New products pipelines: TB

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Director
Global Tuberculosis Programme

World Health Organization

TB REMAINS ONE OF THE TOP

INFECTIOUS KILLERS IN THE WORLD

It is the leading cause of death of people with HIV and a major contributor of antimicrobial resistance related deaths

In 2022,

- **1.3 million** people died from TB
- **10.6 million** people fell ill with TB
- **Two in five people with drug-resistant TB** did not access treatment

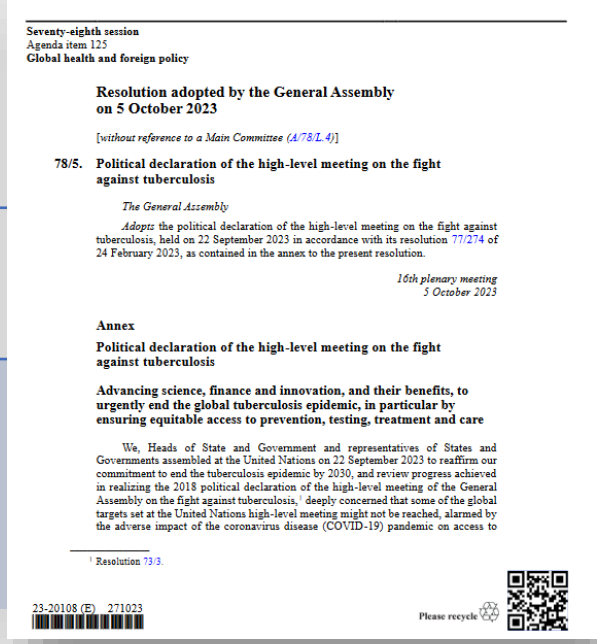
About a quarter of the global population is estimated to have been infected with TB bacteria

Global tuberculosis targets -2023 UNGA political declaration on TB






TB treatment coverage	**90% by 2027**
Coverage of TB preventive treatment for priority groups (household contacts of people with TB; people living with HIV)	**90% by 2027**
Coverage of rapid diagnostic testing for TB	**100% by 2027**
Coverage of health and social benefits package for people with TB	**100% by 2027**
Development and availability of new TB vaccines that are safe and effective	**Rollout initiated, preferably within 5 years**
Annual funding for universal access to quality prevention, diagnosis, treatment and care for TB	**US$ 22 billion by 2027, US$ 35 billion by 2030**
Annual funding for TB research	**US$ 5 billion by 2027**



Seventy-eighth session
Agenda item 125
Global health and foreign policy

Resolution adopted by the General Assembly on 5 October 2023

[*without reference to a Main Committee (A/78/L.4)*]

78/5. Political declaration of the high-level meeting on the fight against tuberculosis

The General Assembly

Adopts the political declaration of the high-level meeting on the fight against tuberculosis, held on 22 September 2023 in accordance with its resolution 77/274 of 24 February 2023, as contained in the annex to the present resolution.

16th plenary meeting
5 October 2023

Annex

Political declaration of the high-level meeting on the fight against tuberculosis

Advancing science, finance and innovation, and their benefits, to urgently end the global tuberculosis epidemic, in particular by ensuring equitable access to prevention, testing, treatment and care

We, Heads of State and Government and representatives of States and Governments assembled at the United Nations on 22 September 2023 to reaffirm our commitment to end the tuberculosis epidemic by 2030, and review progress achieved in realizing the 2018 political declaration of the high-level meeting of the General Assembly on the fight against tuberculosis,[1] deeply concerned that some of the global targets set at the United Nations high-level meeting might not be reached, alarmed by the adverse impact of the coronavirus disease (COVID-19) pandemic on access to

[1] Resolution 73/3.

23-20108 (E) 271023

Please recycle

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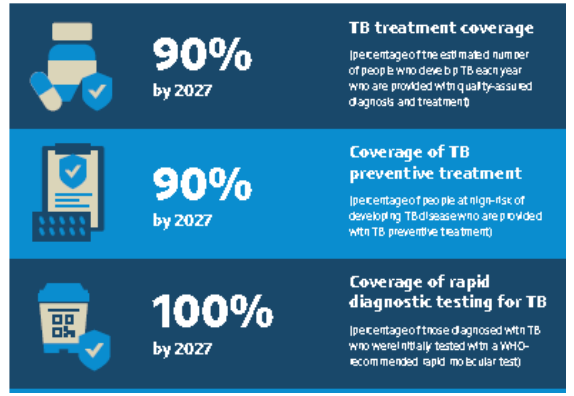
RAPID UPTAKE OF WHO POLICIES, TOOLS AND RECOMMENDATIONS



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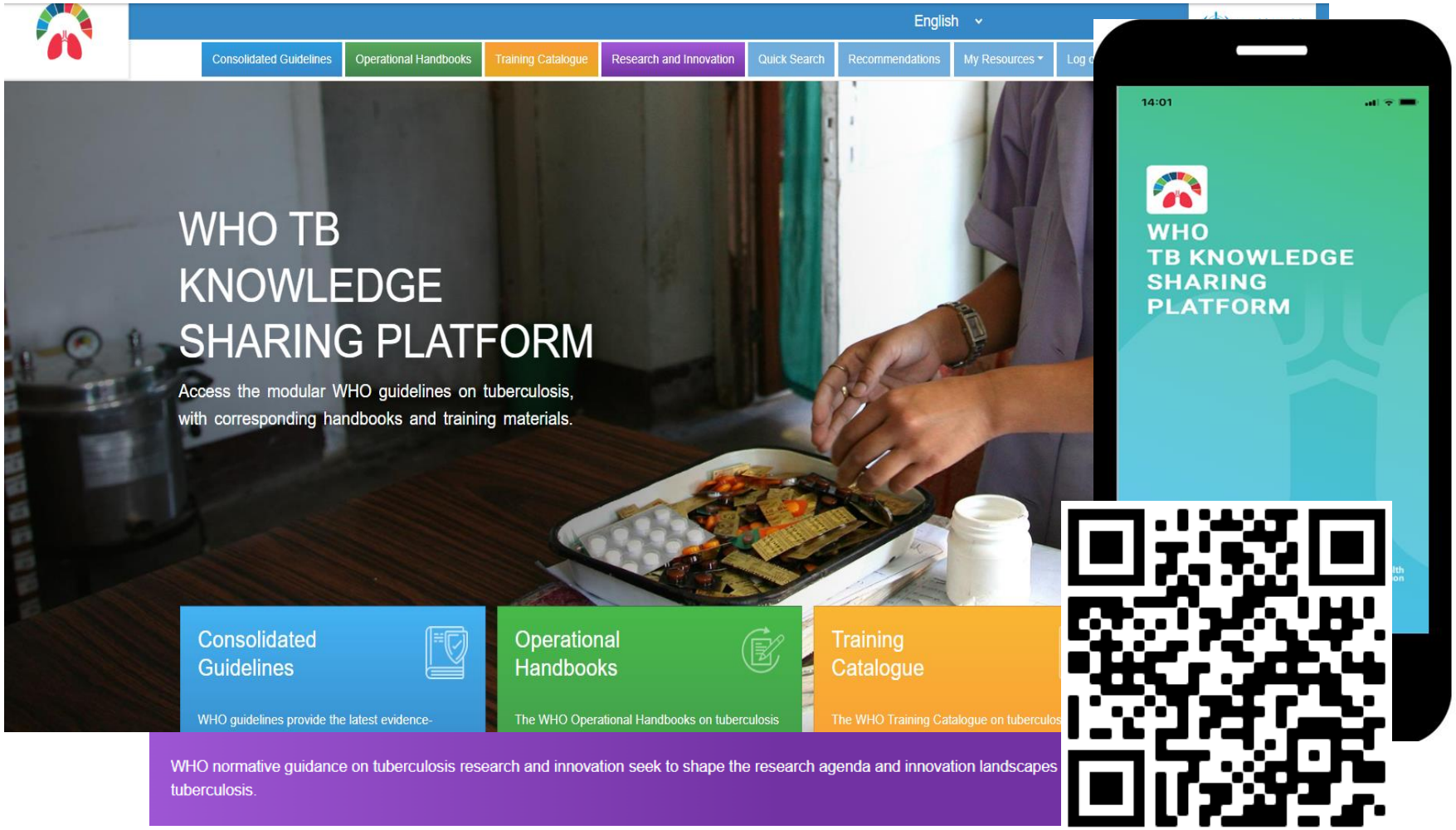
Android -

https://play.google.com/store/apps/details?id=com.whotbksp

iOS -

https://apps.apple.com/us/app/who-tb-guide/id1569546750



New developments: Guidelines & Handbooks

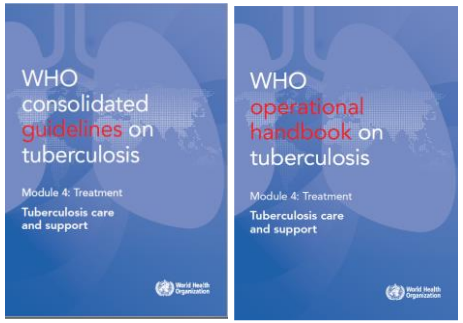
DS-TB

DS-TB guidelines & handbook 2022

- **4-month 2HPMZ/2HPM** regimen
- **4-month 2HRZ(E)/2HR** regimen for children and adolescents
- Consolidating all recommendations on DS-TB (2022)

TB Care & Support

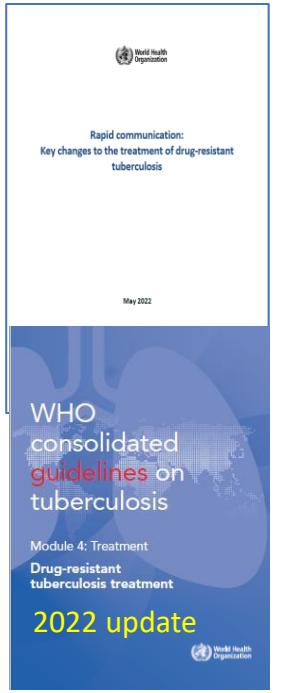
Guidelines & Handbook 2022



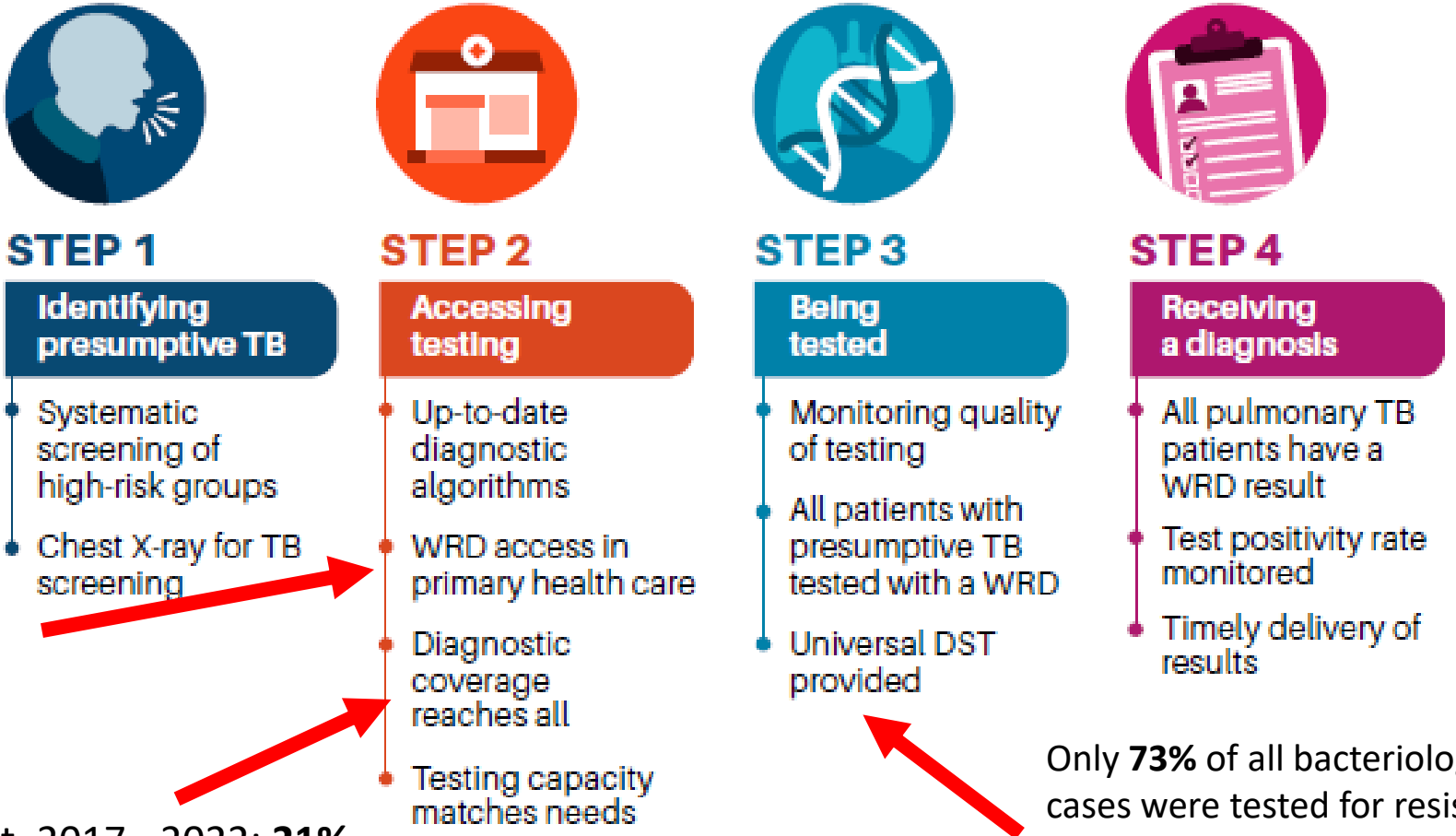
DR-TB

Guidelines and handbook 2022 update

- **6-month BPaLM regimen, comprising bdq, Pa, Lzd (600 mg) & Mfx**, may be used programmatically in place of 9-month or longer (>18 months) regimens, in patients (aged ≥15 years) with MDR/RR-TB
- **9-month, all-oral, bedaquiline-containing regimens*** are preferred over the longer (>18 months) regimen in adults and children with MDR/RR-TB
- Longer regimen for patients with extensive forms of DR-TB (e.g., XDR-TB)



WHO Standard: Universal access to rapid TB Diagnostics



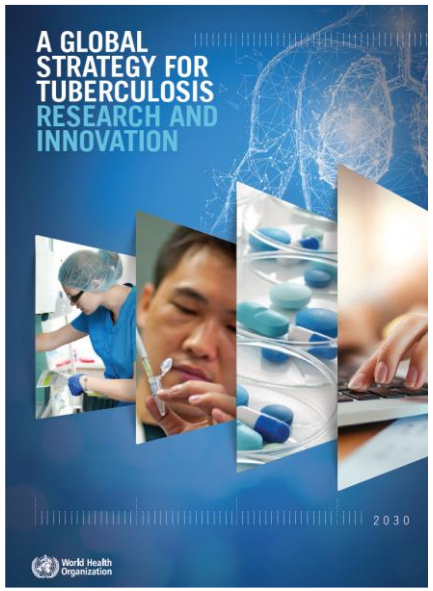
More than **80%** of individuals with symptoms of TB enter at **primary health care**

WRD as the initial test, 2017 - 2022: **21%**, 22%, 28%, 33%, **38% and 47%.**

Only **73%** of all bacteriologically confirmed TB cases were tested for resistance at least to RIF. FQ resistance testing **53%**
Group A drugs (e.g. bedaquiline and linezolid) **much lower ~30%**.

Progress with respect to TB research and innovation

Examples of progress in 2023



Implementation of the global strategy for TB research and innovation

WHO launch of global **individual patient data platform** for tuberculosis treatment

WHO launch of **TB research tracker**, an online platform to track progress in TB research

WHO launch of **target product profiles** to shape product development towards public health impact

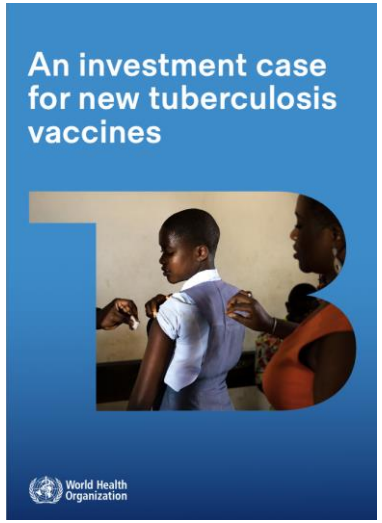
Global research agenda for antimicrobial resistance in human health

For more information: Global TB Report 2023

Full public value assessment of new TB vaccines

Over a 25-year period, a partially effective (50%) TB vaccine for adolescents and adults

Saving lives	could cumulatively avert 37.2–76.0 million cases and 4.6–8.5 million deaths
Antimicrobial stewardship	could avert 21.9–42.3 million treatments with antibiotics
Cost-effective and cost-saving	Estimated to be cost–effective in nearly all high TB-burden countries and cost-saving from a societal perspective.
Return on investment	Would return US $7 in health and economic benefits to the economy For every US$ 1 invested in the full set of interventions
Market potential	The population that requires vaccination could be up to 1.32–1.43 billion adolescents and adults



https://www.who.int/publications-detail-redirect/9789240064690

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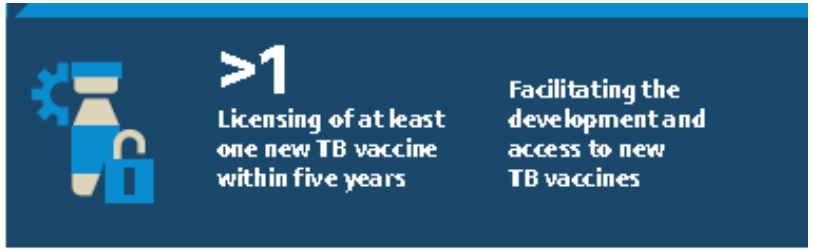
WHAT IT WILL TAKE TO REACH UNHLM COMMITMENTS

VACCINE DEVELOPMENT

Establishment of the WHO TB vaccine accelerator council

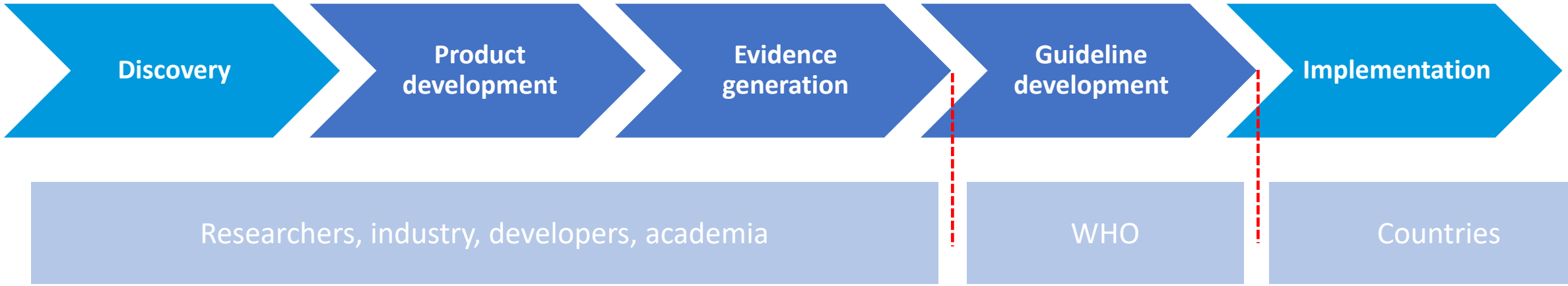
- WHO Director-General, Dr Tedros Adhanom Ghebreyesus, officially launched the **TB vaccine accelerator council** to facilitate the facilitate the development, testing, authorization, and use of new TB vaccines, drawing on lessons learned from the response to the COVID-19 pandemic.
- It is the **first global multi-sectoral collaboration platform to facilitate tb vaccine development and access**
- The Council, supported by the WHO secretariat, will be led by a ministerial board**, **co-chaired by the health ministers of Brazil (Dr Nisia Trindade Lima) and Indonesia (Dr Budi Gunadi Sadikin)**

**France, Viet Nam, South Africa, Pakistan, Philippines, USA



Pathway of novel medicines/regimens

from a health policy perspective



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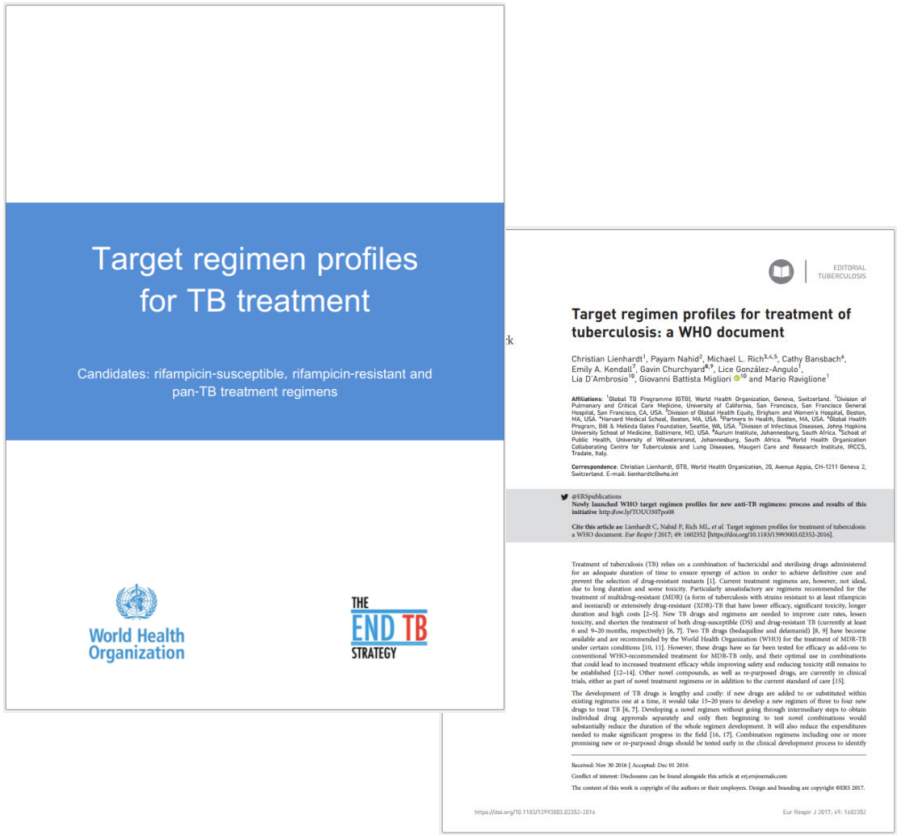
Product development

Target Regimen Profiles

- Purpose of Target Regimen Profiles (TRPs)
  - identify and prioritize characteristics of TB treatment regimens to align decisions made at the time of regimen development with patient and programmatic needs at country level
- 2016 WHO published the first TRPs for TB treatment
  - 17,555 downloads from WHO website, 32 citations of accompanying journal publication
- Why update
  - landscape of drugs and regimens has changed
  - new guidelines available
  - further improvements are urgently needed



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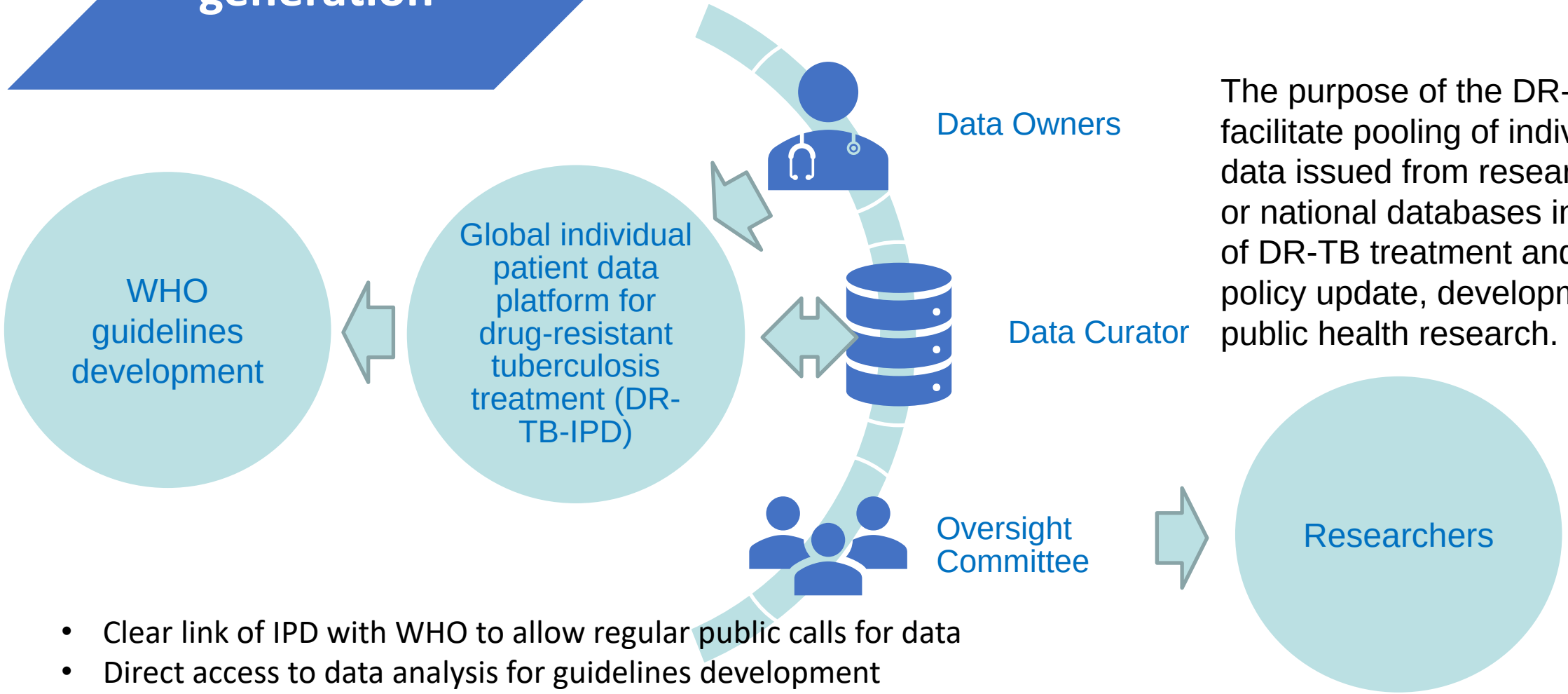
Evidence generation

TB-IPD platform



The purpose of the DR-TB-IPD is to facilitate pooling of individual patient data issued from researchers, local or national databases in the context of DR-TB treatment and facilitate policy update, development and public health research.

- Clear link of IPD with WHO to allow regular public calls for data
- Direct access to data analysis for guidelines development
- Flexibility in systematic review team selection
- Open access to external researchers

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Global clinical development pipeline: new evidence expected in 2023-25

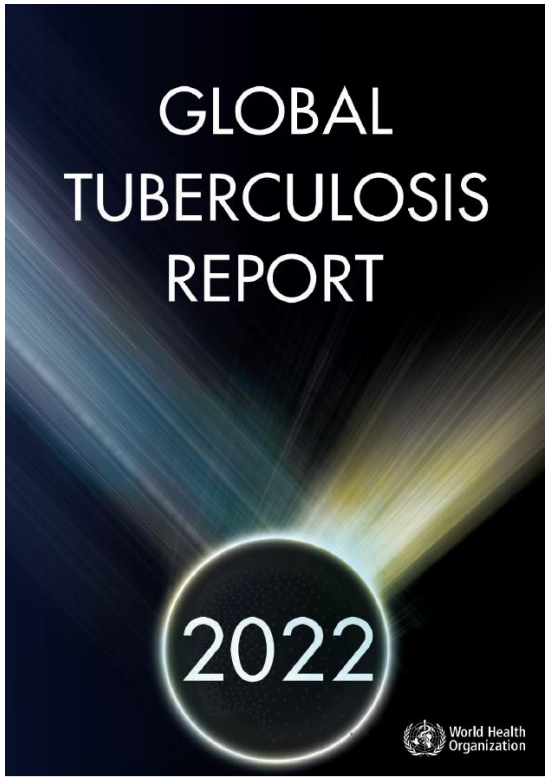
Phase III[a]
Bedaquiline–delamanid–linezolid–levofloxacin–clofazimine (6-month oral regimen for RR-TB) or bedaquiline–delamanid–linezolid–clofazimine (6–9 month oral regimen for pre-XDR and XDR-TB) **(BEAT TB trial)**[g]
Bedaquiline–pretomanid–moxifloxacin–pyrazinamide (BPaMZ) **(SimpliciTB trial)**
Bedaquiline with two OBRs[c] (all-oral, 9 months; with injectable, 6 months) **(STREAM Stage 2)**
Bedaquiline and delamanid with various existing regimens for MDR-TB and XDR-TB **(endTB trial)**
Bedaquiline-delamanid-linezolid-clofazimine for fluoroquinolone-resistant MDR-TB **(endTB-Q)**
Rifampicin High-dose rifampicin and linezolid to reduce mortality among people with TB meningitis (**INTENSE-TBM**)[g] High-dose rifampicin to shorten drug-susceptible TB treatment (**Hi-DoRi-3**) High-dose rifampicin with standard regimen for drug-susceptible TB treatment (**RIFASHORT**)
Several 2-month regimens for drug-susceptible TB **(TRUNCATE-TB)**
Short intensive treatment for children with TB meningitis (6 months of daily rifampicin, isoniazid, pyrazinamide and levofloxacin (**SURE**)[e,f,g]
Ultra-short treatment for fluoroquinolone sensitive MDR-TB (**TB-TRUST**)

DR-TB

- End TB trial
- BEAT Tuberculosis trial (SA)
- SimpliciTB
- ZeNix – evidence used in 2022 DR-TB GDG
- NExT – evidence used in 2022 DR-TB GDG
- TB PRACTECAL – evidence used in 2022 DR-TB GDG
- MDR-END

DS-TB

- TRUNCATE-TB
- RIFASHORT
- PredictTB



Evidence generation

TB research tracker

World Health Organization

World Health Organization | Global Tuberculosis Programme | External Links | Select Language

Home / TB Research Tracker

TB Research Tracker

Use the table below to access the most up-to-date information on clinical trials, operational research and other studies on TB and MDR-TB

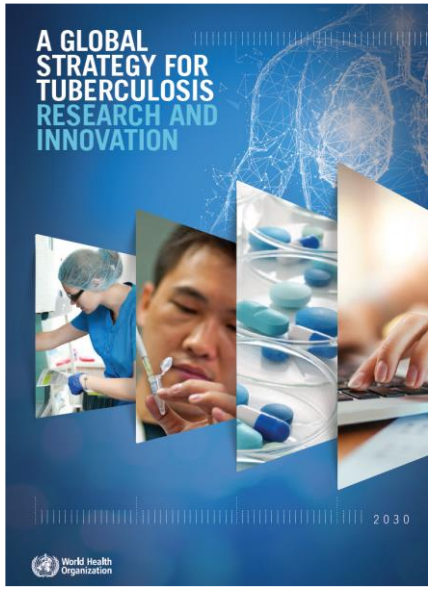
Filters Reset

Clinical Trials | Operational Research | Search by Keywords... | Search

Indication: DR-TB | Theme | Location | Cohort Size | End Date

Name	Indication	Theme	Research Topic	Location	Cohort Size	End Date	Select
Janssen Japan Trial	DR-TB	New drug research	MDR TB	Mozambique, Philippines, Russian Federation, South Africa, Uganda, Ukraine	60	Jul 2025	
Nix-TB	DR-TB	New regimen research	BPaL regimen for XDR-TB	South Africa	109	Jul 2020	
ZeNix	DR-TB	Dose optimization	Dosing and duration of linezolid use in the BPaL regimen	Belarus, Georgia, South Africa	180	Dec 2021	
MDR-END	DR-TB	New regimen research	Clinical trial on a regimen for FQ susceptible MDR-TB	Republic of Korea	238	Jun 2021	
NeXT	DR-TB	New regimen research	Clinical trial all oral shorter regimens for MDR-TB	South Africa	300	Dec 2020	
endTB-Q	DR-TB	New regimen research	Clinical trial on treatment regimens for Fq-resistant TB	India, Kazakhstan, Lesotho, Pakistan, Peru, Vietnam	324	Dec 2022	

Progress with respect to TB research and innovation



Status of clinical development pipeline for diagnostics, drugs and vaccines (August 2023)

3 new diagnostic products to detect drug-resistant TB recommended by WHO in 2023

28 drugs for treatment of TB disease in clinical trials

16 vaccine candidates in clinical trials

29+ clinical drug trials and other research studies for treatment of TB infection

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TB diagnostics pipeline

- The diagnostic pipeline has expanded considerably in terms of the number of tests, products or methods in development. These include:
  - molecular tests for the detection of TB disease and drug resistance
  - interferon-gamma release assays (IGRAs) for the detection of TB infection
  - biomarker-based assays for detection of TB infection and disease
  - computer-aided detection (CAD) for TB screening using digital chest radiography

- In 2023, WHO convened a GDG to assess the use of targeted NGS for detecting DR-TB directly from sputum specimens. This newly-recommended class of tests included:
  - Deeplex® Myc-TB (GenoScreen)
  - NanoTB® (Oxford Nanopore Technologies)
  - TBseq® (ShengTing Biotech)

  although not all technologies met the class criteria for some drugs

TB drugs/regimens pipeline

- 28 drugs for the treatment of TB disease in Phase I, Phase II or Phase III trials. These 28 drugs comprise:
  - 18 new chemical entities. These are BVL-GSK098, BTZ-043, delpazolid, GSK-286 (GSK 2556286), GSK-3036656, macozinone, OPC-167832, TBAJ-587, TBAJ-876, TBI-223, TBI-166, TBA-7371, telacebec-(Q203), sanfetrinem, SQ109, SPR720 (fobrepodacin), sutezolid, and sudapyridine (WX-081)
  - 2 drugs that have received accelerated regulatory approval. These are bedaquiline and delamanid;
  - 1 drug that was recently approved by the United States (US) Food and Drug Administration under the limited population pathway for antibacterial and antifungal drugs. This is pretomanid, which is part of the newly-recommended 6-month regimen for MDR/RR-TB and pre-XDR-TB;
  - 7 repurposed drugs. These are clofazimine, levofloxacin, linezolid, moxifloxacin, rifampicin (high dose), rifapentine and tedizolid

- Various combination regimens with new or repurposed drugs, as well as host-directed therapies, are also in Phase II or Phase III/IV trials or being evaluated as part of operational research projects.

- There are at least 29 clinical trials and implementation research studies to evaluate drug regimens and models of delivery for TB preventive treatment.

TB vaccine pipeline

- 16 vaccine candidates of which 11 in active trial

Paediatric Drug Optimization for 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
- Closely linked to other workstreams such as the Technical Advisory Group on dosing of TB medicines

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

PADO-TB

- Convened for the first time in 2019 (virtual review in 2021)
- Second PADO-TB in October 2023 (report with outcomes will be published on the WHO website in Q1 2024)

SUCCESS STORY
Paediatric rifapentine prioritized by PADO-TB in 2021, added to the WHO prequalification list.
November 2023: first manufacturer prequalified

PADO-TB2 PRIORITIES

PADO PRIORITY LIST (short-term priorities)	
Rifapentine 150 mg scored dt	Development ongoing A fixed-dose combination for TPT was not considered a priority for development at the moment
Rifampicin 100 mg scored dt*	Monitoring the longer-term need/feasibility of an FDC **pending dosing guidance by WHO*
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 project)
PADO WATCH LIST (longer-term priorities)	
All compounds in Phase IIa/b as of October 2023	Delpazolid, sutezolid, GSK-656, quabodepistat, BTZ-043, TBI-223: **more advanced in their clinical development, paediatric investigations to be initiated asap.**
Long acting	New technologies
Oral film rifapentine	New technologies

WHO will look into updated dosing guidance for **rifampicin** in 2024 with the newly established **TECHNICAL ADVISORY GROUP ON DOSING**