

# **Tuberculosis preventive treatment**

## **Rapid Communication**





## Background

The World Health Organization (WHO) estimated that in 2022 there were 10.6 million incident tuberculosis (TB) cases and 1.3 million TB deaths globally, making TB the second leading infectious cause of death globally after COVID-19(1). About one fourth of the world's population is estimated to have been infected with *M. tuberculosis*. Several studies have shown that, on average, 5–10% of those infected will develop TB disease over the course of their lives, with the majority of them developing TB within the first 2–5 years after the initial infection(2). Effective treatment of TB infection – known as TB preventive treatment (TPT) – in people at highest risk of progression safely reduces the risk of developing TB disease. The WHO End TB Strategy considers the scale-up of TPT to be a critical component of all efforts to end the global TB epidemic with currently available technologies(3,4). In September 2023, at the UN High Level Meeting on Tuberculosis, Member States committed to increase TPT coverage among contacts and people with HIV, reaching at least 45 million individuals by 2027(5). Major barriers to an expanded access to TPT for people in need include low performance of programmes in identifying opportunities to test and treat target populations, cost of testing and TPT, and the low penetration of shorter and better tolerated TPT regimens containing rifapentine.

Over the years, WHO has released evidence-based recommendations on TPT to facilitate its implementation at country level. The last update of its TPT guidelines was in 2020(6). These consolidated guidelines contain 18 recommendations across four critical points in the cascade of care and programmatic management of TPT. All recommendations have been developed in recent years by WHO through Guideline Development Groups (GDGs) using the GRADE process. The 2020 guidelines were accompanied by an operational handbook with practical advice and job aids(7).

Since 2020, there have been developments that also impact upon TPT policy. These include the revision of WHO guidance on screening for TB disease and new modalities to test for TB infection(8,9). In addition, two landmark trials looking at TPT for contacts of multidrug-resistant TB (MDR-TB) have been completed(10,11). Moreover, more data are becoming available relevant to this question, as well as to dose adjustment and safety of TPT in childhood, pregnancy, and other specific situations.

In light of these new developments, and the continued demand by Member States for guidance on how best to protect people at risk of TB, WHO convened a GDG to examine the latest evidence in order to update its guidelines. The Group met in virtual sessions in December 2023 and proposed one new recommendation related to TPT in people exposed to MDR-TB and approved a number of other changes to the previous guidelines text, in part to address comments received from users. In addition, the WHO Technical Advisory Group on dosing of TB medicines was also engaged in 2024 to advise on necessary changes to WHO guidance on dosage of drugs used for TPT and concurrent use of other medications in different subpopulations.

This Rapid Communication is being issued to help national TB programmes and other stakeholders prepare for the changes that will be introduced with the update of guidelines on TPT.

## Key findings

### TB preventive treatment for contacts of MDR-TB

WHO has recommended TPT for contacts of MDR/RR-TB since 2017. This recommendation was conditional, based on evidence of very low certainty and is not specific to use of any particular drug regimen. Its implementation has thus been poor. A regimen of 6 months of levofloxacin should now be used as TPT for contacts of MDR/RR-TB in light of new evidence from two well-conducted randomized controlled trials in South Africa and Viet Nam supporting the use of levofloxacin of this regimen in people of all ages.

### Other updates

The 2<sup>nd</sup> edition of the TPT guidelines will include a number of other revisions, namely:

- drug dosages of regimens with levofloxacin and rifapentine are being updated in light of new evidence on their use, and the co-administration of dolutegravir
- relevant recommendations from the 2021 WHO screening guidelines and 2022 guidelines on new tests of TB infection are being integrated
- an update of the algorithm for the management of TPT in contacts, people with HIV and other risk groups to reflect updated algorithms included in recent WHO guidelines for screening and testing for TB infection
- the research gaps are being updated to reflect the latest evidence reviewed

## Next steps

- The updates will be released as the 2<sup>nd</sup> edition of the *WHO consolidated guidelines on tuberculosis: Module 1: Prevention - tuberculosis preventive treatment* by July 2024. These guidelines will replace the previous WHO guidance on TPT from 2020. The updated summary of findings and the evidence to decision tables will be produced in conformity with the GRADE method and made available on the WHO Global Tuberculosis Programme website.
- The guidelines will be accompanied by an updated operational handbook. This will include further details on implementing the recommendations in the target populations and the latest advice on drug dosage, algorithms, and other aspects of the programmatic management of TPT.
- The WHO Global Tuberculosis Programme and WHO regional and country offices will disseminate the new documents through the WHO TB Knowledge Sharing Platform as well as webinars and regional meetings, and support countries to update their national guidelines, train staff, inform programme budgets and facilitate the rapid transition to more effective interventions. The concerted efforts of staff from national programmes, technical partners, donors, civil society and other stakeholders will be important for the successful scaleup of the novelties being recommended in our new guidelines.

WHO gratefully acknowledges the work of the GDG, the WHO Technical Advisory Group on dosing of TB medicines, the evidence reviewers, study investigators, drug manufacturers, national TB and HIV programmes, WHO colleagues, other technical partners, funding agencies, civil society, patients and all others who contributed data to inform this guideline update.

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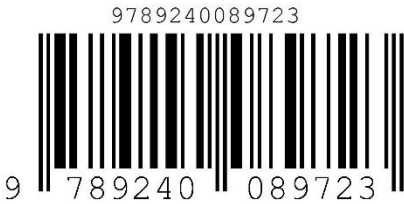
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