

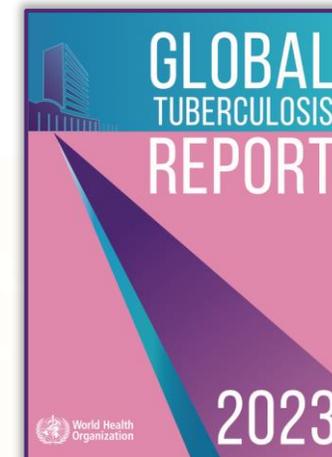


WHO updates

Annemieke Brands, Sabine Verkuijl, Kerri Viney & Tiziana Masini, WHO GTB

Annual meeting of the Child and Adolescent TB Working Group
Hyatt Regency Paris Etoile, Paris, France
14 November 2023

TB incidence and mortality in children and adolescents, 2022



10.6 million → **1.3 million**
TB among all ages in 2022 TB deaths in 2022

1.25 million → **214 000**
children (0–14 years) developed TB in 2022 (12% of all TB) TB deaths in 2022 (16% of all TB deaths)



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 years,

76% were in children <5 years



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

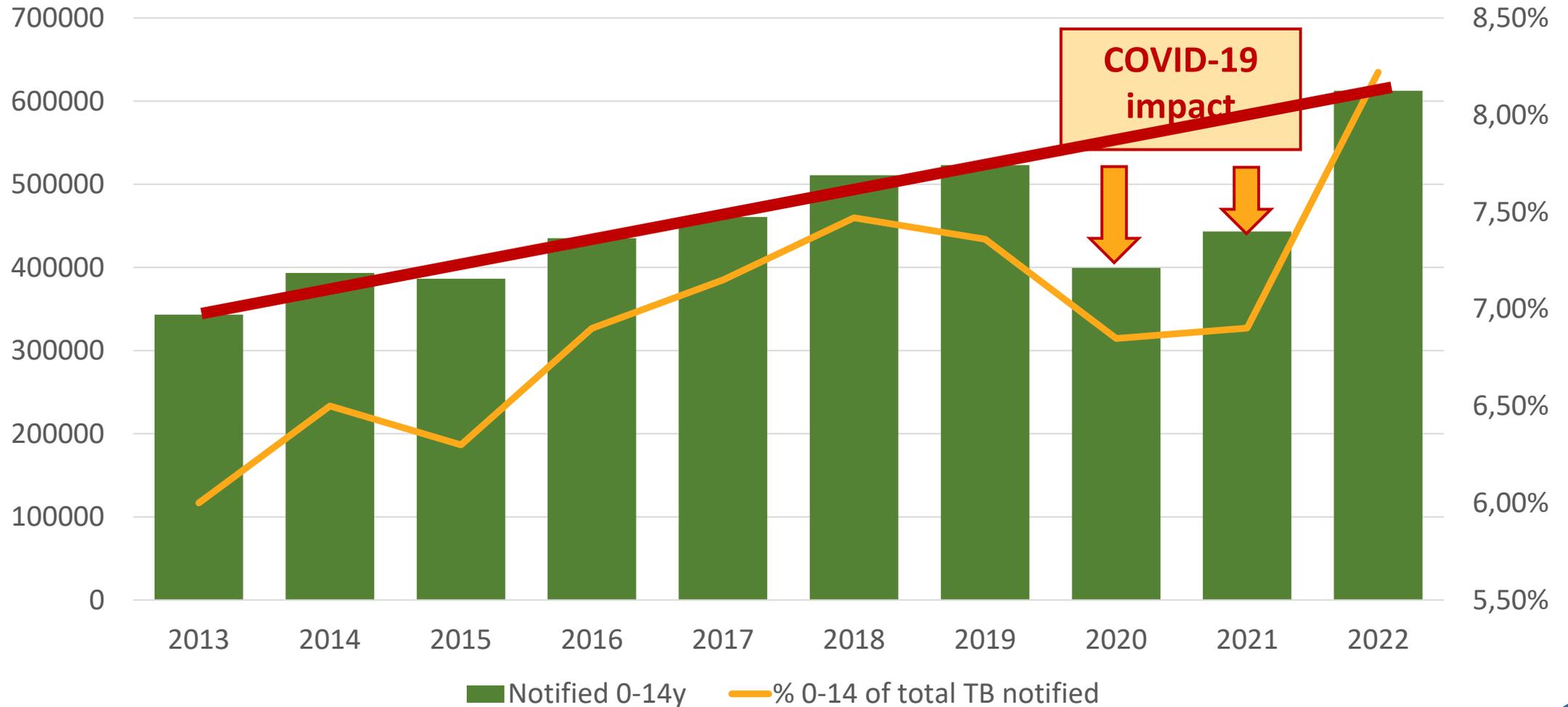
(Dodd et al, 2017)



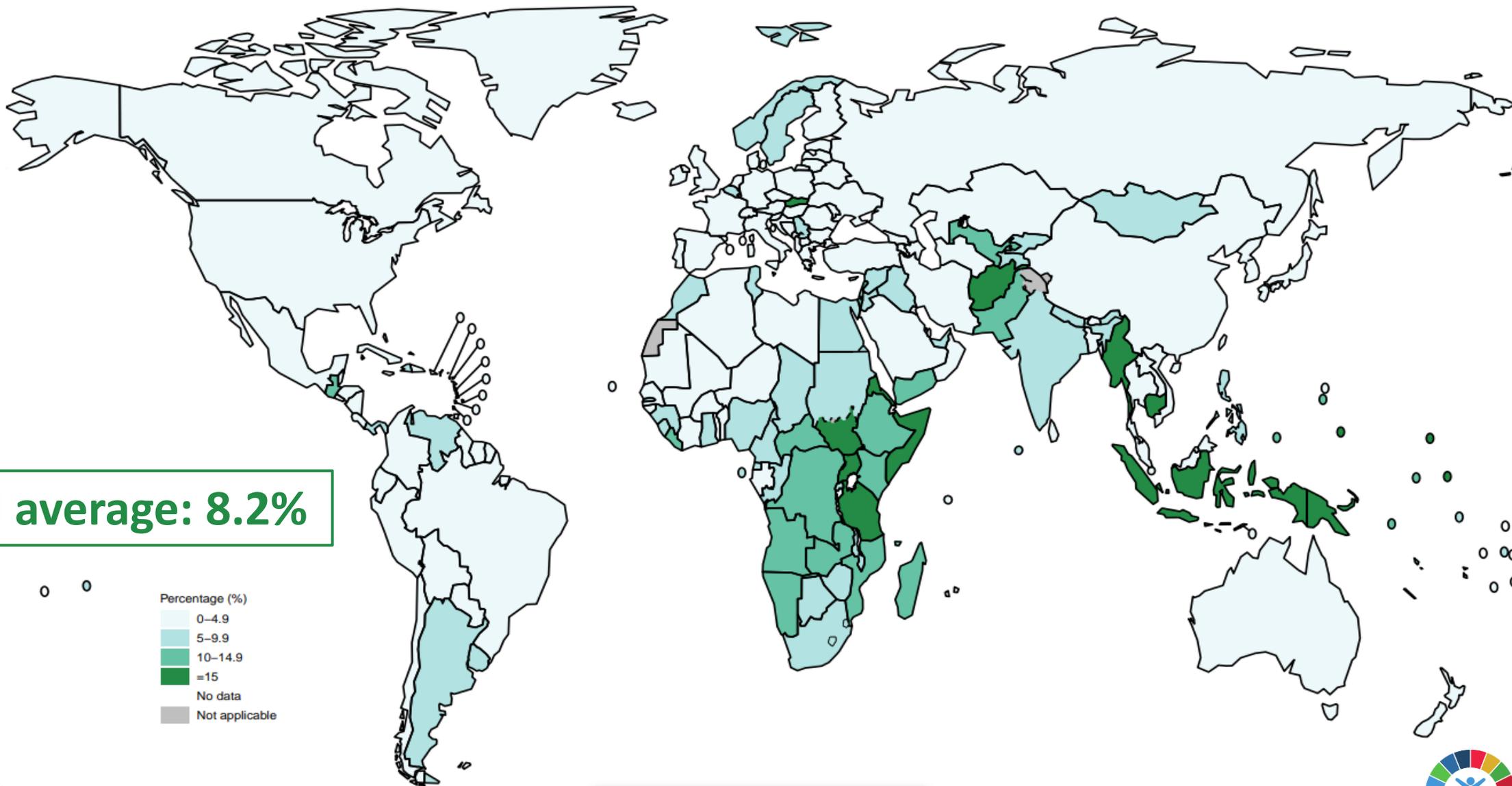
31 000 (14%) TB deaths in the 0–14 year age group were among children living with HIV

Trends in global TB notifications <15 years

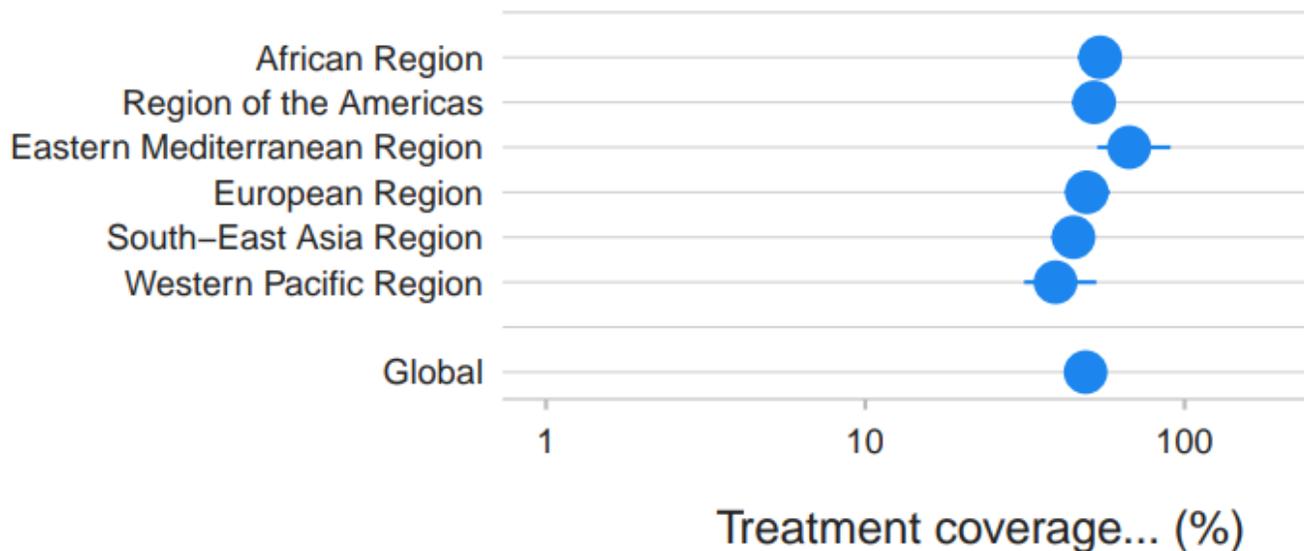
Trends in case detection in children and young adolescents (<15y), 2013-2022



% of people with a new / relapse episode of TB <15 years, 2022

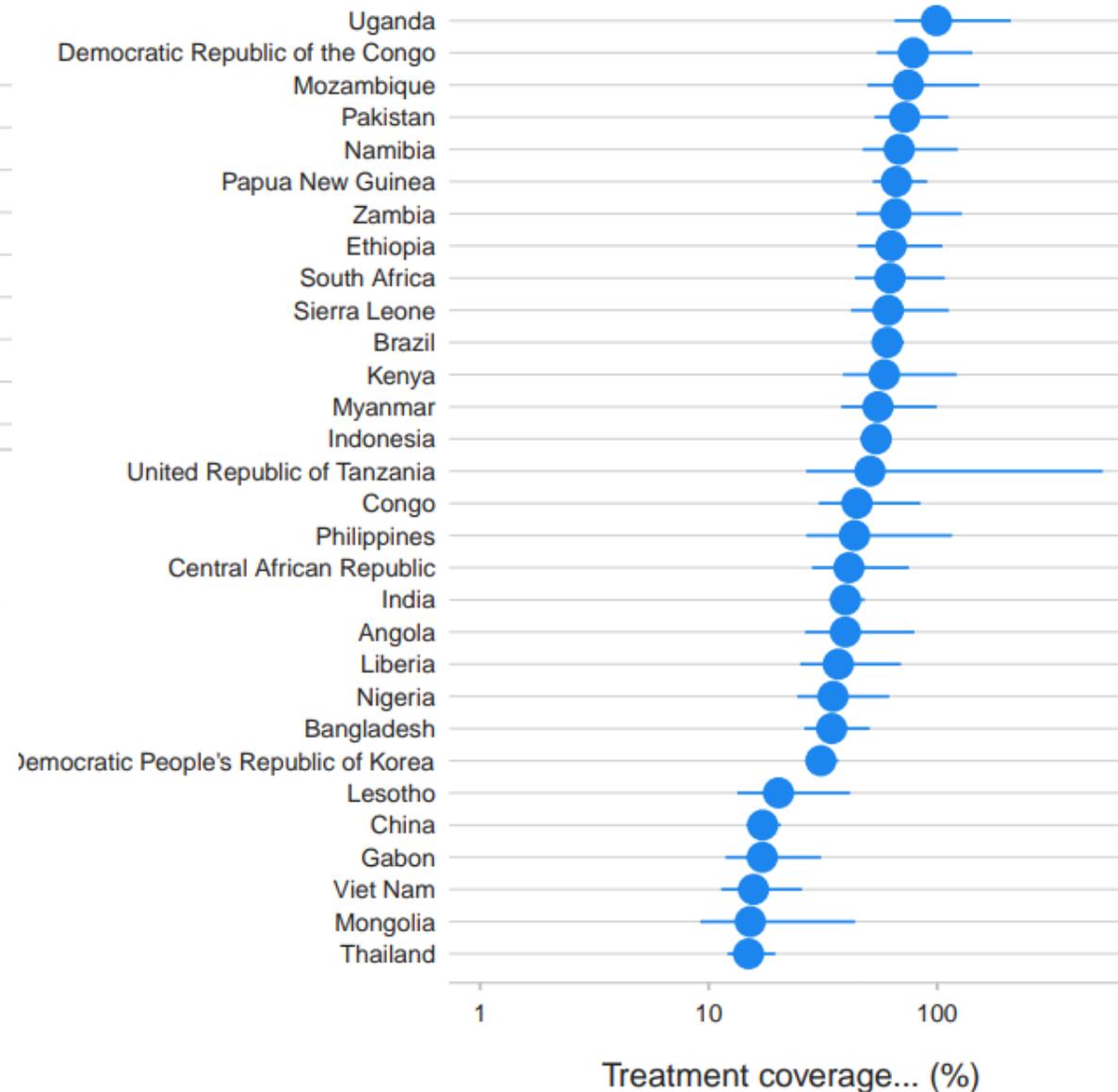


TB treatment coverage in <15 years



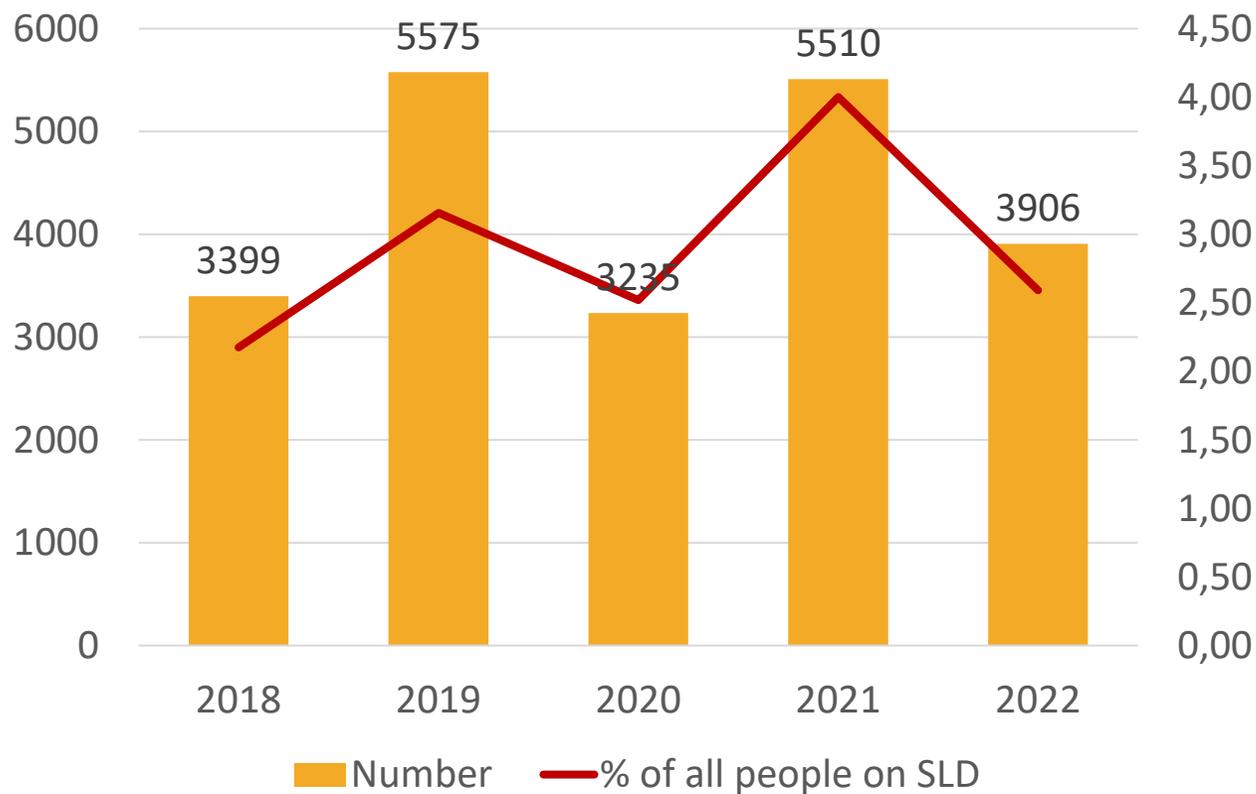
Global average: 49%

People aged 0–14 years

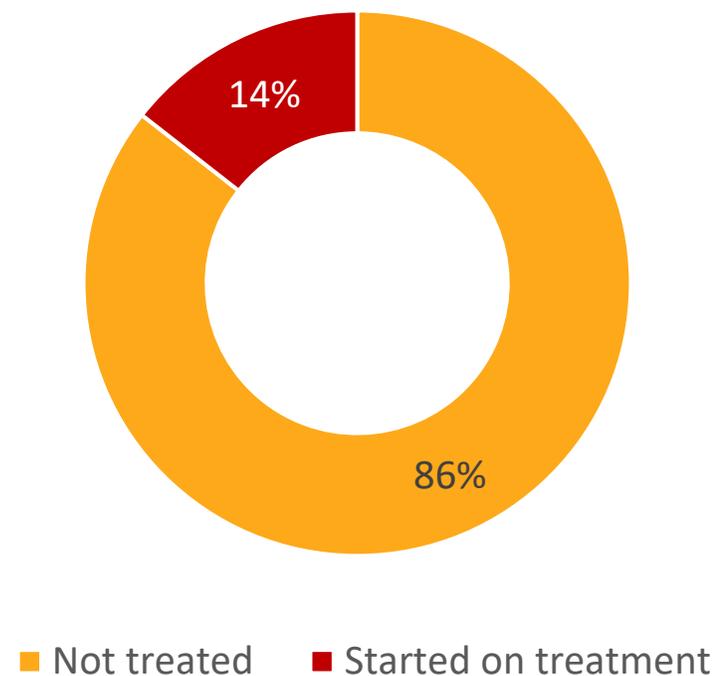


Treatment initiation in children with MDR/RR-TB

Second-line treatment initiation in <15 year olds, 2018-2022

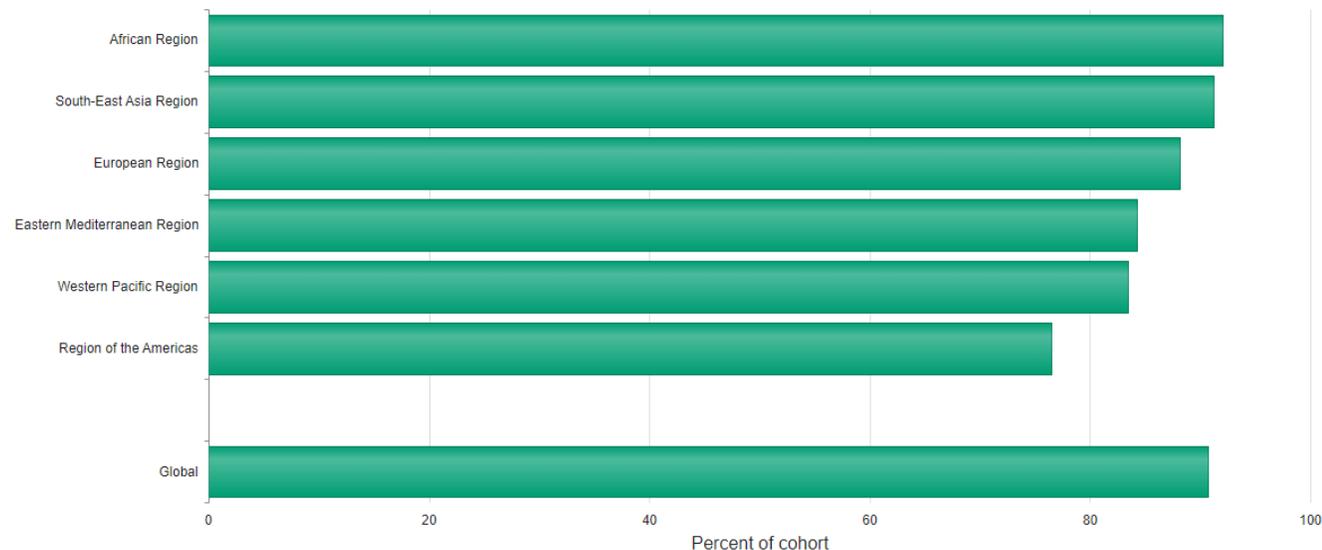
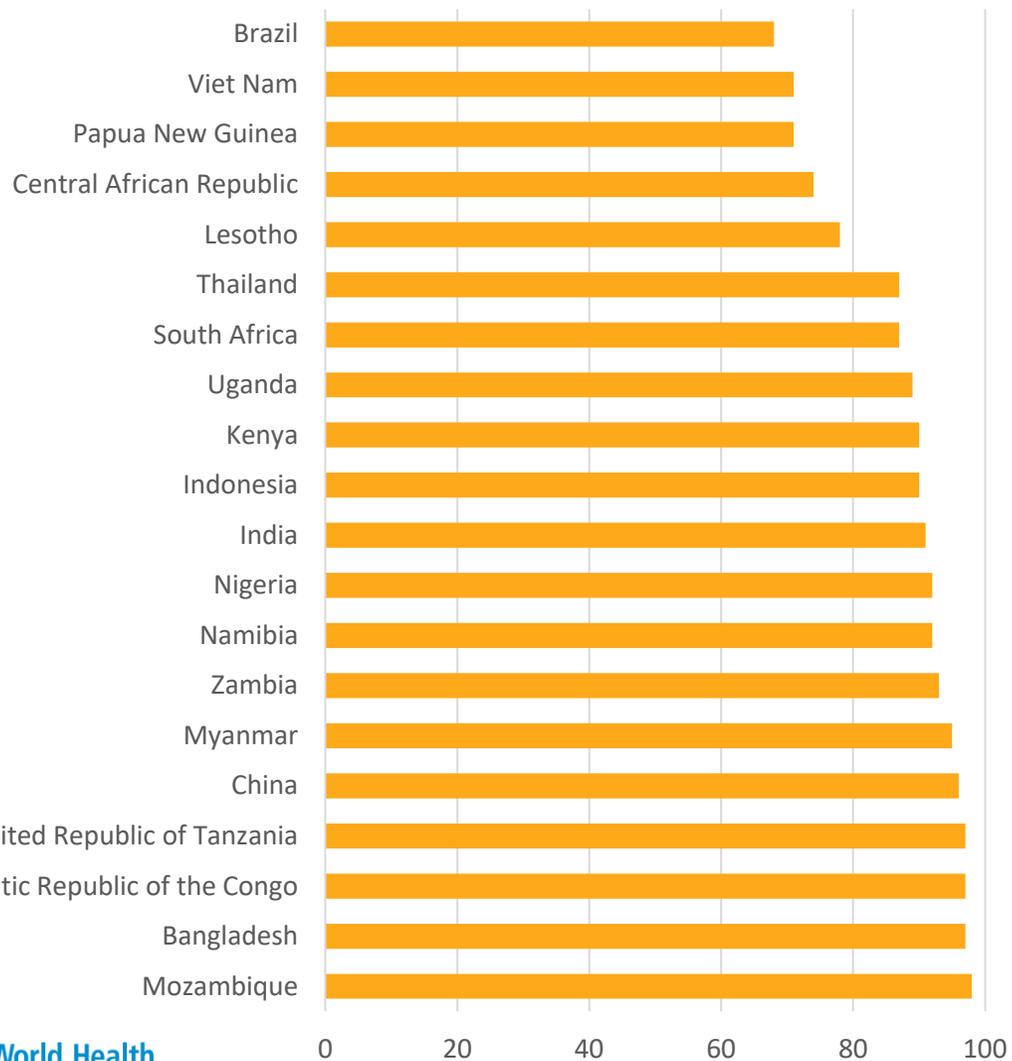


Treatment coverage: MDR/RR-TB in children and young adolescents, average for 2018-2022 (out of an estimated 30 000 per year)



Treatment success rates <15 years

Treatment success rate (%), 0-14y, 20 TB HBCs, 2021 cohort,
N=283 392

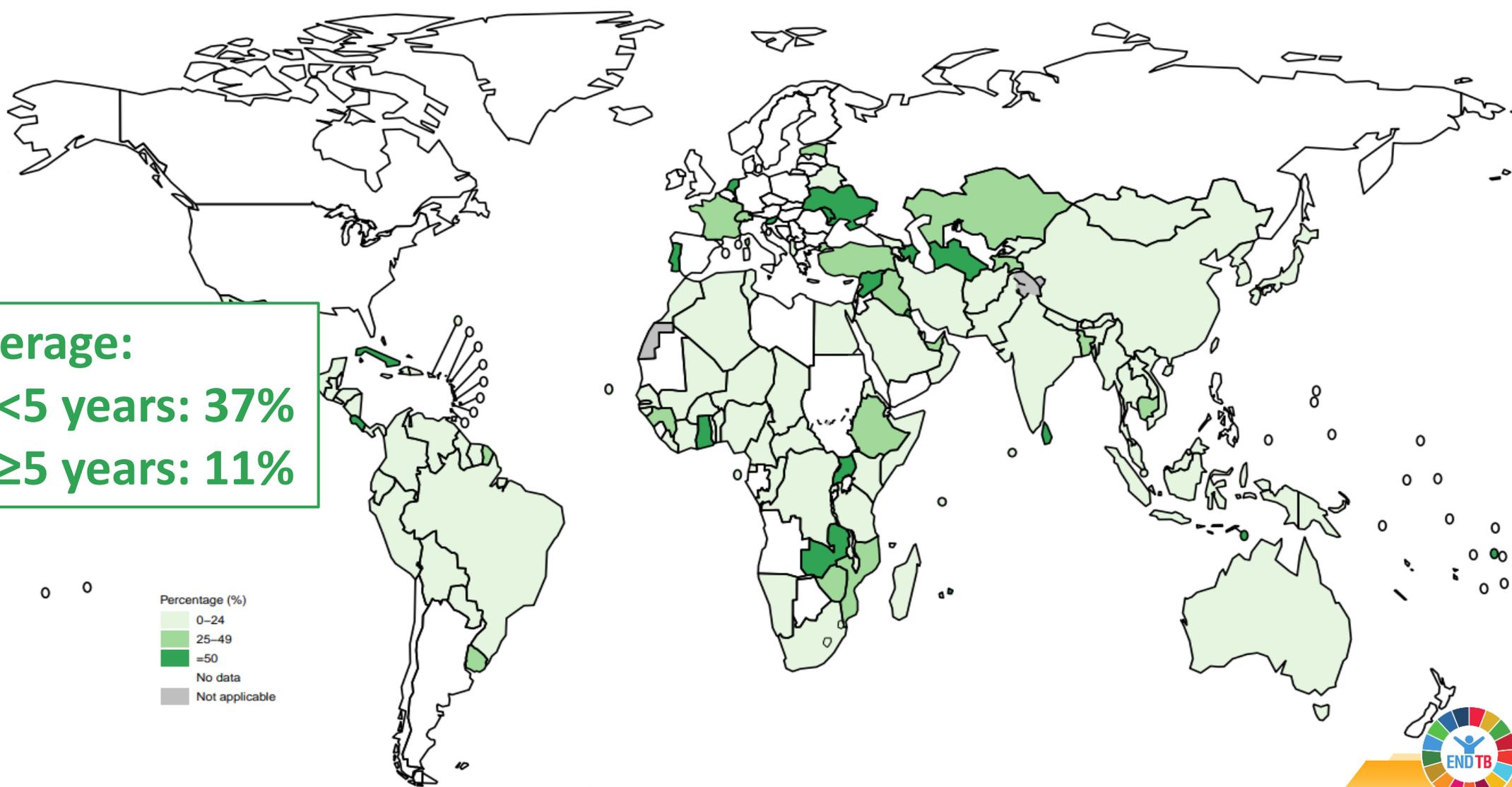


^a Data were reported by 136 countries on outcomes for 309 535 children aged 0-14 years, equivalent to 70% of the 443 648 cases among children aged 0-14 years that were notified in 2021.

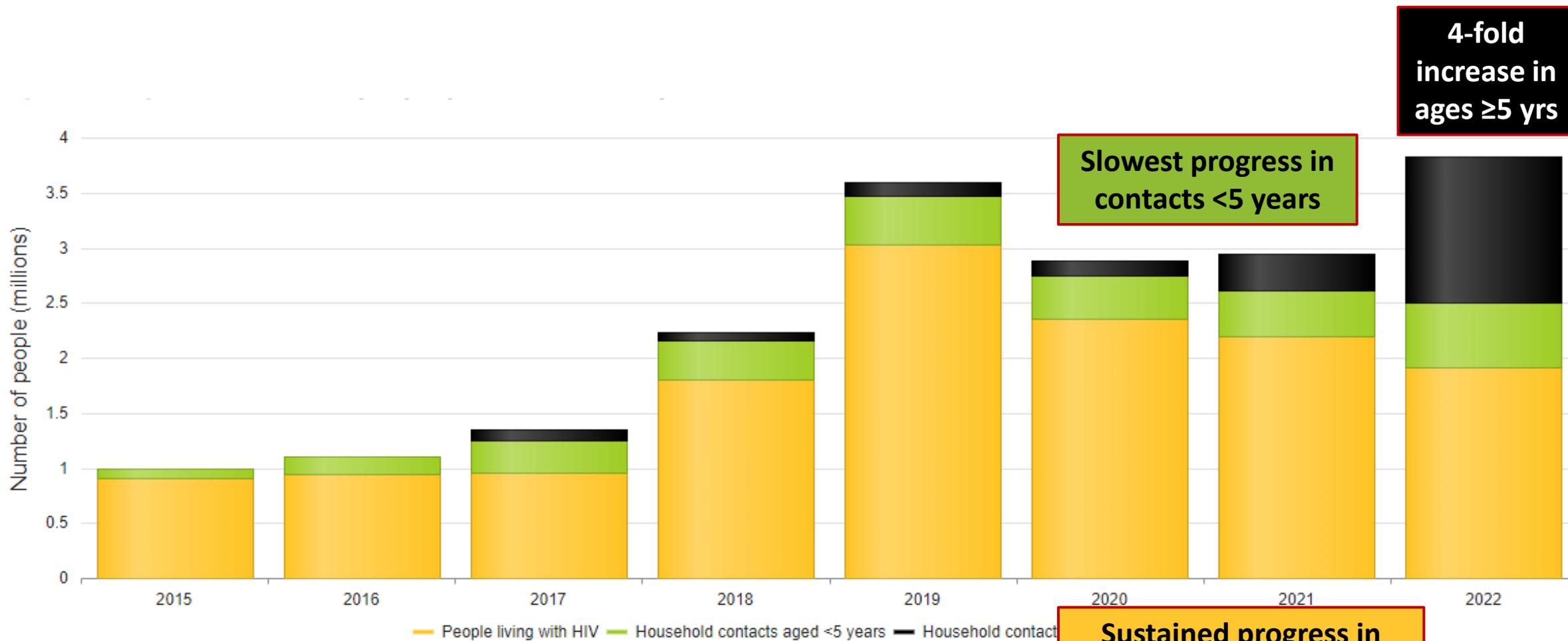
Global average: 91%

% of household contacts (all ages) provided with TPT, 2022

Global average:
Contacts <5 years: 37%
Contacts ≥5 years: 11%



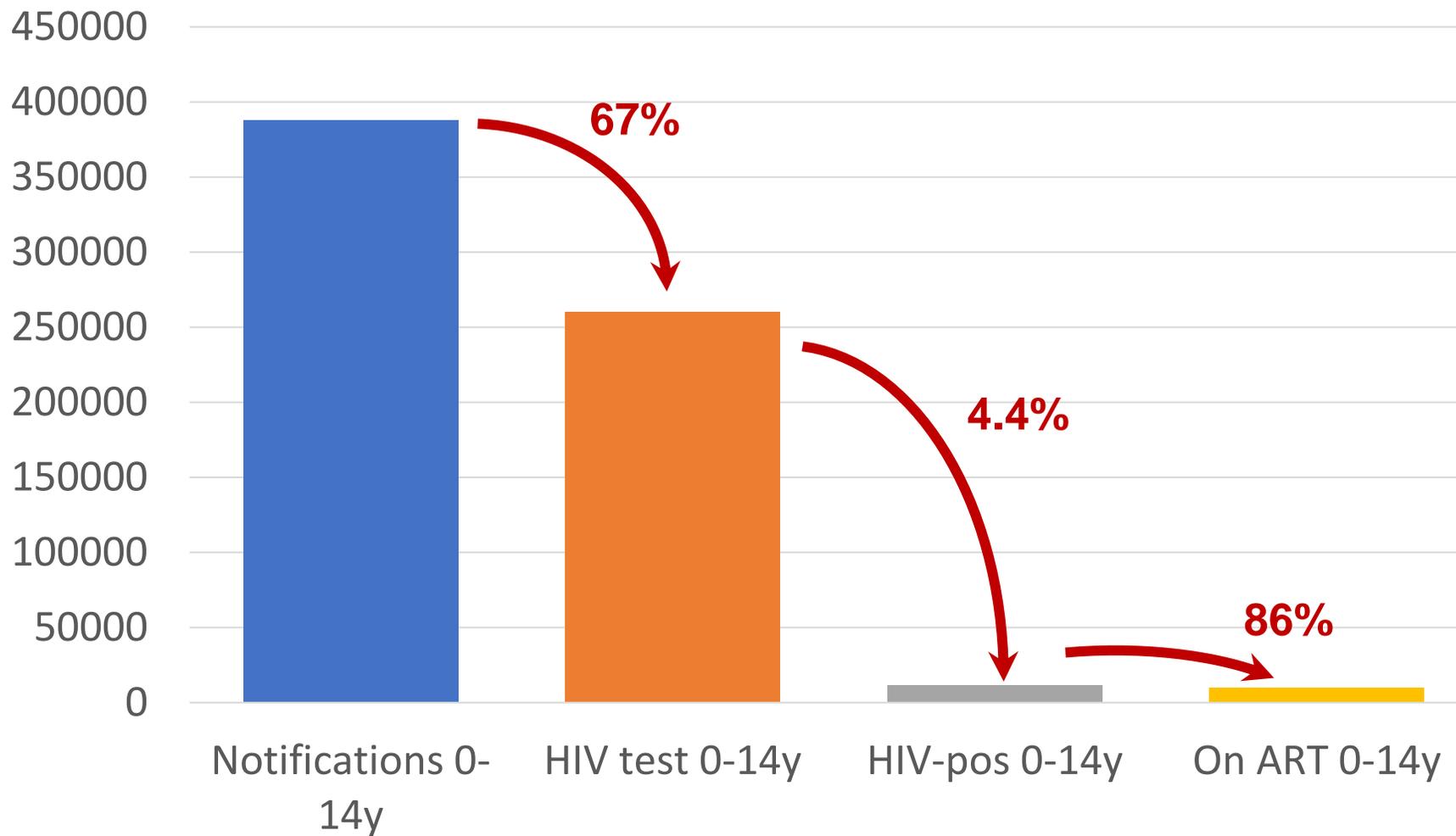
Number of people provided with TPT, 2015-2022



Sustained progress in PLHIV, but no age-disaggregated data

TB/HIV co-infection

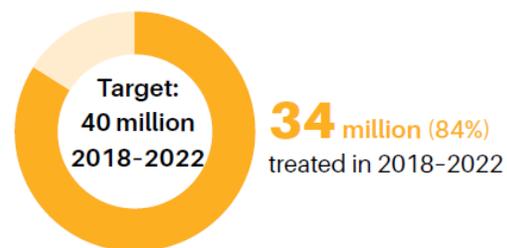
TB/HIV care cascade 0-14y in 20 TB/HIV HBCs



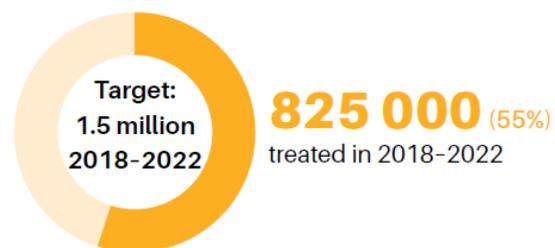
Progress against UNGA HLM targets, 2018-2022

Treatment for DS- and DR-TB

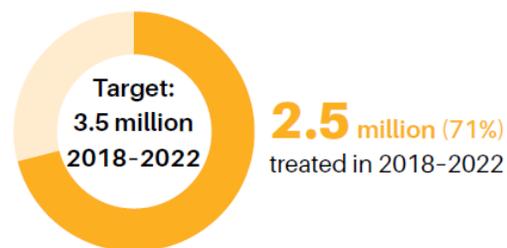
TB treatment (all ages)



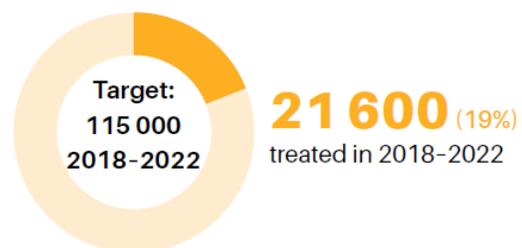
MDR/RR-TB treatment (all ages)



TB treatment (children)

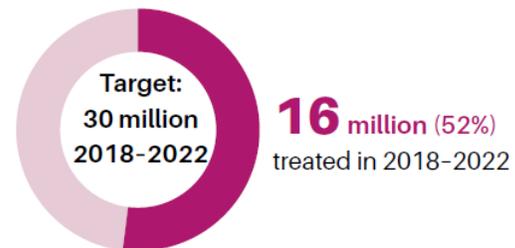


MDR/RR-TB treatment (children)

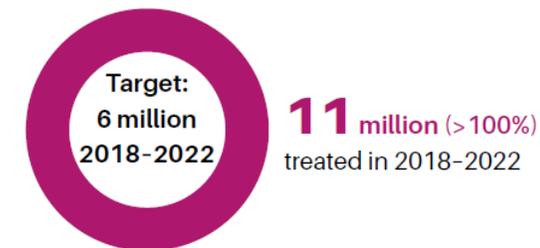


TB Preventive Treatment

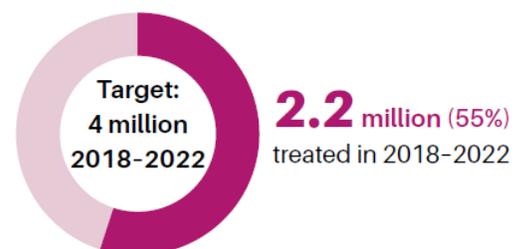
All ages



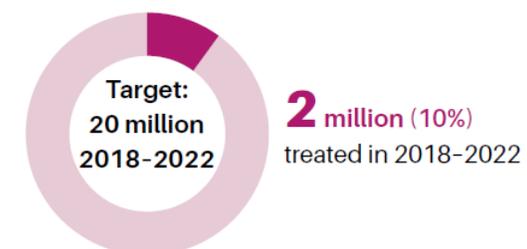
People living with HIV



Household contacts aged <5 years

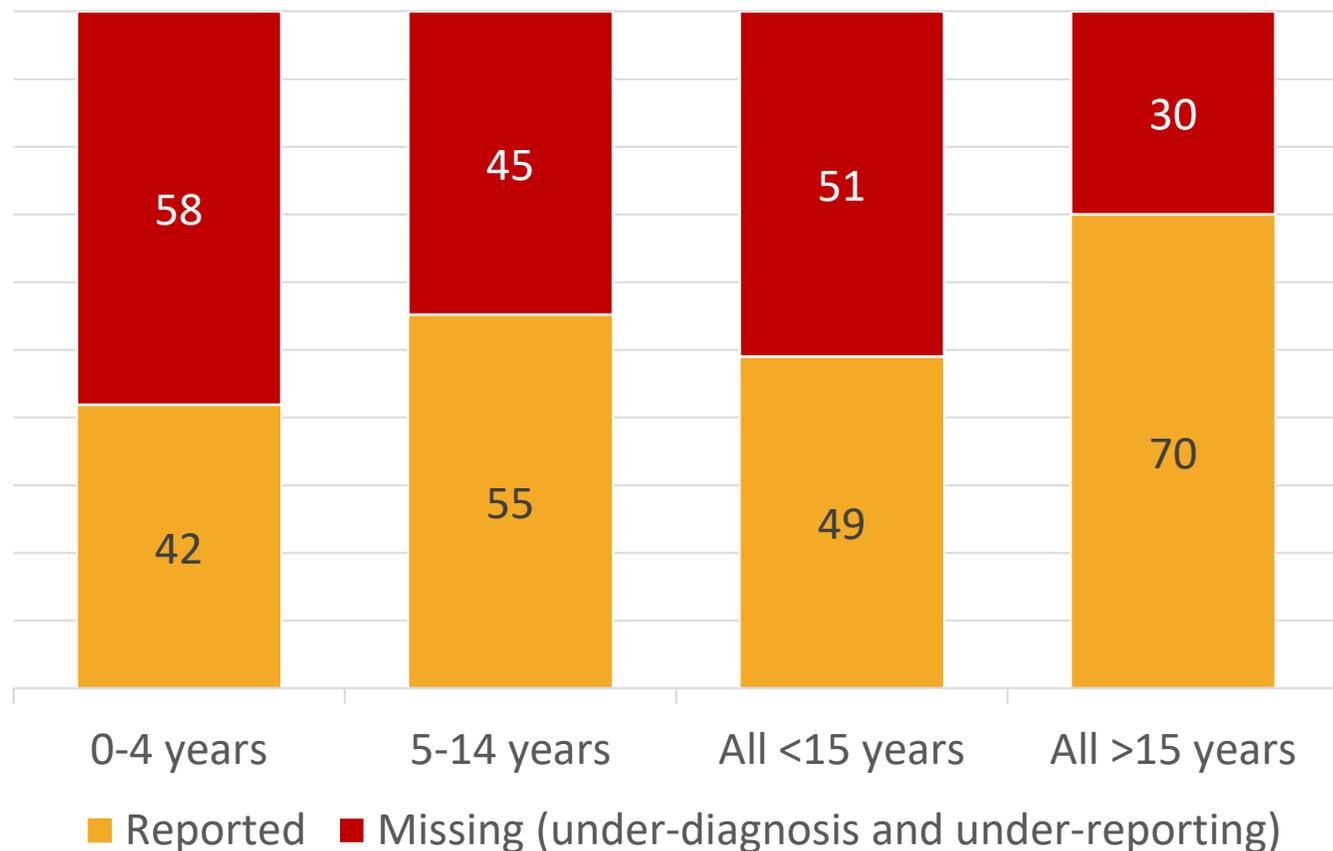


Household contacts aged ≥5 years

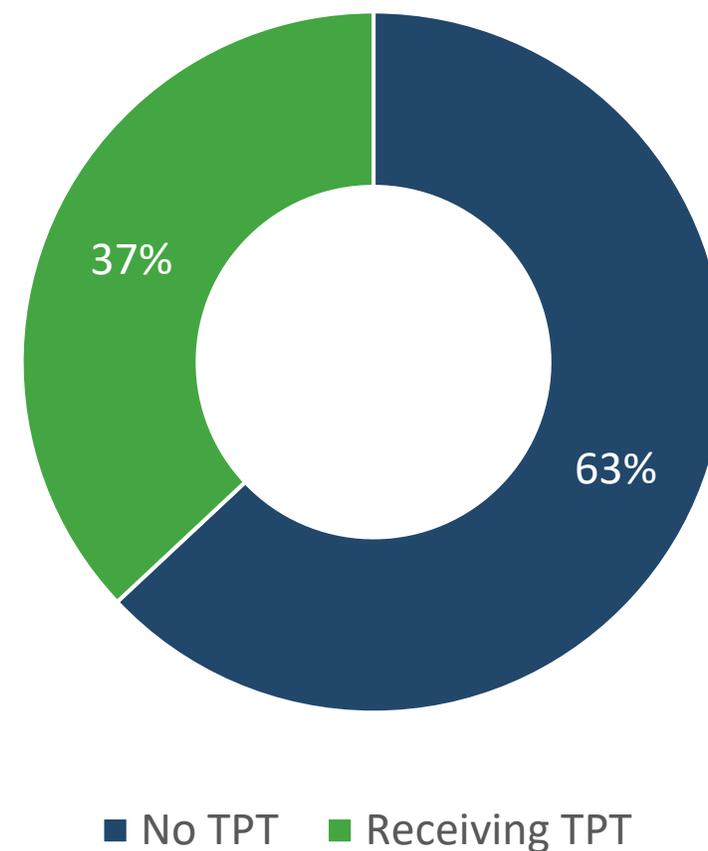


Remaining programmatic gaps

% of missing persons with TB in different age groups (2022)



Access to TPT in child contacts <5 years



Summary of data published in IJTLD Open



TB in children and adolescents

EDITORIAL

Global reporting on TB in children and adolescents: how far have we come and what remains to be done?

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In September 2023, the second United Nations High-Level Meeting on the Fight Against Tuberculosis (UN HLM) provided an important opportunity to reflect on progress towards ending TB in children and adolescents, based on the most recent data reported to the WHO.^{1,2} Following a 'Call to action for childhood TB' in 2011,³ the availability of surveillance data and estimates of the burden of TB disease in children has improved and expanded (Figure 1).



Figure 1. Global milestones in reporting on TB in children and adolescents, 2011–2022.

Preprint:

<https://theunion.org/news/global-reporting-on-tb-in-children-and-adolescents-how-far-have-we-come-and-what-remains-to-be-done>

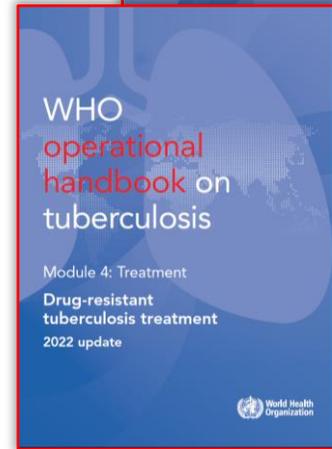
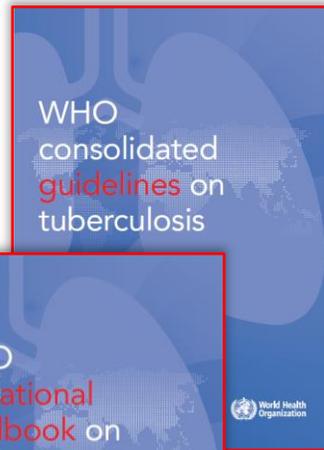


2023 HLM targets

Indicator	Global target
TB treatment coverage	90% by 2027 ~45 million people globally, including 4.5 million children and 1.5 million people with drug-resistant TB
TPT coverage	90% by 2027 ~45 million people globally, including 30 million household contacts, including children and 15 million people living with HIV
Coverage of health and social benefits package for people with TB	100% by 2027
Scale-up of comprehensive efforts to close gaps in care of children with or at risk of TB – equitable access to screening, prevention, testing and treatment services as part of comprehensive primary health care	

Updated WHO guidance

- Updates to Box 5.3 on eligibility criteria for the 4-month regimen for non-severe TB (Module 5 operational handbook)
- DR-TB guidelines and Operational Handbook, December 2022
 - BPaLM/BPaL for ages ≥ 14 years
 - Linezolid variation for 9-month oral regimen
 - Children with clinical diagnosis eligible for the 9-month regimen
 - Updated dosing table covering 3kg->70kg in DR-TB operational handbook
- Upcoming Guideline Development Group on TPT
 - Data from TB-CHAMP and V-Quin (DR-TB TPT)
 - Separate advisory group on dosing, including for 3HP < 2 years



<https://iris.who.int/bitstream/handle/10665/370100/9789240074286-eng.pdf?sequence=1>

<https://iris.who.int/bitstream/handle/10665/370099/9789240074309-eng.pdf?sequence=1>



TB is a preventable and curable disease, yet it is a common cause of sickness and death in children and adolescents. Every year, more than 1 million children and young adolescents fall ill with TB. Young children are at increased risk of severe disease and death; adolescents are at increased risk of disease that can be readily transmitted. Important gaps remain in finding children and adolescents with TB and in providing TB treatment and TB preventive treatment (TPT) to children and adolescents.

This e-course gives practical guidance on key elements of the management of TB in children and adolescents. The role of health care workers in preventing, identifying and managing TB in children and adolescents is critical.

-  Coming soon
-  Language: English
-  Intermediate (Intermediaire), Tuberculosis

Enter course

Un-enroll

**BIG thanks
to the Union
team!**

<https://openwho.org/courses/TB-child-adolescent-EN>
Register first on openwho.org before enrolling for the course

A second course for a **programmatic audience** is in preparation

Work on TB and pregnancy

- WHO co-convened meeting: *A primer on TB and pregnancy: laying the groundwork for consensus with SMART4TB and the IMPAACT network* (Washington DC, October 2023)
 - Start of a process towards consensus on earlier and optimal inclusion of pregnant women in TB drug and vaccine research
- Inclusion of detail on maternal and infant TB in the 2023 Roadmap
 - *“effectively addressing TB in infants and young children cannot be separated from effectively addressing maternal TB”*



<https://apps.who.int/iris/bitstream/handle/10665/365953/9789240057562-eng.pdf>

Box 6

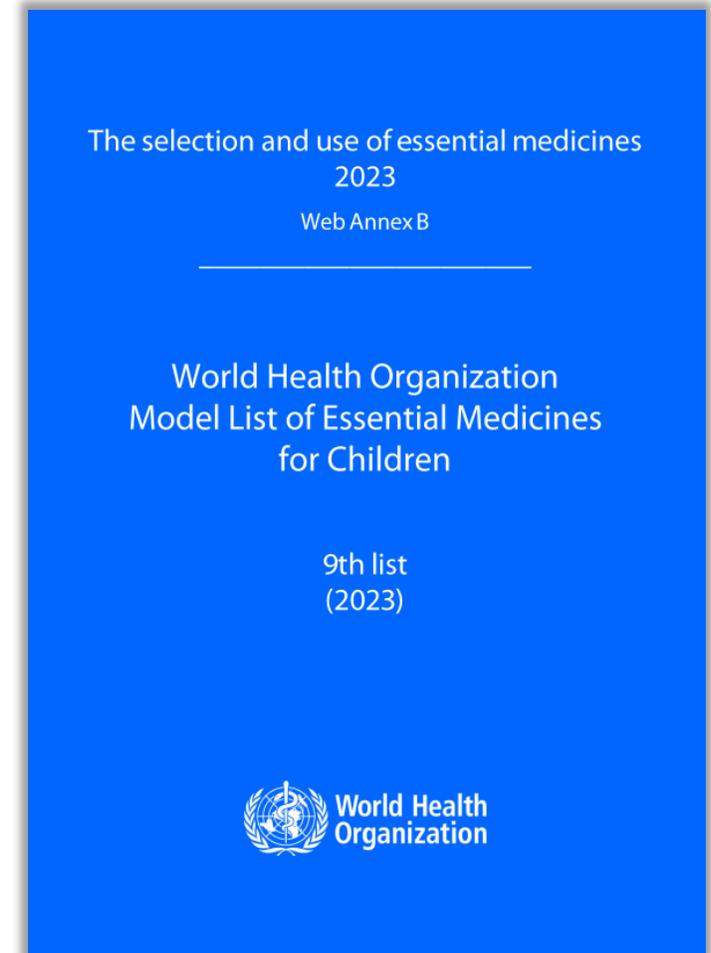
TB in pregnant and post-partum women and their infants

Pregnant and post-partum women are at increased risk of developing TB, with associated risks of maternal hospitalization, death and adverse pregnancy outcomes including eclampsia and miscarriage. Maternal TB increases the risk of premature birth, vertical transmission of HIV, and morbidity and mortality of both the infant and others in the household. Effective TB prevention and timely TB diagnosis and treatment in pregnant and post-partum women are essential to improving outcomes. Given that pregnant women are seldom eligible for inclusion in clinical trials, delays in safety evaluation and dose optimization of TB drugs in this population has resulted in longer, less efficacious, and more toxic regimens particularly for the treatment of DR-TB.



Updated WHO Essential Medicines List for children

- **Bedaquiline and delamanid** listed without age restriction
- **Ethionamide** also listed in core list (to reflect role in DS-TBM)
- Removal of **oral liquid formulations of E, INH, Z** (dispersible tablets now available and are the preferred option)
- Removal of a **powder for oral liquid for linezolid** (dispersible tablets now available and are preferred option)



PAediatric Drug Optimization of TB (PADO-TB)

Objective: To identify TB medicines and formulations to be prioritized for research and development for the prevention and treatment of TB in children

Enable alignment between researchers, funders, procurers, market coordination entities, innovators, generic manufacturers, product development partnerships and regulators

Ensure that the unique needs of children are considered and effectively addressed upfront

PAediatric Drug Optimization of TB

PADO-TB2
3-5 October 2023

PADO PRIORITY LIST (short-term priorities)

Rifapentine 150 mg scored dt	Development ongoing An FDC for TPT was not considered a priority for development at the moment
Rifampicin 100 mg scored dt	Addition on a note on monitoring the longer-term need/feasibility of an FDC
Pretomanid	Flag that it remains a priority for development for children even though development timeline is on the longer term
Moxifloxacin, 100 mg dt	Palatability needs improvement (ongoing)

PADO WATCH LIST (longer-term priorities)

All compounds in Phase IIa/b as of October 2023	Special flag tbc for compounds that are more advanced for development, ie: delpazolid, sutezolid, GSK-656, OPC-167832, BTZ-043, TBI-223
Long acting	New technologies
Oral film rifapentine	New technologies

Technical Advisory Group on dosing

- Aims to complement work done by WHO Guideline Development Groups (WHO recommendations) **to inform dosing updates in WHO Operational Handbooks in a transparent, evidence-based, structured manner**
- 20 experts from geographically diverse settings and relevant technical expertise: clinical pharmacology, pharmacometrics, clinical research, programmatic management, civil society
- Standing group – members appointed for 3 years (and eligible for reappointment)



First TAG meeting
Jan/Feb 2024 to review new evidence on dosing of TB
Preventive Treatment regimens



Acknowledgements

Tereza Kasaeva, Farai Mavhunga, Katherine Floyd & other colleagues from WHO GTB

Core team members of the child and adolescent TB working group

All members of the child and adolescent TB working group

Thank you for your attention!