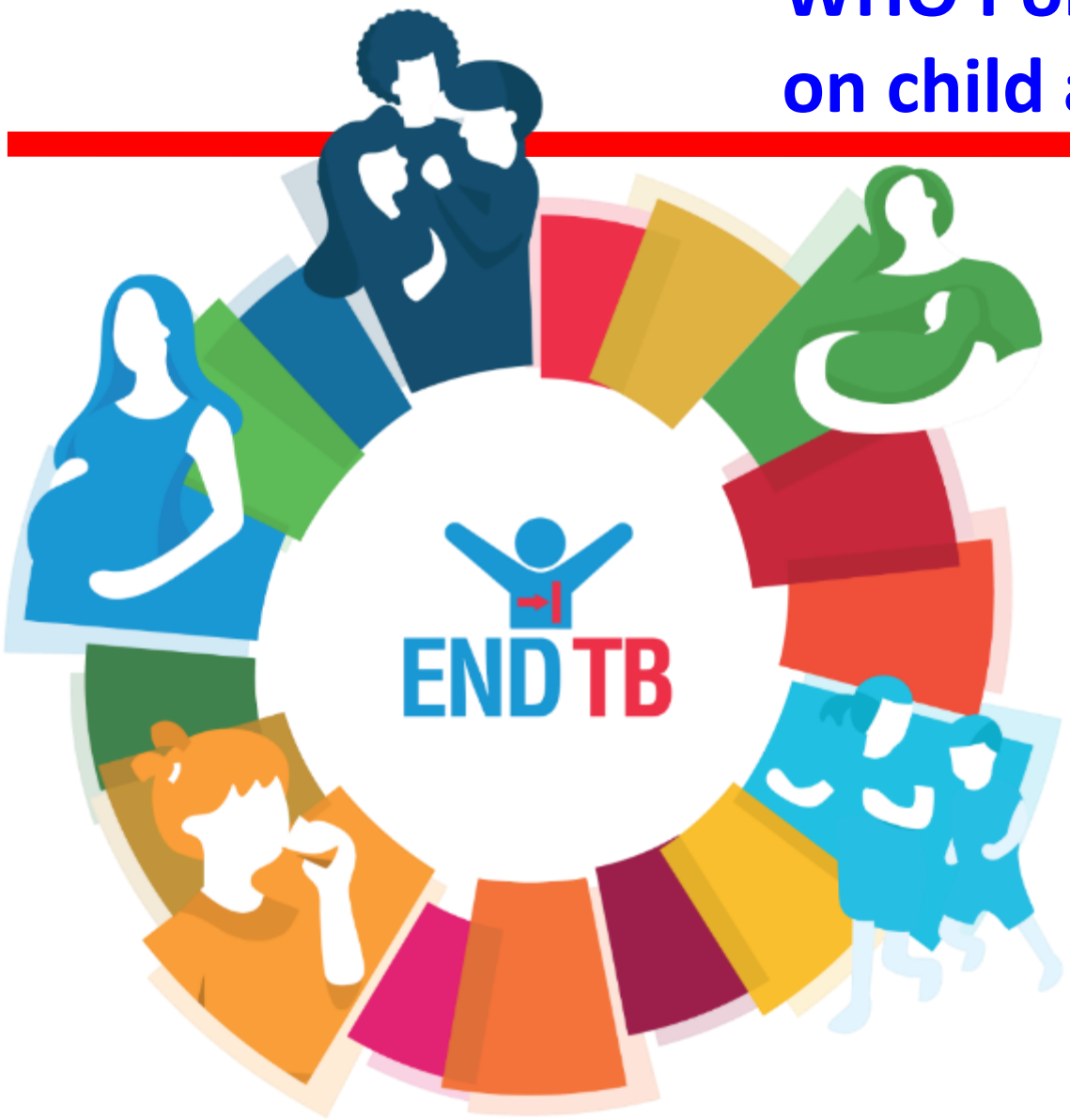
WHO Policy Updates on child and adolescent TB



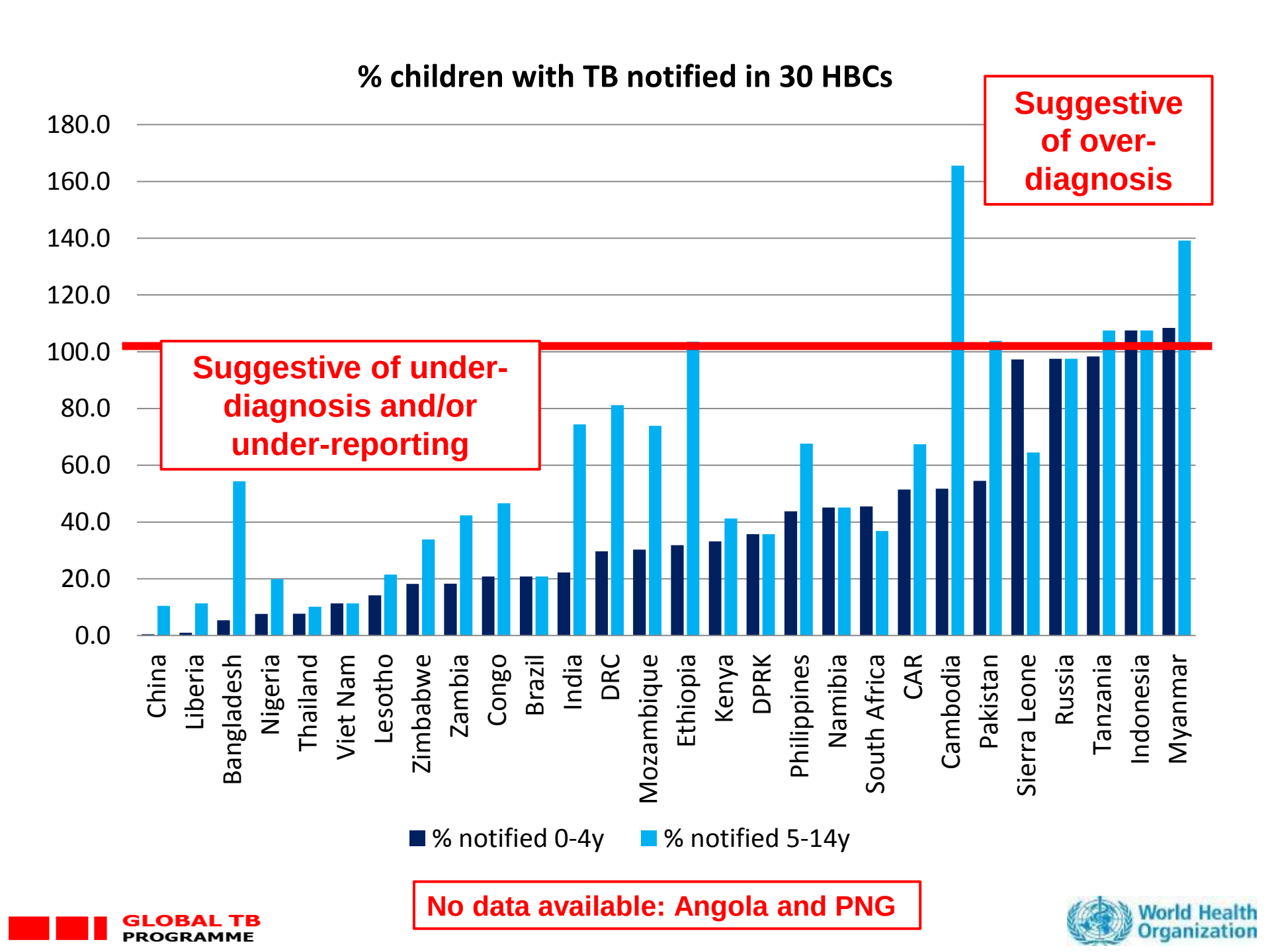
Annual meeting of the Child and Adolescent TB working group

The Hague, The Netherlands,
24 October 2018

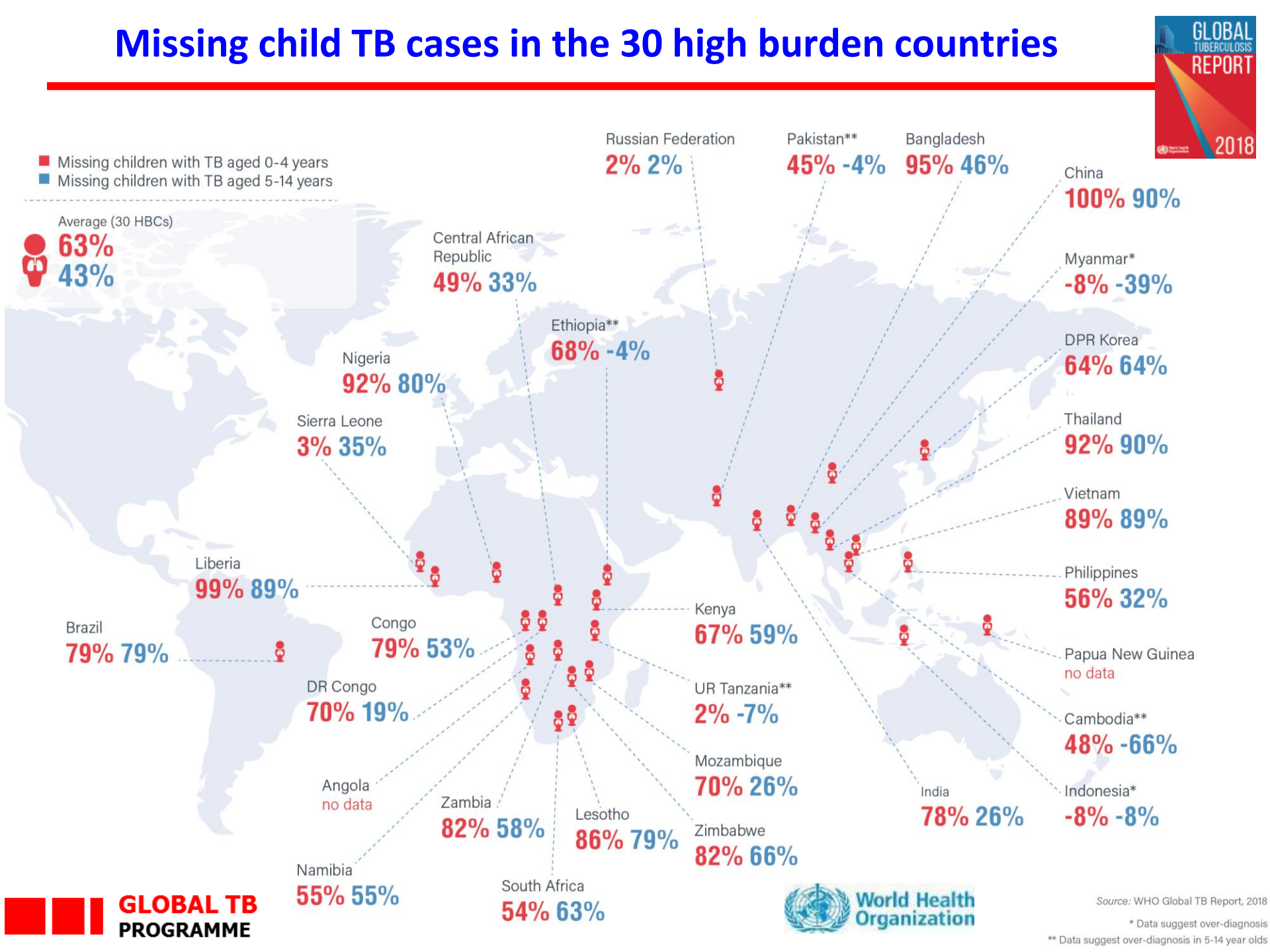
Malgosia Grzemska
Global TB Programme
WHO/HQ

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
180.0
160.0
140.0
120.0
100.0
80.0
60.0
40.0
20.0
0.0
China
Liberia
Bangladesh
Nigeria
Thailand
Viet Nam
Lesotho
Zimbabwe
Zambia
Congo
Brazil
India
DRC
Mozambique
Ethiopia
Kenya
DPRK
Philippines
Namibia
South Africa
CAR
Cambodia
Pakistan
Sierra Leone
Russia
Tanzania
Indonesia
Myanmar
% notified 0-4y
% notified 5-14y
No data available: Angola and PNG
GLOBAL TB PROGRAMME
World Health Organization

Missing child TB cases in the 30 high burden countries



GLOBAL TB PROGRAMME

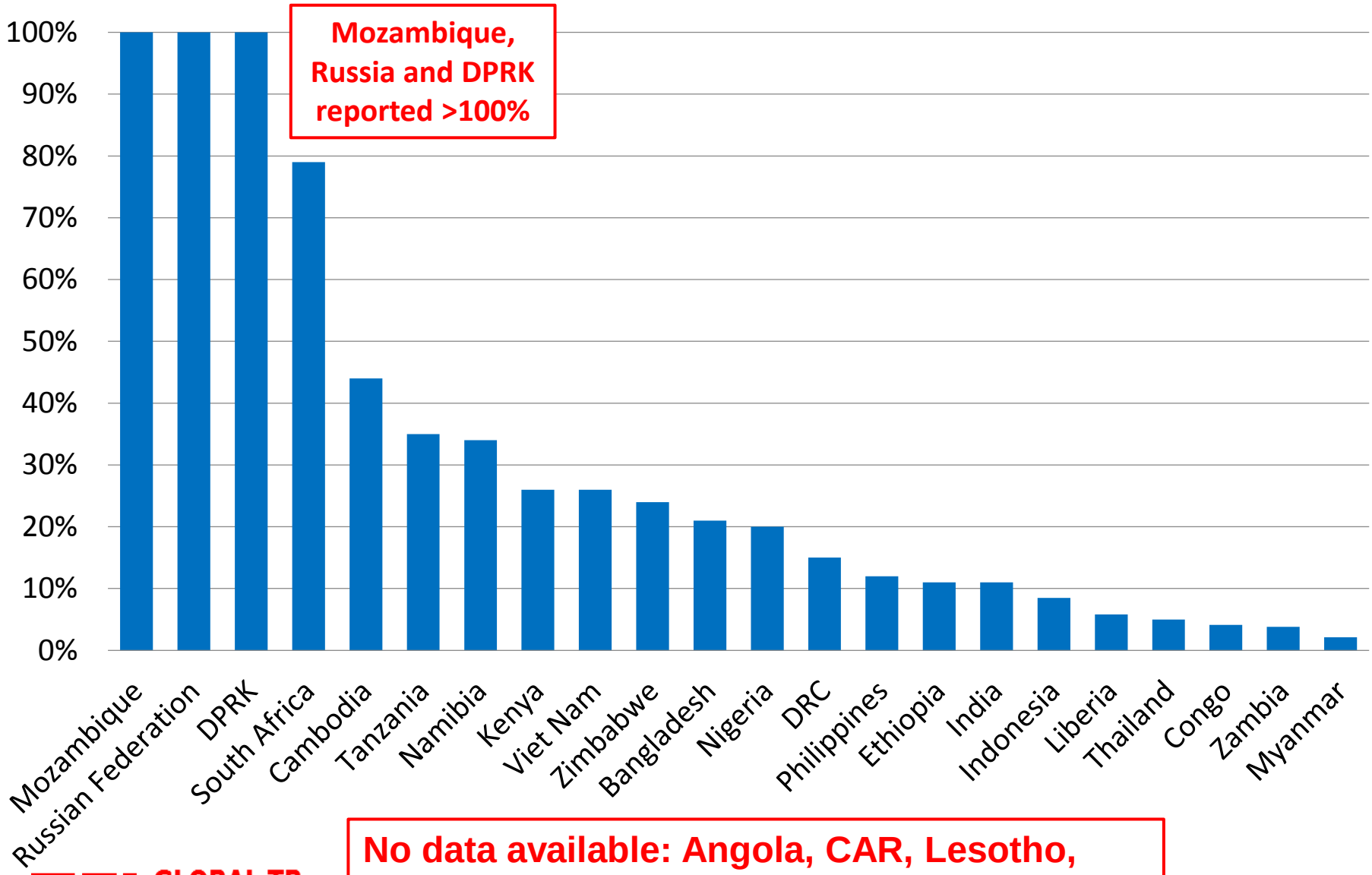
World Health Organization

Source: WHO Global TB Report, 2018

* Data suggest over-diagnosis

** Data suggest over-diagnosis in 5-14 year olds

% eligible children <5y on preventive treatment (2017)



No data available: Angola, CAR, Lesotho, Sierra Leone, Brazil, Pakistan, China, PNG

GLOBAL TB PROGRAMME

World Health Organization

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

HIGH-LEVEL MEETING ON THE FIGHT TO END TUBERCULOSIS
26 SEPTEMBER 2018, UNHQ, NEW YORK

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

Roadmap towards ending TB in children and adolescents

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

World Health Organization

Roadmap is aligned with targets of the political declaration of the UN HLM on TB adopted by UNGA

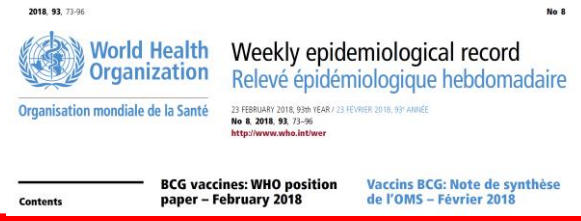
Ending the epidemic of tuberculosis by 2030 requires **Universal Health Coverage, leaving no one behind,** but **also action beyond the health sector** to address the risk factors and determinants of disease. The political declaration of the **UN HLM on TB provides** a major opportunity to galvanize 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).

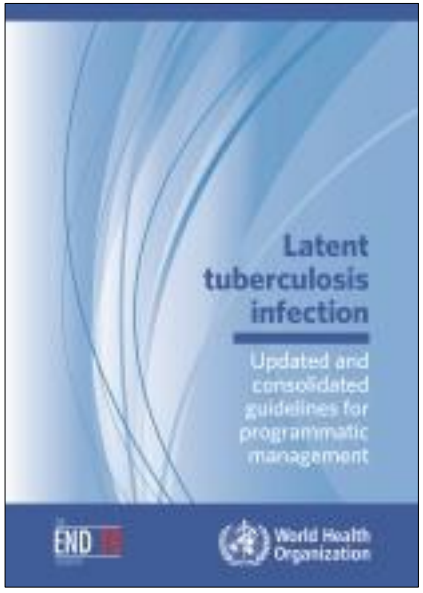
Quick update on TB prevention: WHO position paper on BCG (Feb 2018)



- 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**.

Quick update of TB prevention: WHO LTBI guidance

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

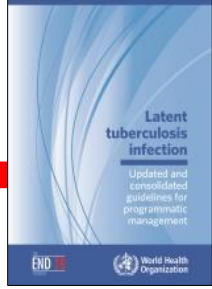


- **Expanding the number of groups prioritized for LTBI testing and treatment** – apart from all living with HIV and under 5 years, additional high risk groups are:
  - HIV-negative children ≥ 5 years, adolescents and adults who are contacts of TB patients
  - Contacts of patients with MDR-TB

- **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

Stop TB Partnership
GLOBAL DRUG FACILITY

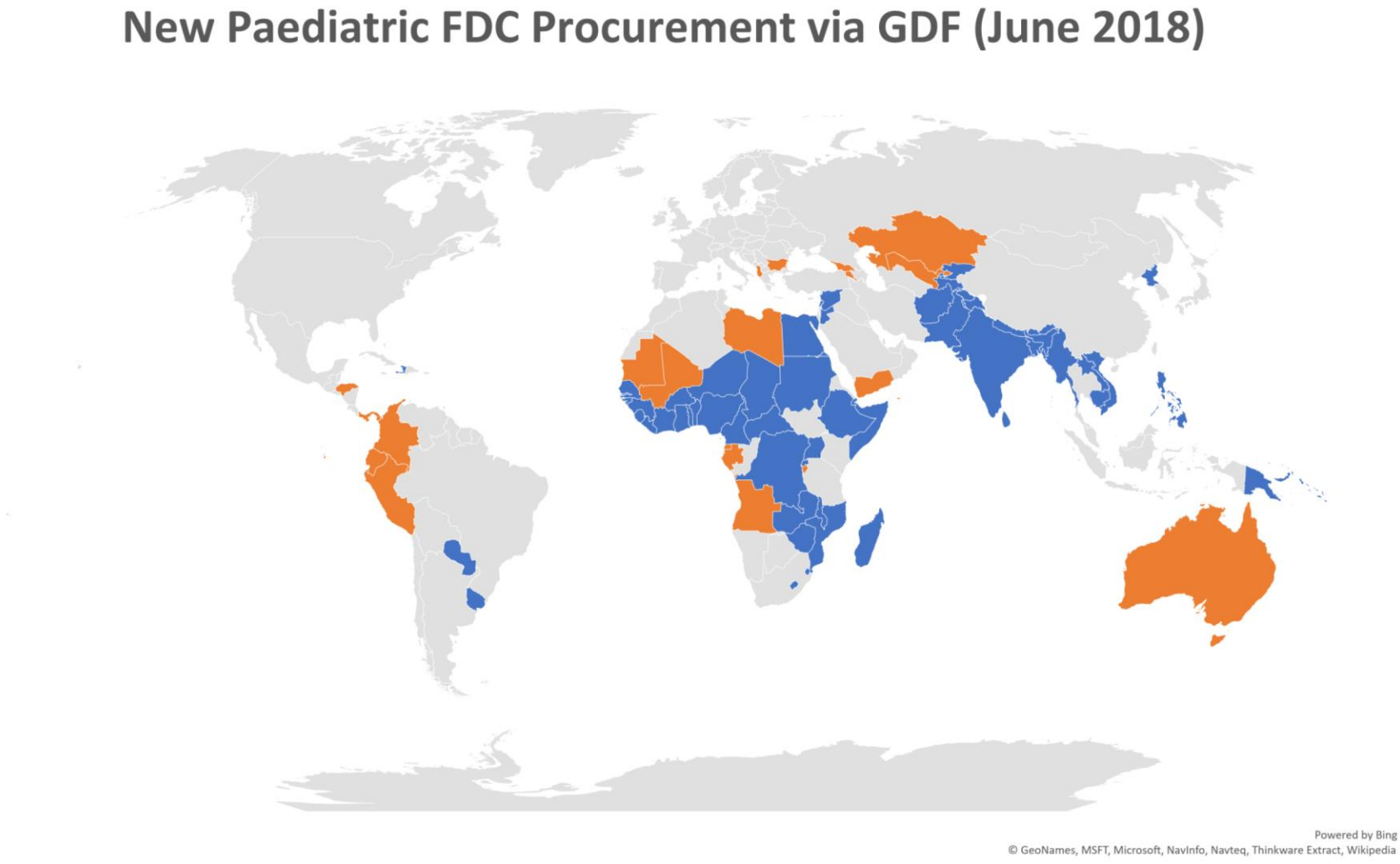
85 Countries have ordered ~789,000 treatment courses* of new pediatric FDCs

- 77 countries have had new pedi FDCs delivered (~464,000 treatments); 8 new countries currently ordering for 1st time

Afghanistan
Albania
Angola
Armenia
Australia
Bangladesh
Benin
Bhutan
Bulgaria
Burkina Faso
Burundi
Cambodia
Cameroon
Central African Republic
Chad
China
Colombia
Comoros
Congo
Cote d'Ivoire
Democratic People's Republic of Korea
Democratic Republic of the Congo
Democratic Republic of Timor-Leste
Djibouti
Ecuador
Egypt
Equatorial Guinea
Ethiopia
Gabon
Gambia
Georgia
Ghana
Guinea
Guinea-Bissau
Haiti
Honduras
India
Jordan
Kazakhstan
Kiribati
Kyrgyzstan
Lao People's Democratic Republic
Lebanon
Lesotho
Liberia
Libyan Arab Jamahiriya
Madagascar
Malawi
Maldives
Mali
Marshall Islands
Mauritania
Mozambique
Myanmar
Nepal
Niger
Nigeria
Pakistan
Panama
Papua New Guinea
Paraguay
Peru
Philippines
Rwanda
Samoa
Sao Tome and Principe
Senegal
Sierra Leone
Solomon Islands
Somalia
Sri Lanka
Sudan
Swaziland
Syrian Arab Republic
Tajikistan
Togo
Tuvalu
Uganda
United Republic of Tanzania
Uruguay
Uzbekistan
Viet Nam
Yemen
Zambia
Zimbabwe

**Treatment courses estimated for children in the third weight band [3 tablets daily] using procurement volumes of 3-FDC formulation*

Child-friendly fixed dose combination formulations



Update on diagnosis: important role of Xpert MTB/RIF in children

Meta-analysis of 15 studies, included 4768 respiratory samples from 3640 children.

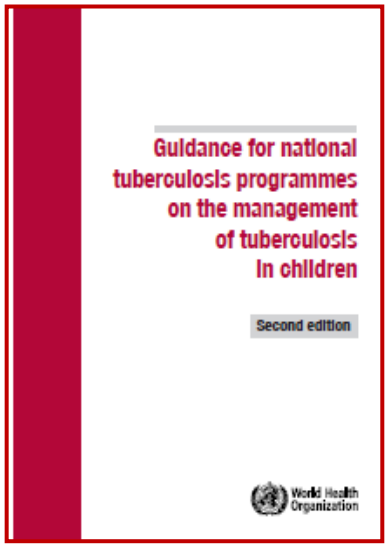
Detjen AK, et al. Lancet Resp Med 2015

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!

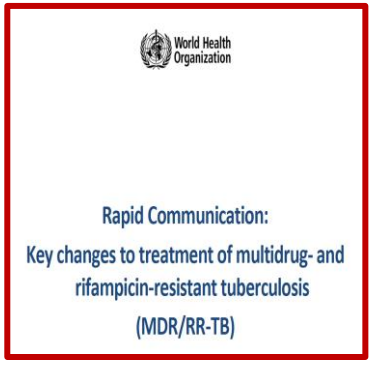
The next generation Xpert MTB/RIF ultra cartridge

- 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

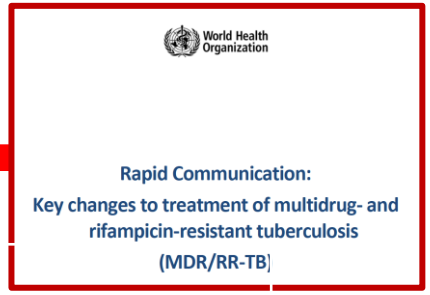
- Feasibility of effective and fully oral treatment regimens for most patients
- Need to ensure drug resistance is excluded before starting patients on treatment
- The need for close monitoring of patient safety and treatment response

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**

http://www.who.int/tb/publications/2018/rapid_communications_MDR/en/

Medicines recommended for use in longer MDR-TB regimens



GROUP	MEDICINE
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)***

http://www.who.int/tb/publications/2018/rapid_communications_MDR/en/

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

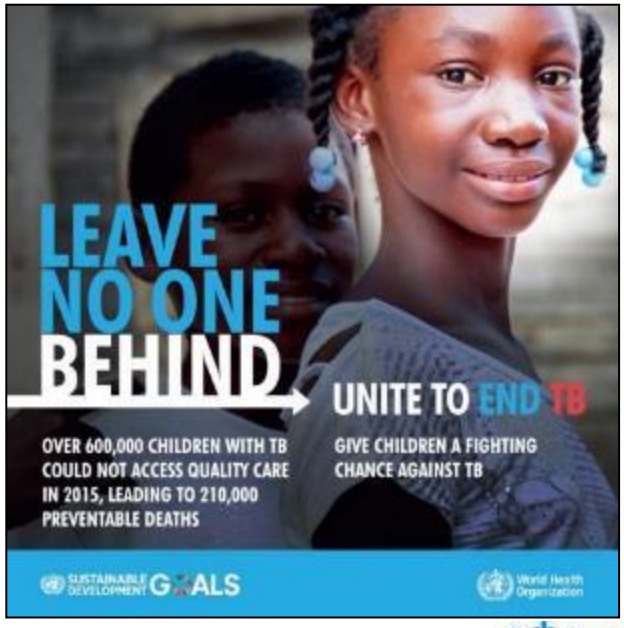
New DR-TB Formulations (Added to GDF Catalog May 2018)
Pyrazinamide 150 mg*
Ethionamide 125 mg*
Levofloxacin 100 mg*
Moxifloxacin 100 mg*
Cycloserine 125mg

New DS-TB Formulations (Added to GDF Catalog May 2018)
Ethambutol 100 mg*
Isoniazid 100 mg*

*dispersible tablet

Plans for 2019 - 21

- Dissemination and adaptation of Roadmap towards ending TB in children and adolescents – regional meetings in Africa and Asia
- Comprehensive Child and Adolescent TB Handbook with new policies and implementation guidance (2019)
- Updated WHO Guidance for National TB Programmes on the Management of TB in Children and Adolescents (2020-2021)



Thank you for your attention!

Acknowledgements

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