

# TPT

## What is Tuberculosis (TB) Preventive Treatment (TPT)?

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TB Preventive treatment prevents TB from developing in persons who have TB infection. Not everyone exposed to TB will get TB disease immediately. Some will go on to develop latent TB infection (LTBI), a state in which the TB does not cause active disease but can be reactivated with time or if there is immune suppression due to HIV or other conditions. TPT uses some of the same drugs that are used to treat TB, but typically only one or two drugs instead of four and sometimes for a shorter period. There have been concerns that using the same drugs in persons with latent TB infection and active TB disease would create drug-resistant strains of TB that would later become active and more difficult to treat.

## Does TPT promote resistant TB?

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**No!** The fact that TPT might promote resistance is a **myth that has prevented programs and individuals from accessing life-saving TB preventive treatment.**

There are a few reasons why the **development of resistance is extremely unlikely:**

- TPT is used for patients who do not currently have active TB
- Active TB can be quickly and easily excluded using simple screening algorithms
- Individuals with TB infection have a small number of slowly replicating bacteria in complexes in the lung. These “hidden” bacteria are at low risk of selecting for drug-resistance
- Most resistance arises from suboptimal treatment of active disease, hence preventing active disease may be beneficial for resistance overall
- Multiple trials have failed to find scientific evidence of a significant association between TB drug-resistance and the use of isoniazid or rifamycins for TPT<sup>1,2</sup>.

## Lack of evidence for isoniazid resistance after IPT

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In a systematic review of 13 published studies since 1951, which included 18,095 people on IPT and 17,985 controls, there was no suggestion of an increased risk of isoniazid-resistant TB after IPT; these results were similar when stratified for HIV<sup>3</sup>.

In addition, in the Thibela study cohort from South Africa, proportions of TB episodes with drug resistance in patients who had received IPT did not significantly differ from those in comparison groups with minimal IPT use<sup>4</sup>.

## Lack of evidence for rifamycin resistance after TPT

In an analysis of six randomised control trials of rifamycin-containing regimens for LTBI treatment versus active control or placebo showed that the occurrence of rifampicin resistant cases was 0.09% in 6,808 individuals receiving rifamycin-based TPT vs 0.01% in 7,415 individuals receiving alternate regimens. (RR = 3.45, 95%CI 0.72–16.56; P = 0.12).

In 3 of these studies *intermittent* rifamycin-based TPT was used and showed 0.06% cases of rifampicin resistance in 4,673 individuals on intermittent rifamycin-containing regimens compared to no cases with rifampicin resistance in 4,427 in control regimens (RR = 3.89; 95%CI 0.44–34.56; P = 0.22).

Therefore, the conclusion in this review was that preventive treatment with rifamycin-containing regimens does not significantly increase rifamycin resistance<sup>5</sup>.

However, it is important to:

- Exclude active TB disease before initiating TPT
- Monitor rigorously to ensure that people who develop active TB while receiving TPT are identified early
- Establish national surveillance systems for resistance to TB drugs in countries that are implementing TPT.

## References

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2. den Boon S, Matteelli A, Getahun H. Rifampicin resistance after treatment for latent tuberculous infection: a systematic review and meta-analysis. *Int J Tuberc Lung Dis* 2016,20:1065-71.
3. Balcells ME, Thomas SL, Godfrey-Faussett P, Grant AD. Isoniazid preventive therapy and risk for resistant tuberculosis. *Emerg Infect Dis* 2006,12:744-51.
4. van Halsema CL, Fielding KL, Chihota VN, Russell EC, Lewis JJ, Churchyard GJ, et al. Tuberculosis outcomes and drug susceptibility in individuals exposed to isoniazid preventive therapy in a high HIV prevalence setting. *AIDS* 2010,24:1051-5.
5. den Boon S, Matteelli A, Getahun H. Rifampicin resistance after treatment for latent tuberculous infection: a systematic review and meta-analysis. *Int J Tuberc Lung Dis* 2016,20:1065-71.