Increase funding for child and adolescent TB programmes
5. Bridge the policy-practice gap
6. Implement and expand interventions for prevention
7. Scale up child and adolescent TB case-finding and treatment
8. Implement integrated family- and community-centred strategies
9. Improve data collection, reporting and use
10. Encourage child and adolescent TB research
Child and Adolescent Roadmap: Key actions

Roadmap towards ending TB in children and adolescents

- Encourage child and adolescent TB research
- Improve data collection, reporting and use
- Scale-up child and adolescent TB case finding and treatment
- Bridge the policy-practice gap
- Foster functional partnerships for change
- Strengthen advocacy at all levels

Note: Many of these key actions can and should be implemented simultaneously
Ending the epidemic of tuberculosis by 2030 requires **Universal Health Coverage**, leaving no one behind, but also **action beyond the health sector** to address the risk factors and determinants of disease. The political declaration of the **UN HLM on TB provides** a major opportunity to galvanize such **multi-sectoral action**.

The declaration includes two major global targets for the next five years:

(i) **40 million people with TB to be reached with care during the period 2018 and 2023**, including **3.5 million children** and 1.5 million people with drug-resistant TB; and,

(ii) **At least 30 million people to be reached with TB prevention services during the period 2018-2023**, including **4 million children under 5 years of age**, 20 million other household contacts and 6 million people living with HIV (including children).
Quick update on TB prevention: WHO position paper on BCG (Feb 2018)

• High TB burden and/or high leprosy burden as well as where Buruli ulcer occurs, a single dose should be given to all healthy neonates at birth or at earliest opportunity thereafter
• BCG can be safely co-administered with other routine vaccines incl. Hep B
• Revaccination not recommended even if TST or IGRA is negative
• Children who are HIV infected should not receive BCG vaccination. However, HIV infected individuals, including children, who are receiving ART, are clinically well and immunologically stable should be vaccinated
• Neonates born to women of unknown HIV status should receive BCG. However, neonates with unknown HIV status born to HIV-infected women should be vaccinated if they have no clinical evidence suggestive of HIV infection, regardless of the mother’s ART status.
• Additionally, neonates with HIV infection should delay BCG vaccination until ART has been started and are immunologically stable.

http://www.who.int/immunization/documents/position_papers/
Quick update of TB prevention: WHO LTBI guidance

WHO updated and consolidated guidance for programmatic management of LTBI (February 2018):

- Expanding the number of groups prioritized for LTBI testing and treatment – apart from all living with HIV and under 5 years, additional high risk groups are:
  - HIV-negative children ≥ 5 years, adolescents and adults who are contacts of TB patients
  - Contacts of patients with MDR-TB

- Expanding testing options in all countries: TST or IGRA. Active TB should always be ruled out before prescribing preventive treatment.

- Expanding preventive treatment options: two new shorter regimens as alternative to 6H: 3HP for adults, adolescents and children; 3RH for children and adolescents < 15 years – should facilitate adherence!

Quick update on TB prevention: WHO LTBI guidance

New recommendations – MDR-TB contacts:

- In selected high-risk household contacts of patients with MDR-TB, preventive treatment may be considered based on individualised risk assessment and a sound clinical justification. *(Conditional recommendation, very low-quality evidence)*
  - Careful assessment of exposure, resistance pattern of source case
  - For household contacts at high risk (e.g. children, PLHIV)
  - Drug selection based on drug susceptibility profile of source case
  - Confirmation of infection with LTBI test required
  - Strict observation and close monitoring of all contacts for 2 years
  - Results of ongoing placebo-controlled trials will be used for updating recommendation
  - Drug choice: later generation fluoroquinolones (e.g. Lfx, Mfx) unless source case resistant. Concern re retardation of cartilage development in children – but not demonstrated in humans.

### Update on the roll out child-friendly TB FDCs via GDF as of end June 2018

85 Countries have ordered ~789,000 treatment courses* of new pediatric FDCs
- 77 countries have had new pedi FDCs delivered (~464,000 treatments); **8 new countries currently ordering for 1st time**

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Child-friendly fixed dose combination formulations

New Paediatric FDC Procurement via GDF (June 2018)

Delivered ▪ First order 2018
Update on diagnosis: important role of Xpert MTB/RIF in children


Compared to culture:
Sensitivity 62% on expectorated or induced sputum; 66% on gastric lavage
Specificity 98%
40% more sensitive than smear microscopy

Xpert MTB/RIF

• should be used as the initial diagnostic test in children suspected of having MDR TB or HIV associated TB – strong recommendation, very low quality of evidence
• may be used as initial test in all children suspected of TB (including extrapulmonary TB) – conditional recommendation acknowledging resource implications, very low quality of evidence

A negative Xpert MTB/RIF result does not exclude TB in children!
The next generation Xpert MTB/RIF ultra cartridge

- Significantly better performance (increased sensitivity) than current cartridge in detecting *M. tuberculosis* specimens with low numbers of bacilli in particular when smear-negative, culture positive specimens (e.g. those from people living with HIV), extrapulmonary specimens (notably cerebrospinal fluid) and in specimens from children.

- Increases sensitivity offset by a decrease in specificity (may lead to false-positives as the Ultra assay also detects TB bacilli that are not replicating).

- Accuracy of detecting rifampicin resistance similar to that of the current Xpert cartridge.

Therefore, current WHO recommendations on the use of Xpert MTB/Rif also apply to the Ultra assay.
Update on MDR-TB: WHO Rapid Communication (August 2018)

- New evidence from meta-analysis of individual data from clinical trials, cohort/observational studies and programmatic implementation of longer and shorter MDR-TB regimens
- Treatment outcome data used for policy formulation

Treatment options are becoming more individualized
- Feasibility of effective and fully oral treatment regimens for most patients
- Need to ensure drug resistance is excluded before starting patients on treatment
- The need for close monitoring of patient safety and treatment response

Key medicine changes:
- Regrouping of medicines recommended for use in longer MDR-TB regimens into three categories, ranked based on the latest evidence about the balance of effectiveness to safety
- Table on the next slide is overall approach to designing longer MDR-TB regimens for adults and children

### Medicines recommended for use in longer MDR-TB regimens

<table>
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<tr>
<th>GROUP</th>
<th>MEDICINE</th>
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| **Group A (to be prioritized):** Include all three medicines (unless they cannot be used) | Levofloxacin (Lfx) or Moxifloxacin (Mfx)  
Bedaquiline (Bdq)\(^1,4\)  
Linezolid (Lzd)\(^2\) |
| **Group B (to be added next):** Include one or both medicines (unless they cannot be used) | Clofazimine (Cfz)  
Cycloserine (Cs) OR Terizidone (Trd) |
| **Group C:** Add to complete the regimen and when medicines from Groups A and B cannot be used | Ethambutol (E)  
Delamanid (Dlm)\(^3,4\)  
Pyrazinamide (Z)\(^5\)  
Imipenem-cilastatin (Ipm-Cln) OR Meropenem (Mpm)\(^6\)  
Amikacin (Am) OR Streptomycin S\(^7\)  
Etionamide (Eto) OR Prothionamide (Pto)  
\(p\)-aminosalicylic acid (**PAS**) |

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New, first-ever, child-friendly medicines for drug-resistant TB now available via Stop TB Partnership’s Global Drug Facility

GDF now offers a full suite of child-friendly formulations for both drug-resistant (DR) and drug-sensitive (DS) TB

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<th>New DR-TB Formulations (Added to GDF Catalog May 2018)</th>
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<tr>
<td>Pyrazinamide 150 mg*</td>
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<td>Ethionamide 125 mg*</td>
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<td>Levofloxacin 100 mg*</td>
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<td>Moxifloxacin 100 mg*</td>
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<td>Cycloserine 125mg</td>
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<th>New DS-TB Formulations (Added to GDF Catalog May 2018)</th>
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<tr>
<td>Ethambutol 100 mg*</td>
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<td>Isoniazid 100 mg*</td>
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*dispersible tablet
Plans for 2019 - 21

- Dissemination and adaptation of Roadmap towards ending TB in children and adolescents – regional meetings in Africa and Asia
Thank you for your attention!

Acknowledgements

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