Update on WHO TB guidelines

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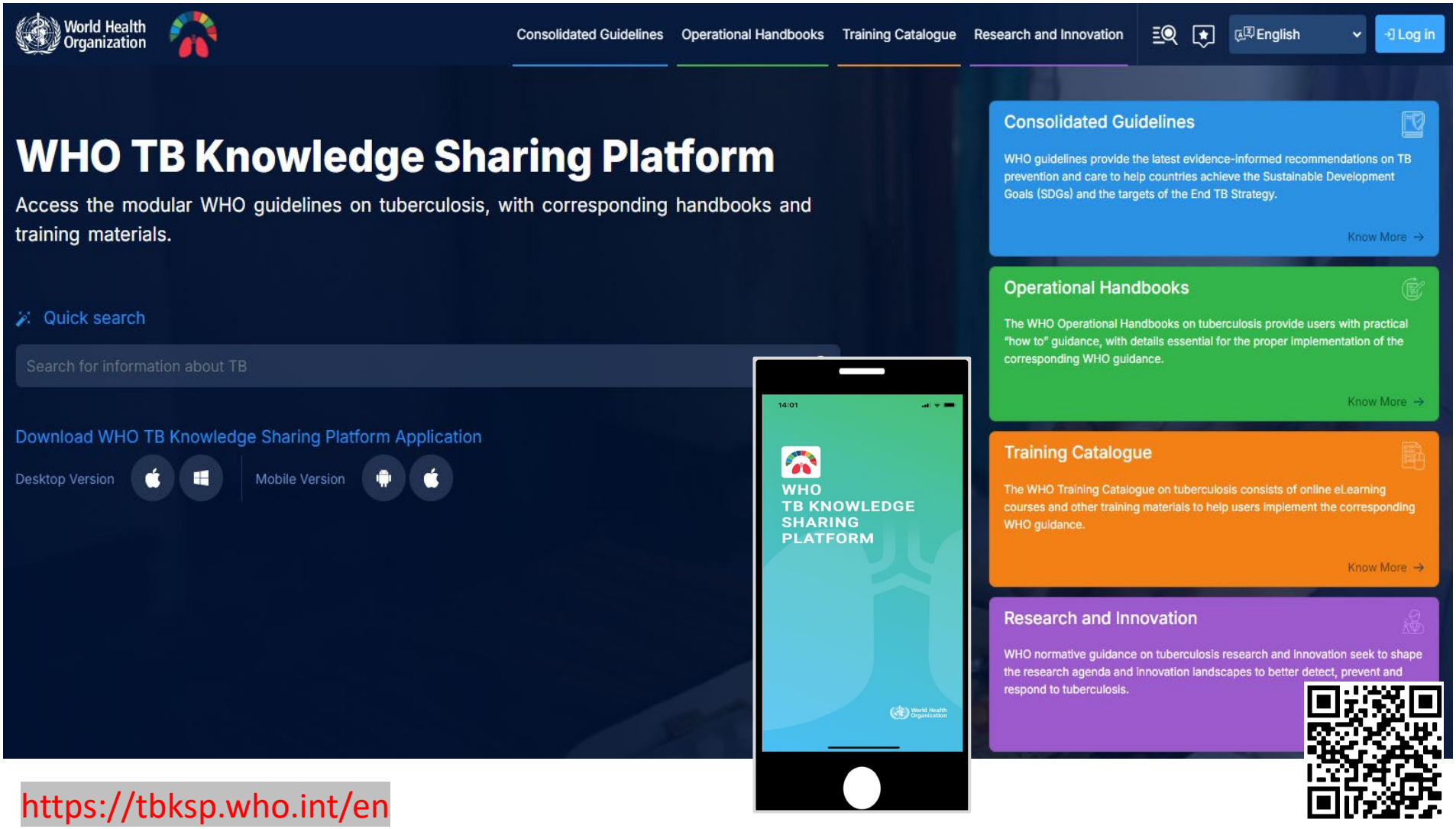
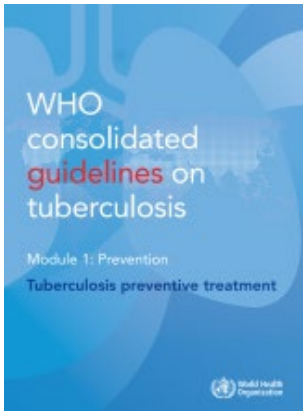
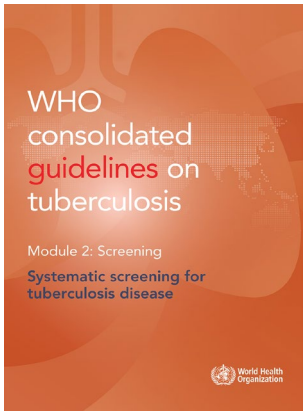
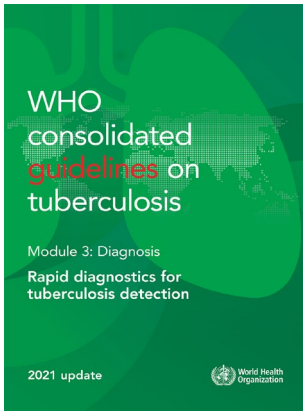


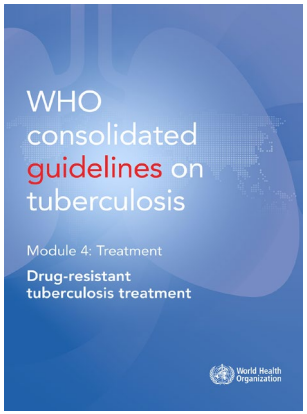
https://tbksp.who.int/en

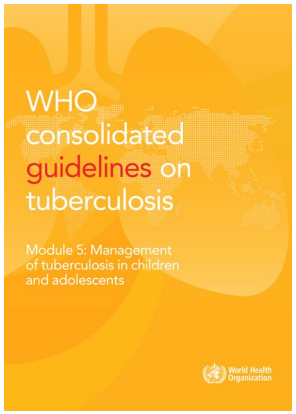
6 Modules

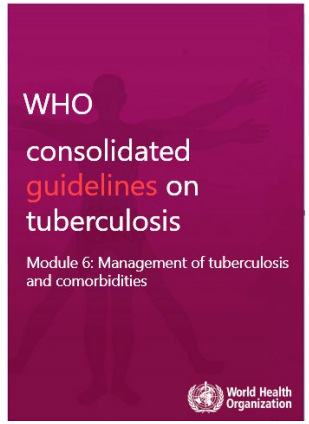

WHO
consolidated
guidelines on
tuberculosis
Module 1: Prevention
Tuberculosis preventive treatment


WHO
consolidated
guidelines on
tuberculosis
Module 2: Screening
Systematic screening for
tuberculosis disease

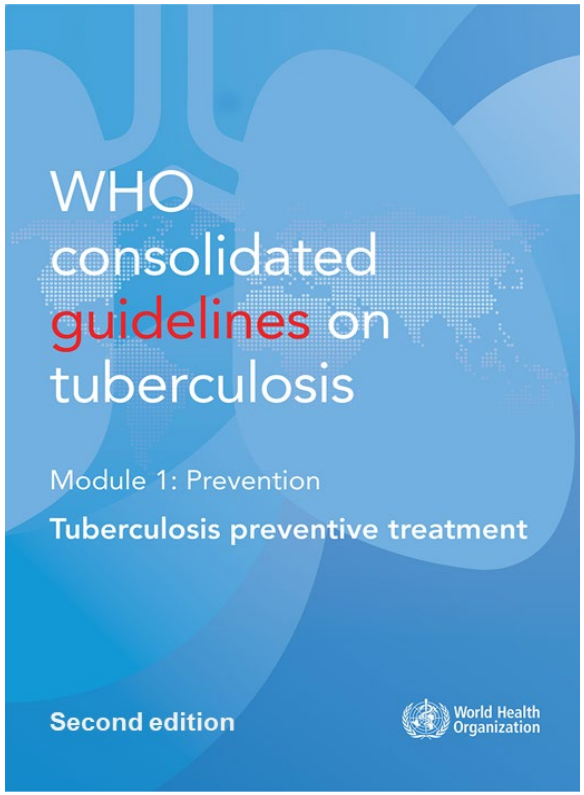

WHO
consolidated
guidelines on
tuberculosis
Module 3: Diagnosis
Rapid diagnostics for
tuberculosis detection
2021 update

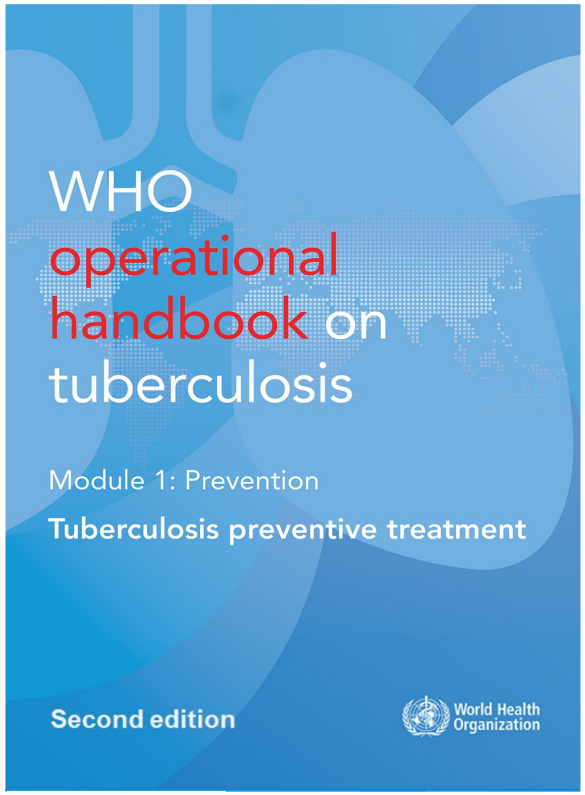

WHO
consolidated
guidelines on
tuberculosis
Module 4: Treatment
Drug-resistant
tuberculosis treatment


WHO
consolidated
guidelines on
tuberculosis
Module 5: Management
of tuberculosis in children
and adolescents


WHO
consolidated
guidelines on
tuberculosis
Module 6: Management of tuberculosis
and comorbidities
World Health
Organization

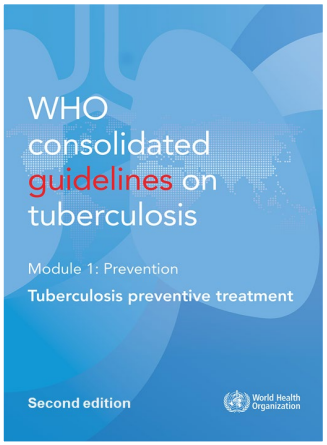
TB preventive treatment





new update issued in Q2 2024

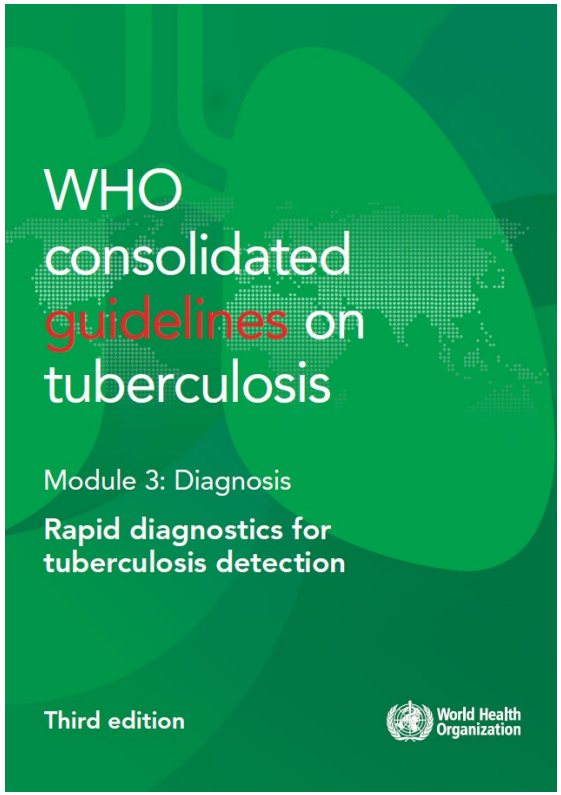
TB preventive treatment

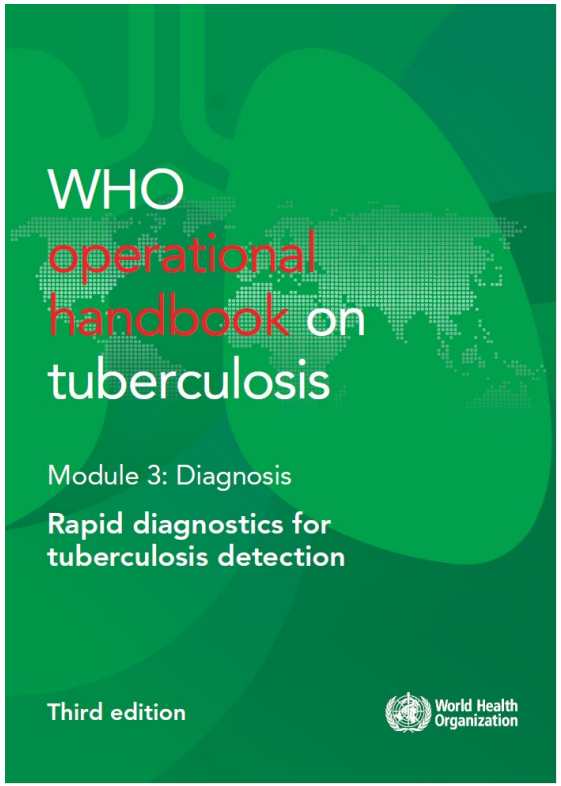


Main changes in 2nd edition of guidelines, 2024

- The recommendation on TPT for MDR/RR-TB is now specific to LFX
- 3 recommendations on newly recommended screening tools were incorporated from the 2021 WHO TB screening guidelines, and 2 other recommendations on TB screening for household contacts and other risk groups from the same guidelines were also added.
- 2 recommendations on TB symptom screening in adults and adolescents with HIV were merged to integrate the pathway of screening and TPT
- 1 recommendation on the use of new *M. tuberculosis* antigen-based tests for TB infection, published by WHO in 2022, was added

TB diagnosis





new update issued in Q1 2024

TB diagnosis: disease → use of targeted NGS

Contents

Table 2.3.6. The accuracy and certainty of evidence of targeted NGS for the detection of resistance to anti-TB drugs among bacteriologically confirmed rifampicin-resistant pulmonary TB

Drug	Reference standard	Accuracy % (95% CI)	Studies (persons)	Certainty in evidence
Isoniazid	Phenotypic DST	Se: 96.5 (93.8–99.2)	12 (1440)	High
	Phenotypic DST	Sp: 95.8 (91.8–99.8)	12 (517)	High
Levofloxacin	Phenotypic DST	Se: 95.8 (90.4–100)	6 (654)	Moderate
	Phenotypic DST	Sp: 96.0 (93.1–98.9)	7 (913)	High
Moxifloxacin	Phenotypic DST	Se: 96.5 (93.6–99.5)	6 (652)	High
	Phenotypic DST	Sp: 95.2 (91.0–99.4)	8 (921)	High
Pyrazinamide	Phenotypic DST+WGS	Se: 90.0 (86.8–93.2)	3 (346)	High
	Phenotypic DST+WGS	Sp: 98.6 (96.8–100)	3 (269)	High
Bedaquiline	Phenotypic DST	Se: 67.9 (42.6–93.2)	3 (31)	Low
	Phenotypic DST	Sp: 97.0 (94.3–99.7)	4 (519)	High
Linezolid	Phenotypic DST	Se: 68.9 (38.7–99.1)	4 (31)	Low
	Phenotypic DST	Sp: 99.8 (99.6–100)	6 (1093)	High
Clofazimine	Phenotypic DST	Se: 70.4 (34.6–100)	4 (36)	Low
	Phenotypic DST	Sp: 96.3 (93.2–99.3)	6 (789)	High
Amikacin	Phenotypic DST	Se: 87.4 (74.5–100)	5 (115)	Very low
	Phenotypic DST	Sp: 99.0 (98.4–99.6)	8 (1003)	Moderate
Ethambutol	Phenotypic DST+WGS	Se: 96.7 (95.0–98.4)	4 (431)	Moderate
	Phenotypic DST+WGS	Sp: 98.4 (96.1–100)	4 (123)	Moderate
Streptomycin	Phenotypic DST	Se: 98.1 (96.1–100)	5 (493)	High
	Phenotypic DST	Sp: 75.0 (59.5–90.5)	5 (250)	Low

CI: confidence interval; DST: drug susceptibility testing; NGS: next-generation sequencing; Se: sensitivity; Sp: specificity; TB: tuberculosis; WGS: whole genome sequencing

TB diagnosis: disease → use of targeted NGS

The products and drugs for which eligible data met the class-based performance criteria are listed below:

Deeplex® Myc-TB (Genoscreen, France): rifampicin, isoniazid, pyrazinamide, ethambutol, fluoroquinolones, bedaquiline, linezolid, clofazimine, amikacin and streptomycin

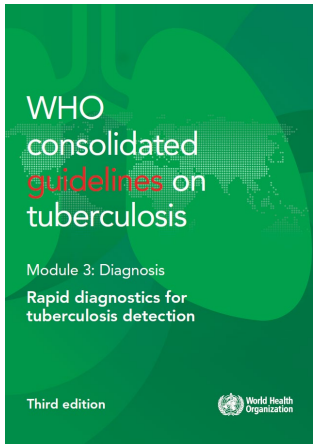
AmPORE-TB® (Oxford Nanopore Diagnostics, United Kingdom): rifampicin, isoniazid, fluoroquinolones, linezolid, amikacin and streptomycin

TBseq® (Hangzhou ShengTing Medical Technology Co., China): ethambutol

Where a product has not yet met the requirements for a specific drug (i.e., the drug is not listed), further improvements to the product are needed, and a review of the evidence is necessary before clinical use.

WHO Technical Advisory Group meeting January 2025: Pathway B – Targeted NGS products

TB diagnosis: disease → new recommendations



new update to be available in Q1 2025

In 2024 WHO has a Rapid Communication on the concurrent use of tests in people with HIV and children

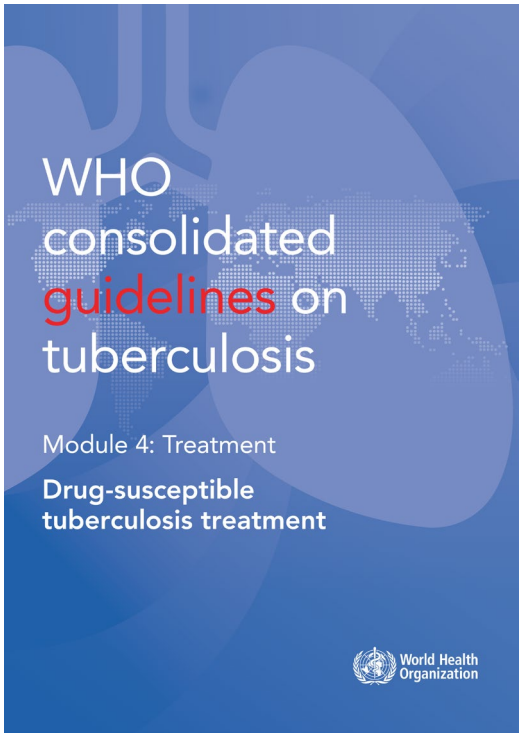
- **In adults and adolescents with HIV who have signs or symptoms or screened positive for TB, or seriously ill, or have advanced HIV disease, concurrent testing using low-complexity automated NAATs on respiratory samples and LF-LAM on urine should be used as the initial diagnostic strategy for diagnosing TB rather than low-complexity automated NAATs on respiratory samples alone (strong recommendation, moderate certainty of evidence).**

- **In children who have signs or symptoms or screened positive for pulmonary TB, concurrent testing using low-complexity automated NAATs on respiratory samples and stool should be used as the initial diagnostic strategy for diagnosing TB rather than low-complexity automated NAATs on respiratory or stool samples alone (strong recommendation, low certainty of evidence for test accuracy).**

TB treatment

new update to be available in Q1 2025

TB treatment: drug-susceptible



New patients with pulmonary TB should receive a regimen containing 6 months of rifampicin: 2HRZE/4HR

Wherever feasible, the optimal dosing frequency for new patients with pulmonary TB is daily throughout the course of therapy

In new PTB patients treated with the regimen containing rifampicin throughout treatment, if a positive sputum smear is found at completion of the intensive phase, the extension of the intensive phase is not recommended

The use of fix-dose combination (FDC) is recommended over separate drug formulations in treatment of patients with DS-TB

In all patients with DS PTB, the use of 3x dosing is not recommended in both the intensive and continuation phases of therapy, and daily dosing remains the recommended dosing frequency

NEW

People aged 12 years or older with drug-susceptible pulmonary TB, may receive a 4-month regimen 2HPMZ/2HPM

NEW

In children and adolescents, 3month-16years, with non-severe TB, a 4- month treatment regimen 2HRZ(E)/2HR should be used

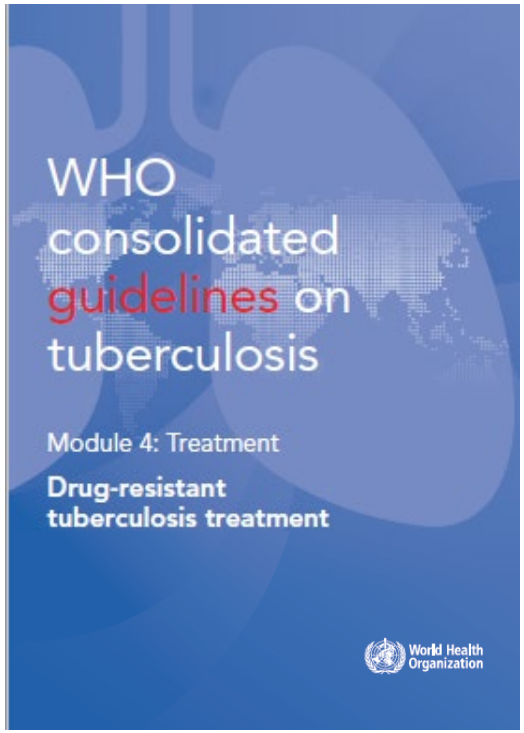
It is recommended that TB patients who are living with HIV should receive at least the same duration of daily TB treatment as HIV-negative TB patients.

ART should be started as soon as possible within two weeks of initiating TB treatment, regardless of CD4 cell count, among people living with HIV.

In patients with TB meningitis, an initial adjuvant corticosteroids with dexamethasone or prednisolone tapered over 6-8 wk should be used

In patients with TB pericarditis, an initial adjuvant corticosteroids may be used

TB treatment: drug-resistant



new update to be available in Q1 2025

- ❖ **Treatment of drug-resistant TB using 6-month regimens.**
  - **Recommendation 1.1 The 6-month bedaquiline, pretomanid, linezolid, and moxifloxacin (BPaLM) regimen**
  - **Recommendation 1.2 The 6-month bedaquiline, delamanid, linezolid, levofloxacin and clofazimine (BDLLfxC) regimen (NEW)**
- ❖ **Treatment of drug-resistant TB using 9-month regimens**
  - **The 9-month all-oral regimen for MDR/RR-TB**
  - **The modified 9-month all-oral regimens for MDR/RR-TB (NEW)**
- ❖ **Treatment of drug-resistant TB using longer regimens**
- ❖ **Regimen for rifampicin-susceptible and isoniazid-resistant tuberculosis**
- ❖ **Monitoring patient response to MDR/RR-TB treatment**
- ❖ **Start of antiretroviral therapy in patients on MDR/RR-TB regimens**
- ❖ **Surgery for patients on MDR/RR-TB treatment**
- ❖ **Hepatitis C virus (HCV) and MDR/RR-TB treatment co-administration (NEW)**

TB treatment: drug-resistant

6-month regimen - BPaLM/BPaL regimen (MDR/RR-TB and pre-XDR-TB)

- in patients (aged ≥14 years) with MDR/RR-TB who have not had previous exposure to bedaquiline, pretomanid and linezolid (defined as >1 month exposure).
- This regimen may be used without moxifloxacin (BPaL) in the case of documented resistance to fluoroquinolones (in patients with pre-XDR-TB).
- DST to fluoroquinolones is strongly encouraged, but DST should not delay treatment initiation.
- Cannot be used during pregnancy
- if DST confirms susceptibility can be used in those exposed to B, Pa, or L for more than 1 month
- no TB meningitis, osteoarticular or disseminated TB

6-month

9-month regimens (MDR/RR-TB)

- 2 months of linezolid (600 mg) can be used as an alternative to 4 months of ethionamide.
- no previous exposure to second-line treatment (including bedaquiline),
- no fluoroquinolone resistance and
- no extensive pulmonary TB disease or severe extrapulmonary TB.
- rapid DST for ruling out fluoroquinolone resistance is required.
- can be used in all age groups
- regimen with linezolid can be used in pregnant women

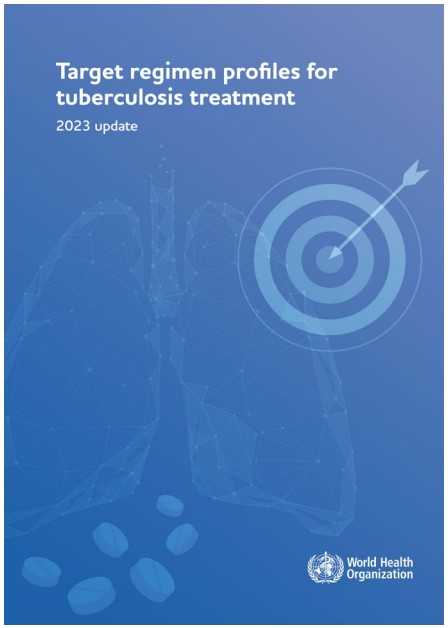
9-month

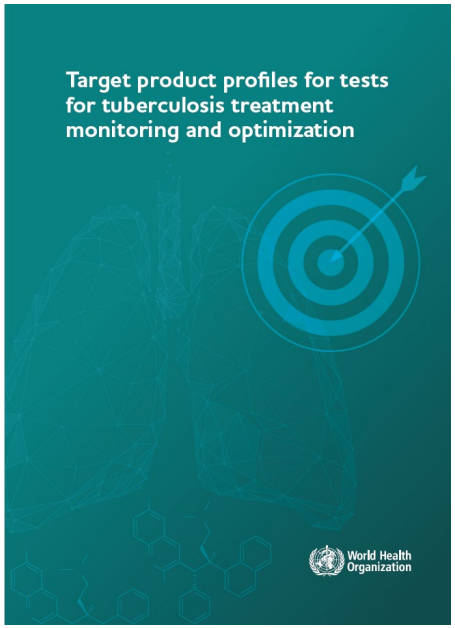
18-month - longer regimens, individualized, mostly in XDR-TB)

- Last resort regimen
- Those who failed or not eligible for two shorter regimens
- XDR-TB patients
- Individualized based on current recommendations

18-month

Target Product/Regimen Profiles & GEG





Guidance on evidence generation on new regimens for TB treatment

Objectives:

- to outline key steps in the WHO guideline development process and the GRADE approach
- provide guidance on how evidence should be generated to optimally inform WHO guideline development

Coming up soon in QIV 2024

Acknowledgments

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