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INPLASY

# Preferred TB Prevention Therapy Regimen for people living with HIV

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None.

## ADMINISTRATIVE INFORMATION

**Support -** World Health Organization.

**Review Stage at time of this submission -** Completed but not published.

**Conflicts of interest -** None declared.

**INPLASY registration number:** INPLASY202520092

**Amendments -** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 20 February 2025 and was last updated on 20 February 2025.

## INTRODUCTION

**Review question / Objective** Aim To compare effectiveness and safety of 1HP, 3HP and 6H for TB preventative therapy (TPT) amongst adults and adolescents (≥13 years) living with HIV.

Primary Objectives
1) To compare, for 1HP and 3HP (combined) vs. 6H, rates of TPT completion, Grade 3 and 4 adverse events (AEs), TB incidence and HIV Viral Load Suppression (VLS)
2) To compare, for 1HP vs 3HP vs. 6H, rates of TPT completion, Grade 3 and 4 AEs, TB incidence and HIV VLS.
Secondary objectives
1) To conduct a subset analysis of studies reporting Grade 3 and 4 AEs to compare Grade 3 and 4 hepatotoxicity across eligible TPT regimens.

PICO question

• Population: Adults /adolescents (≥13 years) living with HIV
• Interventions: 1HP (daily isoniazid-rifapentine for 1 month) regimen use to prevent TB in people living with HIV; 3HP (weekly isoniazid-rifapentine for 3 months) regimen use to prevent TB in people living with HIV
• Control: 6H (6 months of daily isoniazid) regimen to prevent TB in people living with HIV
• Outcomes: TPT completion, Grade 3 and 4 adverse events (incl. Hepatotoxicity), TB incidence, HIV Viral Load Suppression (VLS).

**Rationale** Tuberculosis (TB) is the leading cause of death amongst people living with HIV (PLHIV), with 161,000 individuals estimated to have died in 2023 . TB preventive therapy (TPT) is effective in reducing progression to active TB and TB related mortality among PLHIV .

Historically TPT regimens of 6-36 months of isoniazid (INH) have been recommended for adolescents and adults living with HIV. However,

lengthy INH based TPT regimens are associated with significant hepatotoxicity risks and low completion , and there is now evidence for comparable effectiveness, improved safety and better completion rates with shorter TPT regimens . World Health Organization (WHO) guidance has evolved to include shorter-duration TPT regimens that include rifapentine, such as 1HP (daily isoniazid-rifapentine for 1 month) and 3HP (weekly isoniazid-rifapentine for 3 months).

PLHIV are a key high TB risk group for TPT and there is a need for enhanced guidance on preferred short course regimens. To evaluate whether a preferred regimen can be recommended for PLHIV in high TB burden settings we have conducted a systematic review to compare effectiveness and safety of 1HP, 3HP and 6H.

**Condition being studied** Tuberculosis prevention.

## METHODS

### Search strategy

• We searched: i) Medline, Embase and the Cochrane central register (2014 to 30 November 2024) ii) Conference abstracts from The Union World Conference on Lung Health TB, International AIDS society conferences and the Conference on Retroviruses and Opportunistic Infections (CROI) from 2022-2024.
• Search terms included HIV, TB and TB preventative agents (e.g. isoniazid, rifapentine, and TPT regimen acronyms [e.g. 6H, 3HP, 1HP])
• Medical subject heading (MESH terms) and different combinations of text words were combined using Boolean operators.
• Additional articles were sought in reference lists of identified articles.
• There was no restriction on study setting or language of publication.

**Participant or population** • Population: Adults / adolescents (≥13 years) living with HIV.

**Intervention** • Interventions: 1HP (daily isoniazid-rifapentine for 1 month) regimen use to prevent TB in people living with HIV; 3HP (weekly isoniazid-rifapentine for 3 months) regimen use to prevent TB in people living with HIV.

**Comparator** • Control: 6H (6 months of daily isoniazid) regimen to prevent TB in people living with HIV.

**Study designs to be included** Randomized controlled trials (RCTs) and prospective observational studies.

**Eligibility criteria** • PLHIV must be included and results stratified by HIV status;
• Studies must include participants ≥ 13 years;
• One of the following outcomes must be evaluated: TPT completion, graded drug-related adverse events (including hepatotoxicity), TB incidence or HIV VL suppression;
• For the TB incidence outcome, studies should include 1HP or 3HP in one of the study arms;
• Given the effect of background TB burden on TB incidence, we decided a priori to restrict analysis of TB incidence to RCTs that compared 2 TPT regimens (either 1HP or 3HP versus each other or versus 6H). For the other outcomes we included RCTs and prospective observational studies.

**Information sources** • We searched: i) Medline, Embase and the Cochrane central register (2014 to 30 November 2024) ii) Conference abstracts from The Union World Conference on Lung Health TB, International AIDS society conferences and the Conference on Retroviruses and Opportunistic Infections (CROI) from 2022-2024.

**Main outcome(s)** TPT completion, Grade 3 and 4 adverse events (including Hepatotoxicity), TB incidence, HIV Viral Load Suppression (VLS).

**Additional outcome(s)** Subset analysis of studies reporting Grade 3 and 4 AEs to compare Grade 3 and 4 hepatotoxicity across eligible TPT regimens.

**Data management** All search results were imported to EndNote and duplicates removed. Primary screening of titles and abstracts was conducted by Peter Bock and validated by a second reviewer (Helen Cox). Conference abstracts were compiled into a word document and reviewed manually. Data were extracted into a pre-defined Excel spreadsheet tool and validated by the second reviewer. Studies that reported additional data in subsequent publications were also included in the data extraction process. Meta-analyses were completed using random effects models in Stata TM (Version 18).

**Quality assessment / Risk of bias analysis** Risk of Bias and GRADE assessments were completed as per Cochrane guidelines. Domains for Risk of Bias were based on the Cochrane ROB and ROBINS tools. GRADE assessment included risk of bias, imprecision inconsistency and indirectness.

**Strategy of data synthesis** For the primary analysis we completed meta-analysis using random effects models.

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**Subgroup analysis** We present present forest plots comparing 1HP vs 3HP and 6H. We also compare 1HP and 3HP combined vs 6H (to be presented in table format).

**Sensitivity analysis** None.

**Language restriction** None.

**Country(ies) involved** South Africa, Australia.

**Other relevant information** None

**Keywords** TB preventative therapy, HIV, 1HP, 3HP, 6H.

**Dissemination plans** This review will be submitted to the WHO and we will complete a manuscript for publication.

**Contributions of each author**

Author 1 - Peter Bock - Completed searches, screening, full text review, meta-analysis and write up.
Email: peterabock@gmail.com
Author 2 - Helen Cox - Validated screening, full text review, meta-analysis and write up.
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