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Understanding treatment discontinuation among latent tuberculosis infection: A scoping review integrating evidence within the COM-B framework

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ABSTRACT

Objective: To identify tuberculosis preventive treatment nonadherence mechanisms *via* the Capability, Opportunity, Motivation, and Behavior (COM-B) framework for latent tuberculosis infection patients.

Methods: This study was conducted in accordance with Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews guidelines. Relevant literature reporting factors associated with tuberculosis preventive treatment discontinuation or completion was included. Identified determinants were synthesized and mapped across the COM-B domains.

Results: Twenty-seven studies were included. Treatment discontinuation rates varied widely (2.0%-66.8%), with consistently higher rates observed in longer regimens (6 months of isoniazid, and 9 months of isoniazid) compared with shorter regimens (3 months of isoniazid plus rifapentine, 3 months of isoniazid plus rifampin, and 4 months of rifampin). Adverse drug reactions, particularly hepatotoxicity, emerged as the most consistent predictor of discontinuation, reflecting impaired physical capability. Opportunity-related factors included healthcare system fragmentation, transportation challenges, and limited access to services. Reduced motivation was associated with stigma, low risk perception, and negative treatment beliefs. Interventions such as shorter regimens, patient-centered care, healthcare worker supervision, and digital adherence technologies were associated with improved treatment completion. These findings suggest that treatment discontinuation results from dynamic interactions between treatment-related burden, healthcare accessibility, and patient motivation.

Conclusions: Clinical tolerance, structural and behavioral factors interact to cause latent tuberculosis infection discontinuation. COM-B guides targeted interventions: shorter regimens, adverse drug reaction management, and improved access and motivation.

KEYWORDS: Latent tuberculosis infection; Preventative treatment; Adherence; Treatment discontinuation; COM-B

1. Introduction

Despite the proven effectiveness of tuberculosis preventive therapy (TPT) in reducing progression from latent tuberculosis infection (LTBI) to active tuberculosis (TB), treatment discontinuation among

Summary

Question: What factors are associated with treatment discontinuation among individuals with latent tuberculosis infection when mapped using the COM-B framework?

Findings: Treatment discontinuation among latent tuberculosis infection is influenced by multidimensional factors, including adverse effects, prolonged treatment duration, limited access to healthcare, and psychosocial factors such as stigma and risk perception.

Meanings: A comprehensive, patient-centered approach that integrates clinical, behavioral, and health system aspects within the COM-B framework is necessary to improve adherence and treatment success for latent tuberculosis infection.

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LTBI remains a serious challenge that significantly reduces the effectiveness of TB control programs and potentially perpetuates the transmission chain in the community[1–3]. The effectiveness of TPT relies on completing the full course of treatment. Several studies indicate that TPT completion rates fluctuate widely, with treatment discontinuation rates remaining high, particularly among high-risk populations[4,5]. This suggests that multifaceted factors influence treatment adherence in LTBI. These factors are not limited to clinical characteristics and treatment regimens but also encompass sociodemographic and psychosocial aspects, risk perception, stigma, social support, adverse effects, and the healthcare system[6–8].

Although several studies have identified factors associated with treatment discontinuation in LTBI, the available evidence remains fragmented. Consequently, current interventions are often developed based on isolated predictors rather than integrated behavioral mechanisms, thereby limiting their effectiveness in improving treatment completion[3,5,9]. In addition, variations in definitions of treatment completion or adherence, differences in TPT regimens, and heterogeneity in study populations complicate drawing robust and generalizable conclusions.

Unlike previous reviews that primarily summarized demographic and clinical predictors of TPT completion, this review systematically synthesizes determinants across behavioral, structural, and psychosocial domains using the Capability, Opportunity, Motivation, and Behavior (COM-B) framework. This approach enables identification of modifiable intervention targets and provides a theoretically grounded basis for designing adherence interventions beyond education-only strategies[10]. Psychosocial issues are important determinants of health behavior and adherence to TB treatment[11]. Therefore, educational or counseling interventions are often insufficiently effective in lowering treatment discontinuation among LTBI[12].

The COM-B framework offers a more comprehensive behavioral perspective because it conceptualizes adherence as the result of dynamic interactions among individual capability, environmental opportunity, and motivational processes, rather than socio-demographic or clinical predictors. Capability includes knowledge about latent TB and TPT, awareness of the benefits of treatment, and the ability to manage adverse effects. Opportunity encompasses both social aspects, such as family support, stigma, and structural aspects, including access to health services, flexibility of service hours, and the quality of follow-up care provided by health workers. Meanwhile, motivation encompasses beliefs in the benefits of treatment, perceptions of the risk of developing active TB, self-efficacy, and both reflective and automatic motivation, which are influenced by previous treatment experiences[13]. Understanding how these determinants interact within behavioral domains is essential for developing targeted and sustainable interventions to reduce treatment discontinuation.

By synthesizing evidence through the COM-B framework, this review moves beyond merely identifying predictors of treatment discontinuation and explains the behavioral mechanisms underlying nonadherence. This approach enables the identification of modifiable intervention targets and provides a stronger theoretical basis for designing patient-centered LTBI adherence strategies.

2. Methods

2.1. Study design

This scoping review aims to systematically map the factors associated with treatment discontinuation among individuals with LTBI. We chose this approach because it is well-suited to identifying the scope, characteristics, and types of available evidence, as well as clarifying concepts and research gaps in complex, multidimensional topics. This scoping review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR) guidelines[14]. The research question in this review is “What factors are identified in the existing literature associated with the discontinuation of TPT in individuals with LTBI according to the Capability, Opportunity, and Motivation (COM-B) framework?”

2.2. Strategy of literature searching

A systematic literature search was conducted in the primary electronic databases, including PubMed/MEDLINE, Scopus, and ScienceDirect. These databases were selected because they provide comprehensive coverage of multidisciplinary research, including medicine, public health, psychology, and health behavior, which are highly relevant to the scope of this review. Although additional databases such as Embase, Web of Science, CINAHL, and PsycINFO may provide broader coverage, this review limited the search to three major databases due to resource accessibility and their extensive indexing of biomedical and public health literature. Nevertheless, this limitation may have resulted in the omission of potentially relevant studies

The literature search included articles published between 2000 and February 2026. Articles published during that period were selected to provide a comprehensive overview of the evolving evidence regarding treatment discontinuation in LTBI. This timeframe encompasses several important changes in the management of LTBI, including advances in diagnostic methods, the use of shorter TPT regimens, the implementation of patient-centered care approaches, and increased attention to psychosocial and behavioral factors that

influence treatment adherence. Furthermore, this period allows for a more comprehensive identification of the determinants of treatment discontinuation across diverse populations and healthcare systems.

The search strategy combined controlled vocabulary and free-text terms related to tuberculosis, latent tuberculosis infection, and treatment adherence. An example of the search string used in PubMed was: ('latent tuberculosis' OR 'LTBI') AND ('treatment adherence' OR 'treatment completion'). In addition, a snowballing approach was employed to search the reference lists of relevant articles and identify further studies. Full search strategies for all databases are provided in Supplementary Table 1.

2.3. Inclusion and exclusion criteria

Inclusion criteria in this review include studies involving (a) individuals with latent tuberculosis infection (LTBI) who received TPT, (b) studies reporting factors associated with discontinuation, non-completion, or completion of TPT, and (c) studies with quantitative, qualitative, or mixed-methods designs. Exclusion criteria include (a) studies involving only active TB patients, (b) articles that do not explicitly discuss the discontinuation of TPT, and (c) articles published as editorials, reviews, case series or reports, letters to the editor, comments, protocols, and conference abstracts without full text.

2.4. Process of study selection

The article selection process was conducted systematically using the web-based application Rayyan, which is designed to facilitate literature screening process in both systematic and scoping reviews. All references retrieved from various electronic databases were first imported into reference management software to identify and remove duplicate records, then exported to Rayyan for further screening. Before the formal screening process, both reviewers conducted a calibration exercise on a subset of articles to ensure a consistent understanding of the eligibility criteria. During the title/abstract

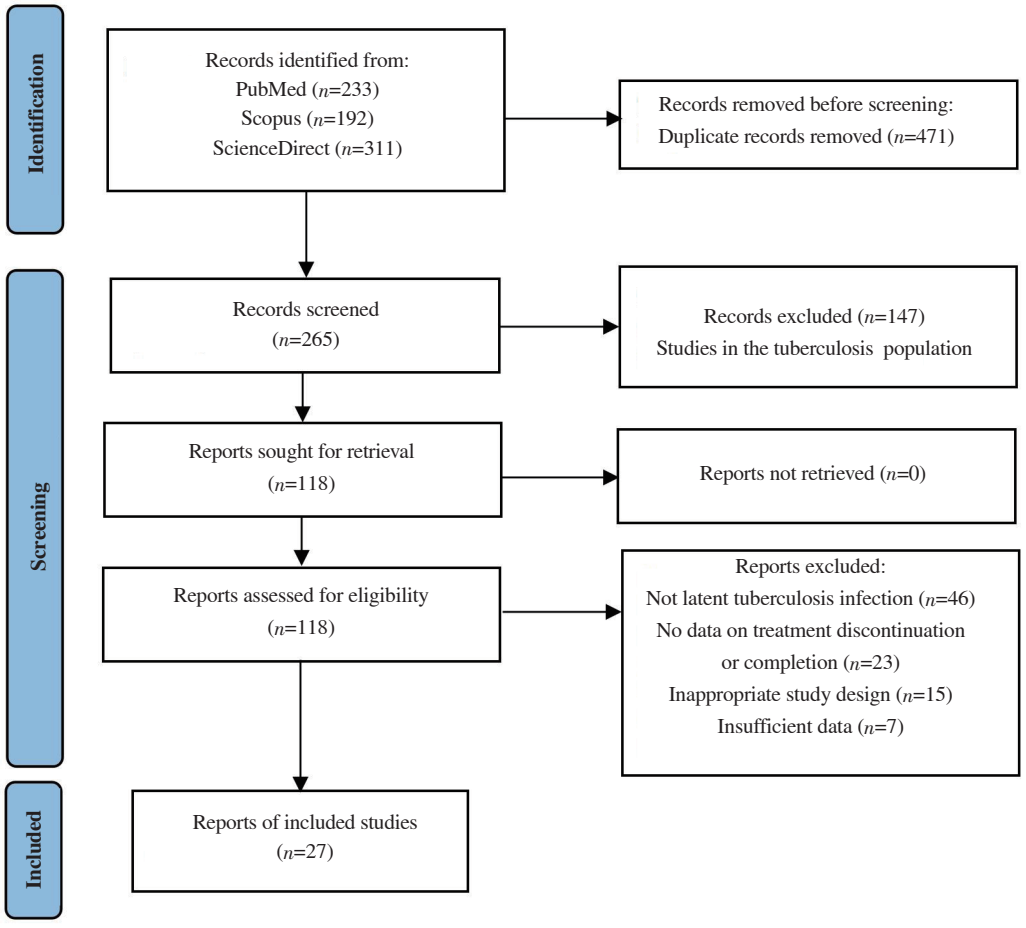

Figure 1. Flowchart of the articles included.

and full-text screening stages, studies were assessed independently by two reviewers (ONP, TP) using the Rayyan platform with the blinding feature enabled to minimize selection bias. All decisions (include, exclude, or unsure) were recorded within Rayyan, and discrepancies between reviewers were systematically documented. Disagreements were resolved through discussion, and when consensus could not be reached, a third reviewer (JJ, EPY, AYN) was consulted to make the final decision. Articles considered relevant or potentially relevant were then advanced to the full-text review stage to determine their final eligibility for inclusion in the review. The study selection process was reported using the PRISMA-ScR flow diagram.

2.5. Data extraction

Data from all studies that met the inclusion criteria were extracted using a standardized data extraction form. The form was designed to collect key information from each included article, including study characteristics, research methods, population characteristics, TPT regimens, and key findings related to treatment discontinuation in LTBI. The extracted information included author names, study location, year of publication, study design, sample size, and factors associated with treatment discontinuation or success. Finally, the identified factors were categorized into the domains of Capability, Opportunity, and Motivation based on the COM-B framework. The categorization process was conducted conceptually by grouping behavioral determinants according to the definitions of each COM-B domain to gain a more comprehensive understanding of the mechanisms underlying treatment discontinuation. Two reviewers independently conducted the categorization process. Any discrepancies in domain allocation were discussed and resolved through consensus.

2.6. Reporting and ethical consideration

The outcomes of this scoping review will be reported in accordance with the PRISMA-ScR guidelines. Since this study utilizes secondary data from publicly available publications, obtaining ethical approval is not required. In accordance with scoping review methodology, variations in study design, sample size, and setting were carefully considered during data interpretation to ensure the robustness of the synthesis. Consistent with the methodological framework for scoping reviews, a formal critical appraisal of study quality was not conducted, as the primary aim of this review was to map the existing evidence rather than evaluate the effectiveness of interventions.

A scoping review does not require PROSPERO registration, as its purpose is to map the existing scientific evidence and identify research gaps without assessing study quality or conducting a quantitative synthesis of intervention effects. Although protocol registration was not conducted, the review methodology was predefined before study selection and consistently applied throughout the review process to minimize methodological bias. In addition, the review process was conducted in accordance with PRISMA-ScR guidelines to ensure methodological transparency.

3. Results

Using a combination of keywords, a total of 736 articles were identified across three databases. Of these, 471 duplicate records were removed. Of the remaining 265 articles, 147 were excluded after title and abstract screening, including studies conducted in active TB, leaving 118 for full-text review. Subsequently, 91 articles were further excluded for various reasons. Finally, according to the PRISMA ScR flowchart, 27 articles were included in the scoping review. Figure 1 presents the PRISMA flowchart for article selection. The characteristics and summary of the included studies in this present review are shown in Table 1.

Mapping the determinants for treatment discontinuation using the COM-B framework from the studies included in this review and the proposed intervention strategies, as shown in Figure 2.

Figure 2 illustrates that treatment discontinuation in LTBI results from a complex interplay between the domains of COM-B. Within the capability domain, factors such as adverse drug reactions, comorbidities, advanced age, and limited knowledge may impair patients' ability to complete therapy. The opportunity domain highlights how healthcare system barriers, limited access to services, financial constraints, and poor continuity of care contribute to treatment non-adherence. Meanwhile, the motivation domain encompasses low perceived risk, stigma, fear of adverse effects, and inadequate social support, all of which may diminish patients' motivation to continue treatment. The interaction among these domains subsequently influences behavior, leading to missed doses, temporary interruption of medication, and ultimately permanent treatment discontinuation. To improve transparency and reproducibility of the COM-B categorization process, a detailed coding framework and determinant mapping are provided in Table 2.

The implications of the included studies for LTBI treatment according to the COM-B model framework are presented in Supplementary Table 2.

Table 1. Characteristics and summary of the included studies.

No.	Author/Year/ Country or region	Study design and sample size	Characteristics of participants	TPT regimens	Summary of findings
1	Chung *et al*., Korea, 2020[15]	Prospective cohort (*n*=114)	●Mean age: 42 years (32-52) ●HCWs: 89 (78.1%) ●Non-HCWs: 25 (21.9%)	9H: 114 (100%)	●37.7% of patients discontinued treatment ●The prevalence of hepatotoxicity was significantly higher in the treatment non-completion group than in the treatment completion group ●Severe hepatotoxicity was an independent risk factor for treatment discontinuation (*HR* 7.99; 95% *CI* 3.05-20.94)
2	Lin *et al*., 2021, Taiwan, China[16]	Prospective cohort (*n*=91)	●Patients with end-stage renal disease receiving maintenance dialysis ●Mean age: (56.6±13.0) years	●9H: 41 (45.0%) ●3HP: 50 (55.0%)	●39% and 18% of patients discontinued treatment in 9H and 3HP regimens, respectively, *P*-value=0.046 ●Hypersensitivity: 29.2% (3HP) *vs.* 10.8% (9H), *P*-value=0.040 ●Grade ≥2 ADR or more was significantly higher in 3HP compared to 9H, 45.8% *vs.* 13.5%, and it was significantly associated with treatment discontinuation, *P*-value=0.002 Grade 2 ADR or more was significantly associated with treatment discontinuation (a*OR* 6.67; 95% *CI* 1.66-26.80), *P*-value=0.008
3	Noh *et al*., 2019, Korea[17]	Retrospective multicentre study (*n*=77)	●Elderly LTBI ●Age 65-78 years ●Major indications for IGRA testing were healthcare workers (42.9%) and household contacts (23.4%)	●9H: 12 (15.6%) ●4R: 22 (28.6%) ●3HR: 43 (55.8%)	●Overall, 16.8% of patients discontinued treatment ●The treatment discontinuation in 3HR, 4R, and 9H regimens was 12.5%, 22%, and 27%, respectively ●The elderly were less likely to discontinue treatment (a*OR* 0.830; 95% *CI* 0.712-0.968), *P*-value=0.017 ●Reasons for treatment discontinuation were loss to follow-up (13.0%) and any adverse events (3.9%)
4	An *et al*., 2024, Cambodia[18]	Retrospective study (*n*=14 262)	Not reported	●3HR: 6 756 (47.4%) ●6H: 4 771 (33.5%) ●3HP: 2 729 (19.1%)	●2.1% of patients discontinued treatment ●Age 15-24 years (a*OR* 1.79; 95% *CI* 1.04-2.78), age 25-34 years (a*OR* 2.09; 95% *CI* 1.29-3.40), initiated with 3HR (a*OR* 2.61; 95% *CI* 1.53-4.46) or 6H (a*OR* 7.01, 95% *CI* 4.19-11.72), and treated at referral hospitals (a*OR* 1.95; 95% *CI* 1.25-3.03) were significantly associated with treatment discontinuation
5	Liu *et al*., 2025, China[19]	Cross-sectional (*n*=399)	College students with LTBI	3HP: 399 (100%)	●8.8% of patients discontinued treatment ●Non-medical students (a*OR* 0.31; 95% *CI* 0.13-0.78), students with higher family income (a*OR* 0.27; 95% *CI* 0.12-0.60), and higher education level (a*OR* 0.08; 95% *CI* 0.02-0.31) were less likely to complete treatment ●Those who experience adverse reactions are more likely to discontinue treatment (a*OR* 9.46; 95% *CI* 2.67-33.64)
6	Moro *et al*., 2016, USA and Canada[9]	Multicenter RCT (*n*=6 232)	●HIV positive: 121 (1.9%) ●Cirrhosis: 194 (3.1%)	●3HP-DOT: 3 230 (51.8%) ●9H-SAT: 3 002 (48.2%)	●1 406/6 232 (22.6%) of patients discontinued treatment ●Of them who discontinued treatment, 317 (5.1%) and 1 089 (17.4%) patients attributed their discontinuation to adverse effects and other factors, respectively ●The incidence of non-completion due to adverse events was similar in 3HP-DOT and 9H-SAT, 6.4% *vs.* 12.7%, *P*-value=0.23 ●The incidence of non-completion due to other factors was significantly higher in 9H-SAT (24.5%) than in 3HP-DOT (12.7%), *P*-value=0.02 ●Those in non-completion related to adverse events, being non-Hispanic and receiving 3HP-DOT (a*OR* 3.0; 95% *CI* 1.93-4.69), having cirrhosis and receiving 9H-SAT (a*OR* 2.93; 95% *CI* 1.52-5.65), alcohol consumption among men (a*OR* 1.64; 95% *CI* 1.05-2.57), and use of concomitant medication (a*OR* 1.86; 95% *CI* 1.42-2.44) were associated with treatment discontinuation ●Those in non-completion related to other factors, receiving 9H-SAT (a*OR* 3.17; 95% *CI* 2.33-4.31), missing for more than one early visit (a*OR* 4.82; 95% *CI* 3.74-6.21), and alcohol abuse (a*OR* 1.73; 95% *CI* 1.30-2.20), were significantly associated with treatment discontinuation
7	Mohamed *et al*., 2025, Malaysia[20]	Retrospective cohort (*n*=895)	●60% were female ●Non-HCW: (88.8%) ●TB contacts: 90.8%	●6H: 877 (98.0%) ●Others: 18 (2.0%)	●9.2% of patients discontinued treatment and 90.8% of patients completed TPT ●Non-HCW occupation (a*OR* 4.21; 95% *CI* 1.25-14.22), residence in Tawau Division (a*OR* 2.00; 95% *CI* 1.10-3.65), and non-TB contact (a*OR* 2.79; 95% *CI* 1.42-5.48) were significantly associated with treatment discontinuation
8	Apriani *et al*., 2021, Australia, Canada, Saudi Arabia, South Korea, Brazil, Indonesia, Benin, Ghana, and Guinea[21]	Multicenter RCT (*n*=1 003)	●Children: 157 ●Adults: 860 ●Male: 34.1%	●4R: 498 (49.6%) ●9H: 505 (50.4%)	●21.2% and 34.5% of patients discontinued treatment in 4R and 9H regimens, respectively, *P*-value=0.001 ●Adverse event of grade 3-5 was 0.4% in 4R and 2.8% in 9H, *P*-value=0.004 ●Patients who discontinued treatment permanently was 1.4% in 4R and 3.0% in 9H, *P*-value=0.088 ●Early discontinuation was 19.1% in 4R and 30.5% in 9H, *P*-value=0.001
9	de Aguiar *et al*., 2022, Brazil[22]	Non-matched case-control study (*n*=518)	Median age: 32.3 years	Not reported	●23.7% of patients discontinued treatment ●Factors associated with non-completion included drug use (a*OR* 23.33; 95% *CI* 1.83-296.1, TB treatment default by the index case (a*OR* 16.97; 95% *CI* 3.63-79.24), and drug intolerance (a*OR* 2.46; 95% *CI* 1.39-4.35)
10	Laza *et al*., 2023, Spain[23]	Retrospective cohort (*n*=2 962)	Median age: 32.3 years	●6H: 1 844 (67.6%) ●3HR: 808 (29.6%) ●4R: 76 (2.7%)	●The overall non-completion rate was 66.8% ●13.5% and 31.7% of patients discontinued treatment in 3HR and 6H regimens, respectively, *P*-value=0.000 1 ●The completion rate was significantly higher among patients monitored by a TB nurse care manager compared with those receiving standard care, 85% *vs.* 67%. *P*-value=0.001 ●Being female (a*OR* 1.26; 95% *CI* 1.06-1.51), provision of a 3HR regimen (a*OR* 2.90; 95% *CI* 2.29-3.70), and nurse telemonitoring (a*OR* 1.75; 95% *CI* 1.27-2.45) were associated with treatment completion

Table continued on next page.

Table 1. Continued.

No.	Author/Year/ Country or region	Study design and sample size	Characteristics of participants	TPT regimens	Summary of findings
11	Sandul *et al*., 2017, USA[24]	Prospective cohort (*n*=3 288)	●Children: 164 (5.0%) ●Adults: 3 124 (95.0%)	3HP: 3 288 (100%)	●12.8% of patients discontinued treatment ●The completion rate was highest in children aged 2-17 years old, 94.5% ●Those who were homeless within the past year (a*OR* 1.72; 95% *CI* 1.25-2.39) and who were current or past smokers (a*OR* 1.43; 95% *CI* 1.08-1.89) were significantly associated with treatment discontinuation ●Individuals who have household contact with TB patients (a*OR* 0.68; 95% *CI* 0.52-0.89) and students (a*OR* 0.45; 95% *CI* 0.21-0.98) were significantly associated with treatment completion
12	Cruz *et al*., 2018, USA[25]	Retrospective cohort (*n*=667)	●Children 0-17 years old with a median age (IQR) of 8.0 (3.6-13.8). ●TPT administered with DOPT 496 (74.4%); SAT 136 (20.4%), and ESAT 35 (5.2%)	●3HP: 283 (42.6%), 3HP was always administered under DOPT. ●9H: 252 (37.7%) 9H DOPT: 178 (70.6%) 9H SAT or ESAT: 74 (29.4%) ●4R: 132 (19.7%) 4R DOPT: 35 (26.5%) 4R SAT or ESAT: 97 (73.5%)	●The overall treatment discontinuation was 3.2%, 20.2%, and 13.2% in 3HP, 9H, and 4R regimens, respectively ●The non-completion rate was 47.4%, 23.5%, 11.2%. 16.5%. 11.1%. 2.9%, and 3.2% in 9H SAT, 9H ESAT, 9H DOPT, 4R SAT, 4R ESAT, 4R DOPT, and 3HP, respectively TPT administration under DOPT (a*OR* 5.72; 95% *CI* 3.47-9.43), increasing age (a*OR* 1.09; 95% *CI* 1.02-1.17), and the absence of any adverse effects (a*OR* 1.70; 95% *CI* 1.43-2.02) were significantly associated with completing therapy
13	Borse *et al*., 2024, India[5]	Prospective cohort (*n*=502)	●All participants were HIV positive ●Mean age: 41 years old	3HP: 502 (100%)	●8.0% of patients discontinued treatment ●53%, 45%, and 2% of patients who discontinued treatment due to TPT toxicity, lost to follow-up, and TB diagnosis, respectively ●Patients who experienced grade II or more adverse events (a*OR* 15.35; 95 *CI* 5.59-42.17), those with diabetes mellitus (a*OR* 12.82; 95% *CI* 1.22-134.75), and those with detectable viral load at baseline (a*OR* 2.39; 95% *CI* 1.02-5.63) were significantly associated with treatment discontinuation
14	Rahman *et al*., 2023, Bangladesh[26]	A community-based implementation study (*n*=1 216)	●Mean age: 27.4 years ●< 5 years: 40 (3.3%) ●5-15 years: 272 (22.4%) ●≥15 years: 904 (74.3%)	3HP: 1 216 (100%)	●3.0% of patients discontinued treatment ●Being female (a*OR* 1.7; 95% *CI* 1.3-2.1), contacts with households with higher monthly income (a*OR* 1.5; 95% *CI* 1.0-2.1), contacts with higher education (a*OR* 1.4; 95% *CI* 1.1-1.9), age > 15 years old (a*OR* 1.5; 95% *CI* 1.1-2.0), those without comorbid conditions (a*OR* 1.7; 95% *CI* 1.1-2.2), and those who did not experience any adverse events (a*OR* 1.6; 95% *CI* 1.2-2.1) were significantly associated with treatment completion ●The provision of reminder phone calls and treatment counseling was significantly associated with treatment completion (a*OR* 1.9; 95% *CI* 1.5-2.4) ●The provision of phone calls, treatment counseling, and follow-up home visits by health workers was significantly associated with treatment completion (a*OR* 2.1; 95% *CI* 1.5-2.7)
15	Mapingure *et al*., 2023, Zimbabwe[27]	Fast-track programme combined with a qualitative study (*n*=50)	●People living with HIV ●Male: 25 (50.0%) ●Female: 25 (50.0%)	3HP: 50 (100%)	●2.0% of patients discontinued treatment due to jaundice ●The provision of a fast-track programme into 3HP includes multi-month dispensing of ARV and 3HP, health facility visits, phone-based monitoring, and adherence support ●Patients reported great satisfaction with the counseling, education, support, and high-quality care received from the providers, as well as the efficient service in the fast-track programme
16	Chen *et al*., 2024, China[28]	Clustered RCT (*n*=2 433)	●Household contact with TB: 1 655 (68.0%) ●Non-household contact: 778 (32.0%)	●3H2P2: 1 160 (47.7%) ●6H: 1 274 (52.3%)	●The overall rate of treatment discontinuation was 12.3% ●Treatment discontinuation was 17.6% and 7.7% in 6H and 3H2P2 regimens, respectively, *P*-value=0.001 ●Of the 313 patients who discontinued treatment, 27.8% due to adverse effects, 3.8% due to loss to follow-up, 1.9% due to TB diagnosis, 60.1% decided not to continue, and 6.4% due to various reasons ●Treatment completion was associated with clinician incentives (a*OR* 2.49; 95% *CI* 1.29-4.81), supervision by HCW (a*OR* 6.40; 95% *CI* 2.64-15.54), and provision of the 3H2P2 regimen (a*OR* 2.09, 95% *CI* 1.11-3.92). ●On the other hand, any adverse effects were found to be a risk factor for abandonment (a*OR* 0.08, 95% *CI* 0.05-0.12, *P*-value=0.001)
17	Alves *et al*., 2024, Brazil[29]	Quasi experimental (*n*=88)	Adult individuals with LTBI (migrants)	●3 HP: 88 (100%), consisting of: SA: 31 (35.3%) DOT: 26 (29.4%) VDOT: 31 (35.3%)	●16.1%, 23.1%, and 19.4% of patients discontinued treatment in SA, DOT, and VDOT, respectively ●After adjusting for sex, age, race, and marital status, individuals under VDOT were more likely to complete treatment (a*OR* 0.26; 95% *CI* 0.7-0.94, P-value 0.04), meanwhile, those under SA were significantly associated with treatment discontinuation (a*OR* 9.93; 95% *CI* 1.96-50.30, *P*-value=0.006)
18	Chiu *et al*., 2022, Taiwan China[30]	Retrospective cohort (*n*=264)	●Long-term care facilities: Private:139 (52.6%) Public: 125 (47.4%) ●History of TB contact: Yes:124 (46.9%) No:140 (50.4%)	●9H: 155 (58.7%) ●3HP: 105 (39.7%) ●4R:4 (1.6%)	●19.6% of patients discontinued treatment ●Those who received 3HP regimens were less likely to discontinue treatment (a*OR* 0.22; 95% *CI* 0.07-0.71), *P*-value<0.05
19	Huang *et al*., 2018, China[31]	Cross-sectional study (*n*=362)	●56 cases in the treatment (TPT) group and 206 cases in the control group ●Age (range): 14-52 years old ●Discrimination (yes): 43.6% ●Worry about adverse effects of TPT (yes): 159 (43.9%) ●Negative opinion provided by non-TB specialist (yes):193 (30.5%)	3 HR: 156 (100%)	●55.8% of patients discontinued treatment ●Those who experienced discrimination (a*OR* 7.17; 95% *CI* 3.36-15.30), accepted a negative opinion from a non-TB specialist (a*OR* 6.01; 95% *CI* 3.07-11.76), worried about the adverse effects of TPT (a*OR* 2.75; 95% *CI* 1.45-5.19), and had parents with low education level (a*OR* 2.60; 95% *CI* 1.42-4.77) were significantly associated with treatment discontinuation

Table continued on next page.

Table 1. Continued.

No.	Author/Year/ Country or region	Study design and sample size	Characteristics of participants	TPT regimens	Summary of findings
20	Asare-Baah *et al*., 2024, USA[32]	Prospective cohort (*n*=993)	●Male: 508 (51.0%) ●Congregate risks (yes): 20 (2.0%)	●3HP: 202 (20.3%) ●4R: 791 (79.7%)	●The overall treatment discontinuation was 27.1% ●13.3% and 30.5% of patients discontinued treatment in 3HP and 4R regimens, respectively, *P*-value=0.001 ●Latino ethnicity (*HR* 1.80; 95% *CI* 1.20-2.90) and those who experienced adverse events (HR 4.30; 95% *CI* 2.60-7.30) were significantly associated with treatment discontinuation in 3HP regimens ●Social-behavioral factors such as substance misuse (*HR* 12.00; 95% *CI* 2.20-69.00) and those with congregate living (*HR* 21.00; 95% *CI* 1.20-360.00) were significantly associated with treatment discontinuation in 4R regimens ●The average time to treatment discontinuation was 4 weeks and it was similar between the two groups, *P*-value=0.12
21	Eastment *et al*., 2017, USA[33]	Retrospective cohort (*n*=391)	●Mean age: 41.6 years old ●Alcohol use: 52 (13.2%) ●Experienced adverse effects (yes): 131 (33.2%)	●9H: 222 (56.7%) ●4R: 82 (21.0%) ●3HP: 87 (22.3%)	●34% of patients discontinued treatment ●48.2%, 14.6%, and 14.9% of patients discontinued treatment in 9H, 4R, and 3HP regimens, respectively, *P*-value=0.001 ●The main reason for treatment discontinuation was loss to follow-up, especially in the 9H regimen ●Those who are unmarried, used tobacco or alcohol, had medical problems more than three, and received charity care were significantly associated with treatment discontinuation.
22	Chang *et al*., 2013, USA[34]	Retrospective cohort (*n*=1 575)	●age (range): 0.5-18 years old ●Family members on treatment (yes): 157 (10.0%) ●Experienced more than one adverse event: 790 (50.0%)	Not reported	●22.0% of patients discontinued treatment ●Age>15-18 years (a*OR* 2.0; 95% *CI* 1.3-3.0), those who had hepatitis (a*OR* 24.6; 95% *CI* 10.5-62.8), and those who experienced symptoms of adverse events (a*OR* 2.0; 95% *CI* 1.2-3.0) were significantly associated with treatment discontinuation
23	Kwara *et al*., 2008, USA[35]	Retrospective cohort (*n*=672)	●Mean age: (33.8±15.2) years old ●Insurance (yes): 325 (48.3%) ●Reported any adverse events (yes): 177 (26.3%)	9H: 672 (100%)	●36.6% of patients discontinued treatment, mostly due to loss to follow-up ●Those without medical assurance (a*OR* 1.7; 95% *CI* 1.1-2.7) and those who demonstrated adverse effects (a*OR* 3.6; 95% *CI* 2.2-6.2) were significantly associated with treatment discontinuation
24	Tegegnework *et al*.,2024, Ethiopia[36]	Cross-sectional (*n*=581)	●People living with HIV on ART ●Median age (range): 36 (21-51) years old ●First-line ARV: 459 (79.1%)	Not reported	●17% of patients discontinued treatment ●27.2% of patients reported adverse effects related to TPT ●Patients who had not experienced adverse events (a*OR* 3.52; 95% *CI* 1.91-6.49) and patients who demonstrated good adherence to ARV (a*OR* 10.38; 95% *CI* 4.14-25.96) were significantly associated with treatment completion
25	Machado *et al*., 2009, Brazil[37]	Prospective cohort (*n*=101)	●Household contacts of patients hospitalized with TB ●Median age: 23 years old	6H: 101 (100%)	●46.5% of patients discontinued treatment ●28.7% of patients were immediately lost to follow-up ●Those who reported adverse events related to TPT (a*OR* 2.69; 95% *CI* 1.3-5.8) and those who required two buses to visit the hospital (a*OR* 1.84; 95% *CI* 1.0-3.3) were significantly associated with treatment discontinuation ●Those who required two buses to visit the hospital (a*OR* 20.69; 95% *CI* 2.1-208.4) were significantly associated with early loss to follow-up
26	Amanya *et al*., 2023, Uganda[38]	Mixed-methods facility-based retrospective cohort (*n*=341)	●People living with HIV ●Median age: 33 years old (IQR 28-40)	Isoniazid	●17% of patients discontinued treatment ●Those who were married or cohabiting (a*OR* 0.31; 95% *CI* 0.17-0.55) were less likely to experience treatment discontinuation ●Lack of health education, high pill burden, distance to the health facilities, and relocation are barriers to treatment completion
27	Macaraig *et al*., 2018, USA[39]	Retrospective cohort (*n*=449)	●Age < 18 years: 85 (18.9%) ●Medical risk factors for LTBI: 57 (12.7%)	●3HP: 125 (28%) ●4R: 269 (60%) ●9H: 55 (12%)	●30%, 21%, and 51% of patients discontinued treatment in 4R, 3HP, and 9H regimens, *P*-value=0.001 ●The main reason for treatment discontinuation was refusal of treatment continuation, 19%, 28%, and 45% in 3HP, 4R, and 9H regimens, respectively ●The provision of 4R (a*OR* 1.39; 95% *CI* 1.07-1.81), 3HP (a*OR* 1.67; 95% *CI* 1.27-2.19), and contacts with TB patients (a*OR* 1.18; 95% *CI* 1.05-1.34) were significantly associated with treatment completion

TB: tuberculosis; LTBI: latent tuberculosis infection; ADR: adverse drug reaction; HCWs: health care workers; TPT: tuberculosis preventive therapy; RCT: randomized-controlled trial; DOPT: directly observed preventive therapy; DOT: directly observed therapy; VDOT: video directly observed therapy; ESAT: enhanced self-administered therapy; SAT: self-administered therapy; SA: self-administered; a*OR*: adjusted odds ratio; 95% *CI*: 95% confidence interval; COM-B: capability, opportunity, motivation, behaviour; 3HP: three months of isoniazid and rifapentine; 3HR: three months of isoniazid and rifampicin; 4R: four months of rifampicin; 6H: six months of isoniazid; 9H: nine months of isoniazid; 3H2P2: three momths of twice weekly of isoniazid and rifapentine; ARV: antiretroviral.

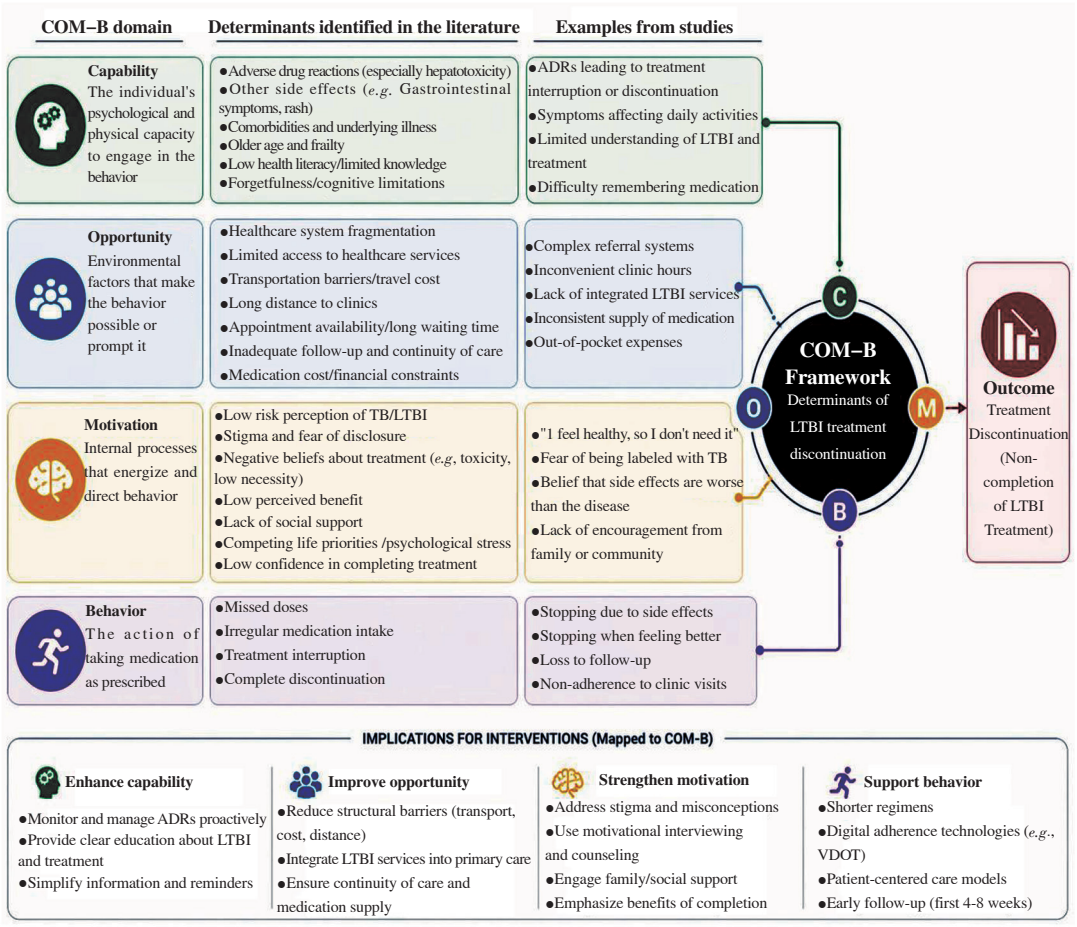

Figure 2. Mapping determinants of tuberculosis preventive treatment discontinuation within the COM-B framework and proposed intervention strategies. TB: tuberculosis; LTBI: latent tuberculosis infection; ADR: adverse drug reaction.

4. Discussion

This review indicates that treatment discontinuation in LTBI is a multifactorial phenomenon resulting from complex interactions among clinical, behavioral, and social factors, as well as the healthcare system. The wide variation in treatment discontinuation rates across studies, ranging from 2.0% to over 60%, reflects heterogeneity in the populations, treatment regimens, and program implementation contexts across various settings.

In our review, we found that ADR during TPT among LTBI is a primary determinant of treatment discontinuation. Various studies indicated that the occurrence of ADR, particularly those of grade 2, increases the risk of nonadherence leading to treatment discontinuation[5,15,16,19]. Severe hepatotoxicity and hypersensitivity reactions have even been identified as independent risk factors, particularly in vulnerable populations such as patients with HIV or other comorbidities[5,34]. These findings underscore the importance of the "capability" component of the COM-B framework, as the physical ability of patients to tolerate treatment directly impacts treatment adherence. Simultaneously, these adverse experiences may negatively shape patients' beliefs and emotional responses toward treatment, thereby influencing the motivation domain within the COM-B framework. Fear of worsening symptoms, anxiety regarding drug safety, and negative expectations about treatment outcomes may reduce patients' willingness to continue therapy, even when the clinical benefits of TPT are well understood[9].

A meta-analysis demonstrated that the incidence of hepatotoxicity due to isoniazid was approximately 2.6% among LTBI patients[40]. Various risk factors have been identified as contributing to hepatotoxicity during TPT, such as the administration of 6H or 9H regimens, those with malnutrition, and those with pre-existing liver dysfunction[41,42]. Nevertheless, several studies in this review that documented adverse effects or hepatotoxicity did not analyze factors associated with it.

The characteristics of the treatment regimen, particularly its duration and complexity, also play a role in determining treatment success.

Table 2. Coding matrix determinants of tuberculosis preventive treatment adherence based on the capability, opportunity, motivation-behaviour framework.

COM-B Domains	Factors	Studies	Capability, opportunity, motivation-behaviour interpretation	Main findings
Capability (Psychological & Physical)	Adverse events (hepatotoxicity, adverse drug reaction)	Chung *et al*., 2020[15]; Lin *et al*., 2021[16]; Borse *et al*., 2024[5]; Liu *et al*., 2025[19]; Chang *et al*., 2013[34]; Kwara *et al*., 2008[35]	Categorized as physical capability because treatment-related physical symptoms may reduce the patient's ability to continue therapy	Adverse events related to tuberculosis preventive treatment were consistently associated with treatment discontinuation
	Comorbid disease (human immunodeficiency virus, diabetes mellitus, cirrhosis)	Borse *et al*., 2024[5]; Moro *et al*.[9]; Eastment *et al*.[33]	Classified under physical capability because underlying medical conditions may impair treatment tolerance and increase vulnerability to adverse events	Comorbid diseases increase susceptibility to adverse events and treatment discontinuation
	Age	Noh *et al*., 2019[17]; Chang *et al*., 2013[34]	Categorized as physical or psychological capability because age-related physical and cognitive factors may influence adherence behavior	Younger age or elderly were associated with treatment adherence (results may vary depending on the context)
	Knowledge or a low level of education	Huang *et al*., 2018[31]; Amanya *et al*., 2023[38]	Classified as a psychological capability because knowledge and educational attainment influence understanding of tuberculosis preventive treatment benefits and adherence	A lack of education increases the risk of treatment discontinuation
Opportunity (Physical & Social)	Longer treatment regimens (9H, 6H)	Lin *et al*., 2021[16]; Apriani *et al*., 2021[21]; Eastment *et al*., 2017[33]	Categorized as a physical opportunity because regimen duration reflects the external treatment structure, influencing adherence	Longer treatment regimens have a higher discontinuation rate than short-term regimens (3HP, 4R)
	Access to services (distance, transportation)	Machado *et al*., 2009[37]; Amanya *et al*., 2023[38]	Classified under a physical opportunity because geographic and transportation barriers limit access to healthcare services	Impediments to access (such as transportation difficulties) increase loss to follow-up and treatment discontinuation
	Healthcare support services (direct observation Treatment, telemonitoring, nurse care manager)	Laza *et al*., 2023[23]; Cruz *et al*., 2018[25]; Chen *et al*., 2024[28]	Categorized as social and physical opportunity because healthcare support provides external facilitation and monitoring	Intensive monitoring and support from healthcare professionals improve completion rates
	Social status (homelessness, substance use, alcohol)	Sandul *et al*., 2017[24]; de Aguiar *et al*., 2022[22]; Asare-Baah *et al*., 2024[32]	Classified as a social opportunity because adverse social environments may hinder adherence behavior	Socially vulnerable individuals significantly increase the risk of treatment discontinuation
	Economic and educational status	Liu *et al*., 2025[19]; Huang *et al*., 2018[31]; Rahman *et al*., 2023[26]	Categorized as physical or social opportunity because financial and educational resources influence healthcare access and continuity	Higher education and wages increase completion rates
	Service systems (fast-track, integrated human immunodeficiency virus care)	Mapingure *et al*., 2023[27]	Classified under a physical opportunity because a service organization may facilitate continuity of care	Innovative service models improve compliance
Motivation (Reflective & Automatic)	Negative perceptions of treatment or fear of side effects	Huang *et al*., 2018[31]	Categorized as an automatic motivation because emotional concerns and fear influence treatment behavior	Worries about adverse effects increase the risk of treatment discontinuation
	Stigma and discrimination	Huang *et al*., 2018[31]	Classified as automatic or social motivation because stigma influences emotional responses and self-perception	Discrimination is a major factor in treatment discontinuation
	Early compliance & follow-up	Moro *et al*[9].; Chen *et al*., 2024[28]	Categorized as a reflective motivation because early engagement reflects intentional adherence behavior	Missing an initial visit increases the risk of treatment discontinuation
	Patient preference/decision to discontinue treatment themselves	Chen *et al*., 2024[28]; Macaraig *et al*., 2018[39]	Classified under a reflective motivation because treatment continuation involves conscious decision-making	Most patients discontinue treatment due to personal reasons (up to 60%)
	Social support (family, tuberculosis contacts)	Sandul *et al*., 2017[24]; Rahman *et al*., 2023[26]	Categorized as a social motivation because interpersonal encouragement may reinforce adherence behavior	Social support improves completion rates
	Behavioral interventions (counseling, reminders)	Rahman *et al*., 2023[26]; Mapingure *et al*., 2023[27]	Classified as a reflective motivation because counseling and reminders strengthen intentional adherence behavior	Educational interventions and reminders significantly improve adherence

6H: 6 months of isoniazid; 9H: 9 months of isoniazid.

Several studies reported higher treatment completion rates among patients receiving the 3HP regimen[16,21,33,39]. This suggests that prolonged treatment duration increases pill burden, the cumulative risk of adverse effects, and patients' psychological fatigue, ultimately diminishing their physical and psychological capacity to maintain adherence. The WHO recommends several treatment options, with a preference for short-course rifamycin-based regimens, as they are more effective at improving adherence[43]. The included evidence suggests that shorter regimens may support improved adherence; however, comparative effectiveness conclusions remain beyond the scope of this review. Therefore, regimen selection should take into account other factors such as treatment duration, adverse effects, potential drug interactions, and patient adherence[44,45].

Limited access to healthcare services, transportation difficulties, financial constraints, homelessness, and substance use reflect deficits in physical and social opportunity within the COM-B framework, thereby reducing patients' ability to sustain treatment adherence[19,22,24,31,35,37,38]. These factors reflect limitations in physical opportunity, thereby underscoring the need to strengthen more accessible, patient-centered service models. In this context, a decentralized approach to health care is recommended. This approach may overcome geographical barriers and improve patient retention in treatment programs, particularly in areas with limited access[46]. In addition, the implementation of community-based care and the involvement of community health workers have proven effective in bridging access gaps[47]. The consistent association between low socioeconomic status and treatment discontinuation observed in this review aligns with the broader social epidemiology of TB[48]. These economic constraints also impact access to healthcare, lead to delayed diagnosis, and result in low participation in TB screening and TPT programs. Furthermore, a low education level contributes to low health literacy, thereby affecting awareness of the importance of TB treatment and prevention[49].

Beyond structural barriers, psychosocial determinants also substantially influence adherence behavior. Stigma, discrimination, and misinformation from non-healthcare professionals further undermine social opportunity and patient motivation by discouraging healthcare-seeking behavior and reducing social support[31]. Stigma was commonly identified as a barrier associated with treatment discontinuation. Stigma may foster negative stereotypes that lead to discrimination across various aspects of life, including education, employment, social relationships, and access to public services. Individuals who experience stigma often face social exclusion, diminished self-confidence, and limited opportunities to build supportive social networks that contribute to their personal development and overall well-being[50].

Furthermore, stigma may exacerbate social inequality in healthcare contexts, as individuals may conceal their condition due to fear of social judgment and discrimination. This can hinder their participation in social activities and limit access to both financial and emotional support. Consequently, stigma not only undermines psychological well-being but also restricts social opportunities and upward social mobility within society[51]. Therefore, to minimize stigma and discrimination, effective interventions, such as community-based education, peer support, psychosocial interventions, and digital media, may be implemented in clinical settings[52].

On the other hand, motivational factors are also key determinants of treatment adherence. Patient refusal to continue treatment is a primary reason for treatment discontinuation, indicating the role of reflective motivation, including risk perception and beliefs about treatment benefits[28,39]. Individuals without a history of contact with TB patients tend to have lower risk perceptions, thereby increasing the likelihood of non-adherence. Conversely, household contact with TB patients has been shown to improve adherence, indicating that risk perception acts as a protective factor[53]. Therefore, to minimize treatment discontinuation among non-household contacts requires a combination of interventions that address clinical, behavioral, and social aspects. The use of shorter regimens, enhanced education and counseling, digital technologies, and socioeconomic support are key strategies, as they tend to have lower risk perception and motivation than close contacts[54].

Interventions at the health system level are consistently shown to improve treatment success. Approaches such as directly observed therapy (DOT), video-observed therapy (VDOT), telemonitoring, reminder systems, and active engagement of healthcare professionals were frequently associated with higher treatment completion rates across included studies[25,26,29]. VDOT may be beneficial and patient-centered innovation compared to DOT. Evidence from controlled clinical trials in patients with LTBI demonstrates that VDOT achieves a treatment completion rate comparable to DOT (73.5% *vs.* 69.4%) at a lower cost. In addition, VDOT not only improves adherence but also reduces the burden on the healthcare system and the stigma associated with face-to-face visits[55]. In countries with a high TB burden, such as Indonesia, strategies that combine simplified digital technologies with community-based approaches and patient-centered care represent the most economically and operationally rational choice.

Nevertheless, the implementation of VDOT and digital health interventions, particularly in low- and middle-income countries, may encounter several structural barriers that cannot be overlooked. First, there are limitations in digital infrastructure, including unstable internet connectivity, limited smartphone availability, and low levels of digital literacy among TB patients. Second, the digital divide may further exacerbate inequities in access to care, particularly among vulnerable populations such as rural communities, older

adults, and low-income groups. Third, challenges related to privacy, data security, and patient trust in digital systems may influence the acceptability and uptake of these interventions[56]. Therefore, implementation strategies in such countries should adopt a phased approach that is grounded in local contexts and supported by inclusive digital health policies.

In addition, the early phase of treatment, particularly the first four weeks, has been identified as a critical period for treatment discontinuation among LTBI[32]. During this phase, patients face initial adaptation to treatment, early onset of adverse effects, and suboptimal support from the healthcare system. A study by Ronald *et al*., indicated that the onset of isoniazid-induced hepatotoxicity typically occurs within the first 2-12 weeks of treatment, reflecting a pattern of idiosyncratic reactions that emerge relatively early after drug exposure[57]. Therefore, more intensive monitoring and targeted interventions are needed during the early phase to prevent premature discontinuation of treatment.

In summary, beyond identifying specific determinants, this review highlights the interconnections among factors across all COM-B domains. Adverse drug reactions affect motivation through fear and perceived negative aspects of treatment, as well as by reducing physical capacity. Similarly, structural barriers such as limited access to healthcare services restrict opportunities, which in turn reduce motivation due to increased treatment burden and reduced interaction with healthcare providers. These findings imply that discontinuation of treatment is driven by a self-reinforcing feedback loop involving ability, opportunity, and motivation, rather than by isolated factors. Therefore, interventions that focus on only one area, such as educational interventions alone, are unlikely to be sufficient. Instead, to achieve long-term improvements in treatment adherence, an integrated approach is required that simultaneously addresses clinical management, access to healthcare, and behavioral support, as illustrated in Figure 2.

Unlike previous reviews that primarily identified isolated predictors of nonadherence, this review demonstrates how determinants interact dynamically across COM-B domains to shape TPT behavior. Nevertheless, this review has several limitations. First, the heterogeneity of study designs, population characteristics, and research settings limits the generalizability of the findings. Second, the predominance of observational designs increases the potential for bias, including selection and information bias, and limits causal inferences. Third, psychosocial factors such as stigma, perceptions, and patient experiences have not been consistently explored across studies. Finally, some studies did not provide detailed reports on treatment regimens or other important variables, which may affect the strength of the synthesis.

The absence of a formal risk-of-bias assessment should be considered when interpreting the findings. The included studies were predominantly observational in design, which may be subject to selection bias, confounding, and limited causal inference. Therefore, the conclusions of this review should be interpreted cautiously, particularly regarding the strength and generalizability of the identified associations.

Complex and interrelated clinical, behavioral, social, and healthcare system factors drive treatment discontinuation among individuals with latent tuberculosis infection. Adverse drug reactions, particularly among patients with comorbidities, remain the most consistent determinants of treatment discontinuation, while prolonged treatment regimens and complex treatment processes further undermine adherence. In addition, structural barriers, socioeconomic challenges, stigma, and low perceived risk substantially influence patients' motivation and opportunity to complete therapy. Conversely, shorter regimens, structured monitoring approaches such as DOT and VDOT, and active involvement of healthcare providers have consistently been associated with improved treatment completion. The early phase of treatment represents a critical window for intervention and intensified follow-up. Overall, the COM-B framework offers a comprehensive behavioral perspective on TPT discontinuation and on identifying modifiable intervention targets. Integrated, patient-centered strategies that enhance capability, improve healthcare access, and strengthen patient motivation are essential for optimizing TPT treatment outcomes.

Based on the findings of this review, several policy and practice implications may be proposed:

1. Latent tuberculosis programs may consider shorter-duration and better-tolerated regimens to improve patient adherence and reduce treatment discontinuation.

2. The system for monitoring adverse effects should be strengthened, particularly during the early phase of treatment, through early detection mechanisms and responsive management.

3. A patient-centered care approach should be widely implemented, incorporating DOT, VDOT, telemonitoring, and home visits to improve patient access and retention.

4. Educational and risk communication interventions should be strengthened to improve patients' perceptions, reduce stigma, and reinforce their motivation to adhere to treatment.

5. Health systems should adopt integrated behavioral approaches that address capability, opportunity, and motivation simultaneously to optimize TPT outcomes.

This review also highlights several priorities for future research:

1. Intervention studies based on behavioral theory, such as COM-B or the Behavior Change Wheel (BCW), are warranted to identify the most effective interventions to improve latent tuberculosis treatment adherence.

2. Prospective longitudinal studies are warranted to identify causal relationships between risk factors and treatment discontinuation.

3. Qualitative and mixed-methods studies should be developed to explore psychosocial factors, including stigma, self-efficacy, perceptions, and patients' experiences with TPT.

4. Evaluations of the implementation and cost-effectiveness of service innovations, such as VDOT and other digital technologies, need to be expanded, particularly in low- and middle-income countries with a high TB burden.

Conflict of interest statement

All authors declare that they have no competing interests

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Authors' contributions

ONP: conceptualization, data curation, literature searching, methodology, writing–original draft, writing–review and editing. TP: conceptualization, methodology, supervision, and writing–review. JJ: conceptualization, literature searching, data extraction. EPY: conceptualization, methodology, data extraction. AYNH: conceptualization, data extraction, writing–original draft.

References

[1] Shresta AB, Siam IS, Tasnim J, Dahal A, Roy P, Neupane S, et al. Prevalence of latent tuberculosis infection in Asian nations: A systematic review and meta-analysis. *Immun Inflamm Dis* 2024; **12**(2): 1200. doi: 10.1002/iid3.1200.

[2] Liyew AM, Gilmour B, Clements ACA, Alene KA. Comparative effectiveness of interventions for preventing tuberculosis: Systematic review and network meta-analysis of interventional studies. *EClinicalMedicine* 2023; **64**: 102209. doi: 10.1016/j.eclinm.2023.102209.

[3] Shah R, Khakhkar T, Modi B. Efficacy and safety of different drug regimens for tuberculosis preventive treatment: A systematic review and meta-analysis. *Cureus* 2023; **15**(4): e38182. doi: 10.7759/cureus.38182

[4] 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**(1): 18458. doi: 10.1038/s41598-024-67845-6.

[5] Borse R, Randive B, Mattoo S, Malik P, Solanki H, Gupta A, et al. Three months of weekly rifapentine plus isoniazid for TB prevention among people with HIV. *IJTLD Open* 2024; **1**(9): 404-409. doi: 10.5588/ijtldopen.23.0609.

[6] Wang J, Zha X, Zhang Q, Chen M, Zhang H, Ding F, et al. Willingness of receiving preventive treatment and its determinants among individuals with latent tuberculosis infection in Shenzhen, China. *BMC Infect Dis* 2025; **25**(1). doi: 10.1186/s12879-025-11026-x.

[7] Xie L, Chen Y, Zhang L, Zhao L, Li T, Shi X, et al. Knowledge and attitudes about screening and preventive treatment of latent tuberculosis infection among patients with rheumatic diseases in Beijing, China. *Infect Drug Resist* 2024; **17**: 3403-3414. doi: 10.2147/IDR.S471448.

[8] Yoopetch P, Anothaisintawee T, Gunasekara ADM, Jittikoon J, Udomsinprasert W, Thavorncharoensap M, et al. Efficacy of anti-tuberculosis drugs for the treatment of latent tuberculosis infection: A systematic review and network meta-analysis. *Sci Rep* 2023; **13**(1): 16240. doi: 10.1038/s41598-023-43310-8.

[9] Moro RN, Borisov AS, Saukkonen J, Khan A, Sterling TR, Villarino ME, et al. Factors associated with noncompletion of latent tuberculosis infection treatment: Experience from the PREVENT TB trial in the United States and Canada. *Clin Infect Dis* 2016; **62**(11): 1390-400. doi: 10.1093/cid/ciw126.

[10] 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. doi: 10.1186/s12879-025-10832-7.

[11] Dhumal G, Nevrekar N, Gupte N, Shrisunder R, Kulkarni P, Sarpotdar S, et al. Improving treatment adherence in youths with multidrug-resistant tuberculosis with psychosocial intervention. *Brain Behav* 2025; **15**(8): e70665. doi: 10.1002/brb3.70665.

[12] 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**(1): 257. doi: 10.1186/s12879-016-1549-4.

[13] Willmott TJ, Pang B, Rundle-Thiele S. Capability, opportunity, and motivation: An across contexts empirical examination of the COM-B model. *BMC Public Health* 2021; **21**(1): 1014. doi: 10.1186/s12889-021-11019-w.

[14] Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA extension for scoping reviews (PRISMA-ScR): Checklist and explanation. *Ann Intern Med* 2018; **169**(7): 467-473. doi: 10.7326/M18-0850.

[15] Chung SJ, Lee H, Koo GW, Min JH, Yeo Y, Park DW, et al. Adherence to nine-month isoniazid for latent tuberculosis infection in healthcare workers: A prospective study in a tertiary hospital. *Sci Rep* 2020; **10**: 6462. doi: 10.1038/s41598-020-63156-8.

[16] Lin SY, Feng JY, Lee CY, Lin YC, Chou YH, Lin KY, et al. 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**(3): e02184. doi: 10.1128/AAC.02184-20.

[17]Noh CS, Kim H I, Choi H, Kim Y, Kim CH, Choi JH, et al. Completion rate of latent tuberculosis infection treatment in patients aged 65 years and older. *Respir Med* 2019; **157**: 52-58. doi: 10.1016/j.rmed.2019.09.004.

[18]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**(1). doi: 10.1038/s41598-024-67845-6.

[19]Liu C, Jing R, Li S, Zhang W, Dong Y, Dong H, et al. Predictors of tuberculosis preventive treatment completion in college students: A high adherence study in China. *Infect Drug Resist* 2025; **18**: 2581-2588. doi: 10.2147/IDR.S523021.

[20]Mohamed AF, Shafei MN, Mohammad WMZW, Teo R, Hui ASM. Factors associated with incomplete latent tuberculosis infection preventive treatment in Sabah, Malaysia. *PeerJ* 2025; **13**: e19736. doi: 10.7717/peerj.19736.

[21]Apriani L, Koesoemadinata RC, Bastos ML, Wulandari DA, Santoso P, Alisjahbana B, et al. Implementing the 4R and 9H regimens for TB preventive treatment in Indonesia. *Int J Tuberc Lung Dis* 2022; **26**(2): 103-110. doi: 10.5588/ijtld.21.0318.

[22]de Aguiar RM, da Silva Vieira MAM, de Almeida IN, de Paula Ramalho DM, Ruffino-Netto A, Carvalho ACC, et al. Factors associated with non-completion of latent tuberculosis infection treatment in Rio de Janeiro, Brazil: A non-matched case control study. *Pulmonology* 2022; **28**(5): 350-357. doi: 10.1016/j.pulmoe.2020.04.004

[23]Ortiz Laza N, Lopez Aranaga I, Toral Andres J, Toja Uriarte B, Santos Zorrozua B, Altube Urrengoechea L, et al. Latent tuberculosis infection treatment completion in Biscay: Differences between regimens and monitoring approaches. *Front Med* 2023; **10**: 1265057. doi: 10.3389/fmed.2023.1265057.

[24]Sandul AL, Nwana N, Holcombe JM, Lobato MN, Marks S, Webb R, et al. High rate of treatment completion in program settings with 12-dose weekly isoniazid and rifapentine for latent *Mycobacterium tuberculosis* infection. *Clin Infect Dis* 2017; **65**(7): 1085-1093. doi: 10.1093/cid/cix505.

[25]Cruz AT, Starke JR. Completion rate and safety of tuberculosis infection treatment with shorter regimens. *Pediatrics* 2018; **141**(2): e20172838. doi: 10.1542/peds.2017-2838.

[26]Rahman MT, Hossain F, Banu RS, Islam MS, Alam S, Faisel AJ, et al. Uptake and completion of tuberculosis preventive treatment using 12-dose, weekly isoniazid-rifapentine regimen in Bangladesh: A community-based implementation study. *Trop Med Infect Dis* 2024; **9**(1): 4. doi: 10.3390/tropicalmed9010004.

[27]Mapingure MP, Zech JM, Hirsch-Moverman Y, Msukwa M, Howard AA, Makoni T, et al. Integrating 3HP-based tuberculosis preventive treatment into Zimbabwe's fast track HIV treatment model: Experiences from a pilot study. *J Int AIDS Soc* 2023; **26**: 26105. doi: 10.1002/jia2.26105/full.

[28]Chen H, Zhang H, Cheng J, Sun D, Wang Q, Wu C, et al. Adherence to preventive treatment for latent tuberculosis infection in close contacts of pulmonary tuberculosis patients: A cluster-randomized controlled trial in China. *Int J Infec Dis* 2024; **147**: 107196. doi: 10.1016/j.ijid.2024.107196.

[29]Alves YM, Berra TZ, Jezus SV, Araújo VMS, Pinheiro JS, Assis LBO, et al. Adherence to short-duration treatment (3HP) for latent tuberculosis among international migrants in Manaus, Amazonas: Evaluation of the efficacy of different treatment modalities. *Microorganisms* 2024; **12**(8): 1629. doi: 10.3390/microorganisms12081629.

[30]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): 1310-1317. doi: 10.1016/j.jmii.2021.09.013.

[31]Huang H, Yuan G, Du Y, Cai X, Liu J, Hu C, et al. Effects of preventive therapy for latent tuberculosis infection and factors associated with treatment abandonment: A cross-sectional study. *J Thorac Dis* 2018; **10**(7): 4377-4386. doi: 10.21037/jtd.2018.06.138.

[32]Asare-Baah M, Salmon-Trejo LTAT, Venkatappa T, Garfein RS, Aiona K, Haas M, et al. Factors associated with the discontinuation of two short-course tuberculosis preventive therapies in programmatic settings in the United States. *Open Forum Infect Dis* 2024; **11**(6): ofae313. doi: 10.1093/ofid/ofae313.

[33]Eastment MC, McClintock AH, McKinney CM, Narita M, Molnar A. Factors that influence treatment completion for latent tuberculosis infection. *J Am Board Fam Med* 2017; **30**(4): 520-527. doi: 10.3122/jabfm.2017.04.170070.

[34]Chang SH, Eitzman SR, Nahid P, Finelli MLU. Factors associated with failure to complete isoniazid therapy for latent tuberculosis infection in children and adolescents. *J Infect Public Health* 2014; **7**(2): 145-152. doi: 10.1016/j.jiph.2013.11.001.

[35]Kwara A, Herold JS, Machan JT, Carter EJ. Factors associated with failure to complete isoniazid treatment for latent tuberculosis infection in Rhode Island. *Chest* 2008; **133**(4): 862-868. doi: 10.1378/chest.07-2024.

[36]Tegegnework AZ, Aemiro MT, Bilchut AH, Mekuria AD, Yehualashet SS. Completion of tuberculosis preventive therapy and associated factors among clients on antiretroviral therapy at Debre Berhan town health facilities, North Shoa Zone, Ethiopia. *AIDS Res Ther* 2024; **21**(1). doi: 10.1186/s12981-024-00629-0.

[37]Machado A, Finkmoore B, Emodi K, Takenami I, Barbosa T, Tavares M, et al. Risk factors for failure to complete a course of latent tuberculosis infection treatment in Salvador, Brazil. *Int J Tuberc Lung Dis* 2009; **13**(6): 719-725.

[38]Amanya I, Muhoozi M, Aruhomukama D, Ssebagereka A, Mugambe R. Isoniazid preventive therapy completion and factors associated with non-completion among patients on antiretroviral therapy at Kisenyi Health Centre IV, Kampala, Uganda. *PLoS One* 2023; **18**(8): e0277739. doi: 10.1371/journal.pone.0277739.

[39]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): 1344-1349. doi: 10.5588/ijtld.18.0035.

[40]Oscanoa TJ, Vidal X, Luque J, Julca DI, Romero-Ortuno R. Hepatotoxicity induced by isoniazid in patients with latent tuberculosis infection: A meta-analysis. *Gastroenterol Hepatol Bed Bench* 2023; **16**(1): 14-23. doi: 10.22037/ghfbb.v16i1.2685.

[41]Oh SH, Lee J, Jo J, Kwon JW. Adverse events of tuberculosis preventive therapy among individuals with latent tuberculosis infection: A nationwide cohort study in South Korea. *Int J Infect Dis* 2025; doi: 10.1016/j.ijid.2025.107914.

[42]Akkahadsee P, Jantharaksa S, Sawangjit R, Phumart P. Incidence, outcomes, and risk factors of antituberculosis drugs induced liver injury in Thailand: A retrospective cohort study. *Pharm Pract* 2024; **22**(2): 2965. doi: 10.18549/PharmPract.2024.2.2965.

[43]World Health Organization. *WHO consolidated guidelines on tuberculosis.* Module 1: Prevention-tuberculosis preventive treatment. Second edition. 2024. [Online]. Available from: https://www.who.int/publications/i/item/9789240096196. [Accessed on 20 May 2026].

[44]Yoopetch P, Anothaisintawee T, Gunasekara ADM, Jittikoon J, Udomsinprasert W, Thavorncharoensap M, et al. Efficacy of anti-tuberculosis drugs for the treatment of latent tuberculosis infection: A systematic review and network meta-analysis. *Sci Rep* 2023; **13**(1): 16240. doi: 10.1038/s41598-023-43310-8.

[45]Winters N, Belknap R, Benedetti A, Borisov A, Campbell JR, Chaisson RE, et al. Completion, safety, and efficacy of tuberculosis preventive treatment regimens containing rifampicin or rifapentine: An individual patient data network meta-analysis. *Lancet Respir Med* 2023; **11**(9): 782-790. doi: 10.1016/S2213-2600(23)00096-6.

[46]Matenga TFL, Chavula MP, Zulu JM, Silumbwe A, Maritim P, Munakampe MN, et al. The effects of decentralisation on patient and service outcomes: A case of the 2018 decentralisation of multidrug-resistant tuberculosis in Zambia. *Arch Public Health* 2025; **83**(1): 193. doi: 10.1186/s13690-025-01672-7.

[47]Bonnet M, Vasiliu A, Tchounga BK, Cuer B, Fielding K, Ssekyanzi B, et al. Effectiveness of a community-based approach for the investigation and management of children with household tuberculosis contact in Cameroon and Uganda: A cluster-randomised trial. *Lancet Glob Health* 2023; **11**(12): e1911-e1921. doi: 10.1016/S2214-109X(23)00430-8.

[48]Saunders MJ, Montoya R, Quevedo L, Ramos E, Datta S, Evans CA. The social determinants of tuberculosis: A case-control study characterising pathways to equitable intervention in Peru. *Infect Dis Poverty* 2025; **14**(1): 53. doi: 10.1186/s40249-025-01324-6.

[49]Purba BB, Sembiring RJS, Sitorus FE, Fahdi F, Purba D. Long-term case-finding of latent tuberculosis infection among household contacts to support tuberculosis elimination efforts in Indonesia. *Mater Sociomed* 2025; **37**(3): 243-249. doi: 10.5455/msm.2025.37.243-249.

[50]Craig GM, Daftary A, Engel N, O'Driscoll S, Ioannaki A. Tuberculosis stigma as a social determinant of health: A systematic mapping review of research in low incidence countries. *Int J Infect Dis* 2017; **56**: 90-100. doi: 10.1016/j.ijid.2016.10.011.

[51]Fuady A, Arifin B, Yunita F, Rauf S, Fitriangga A, Sugiharto A, et al. Stigma, depression, quality of life, and the need for psychosocial support among people with tuberculosis in Indonesia: A multi-site cross-sectional study. *PLoS Glob Public Health* 2024; **4**(1): e0002489. doi: 10.1371/journal.pgph.0002489.

[52]Aitambayeva N, Aringazina A, Nazarova L, Faizullina K, Bapayeva M, Narymbayeva N, et al. A systematic review of tuberculosis stigma reduction interventions. *Healthcare* 2025; **13**(15): 1846. doi: 10.3390/HEALTHCARE13151846.

[53]Mamo AN, Gilo RF, Tesema AF, Worku NF, Kenea TT, Dibisa DK, et al. Household contact tuberculosis screening adherence and associated factors among pulmonary tuberculosis patients on follow-up at health facilities in Shashamane Town, Southeast Ethiopia. *Patient Prefer Adherence* 2023; **17**: 1867-1879. doi: 10.2147/PPA.S411685.

[54]Sazali MF, Rahim SSSA, Mohammad AH, Kadir F, Payus AO, Avoi R, et al. Improving tuberculosis medication adherence: The potential of integrating digital technology and health belief model. *Tuberc Respir Dis* 2023; **86**(2): 82-93. doi: 10.4046/trd.2022.0148.

[55]Garfein RS, Liu L, Cepeda J, Graves S, Miguel SS, Antonio A, et al. Asynchronous video directly observed therapy to monitor short-course latent tuberculosis infection treatment: Results of a randomized controlled trial. *Open Forum Infect Dis* 2024; **11**(4): ofae180. doi: 10.1093/ofid/ofae180.

[56]Sundaram KK, Ahmad Zaki R, Shankar D, Hoe V, Ahmad NAR, Kuan WC, et al. Effectiveness of video-observed therapy in tuberculosis management: A systematic review. *Cureus* 2024; **16**(10): e71610. doi: 10.7759/cureus.71610.

[57]Ronald LA, FitzGerald JM, Bartlett-Esquilant G, Schwartzman K, Benedetti A, Boivin JF, et al. Treatment with isoniazid or rifampin for latent tuberculosis infection: Population-based study of hepatotoxicity, completion and costs. *Eur Respir J* 2020; **55**(3): 1902048. doi: 10.1183/13993003.02048-2019.

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Supplementary Table 1.

Searching Strategy

Pubmed	("Latent Tuberculosis"[Mesh] OR "latent tuberculosis infection" OR LTBI) AND ("Medication Adherence"[Mesh] OR adherence OR compliance OR "treatment discontinuation" OR "treatment interruption" OR default OR nonadherence) AND ("Health Behaviour"[Mesh] OR Behaviour OR behaviour OR capability OR knowledge OR motivation OR belief OR perception OR attitude OR opportunity OR "social support" OR stigma OR access OR barrier)
Science Direct	(latent tuberculosis OR LTBI) AND (treatment discontinuation OR treatment interruption) AND (knowledge OR attitude OR stigma)
Scopus	TITLE-ABS-KEY ("latent tuberculosis" OR "latent tuberculosis infection" OR LTBI) AND ("treatment adherence" OR adherence OR compliance OR "treatment discontinuation" OR "treatment interruption" OR default OR nonadherence) AND (capability OR knowledge OR motivation OR belief OR perception OR attitude OR opportunity OR "social support" OR stigma OR access OR barrier)

Supplementary Table 2.

Implications for LTBI

No	Author/Year/ Country	Implication for LTBI according to the COM-B framework
1	Chung *et al.,* Korea/2020 [15]	HCWs are a vulnerable group to LTBI. Even among HCWs with a high level of TB knowledge, longer regimen duration and tolerability are major barriers to complete treatment.
2	Lin *et al*.,/2021/Taiwan [16]	The high incidence of Grade ≥2 ADRs in 3HP underscores the importance of rigorous monitoring for adverse effects. When selecting an TPT regimen, it is recommended to balance among treatment duration, safety profile, and strategies for managing adverse effects.
3	Noh *et al*., 2019/Korea [17]	Shorter treatment regimens improve treatment completion. A high rate of loss to follow-up as a primary cause of treatment discontinuation underscores the need to strengthen patient monitoring and management of adverse effects to minimize discontinuation.
4	An *et al*.,/2024/Cambodia [18]	The high risk of treatment discontinuation at referral facilities highlights the need to strengthen patient-centered care systems, including improved counseling, active monitoring, and continuity of care to prevent loss to follow-up.
5	Liu *et al*.,/China/2025 [19]	Although the treatment discontinuation rate is relatively low, socioeconomic and educational factors play a significant role in TPT. In addition, adverse effects are a major risk factor for treatment discontinuation; therefore, active monitoring and early management of drug reactions are essential to prevent treatment discontinuation

No	Author/Year/ Country	Implication for LTBI according to the COM-B framework
6	Moro *et al*.,/2016/ USA and Canada [9]	Nonadherence to TPT is not only due to adverse effects but also to non-clinical factors. The 3HP regimen using a DOT approach is superior to the 9H-SAT regimen in reducing discontinuation due to other factors. Therefore, shorter regimens with direct observation should be prioritized.
7	Mohamed *et al*.,/2025/Malaysia [20]	This underscores the need for a more targeted approach through intensified education, particularly among the non-HCW population and individuals with lower risk perception. Furthermore, geographical variations highlight the importance of strengthening access to services and improving program quality at the local level to ensure equitable success in TPT.
8	Apriani *et al*.,/2021/Australia, Canada, Saudi Arabia, South Korea, Brazil, Indonesia, Benin, Ghana, and Guinea [21]	The high rate of early discontinuation in 9H underscores that the longer regimens are a major barrier to adherence. Therefore, shorter regimens should be prioritized, accompanied by intensive early monitoring for adverse effects to prevent treatment discontinuation.
9	de Aguiar et al.,/2022/Brazil [22]	Substance use and a history of nonadherence in the index cases are strong indicators of the need for a risk-based approach, including early behavioral screening and more intensive supportive interventions.
10	Laza *et al*.,/2023/Spain [23]	The involvement of healthcare workers through active monitoring improves treatment success; thus, this approach should be integrated into routine care. The combination of appropriate regimen selection and strengthening of a healthcare-worker-based monitoring system is key to minimizing treatment discontinuation.
11	Sandul *et al*.,/2017/USA [24]	Vulnerable groups, such as individuals with a history of homelessness and smokers, require special attention through social support and behavior-based interventions. Protective factors, such as student status and contact with TB patients, underscore the importance of risk perception and a supportive environment in improving adherence.
15	Cruz *et al*.,/2018/USA [25]	The DOPT model has been shown to improve treatment completion, underscoring the importance of a structured healthcare system. Factors such as increasing age and the absence of adverse effects also contribute to adherence, suggesting that monitoring for adverse effects and a personalized treatment approach are key in improving the success of TPT.
12	Borse *et al*.,/2024/India [5]	Adverse effects underscore the importance of close monitoring and early management. Strengthening follow-up systems is also necessary to prevent patient loss, highlighting the importance of an integrated approach between TB and HIV services in improving the outcome of TPT.
13	Rahman *et al*.,/2023/Bangladesh [26]	The low treatment discontinuation rate indicates that successful TPT depends on a combination of individual factors and healthcare support. In addition, simple interventions such as telephone reminders, counseling, and home visits have proven effective in improving treatment completion rates. Therefore,

No	Author/Year/ Country	Implication for LTBI according to the COM-B framework
		strengthening patient education and active monitoring systems by healthcare workers should be integrated into LTBI programs to maintain and improve treatment success.
15	Mapingure *et al*.,/2023/Zimbabwe [27]	An approach incorporating multi-month dispensing, telephone-based monitoring, and educational and counseling support has been shown to improve patient satisfaction and adherence. Therefore, the integration of TB-HIV services into an efficient, flexible, and patient-centered care model needs to be adopted more widely to increase the coverage and success of TPT.
16	Chen *et al*.,/2024/China [28]	The high proportion of patients who discontinue treatment on their own initiative underscores the importance of strengthening motivation through ongoing education and counseling. Furthermore, the healthcare system plays a crucial role, as incentives for clinicians and active supervision by healthcare professionals significantly improve treatment success. Since adverse effects remain a major risk factor, optimal monitoring and management are necessary to prevent treatment discontinuation.
17	Alves *et al*.,/2024/Brazil [29]	The high risk of treatment discontinuation among SA underscores that an unsupervised approach is suboptimal, particularly among vulnerable groups. Therefore, the implementation of flexible, digital-based monitoring models such as VDOT should be prioritized to improve the success of LTBI therapy among migrant populations.
18	Chiu *et al.*,/2022/Taiwan [30]	Since nearly half of patients have no history of TB exposure, strengthening education on the benefits of preventive therapy is crucial for improving risk perception and adherence. Additionally, the implementation of consistent and standardized facility-based strategies (in both public and private settings) is necessary to ensure the success of TPT.
19	Huang *et al.*,/2018/China [31]	The high rate of treatment discontinuation indicates that social factors and perceptions play a crucial role in the success of TPT. Discrimination, the influence of negative opinions from non-specialists, and concerns about adverse effects underscore the importance of appropriate and consistent educational interventions by competent healthcare professionals. In addition, the low level of family education highlights the need for a simpler and more context-sensitive communication approach.
20	Asare-Baah *et al.*,/2024/USA [32]	The 3HP regimen had a lower rate of treatment discontinuation compared to the 4R regimen. However, the clinical and sociobehavioral factors increase the risk of treatment discontinuation. Furthermore, the discontinuation occurs around 4 weeks, underscoring the importance of intensive monitoring during the initial phase of treatment. Therefore, LTBI program strategies should integrate appropriate regimen selection with social and behavioral interventions, along with strengthened early follow-up to prevent treatment discontinuation.
21	Eastment *et al.*,/2017/USA [33]	The loss to follow-up as the primary reason for treatment discontinuation highlights the need to strengthen patient

No	Author/Year/ Country	Implication for LTBI according to the COM-B framework
		monitoring and retention systems, particularly during the early stages of therapy. Additionally, social and clinical factors underscore the importance of a risk-based approach with more intensive support for vulnerable groups to improve the success of TPT.
22	Chang *et al.*,/2013/USA [34]	Adolescents are at higher risk of treatment discontinuation, thus requiring an approach better suited to their age-specific characteristics, such as engaging education and more intensive monitoring. Additionally, comorbidities such as hepatitis and the emergence of adverse effects are major risk factors; therefore, early screening and rigorous clinical monitoring are crucial.
23	Kwara *et al.*,/2008/USA [35]	The lack of health insurance underscores the need for financial support or policies that improve access to health care. In addition, adverse effects remain a major risk factor, highlighting the importance of early monitoring and management of adverse events to prevent treatment discontinuation.
24	Tegegnework *et al.*,/2024/Ethiopia [36]	In HIV-positive populations, adverse effects are a major barrier to the success of TPT, thus necessitating enhanced monitoring and management of adverse events. Furthermore, good adherence to ARV has been shown to improve the success of TB treatment, underscoring the importance of integrated TB-HIV services and an overall adherence-based approach.
25	Machado *et al.*,/2009/Brazil [37]	The high rates of treatment discontinuation and loss to follow-up in the 9H regimen indicate that barriers to accessing services and side effects are major factors contributing to nonadherence. Complex transportation needs reflect significant geographical constraints, necessitating more accessible and flexible service approaches, such as decentralizing services or providing transportation support. Additionally, monitoring and management of side effects must be strengthened to prevent treatment discontinuation.
26	Amanya *et al.*,/2023/Uganda [38]	In the HIV-positive population, social and structural factors play a crucial role in the success of TPT. Social support, such as marital status or cohabitation, has been shown to improve adherence; therefore, the involvement of family members or caregivers needs to be strengthened. Conversely, barriers such as lack of education, high medication burden, distance to healthcare facilities, and patient mobility underscore the need for a more flexible, patient-centered service approach. Therefore, LTBI strategies must integrate adequate education, regimen simplification, and improved access and continuity of care to reduce treatment discontinuation.
27	Macaraig *et al.*,/2018/USA [39]	The high proportion of treatment discontinuations due to patient refusal underscores the importance of strengthening motivational factors through effective education and counseling. Furthermore, a history of contact with TB patients improves adherence, indicating that risk perception plays a key role in treatment

No	Author/Year/ Country	Implication for LTBI according to the COM-B framework
		success. Therefore, LTBI strategies need to integrate the selection of appropriate regimens with educational interventions to enhance patient motivation and treatment acceptance.