

# Determinants of Acceptance of Tuberculosis Preventive Therapy among Household Contacts of Tuberculosis Patients: A Systematic Review

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## ABSTRACT

**Background:** Tuberculosis Preventive Therapy (TPT) constitutes a central pillar in global TB elimination efforts; however, its implementation remains substantially below international targets. Data from the World Health Organization Regional Office for South-East Asia indicate that between 2018 and 2020, only 1.2 million household contacts aged <5 years (29% of the target) and 320,000 contacts aged ≥5 years (1.6% of the target) initiated TPT. This study aimed to identify the determinants influencing acceptance of TPT among household contacts of tuberculosis patients.

**Subjects and Method:** This systematic review followed PRISMA 2020 guidelines and the PICOS framework. It included analytical observational studies on household contacts of tuberculosis patients reporting determinants of TPT acceptance (acceptance, uptake, or initiation) with measures of association. Literature searches were conducted in PubMed, Scopus, Embase, or Web of Science, and Google Scholar for studies published between 2015 and 2026. Study selection involved screening of titles, abstracts, and full texts. Risk of bias was assessed using a modified Critical Appraisal Checklist for quantitative observational studies.

**Results:** A total of 14 studies were included, comprising 45,076 household contacts of tuberculosis patients. TPT acceptance ranged from 17% to 95% across studies. The most influential determinants of higher acceptance included active contact investigation and counseling, prior TB screening, shorter treatment regimens, and strong health system support. Key barriers were low perceived benefit, concerns about adverse effects, stigma, and limited access to healthcare services.

**Conclusion:** TPT acceptance among household contacts is primarily influenced by active contact investigation and counseling, prior TB screening, use of shorter treatment regimens, and strong health system support. In contrast, low perceived benefit, concerns about adverse effects, stigma, and limited healthcare access remain key barriers. Addressing these determinants through targeted, patient-centered interventions is essential to improve TPT uptake.

**Keywords:** acceptance, preventive therapy, risk factors, treatment uptake, tuberculosis

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## BACKGROUND

Tuberculosis (TB) remained the leading cause of death attributable to a single

infectious agent worldwide in 2023. Following the COVID-19 pandemic, global TB incidence increased; however, by 2023

it had stabilized at approximately 134 new cases per 100,000 population (WHO, 2024a). According to the Global Tuberculosis Report 2023 and 2024, the global burden of TB remains substantial, with an estimated 10.6–10.8 million new cases and 1.25 million deaths reported in 2023, corresponding to an incidence rate of approximately 130 cases per 100,000 population. The South-East Asia Region accounts for the largest proportion of cases (46%), followed by the African Region (23%) and the Western Pacific Region (18%), underscoring marked regional disparities in disease distribution. Indonesia ranks second worldwide, with an estimated 1.09 million cases and 125,000 deaths in the same year. Although the World Health Organization (WHO), in partnership with United Nations Member States, has reaffirmed its commitment to the End TB Strategy—aiming to reduce TB mortality by 90% and incidence by 80% by 2030—the continuing rise in reported cases highlights the urgent need to strengthen early detection, preventive measures, and comprehensive TB management in order to achieve global epidemic control. (Bhatia et al., 2023; Floyd et al., 2018; WHO, 2024a).

Notwithstanding the robust evidence supporting its effectiveness, global TPT coverage remains suboptimal. In 2023, TPT coverage reached only 56% among people living with HIV and was considerably lower among household contacts, at 21% (WHO, 2024a). TPT is a key intervention aimed at preventing the progression from latent tuberculosis infection to active disease, particularly among high-risk populations such as household contacts and immune-compromised individuals (Silva Júnior et al., 2025). Evidence derived from systematic reviews of randomized controlled trials (RCTs) indicates that TPT can substantially reduce TB incidence, with risk

reduction of up to 63% among people living with HIV (HR 0.37; 95% CI: 0.28–0.48) (Wang et al., 2025).

Despite its proven effectiveness, barriers such as limited access to healthcare services, concerns about adverse drug effects, low perceived risk, and health system constraints continue to hinder optimal utilization of TPT across different settings (Masini et al., 2020; WHO, 2024a). At the same time, enabling factors including active contact investigation, counseling, and shorter treatment regimens have been shown to improve acceptance and adherence (Ihesie et al., 2024; WHO, 2022). These findings underscore the importance of understanding context-specific determinants that influence TPT acceptance among household contacts..

Although several systematic reviews have examined TPT effectiveness and adherence, limited evidence specifically synthesizes determinants of TPT acceptance among household contacts across diverse settings. Furthermore, existing reviews often focus on clinical efficacy or adherence outcomes rather than acceptance as a critical early step in the care cascade. The objective of this study is to describe the barriers and facilitating factors associated with the implementation of TPT among household members living with TB patients globally, with a particular emphasis on evidence derived from observational studies.

## SUBJECTS AND METHOD

This study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines, an updated framework designed to enhance the transparency and completeness of systematic review reporting (Page et al., 2021).

## 1. Eligibility criteria

The inclusion and exclusion criteria were established using the PICOS framework (Population, Exposure, Comparison, Outcome, Study design). The population comprised household members or individuals residing with TB patients (household contacts). The exposures of interest included factors potentially influencing TPT acceptance, such as sociodemographic characteristics, educational level, knowledge and perceptions of TB, access to healthcare services, family support, and health system-related determinants. The comparison group consisted of household contacts who did not accept or initiate TPT. The primary outcome was TPT acceptance, operationalized through indicators such as acceptance, uptake, or initiation of TPT. This review focused exclusively on observational studies examining associations between these determinants and TPT acceptance. Studies were excluded if they did not employ an analytical observational design, did not involve household contacts, were review articles, editorials, commentaries, case reports, or available only as abstracts, or failed to report clear data on factors associated with TPT acceptance.

## 2. Literature search strategy

A comprehensive literature search was conducted across electronic databases, including PubMed, Scopus, Embase, or Web of Science, and Google Scholar for articles published in English. The search strategy incorporated predefined Boolean operators: ("tuberculosis preventive therapy" OR "isoniazid preventive therapy") AND ("household contacts") AND (acceptance OR uptake OR initiation) AND ("risk factors" OR determinants) AND ("observational study"). To further refine results in Google Scholar, title-specific restrictions were applied using the following format: intitle:("tuberculosis preventive

therapy" OR "isoniazid preventive therapy" OR IPT OR TPT) AND intitle:("household contact" OR "household contacts") AND intitle: (acceptance OR uptake OR initiation) AND intitle:("risk factor" OR determinants). The search was limited to studies published between 2015 and 2026 and restricted to relevant observational designs. Additionally, manual searches of reference lists from eligible articles were undertaken to identify potentially relevant studies.

## 3. Study selection

Study selection was performed in a step-wise manner through screening of titles, abstracts, and full texts based on the predefined eligibility criteria. The screening process was conducted independently by two reviewers. Articles deemed irrelevant, lacking an observational design, or not involving household contacts of TB patients were excluded. Any disagreements between reviewers were resolved through discussion, and when necessary, a third reviewer was consulted to reach consensus. The selection process was conducted systematically to ensure that only studies aligned with the research objectives were included in the review.

## 4. Data extraction

Extracted data included author names, year of publication, study setting, population characteristics, number of cases and controls, analyzed determinants, and measures of association such as odds ratios (ORs) with corresponding confidence intervals. All extracted information was organized into tabular form to facilitate synthesis and review. The findings were synthesized using a narrative synthesis approach, in which determinants were grouped and summarized thematically across studies based on their direction and consistency of association with TPT acceptance.

## 5. Risk of bias and quality assessment

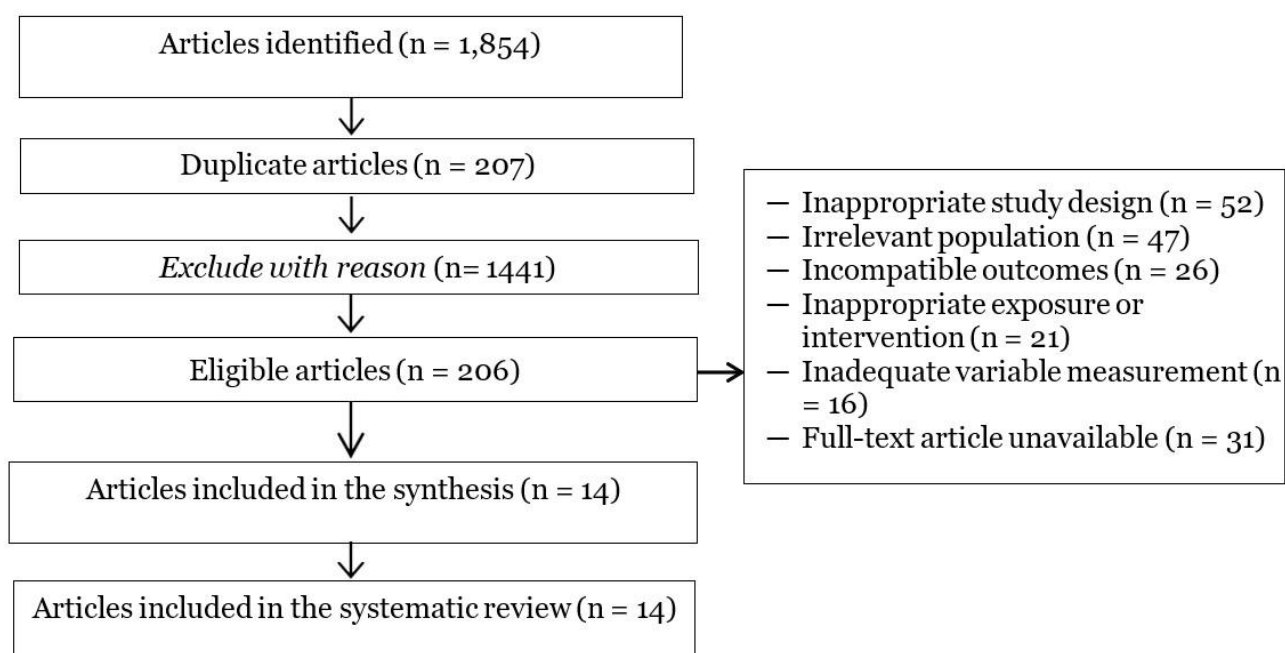
Risk of bias was independently assessed using a modified Critical Appraisal Checklist based on CASP, tailored for quantitative observational studies. Each article was evaluated against 12 assessment criteria, with a maximum possible score of 24 (Long et al., 2020).

## RESULTS

### 1. Study Selection Process

Figure 1 presents the PRISMA flow diagram illustrating the process of article identification and selection for inclusion in this systematic review. The PRISMA flowchart indicates that the selection process began with 1,854 records initially identified.

Following the removal of 207 duplicate articles, automated screening tools reduced the dataset to 206 articles that met the preliminary eligibility criteria for further assessment. During the full-text eligibility review, several studies were excluded for specific reasons: inappropriate study design (52), irrelevant population (47), incompatible outcomes (26), unsuitable exposure or intervention (21), inappropriate variable measurement (16), and unavailability of full-text articles (31). After completing all stages of screening and eligibility assessment, a total of 14 studies satisfied the inclusion criteria and were incorporated into the final synthesis of this systematic review.



**Figure 1. Result of Prisma Flow Diagram**

### 2. Quality Appraisal of Studies

The methodological quality of the fourteen studies included in this review was assessed using a Critical Appraisal Checklist comprising 12 criteria, adapted from the Critical Appraisal Skills Programme (CASP) for quantitative research. Each study was evaluated according to key methodological

domains, including clarity of research objectives, appropriateness of sampling and recruitment strategies, validity and reliability of exposure and outcome measurements, consideration of potential confounding factors, reporting of findings in the form of adjusted odds ratios (aOR), and the relevance and practical implications of

the results. Each criterion was scored as 0 (no), 1 (unclear), or 2 (yes), with a maximum possible score of 24 points per study.

**Table 1. Modified Critical Appraisal Checklist Based on CASP**

| Primary Studies           | Criteria |   |   |   |   |   |   |   |   |    |    |    | Total |
|---------------------------|----------|---|---|---|---|---|---|---|---|----|----|----|-------|
|                           | 1        | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |       |
| Abelti et al. (2025)      | 2        | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2  | 2  | 2  | 24    |
| Mukherjee et al. (2025)   | 2        | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 2  | 2  | 2  | 23    |
| Kumar et al. (2025)       | 2        | 2 | 2 | 2 | 1 | 1 | 2 | 2 | 2 | 2  | 2  | 2  | 22    |
| Suresh et al. (2025)      | 2        | 2 | 2 | 2 | 1 | 1 | 2 | 2 | 2 | 2  | 2  | 2  | 22    |
| Ihesie et al. (2024)      | 2        | 2 | 2 | 2 | 2 | 2 | 0 | 2 | 2 | 2  | 2  | 2  | 22    |
| Ren et al. (2024)         | 2        | 2 | 2 | 2 | 2 | 1 | 0 | 2 | 2 | 2  | 2  | 2  | 21    |
| Felisia et al. (2023)     | 2        | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2  | 2  | 2  | 24    |
| Rahman et al. (2023)      | 2        | 2 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2  | 2  | 2  | 23    |
| Sharma et al. (2022)      | 2        | 2 | 2 | 2 | 1 | 1 | 0 | 2 | 2 | 2  | 2  | 2  | 20    |
| Isaac & Kizito (2022)     | 2        | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 2  | 2  | 2  | 23    |
| Otero et al. (2020)       | 2        | 2 | 2 | 2 | 2 | 2 | 0 | 2 | 2 | 2  | 2  | 2  | 22    |
| Suryavanshi et al. (2020) | 2        | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 2  | 2  | 2  | 23    |
| Burmen et al. (2019)      | 2        | 2 | 2 | 2 | 1 | 1 | 2 | 2 | 2 | 2  | 2  | 2  | 22    |
| Birungi et al. (2018)     | 2        | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 2  | 2  | 2  | 23    |

#### Description of the question criteria:

- 1 = Does the study address a clearly focused problem?
- 2 = Was the study population recruited appropriately?
- 3 = Were determinants of TPT acceptance measured accurately to minimize bias?
- 4 = Was TPT acceptance measured accurately to minimize bias?
- 5 = Were important confounding factors identified and accounted for?
- 6 = Was follow-up sufficiently complete and adequate?
- 7 = Are the results of this study reported in the aOR?
- 8 = How precise are the results?
- 9 = Can the results be trusted?
- 10 = Can the results be applied to the target population?
- 11 = Are the results of this study consistent with other available evidence?
- 12 = What are the implications of this research for practice?

#### Answer score description:

- 0 = No
- 1 = Can't tell
- 2 = Yes

Based on the modified CASP assessment of the 14 included quantitative studies, most demonstrated strong methodological quality, with total scores ranging from 20 to 24 out of a maximum of 24. Two studies—Abelti (2025) and Felisia (2023)—achieved the highest possible score of 24, indicating that all appraisal criteria were fully satisfied. The majority of the remaining studies scored between 22 and 23,

reflecting high methodological rigor with only minor limitations, primarily related to the identification of potential confounding factors, completeness of participant follow-up, and reporting of adjusted odds ratios (aOR). One study, Sharma (2022), received the lowest score of 20; however, it still fell within the category of acceptable methodological quality. Overall, the modified CASP evaluation suggests that most included

studies possess solid internal validity and reasonably reliable findings, thereby providing an appropriate foundation for evidence synthesis and the formulation of research conclusions.

### 3. Study Characteristics

The following table summarizes the characteristics of the studies included in this systematic review on factors influencing TPT acceptance among household contacts of tuberculosis patients. The information presented includes the country of study, population characteristics, study design, sample size, prevalence of TPT acceptance, and determinants reported to be associated with TPT uptake. Across the 14 included studies, several determinants of TPT

acceptance were consistently identified. Active contact investigation and counseling were the most frequently reported factors, followed by TB screening prior to initiation and individual knowledge or risk perception related to TB. Shorter treatment regimens and strong health system support, including healthcare worker involvement and person-centered care, were also commonly associated with higher acceptance. In contrast, barriers such as concerns about adverse effects, low perceived benefit, stigma, and socioeconomic constraints were repeatedly reported across multiple studies, indicating a consistent pattern of both enabling and limiting factors influencing TPT uptake.

**Table 2. Characteristics of Studies Included in the Systematic Review**

| No | Country  | P                                           | I           | C                                                                                      | O              | S                               | Sample Size | Main Findings                                                                                                                                                                                                                                 |
|----|----------|---------------------------------------------|-------------|----------------------------------------------------------------------------------------|----------------|---------------------------------|-------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1  | Ethiopia | Household contacts of TB patients           | TPT program | Age, enrollment period, TPT regimen type, site of initiation, adherence support        | TPT acceptance | Cross-sectional mixed methods   | 4,367       | TPT acceptance prevalence was 95.4%. Determinants included regimen type, site of therapy initiation, and adherence support.                                                                                                                   |
| 2  | India    | Household contacts of drug-sensitive TB     | TPT program | Sex, contact tracing, counseling, TB symptom screening, sociodemographic factors       | TPT acceptance | Cross-sectional                 | 301         | Acceptance prevalence was 74.8% (225/301). Significant factors: male sex (aOR = 1.98; 95% CI 1.00 – 3.91), traced contacts receiving counseling (aOR = 13.51; 95% CI 6.78 – 26.91), and TB symptom screening (aOR = 5.69; 95% CI 2.22–14.59). |
| 3  | India    | Household contacts of pulmonary TB patients | TPT program | Age, sex, family structure, housing density, TPT awareness, TB screening, regimen type | TPT acceptance | Community-based cross-sectional | 430         | Acceptance prevalence was 43.7%. Influencing factors included awareness of TPT, active TB screening, and regimen type.                                                                                                                        |
| 4  | India    | Household contacts of TB                    | TPT program | Sex, age, BMI, tobacco use, alcohol use, diabetes,                                     | TPT acceptance | Observational                   | 264         | Acceptance prevalence was 81.3%. Determinants included age, nutri-                                                                                                                                                                            |

| No | Country    | P                                            | I           | C                                                                                                               | O              | S                                    | Sample Size | Main Findings                                                                                                                                             |
|----|------------|----------------------------------------------|-------------|-----------------------------------------------------------------------------------------------------------------|----------------|--------------------------------------|-------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|
|    |            | patients                                     |             | hypertension                                                                                                    |                |                                      |             | tional status (BMI), and comorbidities such as diabetes.                                                                                                  |
| 5  | Nigeria    | Household contacts of TB patients            | TPT program | Age, bacteriological contact status, health system factors, perceived effectiveness, concern about side effects | TPT acceptance | Cross-sectional mixed methods        | 30,012      | Acceptance prevalence was 40.1%. Determinants included age, perceived treatment effectiveness, health system support, and concerns about adverse effects. |
| 6  | China      | Household contacts of TB patients            | TPT program | Sex, age, education, occupation, perceived effectiveness, stigma, economic burden                               | TPT acceptance | Multicenter cross-sectional          | 1,077       | Acceptance prevalence was 17.0%. Determinants included education level, perceived effectiveness, concerns about side effects, and social stigma.          |
| 7  | Indonesia  | Household contacts of TB patients            | TPT program | Person-centered care, short-course regimens (3RH/ 3HP), adverse event monitoring, nurse support                 | TPT acceptance | Cross-sectional                      | 1,016       | Acceptance prevalence was 78.8%. Determinants included person-centered care, use of short regimens, and healthcare worker support.                        |
| 8  | Bangladesh | Household contacts of TB patients            | TPT program | Education, income, residence, drug side effects                                                                 | TPT acceptance | Community-based implementation study | 3,193       | Acceptance prevalence was high (>70%). Determinants included education level, income, and experience of drug side effects.                                |
| 9  | India      | Adult household contacts of TB patients      | TPT program | Demographics, TB knowledge, risk perception, BMI, diabetes                                                      | TPT acceptance | Cross-sectional                      | 536         | Acceptance prevalence was 73.5%. Determinants included TB knowledge, perceived infection risk, and health status.                                         |
| 10 | Uganda     | Household contacts of TB patients (<5 years) | IPT program | Age, marital status, income, education, TB screening                                                            | IPT acceptance | Analytical cross-sectional           | 207         | IPT acceptance prevalence was 36.7%. Determinants included age, education, socioeconomic status, TB screening, and health worker counseling.              |
| 11 | Peru       | Household contacts of TB patients            | IPT program | Age, relationship to index case, smear status, facility characteristics                                         | IPT acceptance | Retrospective longitudinal           | 2,323       | IPT acceptance was 70.2% among children <5 years and 36.7% among those aged 5–19                                                                          |

| No | Country       | P                                 | I               | C                                                                                        | O                  | S                              | Sample Size | Main Findings                                                                                                                                                                   |
|----|---------------|-----------------------------------|-----------------|------------------------------------------------------------------------------------------|--------------------|--------------------------------|-------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|    |               |                                   |                 | tics, TST implementation                                                                 |                    |                                |             | years. Determinants included relationship to index case, smear status, and health facility characteristics.                                                                     |
| 12 | Multi-country | Household contacts of TB patients | MDR-TPT program | TB knowledge, employment/school status, attitude, self-efficacy                          | MDR-TPT acceptance | Multisite cross-sectional      | 743         | MDR-TPT acceptance prevalence was 79%. Determinants included TB knowledge, treatment attitude, and self-efficacy.                                                               |
| 13 | Kenya         | Child contacts of TB patients     | IPT program     | Index case characteristics, family relationship, residential location                    | IPT acceptance     | Retro-spective cross-sectional | 337         | IPT acceptance prevalence was 15%. Determinants included family relationship to index case, smear-positive status, and residence location.                                      |
| 14 | Rwanda        | Child contacts of TB patients     | IPT program     | Child age, relationship to index case, healthcare worker attitude, index case HIV status | IPT acceptance     | Cross-sectional                | 270         | IPT acceptance prevalence was 89% among children <5 years. Determinants included child age, relationship to index case, healthcare worker attitudes, and index case HIV status. |

TB: Tuberculosis; TPT: Tuberculosis Preventive Therapy; IPT: Isoniazid Preventive Therapy; MDR-TPT: Multidrug-Resistant Tuberculosis Preventive Therapy; 3RH: 3 months of Rifampicin plus Isoniazid; 3HP: 3 months of weekly Isoniazid plus Rifapentine; BMI: Body Mass Index; TST: Tuberculin Skin Test; aOR: Adjusted Odds Ratio; CI: Confidence Interval. 1 = (Abelti et al., 2025); 2 = (Mukherjee et al., 2025); 3 = (Kumar et al., 2025); 4 = (Suresh et al., 2025); 5 = (Ihesie et al., 2024); 6 = (Ren et al., 2024); 7 = (Felisia et al., 2023); 8 = (Rahman et al., 2023); 9 = (Sharma et al., 2022); 10 = (Otero et al., 2020); 11 = (Isaac & Kizito, 2022); 12 = (Suryavanshi et al., 2020); 12 = (Burmen et al., 2019); 13 = (Birungi et al., 2018)

Table 2 illustrates that the prevalence of TPT acceptance among household contacts of tuberculosis patients varies considerably across studies, ranging from 15% to 95.4%. Such variability is likely attributable to differences in population characteristics, healthcare system capacity, and the implementation of TPT programs across countries. Several determinants were consistently reported, including individual-level factors (age, sex, educational attainment, knowledge, and perceived risk of TB), socioeconomic conditions (income and

housing status), and health service-related components such as contact tracing, counseling provided by healthcare workers, medication availability, and patient-centered care approaches. In addition, perceptions of treatment effectiveness and concerns regarding potential adverse drug effects emerged as important influences on individuals' decisions to initiate TPT. Overall, the findings of this systematic review indicate that improving TPT acceptance extends beyond ensuring drug availability; it requires comprehensive strategies

encompassing enhanced health education, strengthened healthcare systems, and programmatic approaches that are responsive to the needs of patients and their families.

## DISCUSSION

The findings of this systematic review demonstrate substantial variation in TPT acceptance among household contacts of TB patients, with reported prevalence ranging from 17% to over 95%. This wide range reflects differences in health system capacity, programmatic approaches, and implementation strategies across settings, including variations in healthcare infrastructure, socioeconomic conditions, and policy implementation across countries. Abelti et al. (2025) in Ethiopia documented an increase in acceptance from 81.7% to 95.4% following a community-based intervention, with a significant effect size (OR 4.67). Similarly, Felisia et al. (2023) in Yogyakarta reported a high acceptance rate of 78.8% through a person-centered care approach. In contrast, Ren et al. (2024) in China identified a markedly low prevalence of 17%, highlighting implementation gaps shaped by both perceptual and systemic factors, suggesting that differences in national program delivery and community engagement may explain cross-country variation.

Determinants of TPT acceptance encompass cognitive, psychological, and health system–related dimensions. Low uptake is frequently linked to uncertainty regarding treatment effectiveness and concerns about adverse drug reactions, as reported by (Ren et al., 2024). Studies conducted in India indicate moderate acceptance levels (43%–75%), with contact counseling, TB symptom screening, and improved knowledge of TPT emerging as key contributors. Notably, contact investi-

gation and individualized counseling demonstrated strong associations with acceptance (aOR 13.51), underscoring the central role of direct engagement with healthcare providers (Kumar et al., 2025; Mukherjee et al., 2025). These findings suggest that TPT acceptance is shaped by a complex interplay between individual perceptions and the quality of health system support and indicate that strengthening service delivery mechanisms may yield greater impact than focusing solely on individual-level factors (Kumar et al., 2025; Mukherjee et al., 2025).

The results of this study suggest that determinants of TPT acceptance can be grouped into three principal domains: individual factors (age, sex, comorbidities, and education), perceptual factors (perceived effectiveness, fear of side effects, and perceived need for therapy), and health system factors (counseling, active screening, community-based service delivery models, and regimen type). Importantly, health system–related determinants appear to exert a more consistent and substantial influence than individual demographic characteristics. This pattern indicates that low TPT acceptance is less a function of patient attributes and more a consequence of how services are structured and delivered—particularly the quality of counseling, proactive engagement strategies, and integrated care models that shape perceptions and facilitate informed decision-making, highlighting the need for system-level interventions to address persistent gaps in implementation (Felisia et al., 2023; Isaac & Kizito, 2022; Otero et al., 2020; Rahman et al., 2023; Sharma et al., 2022).

These conclusions align with the policy framework described by Salazar-Austin et al. (2022), while also reflecting findings derived from the studies included

in this review, which identified a gap between global TPT recommendations and field-level implementation. Short-course regimens such as 3HP have been shown to enhance both acceptance and treatment completion, particularly when supported by price reductions and formulation innovations (Servello et al., 2026). Nevertheless, limitations in rifapentine production and restricted availability of pediatric formulations continue to constrain implementation in many low- and middle-income countries. Concurrently, screening and counseling remain critical levers for improving TPT uptake, with strong reported associations (aOR up to 13.51), although current programmatic screening strategies are often limited by the underutilization of more sensitive and specific TB infection diagnostics (Fox et al., 2020; Scriba et al., 2021; WHO, 2024b), indicating gaps between evidence and real-world practice.

Comprehensive contact investigation and systematic screening are therefore essential components of effective TPT implementation. Reliance solely on symptom-based screening has proven suboptimal, given that a substantial proportion of subclinical TB cases remain undetected under this approach (Onozaki et al., 2015). Molecular diagnostic technologies such as Xpert MTB/RIF demonstrate higher sensitivity, strong acceptance, and the capacity to identify asymptomatic cases (Kweza et al., 2018), thereby offering the potential to strengthen program effectiveness. Furthermore, community-based and person-centered care models consistently outperform facility-based approaches in terms of contact identification, treatment initiation, and completion (Kay et al., 2022). These findings reinforce the conclusion that proactive and integrated service design plays a more decisive role in program success than individual patient

characteristics, providing clear direction for programmatic improvement..

Expanding TPT coverage and strengthening monitoring systems are strategic priorities for enhancing overall program impact. Extending TPT to all household contacts and considering contact investigation beyond the household setting may broaden TB detection and prevention efforts (Hoang et al., 2019). The implementation of standardized cascade-of-care indicators and the development of individual-based electronic registries are equally critical for identifying losses to follow-up and improving program evaluation (WHO, 2024b). Collectively, these results emphasize that optimizing TPT requires a systemic approach encompassing regimen innovation, strengthened screening strategies, adaptive service delivery models, and integrated monitoring frameworks, with direct implications for policymakers and TB control programs in designing more effective and context-specific interventions.

Despite offering a comprehensive synthesis, this review should be interpreted in light of several limitations. Most included studies employed cross-sectional designs, precluding causal inference. Moreover, variability in operational definitions—such as “acceptance,” “uptake,” and “coverage”—introduces conceptual heterogeneity across studies. Not all investigations reported comprehensive multivariable analyses, limiting direct comparison of effect sizes among determinants. In addition, potential publication bias, language bias, and database selection bias may have influenced the inclusion of studies, thereby affecting the overall representativeness of the evidence. Furthermore, the absence of a meta-analysis limits the ability to quantitatively synthesize findings and estimate pooled effects.

In conclusion, the findings of this systematic review indicate that improving TPT acceptance among household contacts of TB patients cannot be achieved solely through individual-level education; rather, it must be anchored in strengthening health system performance. Key determinants identified include active contact screening, availability of short-course regimens, and quality of counseling. Programs should ensure that contact screening is conducted actively and systematically, provide affordable short-course regimens with consistent availability, reinforce individualized counseling, and develop community-based, household-centered service delivery models. Through a more proactive, integrated, and family-centered approach, TPT coverage and acceptance can be sustainably enhanced at the population level. Future research should therefore prioritize longitudinal or experimental designs to strengthen causal inference, adopt standardized definitions and indicators, and conduct more robust multivariable analyses to identify key determinants with greater precision and depth.

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#### **CONFLICT OF INTEREST**

All authors disclose no competing interests

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