BMC Infectious Diseases

SYSTEMATIC REVIEW Open Access

Clinical effectiveness of three months once-weekly Isoniazid and Rifapentine regimen for treatment of Latent TB Infection: a systematic review and meta-analysis

Malaisamy Muniyandi[1*], Bhaskara Chary Kothoju[1], Karthick Chelvanayagam[1], Balagopal Balachandran[1], Bharathidasan Palani[1], Venkateshprabhu Janagaraj[1], Vijaykaravell Thirupathi[1] and Karikalan Nagarajan[2]

Abstract

Background Globally, multiple TB preventive treatment (TPT) regimens are available for Latent Tuberculosis Infection (LTBI) and implementing TPT is essential for achieving TB elimination. Standard treatments for LTBI include 9 and 6-month isoniazid monotherapy (9H and 6H) regimens, recent clinical trials also introduced the shorter once-weekly 3-month isoniazid plus rifapentine (3HP) regimen. To evaluate the clinical effectiveness of 3HP in adults, we performed a comprehensive synthesis on the clinical effectiveness (treatment completion, adverse drug reactions (ADRs) and exploratory analysis of incident active TB) of the 3HP regimen compared with 9H and 6H.

Methods A systematic search was carried out in PubMed, EMBASE, ScienceDirect, and Cochrane Library. An excel data collection tool was used for collecting the required data. Pooled estimates of effectiveness were calculated through random-effects meta-analysis model using odds ratio (OR) and risk ratio (RR) as summary measures. Risk of bias was assessed using the RoB 2.0 and ROBINS-I tools, and publication bias was evaluated. The certainty of the evidence was assessed using the GRADE approach.

Results Twenty studies met eligibility criteria, of which 5 were trials and 15 were observational studies. Meta-analysis showed that participants receiving the 3HP regimen were nearly three times more likely to complete treatment compared to 9H regimen (OR = 2.81; 95% CI: 2.05–3.86; low certainty) and the OR was 2.91 compared to 6H regimen. The risk of ADRs was 1% higher with 3HP when compared to 9H (RR = 1.01; 95% CI: 0.76–1.33; very low certainty). The pooled RR of adverse events, such as grade 1–2, grade 3–4, grade 5 and hepatotoxicity were 1.38 (95% CI: 0.73–2.59; $I^2 = 75.9\%$), 1.19 (95% CI: 0.78–1.82; $I^2 = 16.6\%$), 0.77 (95% CI: 0.49–1.22; $I^2 = 0\%$) and 0.26 (95% CI: 0.18–0.38; $I^2 = 17.7\%$) respectively. Exploratory analysis suggested a lower incidence of active TB with 3HP compared to 9H; however, the difference was not statistically significant (RR = 0.47; 95% CI: 0.16–1.38; moderate certainty).

Conclusion The shorter 3HP regimen is associated with higher treatment completion and lower hepatotoxicity compared to 9H, with evidence on progression to active TB remains exploratory and imprecise. Limited evidence

*Correspondence:
Malaisamy Muniyandi
muniyandi.m@icmr.gov.in

Full list of author information is available at the end of the article

on 6H showed improved treatment completion with 3HP. These findings should be interpreted cautiously as most evidence was derived from heterogeneous observational studies, and the certainty of evidence for main outcomes was low to very low.

Clinical trial number Not applicable.

Keywords Latent tuberculosis infection, Tuberculosis preventive therapy, 3HP regimen, 6H regimen, 9H regimen, Adverse drug reactions, Treatment completion, TB incidence

Introduction

Latent Tuberculosis Infection (LTBI) refers to a condition in which the immune system contains the infection caused by *Mycobacterium tuberculosis* (M. tb), without exhibiting the clinical signs or symptoms of active tuberculosis (TB) [1, 2]. Globally, approximately one-quarter of the world's population, that is about 1.7 to 2 billion people were estimated to have LTBI [3]. The prevalence is substantially higher in low and middle-income countries with high TB incidence, reaching up to one-third of the population, whereas it remains below 15% in most high-income, low-incidence settings [3, 4]. The high TB prevalence in low and middle income countries could be attributed to a large reservoir of LTBI cases and higher rate of progression to active TB [5, 6]. As per the World Health Organisation (WHO), about 1.6 million children under 5 years old who are household contacts of people with bacteriologically confirmed pulmonary TB were eligible for TB preventive treatment (TPT) in 2023 [7]. A higher proportion of the population were susceptible to progression to active TB disease from LTBI due to the presence of risk factors such as diabetes, malnutrition, Human Immunodeficiency Virus (HIV), smoking, poverty, silicosis and immunosuppressive conditions [8].

The identification and management of LTBI is central to global TB control efforts. The WHO recommends TPT for individuals at increased risk of progression to active TB, including people living with HIV (PLHIV) and household contacts, irrespective of HIV status [9]. In the 2018 WHO consolidated guidelines, regimens like six months of daily isoniazid monotherapy (6H), once-weekly isoniazid plus rifapentine for three months (3HP), three months of daily isoniazid plus rifampicin (3HR), and four months of daily rifampicin (4R) received strong recommendations. Additionally, one month of daily isoniazid plus rifapentine (1HP) was also recommended, primarily to improve treatment completion, tolerability, and programmatic feasibility, based on moderate to low certainty evidence [2].

Traditionally, nine months of daily isoniazid (9H) preventive treatment and a 6-month chemoprophylaxis regimen have been widely used under programmatic conditions, particularly for under five children who have been in close contact with individuals exposed to active pulmonary TB as well as PLHIV [10]. Recent evidence increasingly supports the safety and effectiveness of shorter, newer TPT regimens [11–13]. Recent studies have shown that these shorter regimens offer similar preventive efficacy, whether delivered in a monotherapy or as a combination alongside isoniazid [13, 14]. It was reported that the 3HP regimen, with shorter duration leads to improved completion rates [15].

The 3HP regimen is recommended for LTBI as an effective option for eligible populations [16]. Although several LTBI regimens exist, evidence on the 3HP regimen's comparative effectiveness is limited and treatment options differ in duration, feasibility and cost. However, existing reviews differ from our present study in important aspects. The recent systematic review assessed the effectiveness of 3HP across heterogeneous populations at risk, without restricting the comparator to the reference standard isoniazid regimens or focusing exclusively on adults [13]. Similarly, the network meta-analysis relied primarily on indirect comparisons across different regimens, unable to provide regimen-specific, comparative estimates relevant for clinical and policy decisions [17]. Whereas this review focuses exclusively on adults and uses direct pairwise meta-analysis to compare 3HP with the reference 9H regimen as primary comparator and 6H as secondary comparator. The primary outcomes were treatment completion and adverse drug reactions (ADRs). Incidence of active TB was evaluated as an exploratory outcome.

Methodology

Study design

This systematic review was conducted to synthesis the published evidence on the clinical effectiveness of the 3HP regimen for treating LTBI. The review methodology was guided by the principles recommended in the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) framework. This review has been registered with the International Prospective Registry of Systematic Reviews (PROSPERO) (Reg. No: CRD420251079283).

Information sources

A literature search encompassing multiple scientific databases such as PubMed, EMBASE, Cochrane Library and ScienceDirect was performed. We have retrieved all the

pertinent articles which compared the 3HP regimen to the 9H–6H regimens for treating LTBI.

Search strategy

To explore the clinical impact of the 3HP regimen, we developed a structured search strategy grounded in PICO (population, intervention, comparator and outcome) framework. This approach was combined with Medical Subject Headings (MeSH) and Emtree terms to maximize sensitivity across databases. Outcome related terms were used selectively and did not restrict the core search strategy. To ensure comprehensive retrieval, we conducted manual screening of reference lists of included studies and relevant reviews. The detailed search strategies used for each database are presented in supplementary Table S1. The review included studies published between 2001 and 2025.

Inclusion criteria

This review includes studies if they (i) assessed the clinical effectiveness of the 3HP with 9H–6H LTBI regimens, among the adult population aged ≥ 15 years, and (ii) reported at least one of the primary outcome, including treatment completion rates, ADRs and incidence of TB. Eligible articles include both randomized controlled trials (RCTs) as well as observational studies. The studies conducted among general and high-risk groups were also included. The studies were considered irrespective of follow-up status.

Exclusion criteria

Studies were excluded if they were unpublished. Additionally, articles that were not available in English language were excluded unless a translation was available. In this review, the abstract published in conference proceedings and presentations were also excluded.

PICO elements

PICO included persons aged 15 years and above with LTBI. The intervention involved administering three months once weekly rifapentine plus isoniazid (3HP). The primary comparator was nine months of daily isoniazid (9H), while six months of daily isoniazid (6H) was included as a secondary comparator. The main outcomes assessed were treatment completion rate, ADR. Incidence of active TB was evaluated as an exploratory outcome.

Study screening process

The screening of studies was conducted individually by two reviewers (BCK and KC). Any discrepancies were resolved through a third reviewer (MM). Duplicate records were independently identified and removed by two reviewers prior to screening (BCK and KC). The selection process followed a two-stage approach. One was title and abstract screening to identify potentially relevant studies. The next stage was full text screening to assess eligibility based on inclusion criteria. The studies that met all criteria were included in the final analysis. The relevant data from the included studies were summarized. The total number of records identified, along with stepwise filtering process based on eligibility criteria was picturized in PRISMA flow diagram.

Data extraction

A structured extraction form was used to systematically extract data from the eligible studies (Supplementary Annexure), and the data extraction process was piloted on one RCT and one observational study to assess the availability, completeness and consistency of relevant data prior to full extraction. The following information for intervention and comparator groups were collected: name of the author, year of publication, country of study, study population (general, high risk groups), age of the participant, follow-up years and sample sizes. The adherence strategy directly observed therapy (DOT) or self-administered treatment (SAT) was also recorded. The outcome information on treatment completion rates, ADR (Grade 1–5 and Hepatotoxicity) and incidence of TB were also collected. The ADRs were categorized by severity, including hepatotoxicity and grade 1–2 (mild-moderate), grade 3–4 (severe-life-threatening), and grade 5 (fatal) events, as defined in the individual studies. Attempts were made to contact corresponding authors of included studies to obtain missing or unclear data, however no additional information was received.

Data analysis

Extracted data were systematically organized using Microsoft Excel 2013. Quantitative meta-analysis was conducted using R (version 4.5.2) with the "meta" statistical package. The characteristics of the studies were described by frequencies and percentages. Clinical outcomes such as treatment completion rate, ADR and TB incidence were compared between 3HP with 9H and 6H regimens. Clinical effectiveness was quantified using odds ratio (OR) and risk ratio (RR) with 95% confidence interval (CI). For studies with zero events in both arms, a continuity correction was applied by adding 0.5 to the cells. The pooled clinical outcome estimates for the 3HP regimen were synthesized using an inverse-variance weighted random-effects meta-analysis, with between studies heterogeneity estimated using the DerSimonian and Laird method and presented in a forest plot. The 95% CI derived using a normal approximation method. Heterogeneity was assessed across studies using the I^2 statistic. Potential publication bias was also assessed by generating funnel plot. To statistically evaluate the

presence of bias, Egger's test was performed. Further, we performed subgroup analysis for study designs and treatment delivery strategies.

Quality assessment

The included studies were assessed based on its methodological quality using risk of bias assessments. They were conducted using two validated tools (i) RoB 2.0 tool was used for the RCTs [18] and (ii) ROBINS-I tool for observational studies [19]. This was presented using traffic light figures to visually assess potential risk of bias.

Certainty of evidence

The certainty of the evidence was evaluated using a modified GRADE approach tailored for OR and RR estimates. For RCTs, the certainty rating started as high and was downgraded based on risk of bias, inconsistency, indirectness, imprecision and publication bias [20]. For observational studies, the certainty rating began at low and was upgraded based on factors such as larger effect size, dose response gradient and direction of plausible effect.

Sensitivity analysis

The robustness of our meta-analysis findings was assessed using a sensitivity analysis. This was conducted by excluding studies having the high risk of bias. A forest plot was generated to present the pooled estimates for the clinical outcomes associated with the 3HP regimen. The influence of this exclusion was assessed by examining changes in effect size, heterogeneity and statistical significance.

Results

Search results

A total of 260 articles were identified through comprehensive electronic searches across PubMed, EMBASE, Cochrane Library and ScienceDirect databases. Out of these, 34 were removed for being duplicates, 140 were excluded based on title reading and 43 were removed after abstract screening. Due to the lack of effectiveness data, an additional 23 articles were excluded. Following the application of predefined exclusion criteria, a total of 20 studies met the eligibility requirements and were included in the meta-analysis [21–40] (Fig. 1).

Study characteristics

Table 1 shows the characteristics of the included studies comparing the 3HP regimen with 9H and 6H. Of the 20 included studies, only two studies compared 3HP with 6H regimen [21, 37]. Fifteen studies reported adverse events [21–25, 27–29, 31, 33, 35, 36, 38–40], while four studies reported TB incidence [21–23, 29]. Treatment completion reported in all studies except one [27]. With exception of four studies, the 3HP regimen was administered under DOT [24–25, 32, 37], while seven studies reported the use of the 9H regimen with SAT [22, 25–28, 33, 40]. Overall, five studies were RCTs [21–25] and 15 were observational studies [26–40]. All RCTs, except one in South Africa were conducted in developed countries from 2011 to 2018, mostly among high-risk population. However, one was conducted on pregnant women in the USA and another included the general population. Most observational studies (7/15) were done in the USA during 2015–2019 among general population. RCTs had 2–4 years follow-up and observational studies mostly had one year. Sample size ranged from 31 to 3,986 in RCTs and 41 to 4771 in observational studies. The supplementary Table-S2 presents ADR outcomes, including hepatotoxicity, grade 1–2 (mild-moderate), grade 3–4 (severe-life threatening) and grade 5 (death) events reported in 9 [22–24, 27, 31, 35, 36, 38, 39], 6 [22–24, 29, 35, 36], 8 [21–24, 29, 35, 36, 38] and 4 [21, 22, 24, 29] studies, respectively.

Quality assessment

For RCTs, ROB 2.0 tool was used to assess the risk of bias. All five RCT studies had moderate risk of bias, none of them had low and high risk of bias, as illustrated in Fig. S1 [21–25]. Risk of bias for observational studies was evaluated using the ROBINS-I tool. Among 15 studies, 8 had high risk of bias [29–31, 34, 35, 37, 38, 40], another 6 had moderate risk [26–28, 32, 33, 39] and the remaining one had low risk of bias [36] (Supplementary Fig. S2).

LTBI treatment completion rate

In RCTs, the treatment completion rate of 3HP regimen compared with 6–9H, except in one (29% in 3HP and 25% in 9H), was ranged from 82 to 99% and 64–99% respectively (Table 1). Individuals receiving the 3HP regimen were approximately twice as likely to complete treatment compared to those on 9H (OR = 2.05; 95% CI: 1.85–2.28; $p = 0.71$; $I^2 = 0\%$; 8161 persons; high certainty) (Fig. 2a). In the observational subgroup, the treatment completion rate of 3HP regimen and 9H regimen ranged from 65 to 99% and 18–96% respectively (Table 1). Individuals receiving the 3HP were approximately three times likely to complete the treatment as compared to 9H (OR = 3.19; 95% CI: 2.04–4.99; $p < 0.0001$; $I^2 = 80.5\%$; 3287 persons; very low certainty) (Fig. 2a). Inconsistency and risk were observed in included studies (Supplementary Table-S3). The pooled OR of treatment completion of 3HP compared with 6H regimen from two reported studies was 2.91 (95% CI: 0.46–18.55; $p = 0.01$; $I^2 = 84.1\%$; 8155 persons; very low certainty) (Fig. 2b). In the certainty assessment, inconsistency, imprecision and one study with high risk of bias were observed (Supplementary Table-S4).

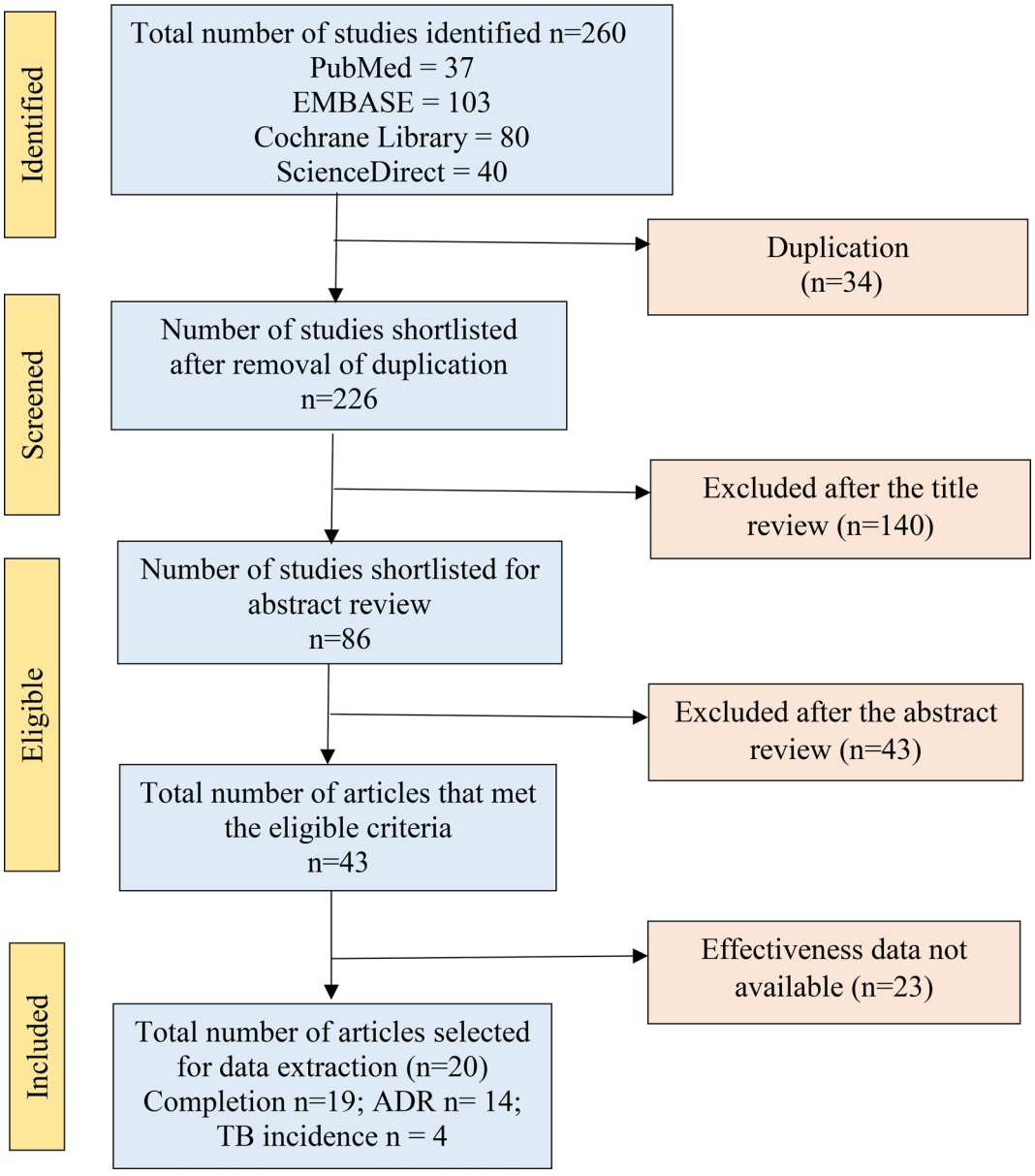

Fig. 1 PRISMA Flow diagram for the review on clinical effectiveness and safety of 3HP for LTBI

When aggregating data across all included studies, the treatment completion rate for the 3HP regimen ranged from 65 to 99%. Persons in the 3HP regimen is about three times more likely to complete the treatment as compared to 9H regimen (OR = 2.81; 95% CI: 2.05–3.86; $p < 0.0001$; $I^2 = 78.9\%$; 11448 persons; low certainty) (Fig. 2a). Inconsistency in the results with heterogeneity noted and risk were observed in the included studies (Supplementary Table-S3). Sensitivity analysis was conducted after excluding seven studies identified as having a high risk of bias [29, 31, 34, 35, 37, 38, 40] and a similar result was found after the analysis (OR = 2.71; 95% CI: 2.06–3.56; $p = 0.03$; $I^2 = 50.5\%$) (Supplementary Fig. S3). Furthermore, assessment of publication bias using a funnel plot (Fig. 3) revealed moderate asymmetry suggesting minimal bias. No visual evidence of publication bias was detected, a finding further supported by results of Egger's test (t = 1.43, df = 17, $p = 0.17$).

Additionally, subgroup analyses were performed based on treatment delivery strategies. In the DOT subgroup, persons receiving the 3HP regimen under DOT were about 3.5 times more likely to complete treatment compared to those receiving 9H regimen under DOT (OR = 3.49; 95% CI: 1.97–6.20; $p < 0.0001$; $I^2 = 80.5\%$) (Supplementary Fig. S4). In the DOT vs. SAT subgroup, persons receiving 3HP under DOT were about two times more likely to complete treatment compared to those receiving 9H under SAT (OR = 2.12; 95% CI: 1.45–3.09;

Table 1 Basic characteristics, treatment outcomes and adverse drug reactions of 3-months once-weekly isoniazid and rifapentine regimen (3HP) and Daily isoniazid monotherapy regimen for 6-9-months (6H/9H) for the treatment of LTBI

Author & yr.	Country	Risk group	Age (yr.), (Mean ± SD /median IQR)	Follow-up (yr.)	Regimen		Sample Size		Treatment completion				Any Adverse Drug Reaction				TB cases (Exploratory)			
					Intervention	Control	Intervention	Control	Intervention		Control		Intervention		Control		Intervention		Control	
RCT									*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
Martinson et al. [20], 2011	South Africa	PLHIV	30.4 (26.4–34.7)	4	3HP + DOT	6H + SAT	328	327	324	99	323	99	217	66	216	66	24	7	22	7
Sterling et al. [21], 2011	USA, Brazil, Spain & Canada	Close contact	35 (25–46)	3	3HP + DOT	9H + SAT	3986	3745	3273	82	2585	69	195	5	139	4	4	0.1	8	0.3
Sun et al. [22], 2018	Taiwan	Close contact	31.7 ± 15	2	3HP + DOT	9H + DOT	132	131	118	89	102	78	65	49	33	25	0	0	0	0
Moro et al. [23]. 2018	USA	Pregnant	23 (21–30)	3	3HP + DOT/Self	9H + DOT/ SAT	31	56	9	29	14	25	0	0	7	13	NA	-	NA	-
Denholm et al. [24], 2017	Australia and new Zealand	General	NA	NA	3HP + SAT	9H + SAT	40	40	36	90	34	85	3	8	0	0	NA	-	NA	-
Observational																				
Lines et al. [25], 2015	USA	General	38.7 ± 16.2	1	3HP + DOT	9H + SAT	45	94	35	78	49	52	NA	-	NA	-	NA	-	NA	-
Bliven -Sizemore et al. [26], 2015	USA, Canada, Brazil & Spain	HCV	45	NA	3HP + DOT	9H + SAT	3545	3317	NA	-	NA	-	15	0	61	2	NA	-	NA	-
Stennis et al. [27], 2015	USA	General	32 (22–47)	1	3HP + DOT	9H + SAT	302	92	196	65	42	46	13	4	0	0	NA	-	NA	-
Huang et al. [28], 2016	Taiwan	Contacts	35 (13–75)	1	3HP + DOT	9H + DOT	101	590	98	97	515	87	3	3	28	5	0	0	2	0
Juarez-reyes et al. [29], 2016	USA	Prisoner	39 (31–48)	1	3HP + DOT	9H + DOT	91	154	77	85	28	18	20	22	NA	-	NA	-	NA	-
Yamin et al. [30], 2016	USA	General	41.6 ± 12.9	1	3HP + DOT	9H + DOT	53	115	42	79	75	65	11	21	25	22	NA	-	NA	-
Mcclintock et al. [31], 2017	USA	General	43.6	1	3HP + DOT/ SAT	9H + DOT/ SAT	87	224	74	85	115	51	NA		NA	-	NA	-	NA	-
Macaraig et al. [32], 2018	USA	General	35.6 ± 17	1	3HP + DOT	9H + SAT	125	55	99	79	27	49	2	2	2	4	NA	-	NA	-
Wheeler et al. [33], 2019	USA	Prisoner	NA	4	3HP + DOT	9H + DOT	122	92	79	65	39	-	NA	-	NA	-	NA	-	NA	-
Feng et al. [34], 2020	Taiwan	General	54.9 ± 17.2	1	3HP + DOT	9H + DOT	166	65	147	89	47	72	15	9	7	11	NA	-	NA	-

Table 1 (continued)

Author & yr.	Country	Risk group	Age (yr.), (Mean ± SD /median IQR)	Follow-up (yr.)	Regimen		Sample Size		Treatment completion				Any Adverse Drug Reaction				TB cases (Exploratory)			
					Intervention	Control	Intervention	Control	Intervention		Control		Intervention		Control		Intervention		Control	
RCT									*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
Shu-yung lin et al. [35], 2021	Taiwan	Dialysis	56.6 ± 13.0	6	3HP + DOT	9H + DOT	50	41	41	82	25	61	48	96	37	90	NA	-	NA	-
Yom An et al. [36], 2024	Cambodia	General	27 ± 20.4	6	3HP	6H	2729	4771	2713	99	4589	96	NA	-	NA	-	NA	-	NA	-
Huang et al. [37], 2021	Taiwan	Diabetes	64.2 ± 9.7	NA	3HP + DOT	9H + DOT	138	62	116	84	49	79	108	71	33	53	NA	-	NA	-
Ting-Fang et al. [38], 2021	Taiwan	General	70.4 ± 19.8	NA	3HP + DOT	9H + DOT	105	155	96	91	108	72	14	13	31	29	NA	-	NA	-
Sweeney et al. [39], 2017	Bhutan	General	NA	NA	3HP + DOT	9H + SAT	82	81	58	71	61	75	19	23	12	15	NA	-	NA	-

$p = 0.0136$; $I^2 = 66.7\%$). Furthermore, persons those receiving treatment under mixed deliveries the odds of the treatment completion was 2.70 times higher compared to 9H.

ADR due to LTBI treatment regimens

A wide range of ADRs (0–96%) was reported across LTBI treatment regimens in the included studies (Table 1). In RCTs, the reported ADR due to 3HP regimen ranged from 0 to 66%, in 6H regimen 66% and 9H regimen ranged from 0 to 25%. Among observational studies, only in two studies, the ADR was 50–96% and in other studies, a similar range of ADR (0–29%) was observed (Table-1). In RCTs subgroup, the pooled estimate of ADR due to 3HP was 53% higher as compared to 9H regimen (RR = 1.53; 95% CI: 0.96–2.44; p = 0.05; I^2 = 61.5%; 8161 persons; moderate certainty). However, the CI included unity, indicating that the difference was not statistically significant. Moderate heterogeneity and the wide CI indicate the presence of inconsistency and imprecision in the estimates (Supplementary Table-S5). Among observational subgroup, the pooled estimates of ADR due to 3HP was 14% lesser as compared to 9H regimen (RR = 0.86; 95% CI: 0.61–1.23; $p < 0.0001$; I^2 = 78.9%; 9240 persons; very low certainty). Overall estimates of ADR due to 3HP was 1% higher as compared to 9H regimen (RR = 1.01; 95% CI: 0.76–1.33; $p < 0.0001$; I^2 = 78.5%; 17401 persons; very low certainty) (Fig. 4). Sensitivity analysis after removing five high risk studies showed that ADR due to 3HP was 8% lesser as compared to 9H regimen (RR = 0.92; 95% CI: 0.61–1.38; $p < 0.0001$; I^2 = 85%) (S5 Fig) [29, 31, 35, 38, 40]. No evidence of publication bias was detected, a finding further supported by results of Egger's test (t=-0.27; df = 13; p = 0.79) (Supplementary Fig. S6).

The supplementary Table-S2 shows hepatotoxicity across studies due to 3HP and 9H regimen except one study (12% and 27%) ranges from 0 to 2% and 0–9% respectively. In RCTs, the pooled estimate of hepatotoxicity in 3HP was 71% lesser as compared to 9H regimen (RR = 0.29; 95% CI: 0.12–0.70; p = 0.02; I^2 = 73.7%). Among observational subgroup, the pooled estimate of 3HP was 0.24 (95% CI: 0.14–0.39; p = 0.85; I^2 = 0%). Overall, the pooled estimate of hepatotoxicity was 74% lesser in 3HP as compared to 9H regimen (RR = 0.26; 95% CI: 0.18–0.38; p = 0.29; I^2 = 17.7%) (Supplementary Fig. S7).

Grade 1–2 (mild-moderate ADR) event reported across studies due to 3HP and 9H regimen except one study (66% and 34%) ranges from 0 to 13% and 0–11% respectively. In RCTs, the pooled estimate of grade 1–2 ADR due to 3HP was 12% higher as compared to 9H regimen (RR = 1.12; 95% CI: 0.33–3.84; p = 0.01; I^2 = 78.3%). Among observational subgroup, the pooled estimate of 3HP was 1.76 (95% CI: 1.09–2.82; p = 0.35; I^2 = 4.8%). Overall, the pooled estimate was 38% higher as compared

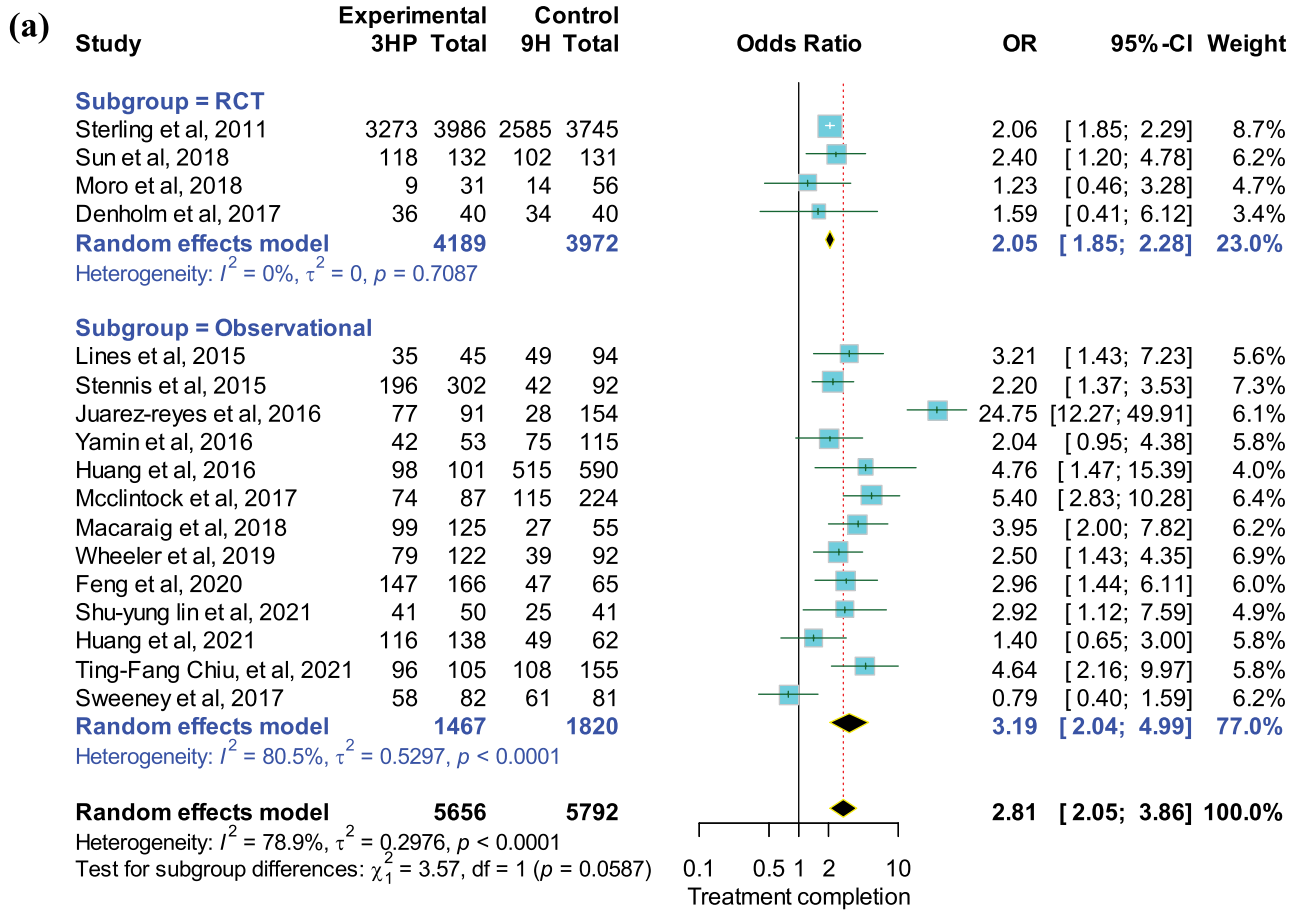

Fig. 2 Forest plot depicting odds ratios comparing treatment completion rate for (**a**) 3HP vs. 9H; (**b**) 3HP vs. 6H regimen among persons with LTBI

to 9H regimen (RR = 1.38; 95% CI: 0.73–2.59; p = 0.0009; I^2 = 75.9%) (Supplementary Fig. S8a). Grade 3–4 (severe-life threatening ADR) event reported across studies due to 3HP and 9H regimen ranges from 0 to 13% and 0–9% respectively. In RCTs, the pooled estimate of 3HP was 0.91 (95% CI: 0.77–1.08; p = 0.39; I^2 = 0%). Among observational subgroup, the pooled estimate of 3HP was 1.85. Overall, the pooled estimate of grade 3–4 ADR due to 3HP was 19% higher as compared to 9H (RR = 1.19 95% CI: 0.78–1.82; p = 0.30; I^2 = 16.6%) (S8b Fig). Grade 5 (death) event reported across studies due to 3HP and 9H regimen except one study (5% in 3HP and 8% in 6H) ranges from 0 to 2% and 0–1% respectively. Overall, the pooled estimate of grade 5 ADR due to 3HP was 23% lesser as compared to 9H regimen (RR = 0.77; 95% CI: 0.49–1.22; p = 0.77; I^2 = 0%) (S8c Fig). Since, CI crossed unity, there is an uncertainty in the effect estimate and the difference was not statistically significant.

Incidence of TB (exploratory outcome)

The RCTs subgroup reported the incidence of TB after the LTBI treatment, out of 3391 patients treated with

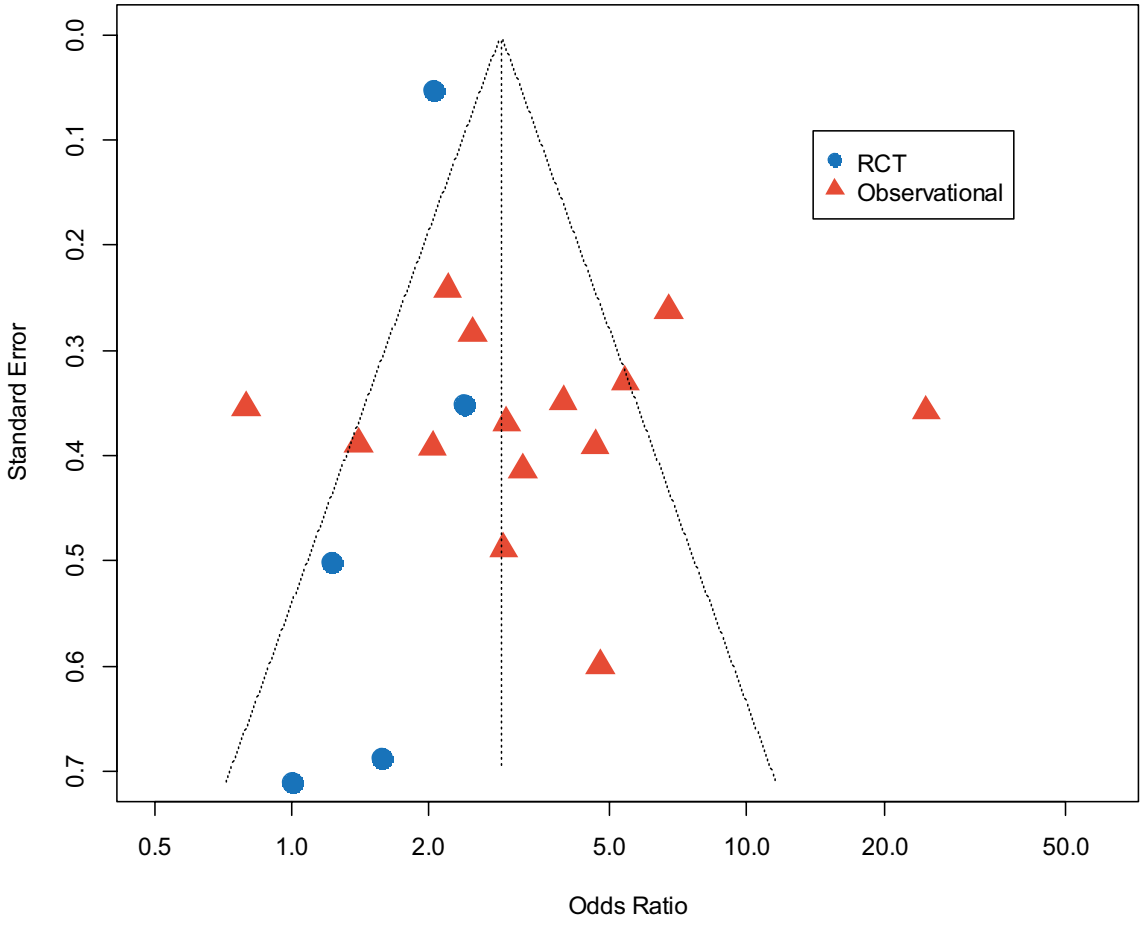

Fig. 3 Funnel plot for odds ratio for comparing the completion rate of 3HP vs. 6H and 9H

3HP, 4 developed TB and among 2687 treated with 9H, 8 developed TB. The estimated incidence of TB was 118 and 298 per 100,000 in 3HP and 9H respectively (Table-1). The exploratory pooled analysis revealed that individuals completing the 3HP regimen had a lower risk of developing TB compared to 9H; however, this difference was not statistically significant (RR = 0.42; 95% CI: 0.13–1.33; $p = 0.70$; $I^2 = 0\%$; 6078 persons; moderate certainty) (Supplementary Table-S6). Overall estimates of incidence of TB after completing LTBI treatment with 3HP was lower as compared to 9H (RR = 0.47; 95% CI: 0.16–1.38; $p = 0.80$; $I^2 = 0.0\%$; 6691 persons; moderate certainty) (Fig. 5) but the CI crossed unity, indicating no statistically significant difference. The wide CI in both analyses indicates there is a considerable uncertainty in the effect estimates. Given the limited number of studies and small number of events, these findings should be interpreted cautiously and do not permit firm conclusions regarding the effect of 3HP on progression to active TB. Only one RCT study directly compared 3HP with 6H, reporting TB incidence 7% in both treatment groups.

Discussion

In this systematic review of studies involving LTBI treatment for adults, we found that 3HP was associated with higher treatment completion compared with the longer 9H and 6H regimens. Our pooled estimates of included studies showed individuals receiving 3HP were nearly three times more likely to complete treatment than those receiving 9H, and they also showed a similarly higher completion rate compared with 6H. The finding of higher treatment completion rates with 3HP highlights the advantage of shorter regimen in improving LTBI treatment adherence and completion. The higher completion rates could be attributed to shortening of treatment duration from nine or six months to three months, ease of medication with reduced drug intake from daily to once weekly and reduced risk of fatigue in individuals [41–43].

Overall ADRs were slightly higher with 3HP and specifically hepatotoxicity and mortality were lower in 3HP compared to 9H regimen, but the difference was not statistically significant. The exploratory analysis of incidence of active TB following LTBI treatment was also lower in the 3HP compared to 9H group, but CIs were wide and the difference was not statistically significant limiting the

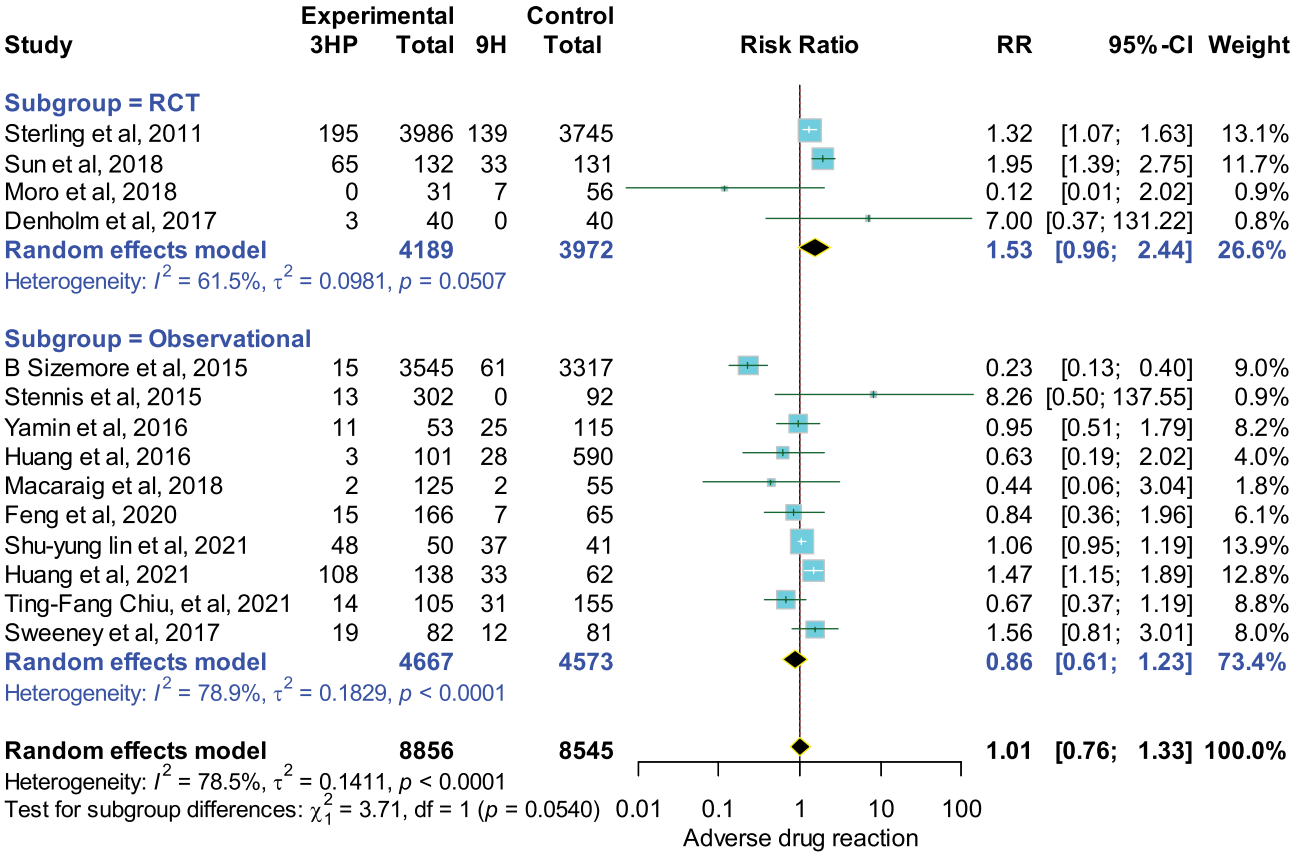

Fig. 4 Forest plot depicting Risk ratio for comparing the any adverse drug reactions of 3HP vs. 9H regimens among persons with LTBI

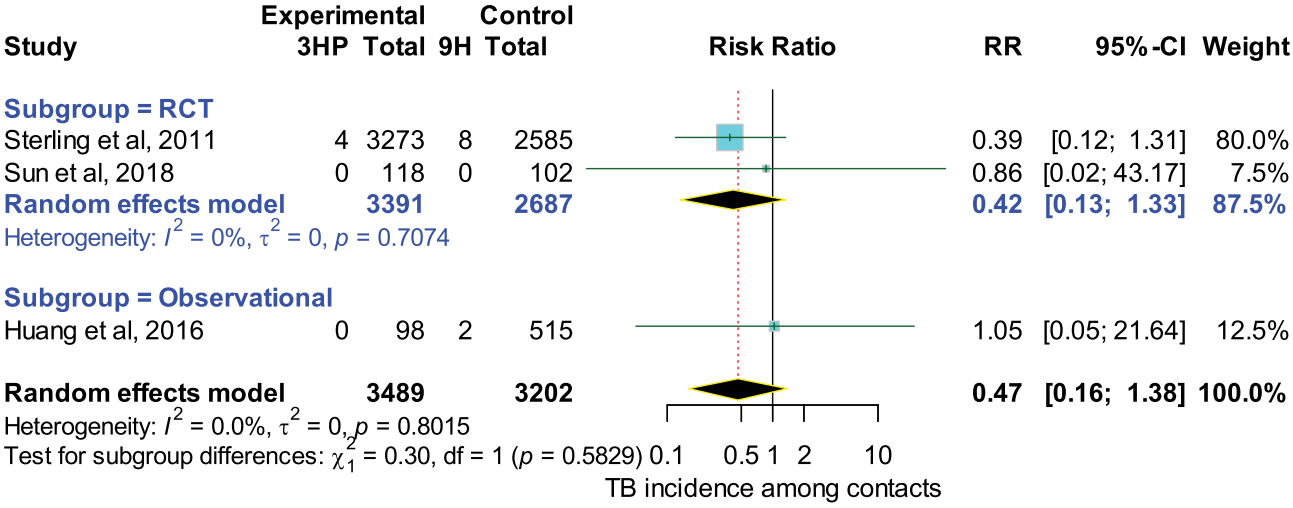

Fig. 5 Exploratory Forest plot depicting Risk ratio for comparing the TB incidence of 3HP vs. 9H regimens among contacts with LTBI

strength of the evidence. Earlier systematic reviews have also reported similar improved completion rates and acceptable safety limits for shorter rifamycin based regimens [17, 44, 45].

Substantial heterogeneity was observed for several outcomes, particularly treatment completion and overall ADRs (I^2 >75%). This variability may be attributed to differences in study populations, intervention delivery methods and outcome definitions across studies. Although a random effects model and subgroup analyses were employed to account for between study variability, residual heterogeneity persisted. Most of the conclusions in this review were driven by observational studies, which showed substantial heterogeneity for several

outcomes (I^2>75%). In contrast, the RCT subgroup analyses demonstrated lower heterogeneity (I^2<75%) across the main outcomes, providing more consistent estimates. In addition, the certainty of evidence for key outcomes, including treatment completion and overall adverse drug reactions, was graded as low to very low using the GRADE approach, primarily because of risk of bias, inconsistency and imprecision. Therefore, findings based predominantly on observational evidence should be interpreted with caution.

An important consideration in interpreting our findings is the mode of treatment delivery. Most randomized trials and many observational studies implemented 3HP using DOT, whereas 9H/6H was often SAT. DOT likely contributed to the higher completion rates observed with 3HP in some settings. However, programmatic data and pragmatic trials have demonstrated that self-administered 3HP can also achieve high completion, particularly when combined with adherence support strategies [25, 46]. The relevance of DOT versus SAT is particularly important for scale-up in resource limited settings, where DOT may not be feasible. Our findings therefore suggest that the shorter duration of 3HP and flexible delivery models can be considered as feasible.

Since the medicines used to treat LTBI can cause side effects, there is a need to consider risk and benefits of a new regimen. Common adverse events include gastrointestinal issues like nausea, vomiting, abdominal pain, fatigue, weakness and rashes. More serious reactions, such as liver problems (indicated by jaundice or dark urine), tingling or numbness in extremities and easy bruising or bleeding, require immediate medical attention [46, 47]. In the current study, our analysis of grade-wise adverse outcomes adds further nuance. While overall ADRs were slightly more in 3HP, this was mainly because of mild to moderate (grade 1–2) events. In contrast, severe (grade 3–4) events were comparable between regimens, as the CI included unity, indicating no statistically significant difference. The hepatotoxicity was lower with 3HP. Moderate heterogeneity and the wide CI indicate the presence of inconsistency and imprecision in the estimates. This finding aligns with prior evidence showing that rifapentine based regimens may be associated with systemic or flu-like reactions but guarantee a substantially lower risk of isoniazid related liver injury [27, 47]. Low rates of ADRs due to 3HP regimen were also reported, which were mild, well-tolerated by patients and manageable by clinicians [46–48]. These low and less serious ADRs leads to fewer treatment interruptions. A cohort study reported that only 2% of patients on 3HP regimen were lost-to-follow-up due to ADRs as compared to 4% in 9H regimen [33].

The 3HP has also shown comparable efficiency in preventing TB disease [22]. In our exploratory analysis, the overall estimates of incidence of TB after completing LTBI treatment with 3HP was lower as compared to 9H regimen, However, this difference was not statistically significant, and the CI were wide, indicating substantial imprecision. Notably, only three studies contributed to this outcome, with a small number of events, thereby limiting the statistical power of the analysis. Given these limitations, the available evidence supports comparable protection rather than definitive superiority of 3HP in preventing active TB. While modelling estimates suggest that in high burden setting shifting to 3HP regimen could lower overall TB incidence due to its higher adherence rate, our synthesis underscore uncertainty of evidence to make such recommendations [48].

Further, shorter duration regimens are increasingly preferred over longer courses for LTBI treatment, owing to their advantages in clinical feasibility and programmatic efficiency. Our findings add to the body of evidence on TB prevention strategies in high burden settings, where losses across the LTBI cascade of care remain substantial. While these findings suggest the probable benefit of 3HP, still the limited number of studies included and higher heterogeneity may impact the quality of the evidence.

Strengths and limitations of the study

This review has several strengths, such as its comprehensive synthesis of both randomized and real-world evidence. Rigorous risk of bias assessment, sensitivity analyses excluding high risk studies and evaluation of publication bias all support the robustness of our findings. Additionally, stratification by grade-wise ADR severity and explicit assessment of hepatotoxicity provide clinically meaningful insights beyond aggregate safety outcomes. Nevertheless, considerable limitations should be noted. This review has the imbalance in comparator evidence, with most studies comparing 3HP to 9H and only a small number evaluating 3HP versus 6H. As a result, conclusions regarding 3HP compared with 6H should be interpreted with caution. Most of the conclusions were driven by observational subgroup, which showed substantial heterogeneity for several outcomes, particularly treatment completion and overall adverse events, reflecting differences in populations, settings, and delivery strategies. Finally, the number of studies reported TB incidence was small, limiting statistical power to detect differences in TB progression. This also limited the ability to assess whether the effectiveness of 3HP varies across different epidemiological settings.

Conclusion

This systematic review and meta-analysis highlights the limited quality of evidence to support the clinical utility of the 3HP regimen for the treatment of LTBI. While

the 3HP regimen was associated with higher treatment completion and lower hepatotoxicity compared to the 9H regimen, with evidence on progression to active TB remains exploratory and imprecise, still the heterogeneity and limited studies constrain strong recommendation. Due to limited evidence directly comparing 3HP with 6H, only treatment completion could be synthesized for this comparison, which favoured 3HP. However, these findings should be interpreted with caution because most estimates were driven by observational studies with substantial heterogeneity, and the certainty of evidence for key outcomes was low to very low using the GRADE approach.

Abbreviations

TB	Tuberculosis
LTBI	Latent tuberculosis infection
TPT	Tuberculosis preventive treatment
3HP	Three months of once-weekly Isoniazid (H) plus Rifapentine (P)
6H	Six months of daily Isoniazid (H)
9H	Nine months of daily Isoniazid (H)
ADR	Adverse drug reaction
HIV	Human immunodeficiency virus
WHO	World Health Organization
DOT	Directly observed therapy
SAT	Self-administered therapy
RCT	Randomized controlled trial
RR	Risk ratio
OR	Odds ratio
CI	Confidence interval
GRADE	Grading of recommendations assessment, development, and evaluation

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12879-026-13607-w.

Supplementary Material 1

Acknowledgements
The authors thank the investigators of the primary studies included in this systematic review for making their data publicly available.

Author contributions
MM: Study conception, design, data collection, analysis & draft manuscript preparation; BCK: Design, data collection, analysis & draft manuscript preparation; KC: Design, data collection, analysis & draft manuscript preparation; BB: Design & data collection; BP: Data collection & draft manuscript preparation; VJ: Design, data collection & analysis; VT: Design & data collection; KN: Study conception, design & analysis. All authors reviewed the results and approved the final version.

Funding
This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data availability
All data analysed during this systematic review are included in this published article and its supplementary materials.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Health Economics, ICMR-National Institute for Research in Tuberculosis, No.1, Mayor Sathyamoorthy Road, Chennai, Tamil Nadu 600031, India
[2]Department of Social Behavioural Research, ICMR-National Institute for Research in Tuberculosis, Chennai, Tamil Nadu 600031, India

Received: 30 January 2026 / Accepted: 12 May 2026
Published online: 04 June 2026

References

1. Alsdurf H, Hill PC, Matteelli A, Getahun H, Menzies D. The cascade of care in diagnosis and treatment of latent tuberculosis infection: a systematic review and meta-analysis. Lancet Infect Dis. 2016;16(11):1269–78.
2. World Health Organization. Latent tuberculosis infection: updated and consolidated guidelines for programmatic management. Geneva: WHO. 2018. Available from: https://www.who.int/publications/i/item/9789241550239. Accessed on 20th June 2025.
3. Cohen A, Mathiasen VD, Schön T, Wejse C. The global prevalence of latent tuberculosis: a systematic review and meta-analysis. Eur Respir J. 2019;54(3):1900655.
4. Houben RMGJ, Dodd PJ. The global burden of latent tuberculosis infection: a re-estimation using mathematical modelling. PLoS Med. 2016;13(10):e1002152.
5. Chauhan A, George N, Sharma A, Gupta S, Chatterjee P, Vashist RP, et al. The prevalence of tuberculosis infection in India: a systematic review and meta-analysis. PLoS ONE. 2023;18(6):e0287313.
6. Kiazyk S, Ball TB. Latent tuberculosis infection: An overview. Can Commun Dis Rep. 2017;43(3/4):62–6.
7. World Health Organization. Global tuberculosis report 2024. Geneva, World Health Organization. 2024. Available from: https://www.who.int/teams/global-programme-on-tuberculosis-and-lung-health/tb-reports/global-tuberculosis-report-2024. Accessed on 18th May 2025.
8. Lönnroth K, Jaramillo E, Williams BG, Dye C, Raviglione M. Drivers of tuberculosis epidemics: the role of risk factors and social determinants. Soc Sci Med. 2009;68(12):2240–6.
9. World Health Organization. WHO consolidated guidelines on tuberculosis: module 1: prevention: tuberculosis preventive treatment. Geneva: WHO. 2020. Available from: https://www.who.int/publications/i/item/9789240001503. Accessed on 07th July 2025.
10. Tadesse Y, Gebre N, Daba S, Gashu Z, Habte D, Hiruy N, et al. Uptake of isoniazid preventive therapy among under-five children: TB contact investigation as an entry point. PLoS ONE. 2016;11(5):e0155525.
11. World Health Organization. Recommended TPT regimens. TB Knowledge Sharing Platform. Available from: https://tbksp.who.int/en/node/1271. Accessed on 26th July 2025.
12. Ruan QL, Li T, Zhang Q, Zhao J, Wang L, Guo H, Chen H, Liu W. Efficacy and safety of a novel short course rifapentine and isoniazid regimen for the preventive treatment of tuberculosis in Chinese silicosis patients: a pilot study (SCRIPT-TB). Emerg Microbes Infect. 2025;14:2502010.
13. Ilavarasan I, Ariharanathan V, Devi CS. Efficacy of short-course weekly isoniazid and rifapentine regimen as tuberculosis preventive treatment among population at risk of developing disease: a systematic review and meta-analysis. J Clin Diagn Res. 2024;18(1):1–9.
14. Radtke KK, Dodd LE, Williams PJ, Deshpande D, Keung CF, Berman J, Peloquin CA, Dooley KE, Weiner M, Savic RM. Comparative efficacy of rifapentine alone and in combination with isoniazid for latent tuberculosis infection: a translational pharmacokinetic-pharmacodynamic modeling study. Antimicrob Agents Chemother. 2021;65(8):e00317–21.
15. Bhargava A. The 3HP regimen for tuberculosis preventive treatment: safety, dosage and related concerns during its large-scale implementation in countries like India. Lancet Reg Health Southeast Asia. 2024;31:100234.
16. Borisov AS, Bamrah Morris S, Njie GJ, Winston CA, Burton D, Goldberg S, et al. Update of recommendations for use of once-weekly isoniazid-rifapentine

regimen to treat latent Mycobacterium tuberculosis infection. MMWR Morb Mortal Wkly Rep. 2018;67(25):723–6.
17. Zenner D, Beer N, Harris RJ, Lipman MC, Stagg HR, van der Werf MJ. Treatment of latent tuberculosis infection: an updated network meta-analysis. Ann Intern Med. 2017;167(4):248–55.
18. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366:l4898.
19. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, Henry D, Altman DG, Ansari MT, Boutron I, Carpenter JR. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ. 2016; 355.
20. Schünemann H, Broz J, Guyatt G, Oxman A, editors. GRADE handbook for grading quality of evidence and.
21. Martinson NA, Barnes GL, Moulton LH, Msandiwa R, Hausler H, Ram M, McIntyre JA, Gray GE, Chaisson RE. New regimens to prevent tuberculosis in adults with HIV infection. N Engl J Med. 2011;365(1):11–20.
22. Sterling TR, Villarino ME, Borisov AS, Shang N, Gordin F, Bliven-Sizemore E, Hackman J, Hamilton CD, Menzies RI, Kerrigan A, Weis SE, Weiner M, Wing D, Conde MB, Bozeman L, Horsburgh CR Jr, Chaisson RE. Three months of rifapentine and isoniazid for latent tuberculosis infection. N Engl J Med. 2011;365(23):2155–66.
23. Sun HY, Huang YC, Huang YS, Su WJ, Huang WC, Chien YJ, Chen YM, Chen SY, Chen MY. Twelve-dose weekly rifapentine plus isoniazid for latent tuberculosis infection: a multicentre randomised controlled trial in Taiwan. Tuberculosis. 2018;111:121–6.
24. Moro RN, Scott NA, Vernon A, Goldberg SV, Schwartzman K, Reves R, Belknap R, Villarino ME, Sterling TR. Exposure to latent tuberculosis treatment during pregnancy. The PREVENT TB and the iAdhere trials. Ann Am Thorac Soc. 2018;15(5):570–80.
25. Denholm JT, McBryde ES, Eisen D, Street A, Matchett E, Chen C, Shultz T, Biggs B, Leder K. SIRCLE: a randomised controlled cost comparison of self-administered short-course isoniazid and rifapentine for cost-effective latent tuberculosis eradication. Intern Med J. 2017;47(12):1433–6.
26. Lines G, Hunter P, Bleything S. Improving treatment completion rates for latent tuberculosis infection: a review of two treatment regimens at a community health center. J Health Care Poor Underserved. 2015;26(4):1428–39.
27. Bliven-Sizemore EE, Sterling TR, Shang N, Benator D, Schwartzman K, Reves R, Swindells S, Mac Kenzie WR, Menzies RI, LoBue P, Villarino ME. Three months of weekly rifapentine plus isoniazid is less hepatotoxic than nine months of daily isoniazid for LTBI. Int J Tuberc Lung Dis. 2015;19(9):1039–44.
28. Stennis NL, Burzynski JN, Herbert C, Nilsen D, Macaraig M. Treatment for tuberculosis infection with 3 months of isoniazid and rifapentine in New York City Health Department clinics. Clin Infect Dis. 2016;62(1):53–9.
29. Huang YW, Yang SF, Yeh YP, Tsao TCY, Tsao SM. Impacts of 12-dose regimen for latent tuberculosis infection: treatment completion rate and cost-effectiveness in Taiwan. Med (Baltim). 2016;95(36):e4126.
30. Juarez-Reyes M, Gallivan M, Chyorny A, O'Keeffe L, Shah NS. Completion rate and side-effect profile of three-month isoniazid and rifapentine treatment for latent tuberculosis infection in an urban county jail. Open Forum Infect Dis. 2016;3(1):ofw038.
31. Yamin A, Bornstein E, Hensel R, Mohamed O, Kempker RR. Predictors of latent tuberculosis infection treatment after introduction of a new regimen: a retrospective cohort study at an inner city clinic. Open Forum Infect Dis. 2016;3(1):ofw039.
32. McClintock AH, Eastment MC, McKinney CM, Narita M, Dhanireddy S, O'Hare AM, Ohl ME, Schwartzman K. Treatment completion for latent tuberculosis infection: a retrospective cohort study comparing 9 months of isoniazid, 4 months of rifampin and 3 months of isoniazid and rifapentine. BMC Infect Dis. 2017;17:146.
33. Macaraig MM, Jalees M, Lam C, Burzynski J. Improved treatment completion with shorter treatment regimens for latent tuberculous infection. Int J Tuberc Lung Dis. 2018;22(11):1344–9.
34. Wheeler C, Mohle-Boetani J. Completion rates, adverse effects, and costs of a 3-month and 9-month treatment regimen for latent tuberculosis infection in California inmates, 2011–2014. Public Health Rep. 2019;134(1suppl):S71–9.
35. Feng JY, Lin HH, Lin HC, Su WJ, Hsu YH, Wang JY, Hsieh MJ, Su IJ. Safety and treatment completion of latent tuberculosis infection treatment in the elderly population-A prospective observational study in Taiwan. Int J Infect Dis. 2020;96:550–7.
36. Lin SY, Lin WR, Chang CW, Lee JJ, Chen YH, Lin HH, Yu MC. Completion and adverse drug events of latent tuberculosis infection treatment in patients receiving dialysis: predictors and impacts of different regimens in a prospective cohort study. Antimicrob Agents Chemother. 2021;65(4):e02042–20.
37. An Y, Khun KE. Factors associated with incomplete tuberculosis preventive treatment: a retrospective analysis of six-years programmatic data in Cambodia. Sci Rep. 2024;14.
38. Huang HL, Huang WC, Lin KD, Liu SS, Lee MR, Cheng MH, Chin CS, Lu PL, Sheu CC, Wang JY, Lee IT. Completion rate and safety of programmatic screening and treatment for latent tuberculosis infection in elderly patients with poorly controlled diabetic mellitus: a prospective multicenter study. Clin Infect Dis. 2021;73(6):e1252–60.
39. Chiu TF, Yen MY, Shie YH, Huang HL, Chen CC, Yen YF. Determinants of latent tuberculosis infection and treatment interruption in long-term care facilities: A retrospective cohort study in Taiwan. J Microbiol Immunol Infect. 2022;55(6):1310–7.
40. Sweeney TL, Ahern JW, Alston WK. Completion Rate and Safety of 12-Dose Isoniazid and Rifapentine for Latent Tuberculosis in a Predominantly Refugee Cohort. Infect Dis Clin Pract. 2017;25(5):272–4.
41. Pangprasertkul S, Buawangpong N, Pinyopornpanish K, Jiraporncharoen W, Angkurawaranon C. Treatment completion and safety profile of once-weekly 3HP regimen for tuberculosis preventive treatment in children and adolescents: a systematic review. BMC Infect Dis. 2025;25(1):436.
42. Cruz AT, Starke JR. Completion rate and safety of tuberculosis infection treatment with shorter regimens. Pediatrics. 2018;141(2):e20172838.
43. Jaswal M, Farooq S, Madhani F, Noorani S, Salahuddin N, Amanullah F, Khowaja S, Safdar N, Khan A, Yuen C, Keshavjee S, Becerra M, Hussain H, Malik AA. Implementing 3HP vs. IPT as TB preventive treatment in Pakistan. Int J Tuberc Lung Dis. 2022;26(8):741–6.
44. Stuurman AL, Vonk Noordegraaf-Schouten M, van Kessel F, Oordt-Speets AM, Sandgren A, van der Werf MJ. Interventions for improving adherence to treatment for latent tuberculosis infection: a systematic review. BMC Infect Dis. 2016;16:257.
45. Hamada Y, Ford N, Schenkel K, Getahun H. Three-month weekly rifapentine plus isoniazid for tuberculosis preventive treatment: a systematic review. Int J Tuberc Lung Dis. 2018;22(12):1422–8.
46. Menzies D, Adjobimey M, Ruslami R, Trajman A, Sow O, Kim H, Obeng Baah J, Villarino ME, Bliven-Sizemore EE, Gao L, Sun Q, Bonnet M, Jablonski K, Dodd LE, Sterling TR. Uptake and completion of tuberculosis preventive treatment using 12-dose, weekly isoniazid-rifapentine (3HP) regimen in program settings. MMWR Morb Mortal Wkly Rep. 2018;67(22):586–9.
47. Sterling TR, Moro RN, Borisov AS, Phillips E, Shepherd G, Adkinson NF, Weis S, Ho C, Villarino ME, Tuberculosis Trials Consortium, Sterling TR. Flu-like and other systemic drug reactions among persons receiving weekly rifapentine plus isoniazid or daily isoniazid for treatment of latent tuberculosis infection in the PREVENT tuberculosis study. Clin Infect Dis. 2015;61(4):527–35.
48. Tseng SY, Chen HY, Hsueh PR, Huang YF, Kuo YL, Chen CP. Patterns of symptom occurrence and systemic drug reactions (SDRs) with 3HP (iAdhere study). Clin Infect Dis. 2021;73(6):e1304–12.

Publisher's note